THE BURDEN OF RESPIRATORY FAILURE AMONG PATIENTS ADMITTED IN THE MEDICAL WARDS AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA

KORIR DAISY CHEPKEMOI

A RESEARCH THESIS SUBMITTED TO THE SCHOOL OF MEDICINE, IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTERS OF MEDICINE IN INTERNAL MEDICINE, MOI UNIVERSITY

DECLARATION

Students Declaration

This research thesis is my original work and has not been presented for a degree in any other University. No part of this proposal may be reproduced without prior permission of the author and/or Moi University.

Korir Daisy Chepkemoi, MBchB

SIGNATURE:…….DATE: ……..

Declaration by Academic Supervisors:

This research thesis has been submitted with our approval as Moi University supervisors

Dr. David Lagat, MBchB, MMED.

Lecturer, Department of medicine

Moi University School of Medicine

SIGNATURE:…….DATE: ……..

Prof. Lameck Diero , MBchB, MMED.

Associate professor of Medicine

Department of Medicine

Moi University School of Medicine

SIGNATURE:…….DATE: ……..

DEDICATION

I dedicate this work to my daughter Grace, and my father Nelson Korir who inspired me to do this work.

ACKNOWLEDGEMENT

I would like to appreciate my supervisors, Prof. L. Diero and Dr. D.Lagat for their invaluable input during the course of the development of this proposal.

I also acknowledge my biostatistician, Mr. Alfred Keter, for his tireless effort in refining this proposal. I am indebted to my colleagues and the entire faculty in the department of Internal Medicine for their guidance and encouragement throughout the research process.

I acknowledge my employer Moi Teaching and Referral Hospital for funding my research and allowing me to use the facility to conduct the research. I am also grateful to my research assistants who did a great job in data collection, blood sample collection and analysis.

LIST OF ABBREVIATIONS

ABG	Arterial Blood Gas
AIDS	Acquired Immune Deficiency Syndrome
ALI	Acute Lung Injury
ALS	Amyotropic Lateral Sclerosis
APS	Acute Physiology Score
ARDS	Acute respiratory Distress Syndrome
ARF	Acute Respiratory Failure
ASD	Atrial Septal Defect
AV	Artero- venous
BGA	Blood Gas Analysis
CBC	Complete Blood Count
COPD	Chronic Obstructive Pulmonary Disease
ECG	Electrocardiography
ECMO	Extra Corporal Membrane Oxygenation
FIO2	Fraction of Oxygen in Inspired Air
GBS	Guillain Barre Syndrome
H2O	Water

HIV	Human Immunodeficiency Virus
ICU	Intensive Care Unit
LFT'S	Liver Function Tests
LODS	Logistic Organ Dysfunction Score
MTRH	Moi Teaching and Referral Hospital
PaO2	Arterial Oxygen Tension
PCO2	Arterial Carbon Dioxide Tension
PDA	Patent Ductus Arteriosus
SAPS II	Simplified Acute Physiologic Score II
UEC'S	Urea Creatinine and Electrolytes
US	United States
USD	United States Dollars
VSD	Ventricular Septal Defect

OPERATIONAL DEFINITIONS

Burden of respiratory failure refers to the entire spectrum of the impact of respiratory failure to patients and society including but not limited to the morbidity, time spent in hospital for treatment, money spent to pay hospital bills resulting from the illness and mortality due to respiratory failure.

Hypoxemia is the main manifestation of respiratory failure and it refers to low oxygen in the blood usually defined in terms of reduced partial pressure of oxygen (mm Hg) in arterial blood (PaO2) measured by arterial blood gases, and also in terms of reduced content of oxygen (ml oxygen per dl blood) or percentage saturation of haemoglobin with oxygen (SPO2), measured by pulse oximetry, (Lawrence 1999).

Respiratory Failure:

- **Hypoxemic respiratory failure** is defined as partial pressure of oxygen (mm Hg) in arterial blood (PaO2) that is less than 60 mmHg with a normal or low partial pressure of carbon dioxide (mm Hg) in arterial blood (PaCo2) (D. Pinson, 2014).
- **Hypercapnic respiratory failure** is defined as partial pressure of carbon dioxide (mm Hg) in arterial blood (PaCO2) that is equals to or greater than 50 mmHg with a low or normal partial pressure of oxygen (mm Hg) in arterial blood (PaO2) (D. Pinson, 2014).

Simplified Acute Physiologic Score II (SAPS II) is a severity of illness score that predicts mortality based on a composite of: Age, vital signs, Glasgow coma score, oxygenation, renal function, chemistry, WBC count, hematologic malignancy or metastatic disease, (Le Gall JR et.al., 1993).

Simplified Acute Physiologic Score II (SAPS II) predicts mortality as follows:

SAPS II Score	Estimated Mortality
29 points	10%
40 points	25%
52 points	50%
64 points	75%
77 points	90%

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THE BURDEN OF RESPIRATORY FAILURE AMONG PATIENTS ADMITTED IN THE MEDICAL WARDS AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA

ABSTRACT

Background: Respiratory failure (RF) is a major problem globally with significant morbidity and mortality. It accounts for approximately 56% of all ICU admissions in Europe with at least 40% mortality. World Health Organization estimates the burden of RF in Sub- Saharan Africa (SSA) at 1.6 -2.4 M cases per year. The cost of RF to society is enormous in terms of lost productivity, shortened lives and cost of care since it requires ICU. In SSA, no specific studies have been published on epidemiology of RF and its burden in terms of cost & mortality. Most studies focus on etiologies of RF, making it difficult to anticipate and plan for the management of patients with RF since the extent of the problem is unknown. This study focuses on the gaps that exist in the epidemiology of RF and its burden in Moi Teaching and Referral Hospital (MTRH) and Kenya.

Objectives: To determine the proportion, clinical characteristics and 30-day treatment outcomes of patients with respiratory failure in MTRH medical wards.

Methods: A prospective study was done with a 30 day follow up. The study population was patients admitted in the MTRH medical wards between June and August 2018. Recruitment was done by consecutive sampling and patients followed up for 30 days to describe their clinical features and treatment outcomes. Data was collected using interviewer administered questionnaires. Continuous variables were summarized as means, medians, standard deviations & interquartile ranges while categorical variables were summarized as frequencies & percentages. Association between clinical characteristics and outcomes was tested using chi square and fisher's exact test. Data was presented using tables, graphs & pie charts.

Results: Pulse oxymetry was done on 1607 patients to identify those with hypoxemia (SPO2<92%) who were then subjected to arterial blood gas analysis to confirm the diagnosis of RF. A total of 217 patients with RF were enrolled. The proportion of RF among patients in MTRH medical wards was 13.5% (217), (95% CI 12.0, and 15.2). The mean age for the participants was 49.8 years. Hypoxemic RF accounted for 84.3% (183) while hypercapnic RF accounted for 15.7% (34). The commonest documented diagnosis was pneumonia at 24.4% (53) and the commonest comorbidity was renal disease at 13.4% (29). Parenchymal lung disease was the leading chest x-ray finding with consolidation being the commonest at 76% (165). Severity of illness was assessed by Simplified Acute Physiologic score where most patients had 15 – 35 points at 67.3% (149). Most patients received oxygenation in the general ward. Mortality was 23% (50) at 30 days and 54.8% (97) of those who survived had residual respiratory failure. Severity of illness was associated with mortality ($p<0.0001$). The median length of hospital stay was 11 days with an interquartile range of 7- 18 days. The median cost of treatment was USD 348 with an interquartile range of USD 229-529.

Conclusion: Respiratory failure is common in MTRH with a high morbidity and mortality.

Recommendation: There is need to improve capacity to manage RF in MTRH by doing arterial blood gas analysis for patients with low oxygen saturations, performing severity of illness scores and establishing a medical ICU.

CHAPTER ONE: INTRODUCTION

1.1 Background

Respiratory failure is a condition in which the lungs fail in one of the functions of gas exchange, oxygenation or carbon dioxide elimination (Roussos et al 2003). In practice it is diagnosed when PaO2 is <60mmHg or PaCO2 is ≥50mmHg accompanied by derangements in ABGs and acid-base status of the patient, (Kaynar M D et al, 2017).

Respiratory failure is a major problem all over the world and in Sub- Saharan Africa with significant morbidity and mortality. It accounts approximately for 56% of all Intensive Care Unit (ICU) admissions in Europe and Brazil with at least 40-54%% mortality, (Vincent et al, 2002, Franca et al, 2011). In the United States (US), the number of hospitalisations owing to acute respiratory failure increased from 1,007, 549 in 2001 to 1,917,910 in 2009, (Stefan MS et al, 2013). In Sub Saharan Africa few studies have been done on respiratory failure as an entity and hence there is little data on its prevalence or mortality rate, however due to the increasing need for ICU care and mechanical ventilation which is largely required due to respiratory failure then it shows that this disease has a high burden in Sub Saharan Africa as well. World health organization (WHO) estimates the burden of respiratory failure in Sub Saharan Africa (SSA) (as cases of mechanical ventilation) at 1,600,000-2,400,000 cases per year with acute lung injury a type of respiratory failure at 130, 000-650,000 per year, (Neill K J et al, 2010).

Respiratory failure is not a disease per se but a consequence of the problems that interfere with the ability to breathe. The term refers to the inability to perform adequately the fundamental functions of respiration: to deliver oxygen to the blood and to eliminate carbon dioxide from it. Respiratory failure has many causes and can

come on abruptly (acute respiratory failure) when the underlying cause progresses rapidly or slowly (chronic respiratory failure) when it is associated over months or even years with a progressive underlying process. Typically, respiratory failure initially affects the ability either to take up oxygen (referred to as oxygenation failure/type I) or to eliminate carbon dioxide (referred to as ventilatory failure/type II). Eventually, both functions cease when the respiratory failure becomes severe enough. (American thoracic society)

Hypoxemia is the main manifestation of respiratory failure and it refers to low oxygen in the blood. Hypoxemia is usually defined in terms of reduced partial pressure of oxygen (mm Hg) in arterial blood (PaO2) measured by arterial blood gases, but also in terms of reduced content of oxygen (ml oxygen per dl blood) or percentage saturation of haemoglobin with oxygen (SPO2), measured by pulse oximetry, (Lawrence 1999).

Serious hypoxemia occurs when the partial pressure of oxygen in blood (PaO2) is less than 60 mm Hg, or (2) when hemoglobin oxygen saturation (SPO2) is less than 92%.

Hypoxemia can be caused by several conditions which cause respiratory failure like pneumonia, Chronic Obstructive Pulmonary Disease (COPD), emphysema, pulmonary edema, drugs and poisoning among others. Anemia, a low number of red blood cells/haemoglobin content in blood that carries oxygen can also cause hypoxemia independent of respiratory failure. Heart disease also causes hypoxemia, (Ratini, DO, MS, 2016).

In this study, presence of hypoxemia is used to screen for patients who are likely to be having conditions that can cause respiratory failure.

Different forms of respiratory failure have been described with Acute Respiratory Distress Syndrome (ARDS) being the main focus of studies that have been done.

Respiratory failure is caused by a variety of conditions including: nervous system failure like central hypoventilation, neuropathies, drug overdose (Opioids, benzodiazepines), alcohol, brainstem hemorrhage, infarction, amyotrophic lateral sclerosis (ALS), and cervical spinal cord injury; muscle (pump) failure like muscular dystrophies and myopathies; neuromuscular transmission failure like myasthenia gravis, Gullein Bare Syndrome (GBS) and tetanus; airway failure i.e. obstruction, dysfunction, asthma and COPD; chest wall and pleural space failure like kyphoscoliosis, morbid obesity, pneumothorax, hydrothorax and hemothorax; alveolar unit failure like alveolar collapse, flooding edema, blood, pus, aspiration, fibrosis, pneumonia, ARDS, ALI and cardiogenic edema or pulmonary vasculature failure like pulmonary embolism and pulmonary hypertension, (Luhr et al, 1999).

Some of the recognized independent risk factors for developing respiratory failure include older age>64 years, severity of illness at admission, hematological malignancy and longer time between hospital admission and ICU admission, (S.A. Franca et al., 2010).

Because so many underlying causes contribute to it, respiratory failure is a common and major cause of illness and death. It is the main cause of death from pneumonia and COPD, which together comprise the third-leading cause of death in the United States today. It is also the main cause of death in many neuromuscular diseases, such as ALS, because these diseases weaken the respiratory muscles, rendering them incapable of sustaining breathing. Epidemiologic studies suggest that respiratory

failure will become more common as the population ages, increasing by as much as 80 per cent in the next 20 years, (Carson S.S. 2006).

Because respiratory failure is such a common cause of illness and death, the cost to society in terms of lost productivity and shortened lives is enormous, not to mention the high cost of treatment since it requires ICU admission and mechanical ventilation, (Stefan MS,2013)

However, it is hard to quantify the significance of this problem in SSA because the cause of death is more likely to be listed as pneumonia, COPD, or another underlying condition, rather than respiratory failure. A few specific studies have been conducted on epidemiology of respiratory failure or its burden in terms of cost or mortality.

This study will therefore focus on the gaps that exist in the epidemiology of respiratory failure as a condition and its burden in MTRH and hence Kenya at large.

1.2 Problem Statement

The overall frequency of respiratory failure is unknown in Africa. This makes it difficult to anticipate and plan for the management of respiratory failure patients to improve on outcome. The only data available are estimates for each underlying disease and most of the published literature has focused on the severest form of ARF, namely, ARDS, and few studies have evaluated either the prevalence of or mortality rate of ARF in general among critically ill patients (Vincent J. Et al, 2002). Knowledge about prevalence and risk factors associated with respiratory failure is mandatory in the process of developing new therapeutic interventions that aim to improve clinical outcome, (Lurh.O.R. et al, 1999).

1.3 Justification

Respiratory failure is associated with high mortality and morbidity and there is need for a study to be conducted to determine the prevalence and the common presentation of patients with respiratory failure locally. This will contribute to the knowledge and to the development of guidelines for the management of respiratory failure in Moi Teaching and Referral Hospital, Kenya and Africa at large.

1.4 Study Significance.

The study is significant in giving an estimate of the burden of respiratory failure in MTRH, how the patients present and what the treatment outcomes are to enable the hospital to plan on the treatment by developing treatment guidelines and availing the relevant equipment required to treat respiratory failure like ventilators. It will also inform government policy since no prevalence studies on respiratory failure have been published in Kenya or Africa.

1.5 Research Questions

1. What is the proportion of respiratory failure among patients admitted in MTRH medical wards?
2. What is the clinical presentation, laboratory and chest x-ray findings of patients with respiratory failure in MTRH medical wards?
3. What is the 30-day treatment outcome of patients with respiratory failure in MTRH medical wards?

1.6 Objectives

1.6.1 Broad Objective

To determine the proportion, clinical characteristics and 30 day follow up treatment outcomes of respiratory failure in MTRH medical wards.

1.6.2 Specific Objectives

1. To determine the proportion of patients with respiratory failure among patients admitted in MTRH medical wards.
2. To describe the clinical presentation, laboratory and chest x-ray findings of patients with respiratory failure in MTRH medical wards.
3. To describe the 30-day follow up treatment outcomes of patients with respiratory failure in MTRH medical wards.

CHAPTER TWO: LITERATURE REVIEW

2.1 Definition

A consensus definition of acute respiratory failure is not available and most studies have used the combination of mechanical ventilation (of variable duration) with or without evidence of severe hypoxemia on arterial blood gas analysis. While some studies utilized a stricter definition than others, the essential component in all has been the need for mechanical ventilation. The indications for mechanical ventilation, however, are mostly based on clinical observations (increased respiratory rate, use of accessory muscles, paradoxical chest wall movements or changes in mental state), none of which has sufficient accuracy or precision. Therefore, the epidemiology of acute respiratory failure has so far been restricted to 'treated' acute respiratory failure, possibly explaining the wide variations in the reported incidence and outcomes of acute respiratory failure and associated clinical syndromes. Since the availability of intensive care and mechanical ventilation vary greatly in different parts of the world, the burden of acute respiratory failure maybe severely underestimated depending on the access to these services hence the lack of data from developing countries**,** (Suri H.S. et al. 2008).

Respiratory failure is a condition in which the lungs fail in one of the functions of gas exchange, oxygenation or carbon dioxide elimination, (Roussos et al 2003). Respiratory failure is defined as a syndrome of inadequate gas exchange due to dysfunction of one or more essential components of the respiratory system. For clinical routine purposes, respiratory failure is usually defined by an arterial oxygen tension (PaO2) of less than 60 mmHg (8.0 kpa) and/or an arterial carbon dioxide tension (PaCO2) greater than 45 mmHg (6.0 kpa) accompanied by derangements in ABGs and acid-base status of the patient, (Budweiser et al, 2008).

2.2 Classification of respiratory failure

Type 1 - hypoxemic respiratory failure is characterized by Hypoxemia PaO2 < 60mmhg without hypercapnia. It is due to ventilation perfusion mismatch and is caused by all acute lung diseases that involve fluid filling or collapse of alveolar units, parenchyma disease, pulmonary edema, pneumonia, pulmonary hemorrhage, ARDS, atelectasis, post-surgery change, aspiration, trauma, pulmonary embolism or shunt and interstitial lung disease.

Type 2 - hypercapneic respiratory failure is characterized by hypoxemia with hypercapnia >50mmhg and it occurs due to hypoventilation or decreased area for gas exchange as in emphysema. Common aetiologies of type II respiratory failure include drug overdose, neuromuscular disease, chest wall abnormalities, severe airway disease like asthma and chronic obstructive pulmonary disease.

Type 3 - Peri – operative respiratory failure is generally a subset of type 1(PO2 < 60) or type II (PCO2 > 50 mmHg) respiratory failure following surgery but is sometimes considered separately because it is common. The Mechanisms underlying this type of respiratory failure is decreased functional residual capacity or prolonged collapse of dependent lung units. This can be caused by: Anesthetic effects, airway secretions, abdominal pain incisions/ abnormal movements/ascites and abnormal posturing especially supine position and obesity.

Type 4 – Shock respiratory failure is secondary to cardiovascular instability. It may be present with hypoxemia or hypercapnoea and occurs during resuscitation for shock (Cardiogenic/ Hypovolemic/ Septic) or while in intubation or ventilation, (Kaynar MD. et al, 2017).

Acute/ Chronic Respiratory Failure

Respiratory failure can be acute or chronic. Acute respiratory failure is characterized by life threatening derangements in arterial blood gases, and it develops over minutes to hours with PH<7.3. Chronic respiratory failure on the other hand is less dramatic and may not be readily apparent. It develops over several days or longer, and allows time for renal compensation and increase in bicarbonate concentration leading to a slightly elevated PH. Therefore, respiratory failure developing over 4 to 8 weeks is considered as chronic respiratory failure. Acute episodes (exacerbations) of respiratory failure in patients with chronic compensated respiratory insufficiency are usually referred to as 'acute on chronic' respiratory failure**,** (Kaynar MD. et al, 2017)

Acute respiratory distress syndrome, (ARDS)

The acute respiratory distress syndrome (ARDS) a severe form of respiratory failure is a common, devastating clinical syndrome of acute lung injury that affects both medical and surgical patients, (Ware L.B.2000).

ARDS can be diagnosed once cardiogenic pulmonary edema and alternative causes of acute hypoxemic respiratory failure and bilateral infiltrates have been excluded.

The Berlin Definition of ARDS, 2012 requires that all of the following criteria be present for diagnosis, (The ARDS Definition Task Force, 2012; Ferguson ND. et al.,2012):

- Respiratory symptoms must have begun within one week of a known clinical insult, or the patient must have new or worsening symptoms during the past week.
- Bilateral opacities must be present on a chest radiograph or computed tomographic (CT) scan. These opacities must not be fully explained by pleural effusions, lobar collapse, lung collapse, or pulmonary nodules.

●The patient's respiratory failure must not be fully explained by cardiac failure or fluid overload. An objective assessment (e.g.echocardiography) to exclude hydrostatic pulmonary edema is required if no risk factors for ARDS are present.

●A moderate to severe impairment of oxygenation must be present, as defined by the ratio of arterial oxygen tension to fraction of inspired oxygen (PaO_2/FiO_2). The severity of the hypoxemia defines the severity of the ARDS:

•Mild ARDS – The PaO_2/FiO_2 is >200 mmHg, but ≤300 mmHg, on ventilator settings that include positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) ≥5 cm H_2O.

•Moderate ARDS – The PaO_2/FiO_2 is >100 mmHg, but ≤200 mmHg, on ventilator settings that include PEEP ≥5 cm H_2O.

•Severe ARDS – The PaO_2/FiO_2 is ≤100 mmHg on ventilator settings that include PEEP ≥5 cm H_2O.

2.3 Epidemiology of Respiratory Failure

Acute respiratory failure, and the need for mechanical ventilation, remains one of the most common reasons for admission to the intensive care unit, (Vincent J L 2003, Cartin-Ceba R, 2011). The burden of acute respiratory failure is high in terms of mortality and morbidity as well as the cost of its principal treatment, mechanical ventilation. Very few epidemiologic studies have evaluated the prevalence and outcome of acute respiratory failure and mechanical ventilation in general worldwide. Most of the published literature has focused on specific forms of acute respiratory failure, particularly acute lung injury (ALI) and acute respiratory distress syndrome (ARDS), (Suri H.S et al, 2008).

The setting of most studies on respiratory failure has also focused on ICU patients meaning the findings of these studies done mainly in developed countries cannot be

compared with those done in developing countries since the availability of ICU facilities is a challenge in developing countries. The differences in the incidences and prevalence of respiratory failure found in studies is largely attributable to the definition of respiratory failure which varies greatly since there is no consensus on it. But most studies define respiratory failure as intubation plus mechanical ventilation. Age of the study subjects also varies and the incidence varies with age.

The prevalence of acute respiratory failure found in a multicenter study in sixteen countries in Europe, was 56%, (Vincent J. Et al, 2003). Out of the 1, 449 patients who were enrolled into the study, 458(32%) were admitted to an ICU with ARF, as defined by a PaO2/fraction of inspired oxygen ratio of < 200 mm Hg and the need for respiratory support. Of the 991 patients who were admitted to an ICU without ARF, 352 (35%) developed ARF later during the ICU stay. These were ICU patients however and so this gives prevalence in the setting of critical illness which could influence the prevalence of respiratory failure as opposed to if the study was to be conducted among general patients being admitted in the hospital.

The incidence of acute respiratory failure found in Sweden, Denmark and Iceland was at 77.6/100,000, acute lung injury at 17.9/100,000 and acute respiratory distress syndrome was at 13.5/100,000/year, (Lurh.O.R. et al, 1999). This was comparable the findings of a prospective multi-centre study carried out to determine the incidence, severity, and mortality of acute respiratory failure (ARF) in Berlin, Germany, a metropolis with a population of 3.44 million where the incidence of Acute Respiratory Failure was 88.6 per 100,000/yr, (Lewandowski K. et al, 1991). These two studies were done in similar populations of ICU patients and this could explain the similarity in the incidence found by the researchers.

A study conducted in France to evaluate the prevalence and outcome of the acute respiratory distress syndrome (ARDS) among patients requiring mechanical ventilation employed a prospective, multi-institutional, initial cohort study including 28-day follow-up. Thirty-six French intensive care units (ICUs) from a working group of the French Intensive Care Society (SRLF) participated in the study and included all the patients entering the ICUs during a 14-day period who were screened prospectively. Hypoxemic patients, defined as having a PaO2/FIO2 ratio (P/F) of 300 mmHg or less and receiving mechanical ventilation, were classified into three groups, according to the Consensus Conference on ARDS: group 1 refers to ARDS (P/F:200 mmHg or less and bilateral infiltrates on the chest X-ray);group 2 to acute lung injury (ALI) without having criteria for ARDS (200 < P/F £ 300 mmHg and bilateral infiltrates) and group 3 to patients with P/F of 300 mmHg or less but having exclusion criteria from the previous groups.

The results of this study showed a prevalence of 22% for all groups of respiratory failure but those meeting the criteria for mechanical ventilation were 43%. Among all the ICU admissions, ARDS, ALI and group 3 patients amounted, respectively, to 6.9% (67), 1.8% (17) and 13.3% (129) of the patients, and represented 31.5%, 8.1% and 60.2% of the hypoxemic, ventilated patients, (E. Roupie et al, 1999).

In the US, the number of hospitalisations owing to acute respiratory failure increased from 1,007,549 in 2001 to 1,917,910 in 2009, (Stefan M S et al, 2013). In a study done in the US, an estimated 329,766 patients discharged from non federal hospitals nationwide in 1994 met study criteria for ARF. The incidence of ARF was 137.1 hospitalizations per 100,000 US residents age ≥ 5 years, (Behrendt, C.E. et al, 2000). This is much higher incidence compared to the European studies by Lurh O.R. et al and Lewandowski K. et al which were 77-86/100,000. This difference could be

accounted for by the fact that the US study included everyone above 5 years of age compared to the European studies that focused on patients who were more than 14 years of age. All the studies however used the same definition of ARF as the need for intubation and mechanical ventilation and admission for over 24 hours.

A Brazillian study done to evaluate the prevalence and incidence of respiratory failure among 1732 patients admitted in ICU found a prevalence of acute respiratory failure at (843) 48% at admission and a further 141(16%) developed respiratory failure while in ICU making a total prevalence of 56.81%, Franca MD et al 2011). This is quite similar to the European study by Vincent J. Et al discussed above that also found an overall prevalence of 56% in the setting of critical illness as well.

2.4 Risk Factors for development of Respiratory Failure.

Some of the risk factors for development of ARF include: Older age, hematologic malignancy, severity of illness at admission to hospital, and longer time between hospital admission and ICU admission, (S.A. Franca et al.2011). In this study of the 141 patients who developed ARF while in ICU, those who developed ARF were older with a median age of 63 vs 49 years p <0.001, while those with hematologic malignancy were 6% vs 3% p<0.04. Severity of illness at ICU admission as evaluated by 3 scores showed that those who developed ARF had a higher score than those who did not (SAPS II median 31 vs 20 P<0.00, APS median 15 vs 7 P<0.001 and LODS median 3 vs 1 P<0.001) compared to those who did not develop ARF. A medical reason for admission to ICU also conferred a higher risk for development of ARF compared to surgical or non - medical reasons.

Similarly, more than two-thirds of ARF admissions were associated with medical, rather than surgical, conditions (69.5% in 2001 and 71.2% in 2009) in a US study as well, (Stefan MS et al, 2013).

Additional independent risk factors for the development of ARF were infection developing in the ICU (odds ratio [OR], 7.59; 95% confidence interval [CI], 5.08 to 11.33) or present on ICU admission (OR, 2.3; 95% CI, 1.68 to 3.16), the presence of neurologic failure on ICU admission (OR, 2.73; 95% CI, 1.90to3.91), and older age (OR, 1.70; 95%CI, 1.30 to 2.22). (Vincent J. Et al, 2002).

Incidence increased nearly exponentially each decade until age 85 years in a US study as well, (Behrendt, C.E. et al, 2000).

The incidence also seemed to vary by race and gender as found in a study conducted in the US between 1992-2007 where the average annual incidence of non- cardiogenic acute respiratory failure over the entire study period was 95.1 (95% CI 93.9 – 96.4) cases per 100,000 for black Americans compared to 66.5 (95% CI 65.8 – 67.2) cases per 100,000 for white Americans (rate ratio = 1.43, 95% CI 1.42-1.44), meaning that Black Americans had approximately 1.9 times the incidence and other-race patients had 1.6 times the incidence of acute respiratory failure of white Americans. There was no clinically important difference in case-fatality between black and white patients with acute respiratory failure, but other-race patients with ≥ 2 organ failures experienced greater case-fatality than white patients. Men had a higher annual incidence of acute respiratory failure compared to women, (Colin R. C., 2012).

2.5 Causes of respiratory failure

Respiratory failure is caused by either disease of pulmonary origin or non- pulmonary origin.

Pulmonary origin: Upper airways- Laryngeal obstruction ; Lower airways- Tracheal obstruction, Acute bronchitis, Chronic bronchitis and chronic obstructive pulmonary disease, Asthma; Lung parenchyma- Aspiration, near drowning, inhalation agents, pulmonary burns ,intrapulmonary bleeding, pulmonary contusion, neoplasms of lung

parenchyma, intrapulmonary metastasis, pneumonia (bacterial, viral, opportunistic), miliary tuberculosis, atelectasis; Lung circulation Pulmonary hypertension-pulmonary embolism, lung edema—cardiogenic, lung edema—noncardiogenic.

Non-pulmonary origin: Pleura-pneumothorax, pleural effusion; Chest- trauma and flail chest, mediastinal emphysema; Ventilatory regulation system-central hypoventilation syndrome, drug overdose, cerebrovascular accident, head/brain trauma; Cardiovascular system- hypovolemic shock, polytransfusion, cardiogenic shock; Abdominal disease- Pancreatitis, digestive necrosis, abdominal sepsis, peritonitis ; Urogenital system- uremia- urinary sepsis; Endocrinologic system-Diabetic ketoacidosis; Anaphylaxis; Skeletal system- Traumatic bone fracture; Neurologic disease- Nontraumatic neurological disease including spinal trauma; Other Multisystem trauma, Burns, Immunologic disorder and sepsis of unknown origin, (Lurh O.R. et al, 1999).

Left cardiac failure, COPD exacerbation, direct lung injury with/without infectious pneumonia, aspiration, abdominal sepsis and extra abdominal sepsis were cited as the common aetiologies of respiratory failure in a study conducted by E. Roupie et al, 1999.

2.6 Outcomes of respiratory failure; mortality and risk factors for mortality.

Mortality was found among those with acute respiratory failure in Brazil to be 48% in patients admitted in ICU and 54% overall hospital mortality compared to 4% ICU mortality in patients without ARF, and 11% hospital mortality in patients without ARF, (Franca MD et al 2011).

The overall mortality rate in the French study was 41% and was significantly higher in ARDS patients than in the others (60% vs 31% $p < 0.01$). In group 3, 42 patients

had P/F less than 200 mmHg associated with unilateral lung injury; mortality was significantly lower (40.5%) than in the ARDS group, (E. Roupie et al, 1999).

The mortality rate in the Sweden, Denmark and Iceland study was 41% for acute respiratory failure, 42.2% for acute lung injury and 41.2% for acute respiratory distress syndrome, (Owe R. L. et al, 1999).

In the US, in 2001 to 2009 a decrease in mortality from 27.6% to 20.6% was observed, (Stefan MS et al, 2013).

The wide variations in mortality rate could be attributed to the underlying diseases, the different ages of the patients included in the study and the management strategies employed in these studies**.** The mortality rate is likely to be higher in Sub Saharan Africa than in the developed nations due to unavailability of similar management strategies (ICU and ventilators) and the difference in clinical characteristics of patients as well of aetiologies of respiratory failure**.**

In another study that looked at incidence and mortality at 31 days found that, overall, 35.9% of patients with ARF did not survive to hospital discharge. At 31 days, hospital mortality was 31.4%. According to the proportional hazards model, significant mortality hazards included age (≥ 80 years and≥ 30 years), multiorgan system failure (MOSF), HIV, chronic liver disease, and cancer. Hospital admission for coronary artery bypass, drug overdose, or trauma other than head injury or burns was associated with a reduced mortality hazard, (Behrendt E., 2000).

Other independent risk factors for death described are: multiple organ failure following ICU admission, history of hematologic malignancy, chronic renal failure or liver cirrhosis, the presence of circulatory shock on ICU admission, the presence of infection, and older age**,** (Vincent J. Et al, 2002).

Franca MD et al also found similar findings with non survivors of ARF being older (median 62 vs 49 P<0.001), had longer time between hospital admission and ICU admission (median 3 vs 1 day P<0.001), were more likely to be admitted for medical reasons (64% vs 38% P<0.001) , more frequently had haematological malignancy (7% vs 1% P<0.001), or AIDS 6% vs 2% P<0.001), had greater severity of illness score SAPS II (median 44 vs 30 P<0.001), APS (median 26 vs 18 p<0.001), LODS (median 5 vs 3 P< 0.001) compared to survivors of ARF. Survivors of ARF had similar ICU (median 8 vs 10 days P=0.183) and longer hospital length of stay (median 25 vs 17 days P<0.001) than non survivors of ARF.

The independent risk factors for mortality identified by E. Roupie et al, were similar; SAPS II score, immunosuppression and septic shock.

Race does not appear to influence the mortality following acute respiratory failure. There was no clinically important difference in case-fatality between black and white patients with acute respiratory failure, but other-race patients with ≥ 2 organ failures experienced greater case-fatality than white patients, (Colin R. C., 2012).

2.7 Pathophysiology of respiratory failure

Respiratory failure can arise from an abnormality in any of the components of the respiratory system. This includes the airways, alveoli, central nervous system peripheral nervous system, respiratory muscles and chest wall. Ventilatory capacity is the maximum spontaneous ventilation that can be maintained without development of respiratory muscle fatigue while Ventilatory demand is the spontaneous minute ventilation that results in a stable PaCo2.Ventilatory capacity exceeds ventilatory demand in normalcy but in respiratory failure there is either reduction in the ventilatory capacity or increase in ventilatory demand or both.

In ideal gas exchange the blood flow and ventilation march each other hence no alveolar arterial PO2 gradient. Increase in this gradient above 15-20 mmHg indicates pulmonary disease as a cause of respiratory failure. High V/Q (ventilation/perfusion) units are the optimally ventilated alveoli with no perfusion. They act like dead space. Low V/Q units are alveoli that are optimally perfused but not ventilated. They act like a shunt.

Efficiency of lung function can therefore be evaluated by measuring the alveolar arterial PO2 gradient and the rate of carbon dioxide elimination

The PO2 gradient can be calculated by the following equation:

PAO2=FiO2*(PB-PH2O)-PACO2/R

Where PAO2 is alveolar PO2, FiO2 is fraction of oxygen in inspired gas, PB is barometric pressure, PH2O is water vapour pressure at 37 degrees centigrade, PACO2 is alveolar PCO2 and R is respiratory exchange ratio which depends on oxygen consumption and carbon dioxide production.

The rate of CO2 production is equal to rate of elimination normally.

VA=K*VCO2/PaCO2, K is a constant 0.863, VA is alveolar ventilation, VCO2 carbon dioxide ventilation.

In hypoxemic respiratory failure the pathophysiologic mechanisms are (**V/Q)** mismatch and shunt. They lead to widening of the alveolar arterial gradient. V/Q mismatch is the most common cause of hypoxemia. Alveolar units may vary from low VQ to high VQ in disease processes. Low VQ contributes to hypoxemia and hypercapnia but high VQ wastes ventilation but does not affect gas exchange unless if very severe. Low VQ occurs from decreased ventilation secondary to airway or interstitial lung disease, or overperfusion due to pulmonary oedema. Low VQ is corrected by administration of 100% oxygen. Hypoxemia also increases minute

ventilation by chemoreceptor stimulation. PaCO2 is not affected. Shunt is whereby the deoxygenated blood bypasses the ventilated alveoli & mixes with oxygenated blood that has flown through oxygenated alveoli and lead to reduced arterial blood oxygen content. Anatomic shunt may be normal due to bronchial & thebesian circulations which account for 2-3% of shunt, ASD, VSD, PDA, and AV malformations of the lungs. In this case there is persistent hypoxemia despite 100% oxygen administration. It is caused by cardiogenic pulmonary oedema, non-cardiogenic pulmonary oedema (ARDS), pneumonia, lung haemorrhage, alveolar proteinosis, alveolar cell carcinoma and atelectasis.

In hypercapnic respiratory failure, there is increased level of carbon dioxide being retained in blood due to decreased ventilation or increased carbon dioxide production. At constant level of CO2 production, PaCO2 is determined by level of alveolar ventilation. As ventilation decreases below 4-6l/min, PaCO2 rises. The causes of increased CO2 production are: fever, sepsis, burns and overfeeding. Decreased alveolar ventilation is caused by: decreased respiratory rate, decreased tidal volume (Vt) and increased dead space (Vd), (Kaynar, MD et al, 2017).

2.8 Clinical features of respiratory failure

The clinical features of respiratory failure are related to hypoxemia, hypercapnia or underlying disease.

Symptoms of underlying disease that is due to either:

Cardiogenic pulmonary edema: history of cardiac disease, chest pain, paroxysmal nocturnal dyspnea, lower limb swelling and orthopnea.

Non cardiogenic pulmonary edema: is acute respiratory distress syndrome (ARDS) that presents with features of sepsis, trauma, aspiration, pneumonia, pancreatitis, drug toxicity and multiple transfusion.

The symptoms of hypoxemia are: cyanosis, seizures, confusion, tachypnea, tremor or arrhythmias. Hypercapnia presents with conjunctival hyperemia, tachycardia, tachypnea, altered sensorium, papilledema and asterixis. Dyspnoea is a major feature in both hypercapnic and hypoxemic respiratory failures.

Table 1: Classification, Pathophysiology and Clinical Features of Respiratory Failure

	TypeI	Type II	Type III	Type IV
Mechanism	VIO mismatch Shunt (Os/Ot)	Alveolar hypoventilation	Atelectasis Shunt (Os/Ot)	Hypoperfusion Metabolic acidosis
Anatomic components	Alveolar unit failure Pulmonary vascular failure	CNS*dysfunction Neuromuscular failure Airway dysfunction	Regional alveo lar unit collapse	All tissues Respiratory muscles
Clinical syndromes	Pulmonary edema CPE* Pneumonia Trauma ILD* ALI*	COPD* NMD* Coma Asthma	Perioperative	Shock

ILD: Interstitial Lung Disease; NMD: Neuromuscular Disorder; COPD: Chronic Obstructive Pulmonary disease; ALI: Acute Lung Injury; CPE: Cardiogenic Pulmonary Oedema; CNS: Central Nervous System, (Suri H.S. et al. 2008).

2.9 Diagnosis of respiratory failure

2.9.1 Arterial Blood Gases

The effectiveness of gas exchange can be assessed by measuring the partial arterial pressures of oxygen and carbon dioxide in a sample of blood obtained by arterial puncture. The oxygen content of blood (CaO2) depends upon arterial saturation (%O2Sat), which is set by PaO2, pH, and PaCO2 according to the oxyhaemoglobin dissociation curve; CaO2 can also be measured by oximetry (see below): CaO2 (mL/dL) = 1.34(mL/dL/g) × [haemoglobin] (g) × %O2Sat + 0.003(mL/dL/mmHg) × PaO2 (mmHg), (Harrisons 19th Edition).

2.9.2 Pulse oximetry

Continuous monitoring of arterial blood gases requires either repeated arterial punctures or an indwelling arterial catheter, and so may be difficult in many circumstances. Instead, the oxygen saturation fraction of haemoglobin (SPO2) can be measured continuously using pulse oximetry, a tool that measures the absorbance by haemoglobin of several wavelengths of light transmitted across a finger, toe, or ear by a non - invasive probe. However, since oxygen content varies relatively little with PaO2 at saturations above 90%, it is difficult to know the precise PaO2 using this device. In addition, as noted earlier, PaCO2 is needed to fully assess the mechanism of hypoxemia, a value that is not revealed by pulse oximetry, hence the need for arterial blood gases for full assessment, (Harrisons 19th Edition).

Severe anaemia can affect the pulse oximeter since the reading depends on light absorption by haemoglobin. This is clinically significant when haemoglobin level is less than 5 g/dl. The pulse oximeter will respond as if a state of low perfusion exists, (Schnapp LM, 1990).

2.9.3 Imaging

Chest radiography-may reveal the cause whereby increased heart size, vascular redistribution, peri bronchial cuffing, pleural effusions, septal lines & perihilar batwing distribution of infiltrates suggests hydrostatic (cardiogenic) oedema. Lack of these features suggests ARDS (non-cardiogenic oedema).

ECG is also done to evaluate the possibility of cardiovascular disease as a cause of respiratory failure or arrhythmia due to acidosis and hypoxemia.

Echocardiography- evaluates cardiac cause of respiratory failure. Ventricular dilatation, regional or global wall motion abnormalities, and severe mitral regurgitation support diagnosis of cardiogenic pulmonary oedema.

2.9.4 Other investigations

Pulmonary function tests: define the recovery potential and are useful in evaluating chronic respiratory failure. Normal values of Forced Expiratory volume in 1 second FEV1 & forced vital capacity FVC suggests disturbance in respiratory control. Decrease in FEV1/FVC ratio suggests airflow obstruction. Reduction in both FEV1 &FVC with normal ratio suggests restrictive lung disease. The normal values for the FVC and FEV_1 should be greater than or equal to 80% of predicted, and the FEV_1 -to-FVC ratio should be no more than 8-9 absolute percentage points below the predicted ratio.

Right sided heart catheterization/pulmonary artery catheterization/Swan-ganz catheterization. It's used for monitoring cardiac function, adequacy of volume resuscitation and systemic oxygen delivery. Pulmonary wedge pressure measurement may distinguish cardiogenic and noncardiogenic oedema.

CBC- to assess anaemia due to tissue hypoxemia and polycythaemia from chronic hypoxemic respiratory failure.

LFT'S & UEC'S – assess aetiology and complications of respiratory failure like acute kidney injury, liver failure and also assess abnormalities in electrolytes that may aggravate the respiratory failure**.** (Kaynar, MD et al, 2017).

2.10 Treatment of respiratory failure

The specific treatment for respiratory failure depends on the specific etiology, however since hypoxemia is the immediate threat to organ damage then it should be corrected and the ventilatory and hemodynamic status of the patient stabilized. Patients with acute respiratory failure or acute on chronic failure should be admitted to ICU and offered mechanical ventilation. Most patients with chronic respiratory failure can be treated at home with oxygen supplementation and/or ventilatory assist devices along with therapy for their underlying disease. Treatment of respiratory failure involves ventilator strategies (involving mechanical ventilation) and non-ventilator strategies (pharmacotherapy & positioning).

2.10.1 Correction of hypoxemia

Assurance of an adequate airway is vital in a patient with acute respiratory distress. The most common indication for endotracheal intubation is respiratory failure. Endotracheal intubation serves as an interface between the patient and the ventilator. Another indication is airway protection in patients with altered mental status. Once the airway is secured, attention is turned toward correcting the underlying hypoxemia, the most life-threatening facet of acute respiratory failure. The goal is to assure adequate oxygen delivery to tissues, generally achieved with an arterial oxygen tension (PaO_2) of 60 mm Hg or an arterial oxygen saturation (SaO_2) greater than 90%.

Supplemental oxygen is administered via nasal prongs or face mask; however, in patients with severe hypoxemia, intubation and mechanical ventilation are often required. Coexistent hypercapnia and respiratory acidosis may have to be addressed. This is done by correcting the underlying cause or providing ventilatory assistance.

2.10.2 Ventilatory strategies

Mechanical ventilation is used for two essential reasons: (1) to increase PaO_2 and (2) to lower $PaCO_2$. Mechanical ventilation also rests the respiratory muscles and is an appropriate therapy for respiratory muscle fatigue. Currently, virtually all mechanical ventilatory support for acute respiratory failure is provided by positive-pressure ventilation. Mechanical ventilation requires an interface between the patient and the ventilator. In the past, this invariably occurred through an endotracheal or tracheostomy tube, but there is a growing trend toward non-invasive ventilation, which can be accomplished by the use of either a full-face mask (covering both the nose and mouth) or a nasal mask (see Non-invasive Ventilatory Support), (Girault C., 2009). Care of an endotracheal tube includes correct placement of the tube, maintenance of proper cuff pressure, and suctioning to maintain a patent airway.

Types of mechanical ventilation

These include Positive-pressure versus negative-pressure ventilation, Controlled versus patient-initiated ventilation and Pressure-targeted versus volume-targeted ventilation.

Approximately 16% of deaths in patients with ARDS results from refractory hypoxemia, which is the inability to achieve adequate arterial oxygenation despite high levels of inspired oxygen or the development of barotraumas, (Esan A, MD et al, 2010). A number of ventilator-focused rescue therapies that can be used when

conventional mechanical ventilation does not achieve a specific target level of oxygenation have been recommended and include:

2.10.3 Positive end expiratory pressure (PEEP).

Increasing the level of PEEP often is the first consideration when the clinician is faced with a patient with refractory hypoxemia. If PEEP results in alveolar recruitment, the shunt is reduced, and PaO2 increases. No studies have reported a survival advantage for use of higher PEEP; they have only reported a higher PaO2 /FIO2 ratio in the higher PEEP groups. The use of higher PEEP is recommended on the basis of fewer pulmonary deaths and absence of reported complications with this strategy, (Gattinoni and Caironi, 2008).

2.10.4 Lung Recruitment Manoeuvres

A recruitment manoeuvre is a transient increase in transpulmonary pressure intended to promote reopening of collapsed alveoli, (Fan E et al,2008, Lapinsky SE et al,2005). Recruitment manoeuvres have been shown to open collapsed alveoli, thereby improving gas exchange, (Grasso S et al, 2002).

One approach of lung recruitment involves a sustained high-pressure inflation using pressures of 30 to 50 cm H2O for 20 to 40 s, (Amato M B,1998). A sustained inflation usually is achieved by changing to a continuous positive airway pressure (CPAP) mode and setting the pressure to the desired level. Pressure controlled breaths can be applied in addition to the sustained high pressure**,** (Medoff BD, 2000).

The second approach is use of Pressure-controlled ventilation (PCV) of 10 to 15 cm H2O with PEEP of 25 to 30 cm H2O to reach a peak inspiratory pressure of 40 to 45 cm H 2 O for 2 min. Another approach is to use intermittent sighs, using three consecutive sighs set at a pressure of 45 cm H2O, (Pelosi P et al, 1999). An extended

sigh also has been used in which there is a stepwise increase in PEEP and a decrease in tidal volume over 2 min to a CPAP level of 30 cm H2O for 30 s, (Lim CM et al, 2001).

Another method applies an intermittent increase in PEEP for 2 breaths/ min, (Foti G, 2000). Pressure-controlled ventilation (PCV) of 10 to 15 cm H2O with PEEP of 25 to 30 cm H2O to reach a peak inspiratory pressure of 40 to 45 cm H 2 O for 2 min also has been used as a recruitment manoeuvre, (Medoff BD, 2000). Prone positioning has also been used to improve alveolar recruitment, (Galiatsou E, 2006).

2.10.5 Non ventilatory strategies of managing respiratory failure

Several non-ventilatory adjunctive interventions have been demonstrated to rapidly ameliorate severe hypoxemia in many patients with severe ARDS and therefore may be suitable as rescue therapy for hypoxemia that is refractory to prior optimization of mechanical ventilation. These include neuromuscular blockade, inhaled vasoactive agents, prone positioning, and extracorporeal life support.

Although these interventions have been linked to physiologic improvement, including relief from severe hypoxemia, and some are associated with outcome benefits, such as shorter duration of mechanical ventilation, demonstration of survival benefit has been rare in clinical trials. Furthermore, some of these non-ventilatory interventions carry additional risks and/or high cost; thus, when used as rescue therapy for hypoxemia, it is important that they be demonstrated to yield clinically significant improvement in gas exchange, which should be periodically reassessed, (Suhail R., 2010). Extracorporeal membrane oxygenation (ECMO) may be more effective than conventional management for patients with severe but potentially reversible respiratory failure.

2.11 Cost of treatment

The treatment for respiratory failure is expensive since it requires the use of non-ventilator and ventilator techniques elucidated above (with admission to ICU in most cases) that are very costly. In a study done in the US, the cost of treatment for respiratory failure went up between 2001 and 2009 from 30.1 billion to 54.3 billion USD, (Stefan MS et al, 2013). In Kenya the numbers of ICU facilities that can offer treatment for respiratory failure are few and mainly in the private sector and the cost per day is up to 250 USD. The public ICU facilities are only in the two national referral hospitals Kenyatta National Referral Hospital and Moi Teaching and Referral hospital with a total of 21 and 6 beds only. Since more patients need these facilities daily and they are almost always fully occupied then many families of the respiratory failure patients end up spending huge amounts of funds to pay for this treatment in the private hospitals. The requirements of patients with respiratory failure in terms of ICU admission, drugs, consumable supplies and oxygen is also high and the cost of treatment ends up being higher than for patients with other general medical conditions.

CHAPTER THREE: METHODOLOGY

3.1 Study Setting

The study was conducted among the inpatients in the medical wards at the Moi Teaching and Referral Hospital (MTRH), Eldoret, Kenya. MTRH is located in Uasin Gishu County, in the North Rift region of Western Kenya. This is about 350 Kilometres Northwest of Nairobi, the capital city of Kenya. The MTRH hospital is the second largest referral hospital in Kenya and is a tertiary (level 6) health facility with a bed capacity of 1000 serving as a teaching hospital for Moi University School of Medicine, Public health and Dentistry, and the Kenya Medical Training Centre (KMTC) Eldoret. MTRH is also a training centre for medical, clinical and nursing officer interns from all over the country. It serves the greater western Kenya region's 22 counties representing about 40% (approximately 16.2 million people) of the country's population. It also serves eastern Uganda and parts of Southern Sudan. It admits patients who require specialized treatment that cannot be offered in the county referral hospitals that refer to it including, cancer treatment, renal replacement therapy and transplant, neurosurgical treatment among others. AMPATH centre also partners with MTRH in offering HIV care and the hospital has an ICU with 21 bed capacity that handles all ICU referrals from the 22 counties in the western region. There is therefore a large pool of patients being admitted in MTRH with various conditions that are associated with respiratory failure and hence the hospital provides a good site for our study. On average a total of 35 patients are admitted daily in the medical wards totalling around 12,700 per year and of these 26% have respiratory conditions that may progress to respiratory failure and require ICU admission. About 15 patients are diagnosed with low oxygen saturations daily including the new hypoxemic patients who develop hypoxemia while on admission. The criteria for ICU admission

in MTRH are any patients with reversible medical conditions like acute respiratory failure requiring ventilator support, acute pulmonary embolism with hemodynamic instability and massive haemoptysis and upper airway obstruction. Other conditions include cardiovascular, neurological, renal, endocrine, obstetric and surgical emergencies.

3.2 Study Design

This was a prospective cohort study where participants were followed up for 30 days after recruitment to describe their treatment outcomes.

3.3 Study Population

The study population was patients admitted in the medical wards at the Moi Teaching and Referral Hospital in Eldoret, Kenya.

3.4 Eligibility Criteria

3.4.1 Inclusion Criteria

Patients 14 years and older who were admitted with SPO2<92% and any of:

1 Partial arterial pressure of oxygen (PaO2) level less than (<) 60 millimeters(s) of mercury (mmHg) in arterial blood gases with a normal or low partial arterial pressure of carbon dioxide (PaCO2) or

2. Partial arterial pressure of carbon dioxide (PaCO2) ≥50 mmHg with a normal or low Partial arterial pressure of oxygen.

3.4.2 Exclusion Criteria

Patients with anemia of hemoglobin less than 5 g/dl. Severe anemia can affect the pulse oximetry reading since it depends on light absorption by hemoglobin across several wavelengths. In vitro and animal studies suggest that pulse oximetry readings may be affected by profoundly decreased hemoglobin concentration, (Lindberg LG.et al.,1995.) In vivo, low hemoglobin concentrations appear to cause falsely low readings when the SaO_2 is below 80 percent, (Severinghaus JW. Et al.,1992.) However, this effect is not clinically significant until the hemoglobin level is less than 5 g/dl, (Perkins GD et.al., 2003).

3.5 Sample Size Determination

For sample size determination we will use 56% for the proportion of respiratory failure, and 40% for mortality rate among the patients with respiratory failure, (Vincent et al**,** 2002, Owe R. L.et al, 1999). Thus, in order to be 95% that we estimate the proportion of patients who die among those who have respiratory failure to within plus or minus 5% of 40% the sample was determined using the following formula (Cochran**,** 1963).

$$n = \left(\frac{Z_{1-\alpha/2}}{d}\right)^2 \times P \times (1-P)$$

$$= \left(\frac{1.96}{0.05}\right)^2 \times 0.40 \times (1-0.40)$$

$$= 369$$

Where $Z_{1-a/2}$ is the quantile of the standard normal distribution corresponding to 100x(1-a/2) percentile, a is the type I error, equal to 5%, P is the proportion of patients with respiratory failure who die, and d is the margin of error equal to 5%.

This is the sample size that was sufficient to determine the proportion that dies among the patients with respiratory failure. This implies that 369 represent 56% of the patients admitted. Hence we will require 369/0.56= 659 patients with hypoxemia in our study. However, sampling was done from a finite population of approximately 300 patients with respiratory failure for a period of three months, Thus N = 300. Hence correcting for finite population gave us:

$$\frac{n}{1+n/N} = \frac{659}{1+659/300} = 206$$ as the study size.

3.6 Sampling Procedure

Consecutive sampling technique was used to recruit the participants into the study among those who met the criteria for inclusion. From the ward, the admission list was reviewed every day to establish the patients admitted with hypoxemia (SPO2<92%) and have a HB ≥5g/dl and the new hypoxemic patients who developed hypoxemia while in the ward were also recruited. Patients were then consented and subjected to blood sampling where blood gas analysis was done. Those who met the criteria for respiratory failure based on blood gas analysis were included in the study.

3.7 Study Procedure

The principal investigator (PI) with the help of the research assistants reviewed all patients of 14 years and older with dyspnea and oxygen saturations less than 92% in the medical wards. Informed consent was obtained from the study participants and the guardian/caretaker in cases where the participant was unconscious or less than 18 years old.

Patient demographic & the clinical characteristics were captured using a structured interviewer administered questionnaire. Blood samples were then collected for arterial blood gas analysis, complete blood count, urea and creatinine. The blood sample collection was done by a dedicated lab technician who delivered the labeled samples to MTRH hematology and biochemistry laboratories where the samples were run by a dedicated laboratory technologist.

The cost of treatment was calculated as the total bill accrued by the patient for the entire admission period due to respiratory failure, until discharge or death or 30 days whichever was longer.

3.7.1 Laboratory procedure

3.7.1.1 Blood Gas Analysis

Arterial blood was obtained from an artery in the wrist, arm, or groin, or pre-existing arterial line. The injection site was first sterilized with an antiseptic. Once an artery was located, a needle with a heparinized syringe was inserted into the artery and blood drawn. After the needle was removed, a bandage was put over the puncture wound. Blood drawn was placed in a container with ice packs and delivered to the MTRH biochemistry laboratory where it was analysed using the RAPID point 500 arterial blood gas machine in the MTRH laboratory. The sample was analyzed within 10 minutes of the procedure to ensure an accurate test result. The results were then recorded in a specially designed laboratory results form for analysis.

3.7.1.2 Urea Creatinine and Electrolytes (UEC's) and Complete Blood Count (CBC)

Venous blood was obtained from the cubital fossa or the femoral vein in the inguinal region following the aseptic technique explained above, then blood was placed in a

labelled red top vacutainer for the UEC's and purple top vacutainer for the CBC. Both samples were delivered to and analysed in the MTRH biochemistry and hematology laboratories respectively. The UEC's were analysed using the Cobas Integra 400+ machine and the CBC using Advia 2021 i machine then the results recorded in a specially designed laboratory results form for analysis.

3.7.2 Imaging procedure

A PA view chest radiograph was done for each of the participants in the study who met the criteria for respiratory failure from the blood gas analysis. This was done at the MTRH radiology department by a dedicated radiographer and all images were reported by the principal investigator and a qualified radiologist.

3.7.3 30 Day follow up procedure

Patients were followed up for 30 days to describe outcome. All- cause mortality was documented for those who died within 30 days. For those who were alive at 30 days, an outcome form was filled whereby the symptoms of respiratory failure were documented including: dyspnoea, cough, chest pain, and cyanosis or oxygen dependence.

Oxygen saturations were also taken again to ascertain if they were back to normal, ≥92% (full recovery) or if they were lower than normal <92% with residual symptoms (chronic respiratory failure).

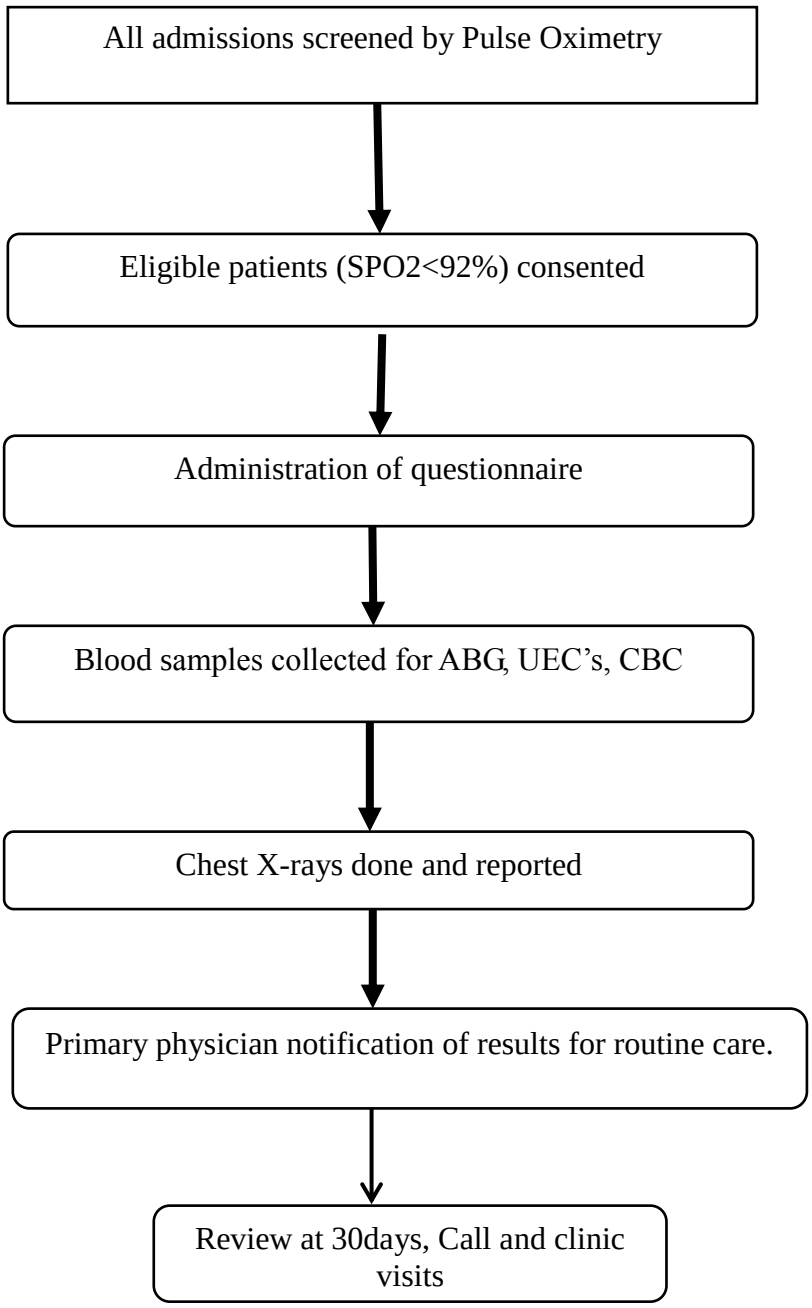

Figure 1: Study procedure

3.7.4 Criteria for Respiratory Failure.

The clinical criteria for diagnosing acute respiratory failure for the purposes of this study were:

Hypoxemic Respiratory failure; Partial pressure of oxygen (PaO2) level less than (<) 60 millimeters(s) of mercury (mmHg) in arterial blood gases with a normal or low partial arterial pressure of carbon dioxide (PaCO2) or

Hypercapnic Respiratory failure; Partial pressure of carbon dioxide (PaCO2) ≥50 mmHg with pH < 7.35, with a normal or low Partial arterial pressure of oxygen (D. Pinson, 2014)

3.8 Data Collection, Management and Storage

Data was collected using structured interviewer administered questionnaires that were filled by the principal investigator and the research assistants.

This questionnaire contained:

Independent variables

Demographic data including: age, gender, race, education level and occupation;

Clinical features of the patients with respiratory failure including: cough, chest pain, dyspnoea, cyanosis, underlying diagnosis, comorbidity, SAPS II score of disease severity, laboratory findings (urea, creatinine, electrolytes, complete blood count and arterial blood gas analysis), treatment/ventilator options and

Dependent variables (outcomes)

These include mortality, full recovery and chronic respiratory failure at 30 days, length of hospital stays and the cost of treatment (total hospital bill paid at the end of

admission due to respiratory failure). All the variables are described in detail in appendix C.

The gathered data was de-identified and entered into an electronic database.

The database was encrypted by assigning labels to ensure confidentiality of the data, and the password was made available to the principal investigator alone. Back-up of the data was done using external drives and memory sticks and kept in separate safe locations to cushion against data loss. Completeness and consistencies was checked regularly. Once the data had completely been converted into the electronic database, the questionnaires were kept in a safe cabinet under a lock, and access was only allowed to the principal investigator. The data will be shredded after five years.

3.9 Statistical Data Analysis

Descriptive statistics including mean and standard deviation (SD) was used to summarize continuous variables that assumed Gaussian distribution. These include age, respiratory rate and SAPS II score. The median and the corresponding inter quartile range (IQR) was used to summarize continuous variables that violated the Gaussian assumptions. Such variables include SPO2, creatinine, PaO2, PaCO2, cost of treatment and duration of hospitalization among other variables. Gaussian assumptions were assessed empirically using Shapiro-Wilk test and graphically using histograms and box plots.

Categorical variables such as gender, education level, occupation, survival outcome among others were summarized using frequencies and the corresponding percentages.

Exploratory associations between the survival outcome and independent categorical variables were assessed using Pearson’s Chi Square test. Fisher’s exact test was used

whenever the Chi Square assumptions were violated. The associated p-value was also reported.

Analysis was done using STATA version 13.1 SE (College Station, Texas 77845 USA).

3.10 Ethical Considerations

Ethical approval was sought from the Institutional Research and Ethics Committee where approval was given with the Final approval number: IREC 2023, the department of internal medicine in Moi University and Moi Teaching and Referral Hospital. An informed written consent was sought from all participants or their next of kin at entry into the study. Assent was sought from the participants aged below 18 years after explaining the study in a language best understood by the participants. Consent was also signed by the guardians for this group. All data collected was kept confidential and was only available to the research team for analysis. Findings for patients diagnosed with respiratory failure were disclosed to the primary care physicians for management. No incentives were offered to participants. Participants were allowed to withdraw consent at any point in the study. There was no conflict of interest in the study.

CHAPTER FOUR: RESULTS

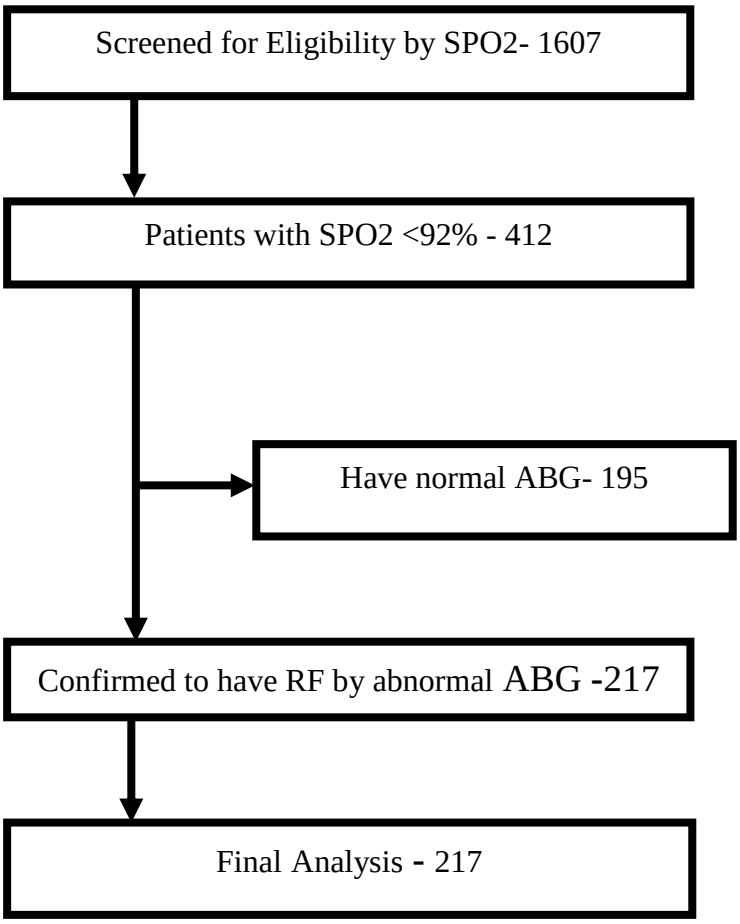

Figure 2: Recruitment Schema

A total of 1607 patients were screened for respiratory failure using pulse oximetry. Of this number, 412 (25.6%) were established to have low oxygen saturations of less than 92% and they were therefore subjected to arterial blood gas analysis.

Consecutive sampling was done to achieve a total of 217 participants with respiratory failure based on the arterial blood gas analysis over the three-month study period representing 13.5% (95% CI: 10.3, 13.3) of all the admitted patients.

Table 2: Socio-demographic characteristics

Variable	**N**	**Mean (SD) or n (%)**
Age (Years), Mean (SD)	**217**	**49.8 (20.4)**
Range (Min. - Max.)		14.0 – 95.0
14 – 34		15 (26.3%)
35 – 64		104 (47.9%)
65+		56 (25.8%)
Gender, n (%)		
Female	217	108 (49.8%)
Male		109 (50.2%)
Education level, n (%)		
None		6 (2.8%)
Primary	217	148 (68.2%)
Secondary		51 (23.5%)
Tertiary		12 (5.5%)
Occupation, n (%)		
None		29 (13.4%)
Casual/Employed		39 (18.0%)
Farming		78 (35.9%)
Housewife	217	23 (10.6%)
Student		23 (10.6%)
Business		15 (6.9%)
Other		10 (4.6%)

SD - Standard Deviation; N - Denominator

The mean age of the participants in the study was 49.8 (SD: 20.4) years with a minimum and a maximum of 14.0 and 95.0 years respectively. Majority of the participants at 47.9% were aged between 35 and 64 years.

Half the participants were male giving a male to female ratio of 1:1.

Less than one third of the participants had secondary or tertiary education and 2.8% had no formal education.

Most of the participants were farmers at 35.9% and 10.6% housewives.

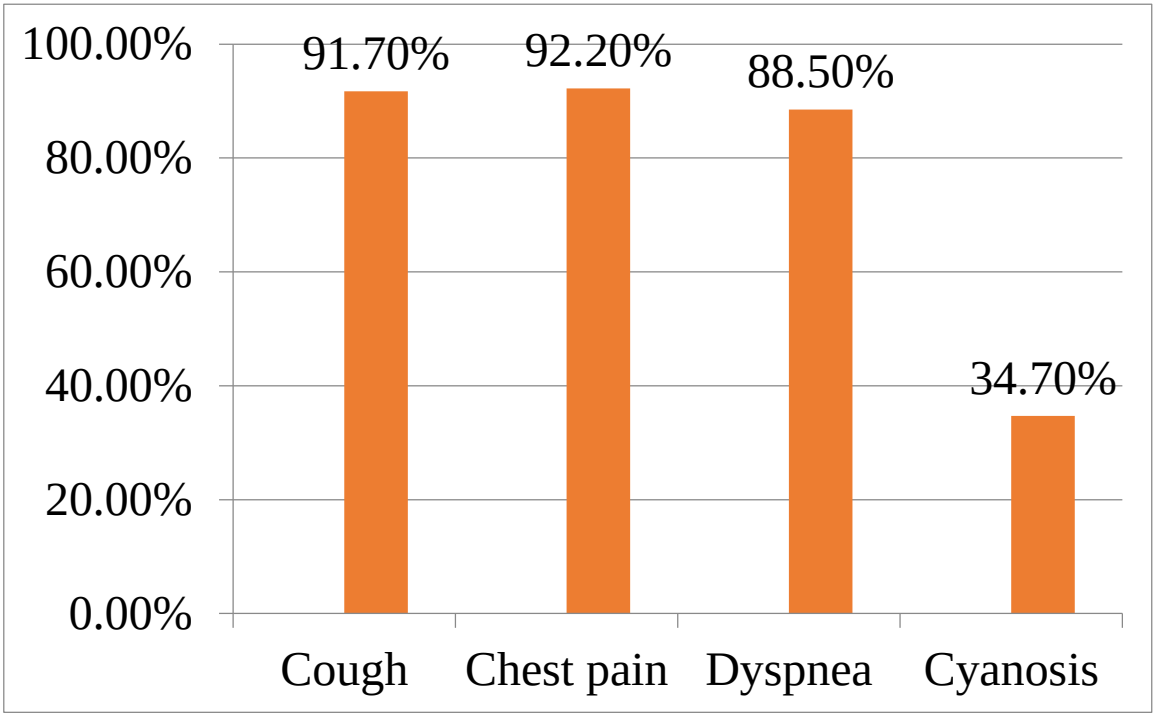

Figure 3: Symptoms and signs of respiratory failure.

The results depict 91.7%, 92.2%, 88.5%, and 34.7% of the participants had cough, chest pain, dyspnea and cyanosis respectively at enrollment.

Table 3: clinical features of Respiratory Failure

Variable	N	Mean (SD) or Median (IQR) or n	(%)
Respiratory rate (breaths/min), Mean (SD)	217	**27.8 (6.6)**	
Range (Min. - Max.)		**6.0 – 58.0**	
Bradypnea (RR<14)		2	0.9
Normal (14-16)		1	0.5
Tachypnea (17-29)		138	63.6
Severe Tachypnea (≥30)		76	35
SPO2 (%), Median (IQR)	217	**80.0 (72.0, 84.0)**	
Range (Min. - Max.)		8.0 – 89.0	
Normal (>92)		0	0
Mild (85 - 92)		53	24.4
severe (<85)		164	75.6
SAPS II, Mean (SD)	217	**27.2 (11.0)**	
Range (Min. - Max.)		6.0 – 57.0	
0 – 14		26	12
15 – 35		146	67.3
> 35		45	20.7

The average respiratory rate was 27.8 (SD: 6.6) breaths per minute with a range of 6.0 – 58.0 breaths per minute and up to 35% having severe tachypnea with a respiratory rate > 30 breaths per minute.

The median oxygen saturation (SPO2) was 80.0% (IQR: 72.0, 84.0) with three quarters of the participants having severely low SPO2 of less than 85%. The average SAPS II score was 27.2 (SD: 11.0) points and 67.3% had SAPS II score ranging from 15 – 35.

The documented diagnosis of the participants was as shown in Table 4.

Table 4: Documented Diagnosis

Diagnosis (n=229)	**n**	**%**
Pneumonia	53	24.40
Cardiovascular diseases	45	20.70
Pulmonary TB	16	7.40
COPD	13	6.00
Neurologic disorders	13	6.00
Hematological disorders	12	5.50
Solid malignancies	11	5.10
Renal disease	9	4.10
Sepsis	9	4.10
Lung cancer	7	3.20
Heart disease	6	2.80
Pleural effusion	5	2.30
Diabetes mellitus	4	1.80
Liver disease	4	1.80
Gastroenteritis	3	1.40
Asthma	2	0.90
Broncospasm	2	0.90
DVT	2	0.90
Interstitial lung disease	2	0.90
OPP	2	0.90
Restrictive lung disease	2	0.90
Alcohol withdrawal	1	0.50
Bronchiectasis	1	0.50
Cellulitis	1	0.50
Dehydration	1	0.50
Malaria	1	0.50
PCP	1	0.50
PE	1	0.50

Denominator = 217

There were 205 (94.5%) who had one condition and 12 (5.5%) who had two conditions.

Pneumonia, cardiovascular diseases, pulmonary TB, COPD, neurologic disorders and hematologic disorders was found in 24.4%, 20.7%, 7.4%, 6.0%, 6.0% and 5.5% of the

participants respectively. Lung cancer was documented in 3.2% of the participants. Other conditions that were diagnosed in less numbers were as shown in the table.

Table 5: Comorbidities

Comorbidity (n=209)	n	(%)
Renal disease	29	13.40
Hypertension	27	12.40
Cardiovascular diseases	26	12.00
HIV	20	9.20
Diabetes mellitus	18	8.30
Hematological disorder	16	7.40
COPD	10	4.60
Gastroenteritis	9	4.10
Solid malignancy	9	4.10
Pneumonia	7	3.20
Pulmonary TB	7	3.20
Liver disease	6	2.80
Pleural effusion	4	1.80
Sepsis	4	1.80
DVT	3	1.40
Alcohol abuse	2	0.90
Lung cancer	2	0.90
Neurological disease	2	0.90
Autoimmune disease	1	0.50
Dysphagia	1	0.50
ILD	1	0.50
Interstitial disease	1	0.50
Pancreatitis	1	0.50
Paralytic ileus	1	0.50
PE	1	0.50
UTI	1	0.50

Denominator =217

The findings in Table 5 present the proportion of participants who had specific comorbidities (the denominator is the number of participants enrolled i.e N = 217).

There were 161 (74.2%) participants who had comorbidities. The rest had none. Of the total participants with comorbidities 120 (55.3%), 34 (15.7%) and 7 (3.2%) had 1, 2 and 3 comorbidities respectively.

Renal disease, hypertension, and cardiovascular diseases were found in 13.4%, 12.4% and 12.0% of the participants respectively. There were 9.2% of the participants who were living with HIV. Diabetes mellitus, hematological disorders and COPD were found in 8.3%, 7.4% and 4.6% respectively.

LABORATORY FINDINGS

Respiratory failure was assessed using arterial blood gas indicators. The findings were as shown in Table 6.

Table 6: Arterial Blood Gas Analysis

Variable	Frequency (n=217)	%
PH		
< 7.35	50	23.0
7.35 - 7.45	98	45.2
> 7.45	69	31.8
PaO2, mmHg		
Normal (≥80)	3	1.4
Mild hypoxemia (60-79)	11	5.1
Moderate hypoxemia (40-59)	170	78.3
Severe hypoxemia (<40)	33	15.2
PaCO2, mmHg		
< 50	183	84.3
≥ 50	34	15.7

IQR – Inter Quartile Range, N - Denominator

The results show that 23% of the patients had acidosis with a PH <7.35, while 31.8 % had alkalosis with a PH > 4.35. 15.2 % of the participants had severe hypoxemia with PaO2 that was < 40 mmHg while 78.3% had moderate hypoxemia. The results also

show that 84.3% of the patients had hypoxemic respiratory failure with a PaO2< 60 mmHg with a PaCO2 <50 mmHg and 15.7% had hypercapnia with a PCO2 that was ≥ 50mmhg.

Table 7: Biochemical findings

Variable	N	Mean (SD) or Median (IQR) or n	(%)
Urea (mmol/l), Median (IQR)	217	5.9 (3.6, 11.1)	
Range (Min. - Max.)		0.7 - 59.7	
≤ 8.3		139	64.1
> 8.3		78	35.9
Creatinine (µmol/l), Median (IQR)	217	73.0 (55.0, 119.0)	
Range (Min. - Max.)		3.7 - 3746.0	
< 44		32	14.7
44-80		92	42.4
>80		93	42.8
Potassium (mmol/l), Median (IQR)	217	4.7 (4.1, 5.3)	
Range (Min. - Max.)		2.5 – 6.4.0	
<3.5		22	10.1
3.5 - 5.1		126	58.1
>5.1		69	31.8
Sodium (mmol/l), Median (IQR)	217	133.7 (128.0, 137.0)	
Range (Min. - Max.)		98.5 - 154.0	
< 136		139	64.1
136-145		67	30.8
> 145		11	5.1

IQR – Inter Quartile Range, **N** - Denominator

The median urea level was 5.9 (IQR: 3.6, 11.1) mmol/l with 35.9% of the participants having urea level above 8.3 mmol/l. The median creatinine level was 73.0 (IQR: 55.0, 119.0) µmol/l with 14.7%, 42.4%, and 42.8% having < 44.0 µmol/l, 44.0 – 80.0 µmol/l and >80.0 µmol/l respectively.

The estimated Glomerular Filtrate as estimated using CKD-EPI equation show that 1.5% of the participants had chronic kidney disease in stage 2 or 3.

The median potassium levels was 4.7 (IQR: 4.1, 5.3) mmol/l with a range of 2.5 – 64.0 mmol/l. There were 58.1% of the participants who had normal (3.5 – 5.1 mmol/l) potassium levels.

One third of the participants had normal sodium levels within 136.0 and 145.0 mmol/l and 64.1% had sodium levels below 136.0 mmol/l.

Analysis of the PH levels show that **23**.0% and 31.8% of the participants had PH levels below 7.35 and above 7.45 respectively.

The median bicarbonate levels was 22.1 (IQR: 17.9, 25.9) units with 49.3% having bicarbonate levels <22.0 and similar proportion having bicarbonate levels between 22.0 and 45.0.

Table 8: Hematological characteristics

Variable	**N**	**Mean (SD) or Median (IQR) or n (%)**
WBC (x 10^3 /µl), Median (IQR)	217	9.3 (6.3, 14.9)
Range (Min. - Max.)		1.8 - 681.1
0 - 5.2		33 (15.2%)
5.2 - 12.4		110 (50.7%)
> 12.4		74 (34.1%)
Platelets (x 10^3 /µl), Median (IQR)	217	238.0 (155.0, 343.0)
Range (Min. - Max.)		6.0 - 901.0
< 130		41 (18.9%)
130 – 145		8 (3.7%)
> 145		168 (77.4%)
Hgb (g/dl), Mean (SD)	217	12.2 (3.7)
Range (Min. - Max.)		5.6 – 12.1
< 12		109 (50.2%)
12 – 18		97 (44.7%)
> 18		11 (5.1%)
RBC (x 10^6 /µl), Median (IQR)	217	4.6 (3.5, 5.3)
Range (Min. - Max.)		1.4 - 10.2
< 4.2		84 (38.7%)
4.2 - 5.4		85 (39.2%)
> 5.4		48 (22.1%)

IQR – Inter Quartile Range, N - Denominator

Analysis of hematological characteristics show that 50.7% of the participants had normal white cell count while 34 % had leukocytosis and 15.2% had leucopenia.

3.7% had between 130.0 – 145.0 x 10^3 /µl platelets, and 39.2% had between 4.2 – 5.4 x 10^6 /µl red blood cells.

The mean hemoglobin levels was 12.2 g/dl (SD: 3.7) with the least and the highest hemoglobin levels of 5.6 and 12.1 g/dl respectively. Half of the participants had hemoglobin levels below 12.0 g/dl while 5.1% had hemoglobin levels above 18.0 g/dl.

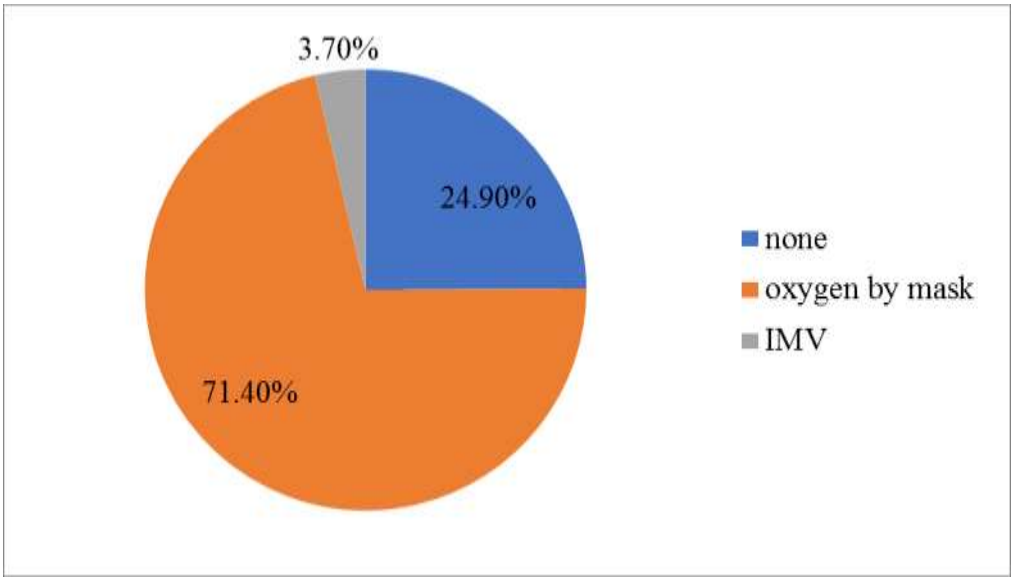

Figure 4: Oxygenation mode

One quarter of the participants were not treated using oxygen. More than two thirds were treated using oxygen by mask and 3.7% were treated using intubation and MV.

Table 9 describes the chest x-ray findings where majority of the participants had parenchymal lung disease with consolidation being the commonest at 76%. Seventy nine percent of the participants also had cardiovascular abnormalities.

Table 9: Chest X-ray Findings.

Finding	Frequency(N=217)	(%)
Parenchymal lung disease		
Consolidation	**165**	**76.0**
Interstitial fibrosis	52	24.0
Lung mass	37	17.0
Pulmonary edema	30	13.8
Hyperinflation bullae	26	12.0
Cavities	26	12.0
Cardiovascular Abnormalities	**172**	**79.3**
Pleural Effusion	89	41.0
Mediastinal abnormalities	33	15.2
Chest wall disorders,	8	3.7
Normal	5	2.3
(Radiology Society of North America.)		

Table 10 presents the outcome at 30 days. The outcomes include survival status at 30 days, cost of treatment and length of stay in the hospital.

Table 10: Outcome: Survival, Mortality, Cost of Treatment and Length of Hospital Stay.

Variable	**N**	**Median (IQR) or n**	**(%)**
Survival, n (%)			
Alive	217	167	77
Dead		50	23
Among those alive			
Had full recovery	166	69	41.6
Recovered with chronic respiratory failure		97	58.4
Cost of treatment (USD), Median (IQR)	217	347.65 (221.55, 528.55)	
Range (Min. - Max.)		61.10 – 8,503.81	
Length of Hospital stay (days), Median (IQR)	217	11.0 (7.0, 18.0)	
Range (Min. - Max.)		1.0 - 101.0	

IQR – Inter Quartile Range, N - Denominator

Of the enrolled participants 23.0% had died by day 30. Of those who survived, 41.6% had full recovery while 58.4% recovered but with chronic respiratory failure.

It cost a median of USD 347.65 (IQR: 221.55, 528.55) for treatment for median duration of stay of 11.0 (IQR: 7.0, 18.0) days.

EXPLORATORY ASSOCIATIONS

The associations done in this study were exploratory based on the variables obtained as outlined in Tables 11 to 16.

Table 11: Association between mortality and age and gender

		Outcome		
		Alive	**Dead**	**P-value**
Variable	**N**	**n = 167**	**n = 50**	
Age (Years), n (%)				
14 – 34		48 (84.2%)	9 (15.8%)	
35 – 64	217	74 (71.2%)	30 (28.9%)	0.133[c]
65+		45 (80.4%)	11 (19.6%)	
Gender, n (%)				
Female		87 (80.6%)	21 (19.4%)	
Male	217	80 (73.4%)	29 (26.6%)	0.210[c]

[c] Pearson's Chi-Square test

The findings show no evidence of association between age and mortality (p = 0.133) as well as between gender and mortality (p = 0.210).

Table 12: Association between clinical findings and mortality

Variable	N	Outcome		P-value
		Alive	**Dead**	
		n = 167	**n = 50**	
PAO2, n (%)				
≥ 60		10 (66.7%)	5 (33.3%)	
< 60	217	157 (77.7%)	45 (22.3%)	0.345[f]
WBC (x 10^3 /µl), n (%)				
0 - 5.2		31 (93.9%)	2 (6.1%)	
5.2 - 12.4	217	86 (78.2%)	24 (21.8%)	0.010[c]
> 12.4		50 (67.6%)	24 (32.4%)	
Chronic Kidney disease, n (%)				
Stage 1		164 (76.6%)	50 (23.4%)	
Stage 2	217	2 (100.0%)	0 (0.0%)	>0.999[f]
Stage 3		1 (100.0%)	0 (0.0%)	
SAPS II Score				
0 – 14		25 (96.2%)	1 (3.9%)	
15 – 35	217	117 (80.1%)	29 (19.9%)	<0.0001[f]
> 35		25 (55.6%)	20 (44.4%)	

[c] Pearson's Chi-Square test

[f] Fisher's Exact test

The findings show that 33.3% of the participants who had PAO2 ≥ 60 died compared to 22.3% among those who had PAO2 < 60. There was no sufficient evidence to demonstrate the presence of a significant difference between the two groups (p=0.345).

Higher levels of WBC were associated with increased risk of death (p=0.010) and higher SAPS II score were also associated with increased risk of death (p<0.0001).

There was no evidence of association between chronic kidney disease and mortality (p>0.999).

Table 13 presents association between diagnosis and mortality.

Table 13: Association between diagnosis and mortality

		Outcome		
Variable	**N**	**Alive n = 167**	**Dead n = 50**	**P-value**
Pneumonia				
No		129 (78.7%)	35 (21.3%)	
Yes	217	38 (71.7%)	15 (28.3%)	0.348[f]
Cardiovascular diseases				
No		127 (73.4%)	46 (26.6%)	
Yes	217	40 (90.9%)	4 (9.1%)	0.015[f]
Pulmonary TB				
No		154 (76.6%)	47 (23.4%)	
Yes	217	13 (81.3%)	3 (18.8%)	>0.999[f]
COPD				
No		154 (75.5%)	50 (24.5%)	
Yes	217	13 (100.0%)	0 (0.0%)	0.043[f]
Neurological disorders				
No		155 (76.0%)	49 (24.0%)	
Yes	217	12 (92.3%)	1 (7.7%)	0.307[f]
Hematological disorders				
No		160 (78.1%)	45 (22.0%)	
Yes	127	7 (58.3%)	5 (41.7%)	0.153[f]
Solid malignancies				
No		160 (77.7%)	46 (22.3%)	
Yes	217	7 (63.6%)	4 (36.4%)	0.282[f]

[f] Fisher's Exact test

Of the participants who were diagnosed with pneumonia, 28.3% died while 21.3% of those who did not have pneumonia died. However, there was no evidence of association between pneumonia and mortality (p = 0.348).

The data show that 9.1% of the participants who had cardiovascular diseases died compared to 26.6% of those who did not have cardiovascular disease. The difference was statistically significant (p=0.015) an indication of a likely influence by another variable on mortality. Similarly, a higher proportion (24.5%) of the participants who did not have COPD died compared to none among those who had COPD (p = 0.043).

Diagnosis of neurological disorder, hematological disorders and solid malignancies were not associated with mortality (p>0.05).

Table 14: Association between comorbidities and mortality

		Outcome		
		Alive	**Dead**	**P-value**
Variable	**N**	**n = 167**	**n = 50**	
HIV				
No		156 (79.2%)	41 (20.8%)	
Yes	217	11 (55.0%)	9 (45.0%)	0.023[f]
Renal disease				
No		145 (77.1%)	43 (22.9%)	
Yes	217	22 (75.9%)	7 (24.1%)	0.817[f]
Hypertension				
No		143 (75.3%)	47 (24.7%)	
Yes	217	24 (88.9%)	3 (11.1%)	0.145[f]
Diabetes mellitus				
No		157 (78.9%)	42 (21.1%)	
Yes	217	10 (55.6%)	8 (44.4%)	0.038[f]
COPD				
No		158 (76.3%)	49 (23.7%)	
Yes	217	9 (90.0%)	1 (10.0%)	0.460[f]
Hematological disorders				
No		157 (78.1%)	44 (21.9%)	
Yes	217	10 (62.5%)	6 (37.5%)	0.213[f]
Number of comorbidities, n (%)				
1		138 (78.4%)	38 (21.6%)	
2	217	25 (73.5%)	9 (26.5%)	0.302[f]
3		4 (57.1%)	3 (42.9%)	

[f] Fisher's Exact test

A significantly higher proportion (45.0%) of participants who were living with HIV died compared to 20.8% among those who were not living with HIV, p = 0.023.

Presence of renal disease and hypertension comorbidities were not associated with mortality (p>0.05).

The findings also indicate that the participants who had diabetes mellitus were more likely to die compared to those who did not have diabetes mellitus, 44.4% vs. 21.1%, p = 0.038.

Presence of hematological disorders as well as the number of comorbidities were not associated with mortality (p>0.05).

Table 15: Association between treatment modality and x-ray findings to mortality

		Outcome		
		Alive	Dead	P-value
Variable	**N**	**n = 167**	**n = 50**	
Ventilation mode, n (%)				
None		46 (85.2%)	8 (14.8%)	
OBM	217	115 (74.2%)	40 (25.8%)	0.243[f]
IMV		6 (75.0%)	2 (25.0%)	
X-ray disorders absent				
No		163 (76.9%)	49 (23.1%)	
Yes	217	4 (80.0%)	1 (20.0%)	>0.999[f]

[f] Fisher's Exact test

Assessment of the association between the mode of treatment and mortality revealed lack of association between the two variables (p = 0.243).

Table 16: Factors associated with abnormal PaO2

Variable	N	PAO2 ≥ 60 n = 14	PAO2 < 60 n = 203	P-value
Age (Years), n (%)				
14 – 34		3 (5.3%)	54 (94.8%)	
35 – 64	217	9 (8.7%)	95 (91.4%)	0.419[c]
65+		2 (3.6%)	54 (96.4%)	
Gender, n (%)				
Female		10 (9.3%)	98 (90.7%)	
Male	217	4 (3.7%)	105 (96.3%)	0.094[c]
Cough, n (%)				
No		5 (33.3%)	13 (6.4%)	
Yes	217	9 (4.5%)	190 (95.5%)	0.003[f]
Chest pain, n (%)				
No		3 (17.7%)	14 (82.4%)	
Yes	217	11 (5.5%)	189 (94.5%)	0.085[f]
Dyspnea, n (%)				
No		1 (4.0%)	24 (96.0%)	
Yes	217	13 (6.7%)	179 (93.2%)	>0.999[f]
Cyanosis, n (%)				
No		5 (3.6%)	136 (96.5%)	
Yes	216	9 (12.0%)	66 (88.0%)	0.021[f]
SPO2, n (%)				
Mild: 85 – 92		2 (3.7%)	51 (96.2%)	
Severe: < 85	217	12 (7.3%)	152 (92.7%)	>0.526[f]
Absence of X-ray disorders, n (%)				
No		14 (6.6%)	198 (93.4%)	
Yes	217	0 (0.0%)	5 (100.0%)	>0.999[f]

[c] Pearson's Chi-Square test

[f] Fisher's Exact test

Association between demographic characteristics and clinical characteristics to respiratory failure was assessed.

The findings indicate that a higher proportion of participants (95.5%) who had a cough compared to those who did not have a cough (6.4%) were more likely to have PAO2 < 60, (p = 0.003).

Among the participants who had cyanosis 88.0% had PAO2 < 60 compared to 96.5% among those who did not have cyanosis (p=0.021).

CHAPTER FIVE: DISCUSSION

In this study the prevalence of respiratory failure was 13.5% which was much higher than the prevalence that was found by Mativa et al., 2009 in Kenyatta National hospital Kenya. The population of patients included in KNH was mixed from the accident and emergency setting and this could explain the differences found. The proportion of patients with respiratory failure in this study was lower than the prevalence found in Europe by Vincent et al, 2002 of 56%. This could be because the European study was conducted purely in an ICU setting and involved multiple intensive care units hence most of the participants could most likely have had respiratory failure at baseline, unlike mine which was done in the general medical wards. The European study also defined respiratory failure as intubation and mechanical ventilation unlike this study which defined respiratory failure as PaO2< 60 and PaCO2 >=50 mmHg. The European study also included patients who developed RF while in the ICU for other reasons like scheduled surgery.

Franca et al, 2011 in Brazil found 57% prevalence of acute respiratory failure and this was higher than our study. Franca's study was done in 24 different ICUs, while my study was conducted in the general wards. This study also included the surgical and nonsurgical patients while mine was purely medical patients.

Male to female ratio was almost 1:1 since males were 49.8% and females were 50.2%. Contrary to KNH study that showed a male to female ratio of 2:1 among patients with respiratory failure. This could be due to the fact that KNH study found trauma as the leading cause of RF and more males were prone to trauma than females. Other studies have however found no gender difference in patients with respiratory

failure, half (51.1%) of all patients were male in the study done by Berhent et al., 2000.

The mean age was 49.8 years with a peak of 35 – 64 years compared with the KNH study where mean age was 39.86 years & peak of 31-40 years. KNH study included trauma patients who were more likely to be of a younger age compared to the ones in my study who had only medical conditions. In a study done by Berhent et al., 2000, the Incidence increased nearly exponentially each decade until age 85 years. Their median age was 69 years (5th to 95th percentile range, 30 to 87 years).

The most common symptom of respiratory failure in this study was chest pain followed by cough. This is comparable to the KNH study which found that cough was the most common symptom followed by loss of consciousness. This could be due to the fact that KNH study had head injury patients among their study participants based on their different inclusion criteria.

Majority of the patients had severe desaturation with SPO2 levels less than 85% at 75.6%. This explains the results of the ABG where majority of the patients had moderate to severe hypoxemia.

This shows that SPO2 served as a good screening tool for hypoxemia in our study. Lee W.W. et al, 2000 did a study where the pulse oximetry had a sensitivity of 0.92 and specificity of 0.90 if COHb is <2%.

This study found that majority of patients had type 1(hypoxemic) respiratory failure at 85.2%, contrary to the KNH study where they found majority of patients had mixed respiratory failure at 79.5% with type 1 being only 20.5% which could be explained by the mixed population in the KNH study where surgical patients were included.

Most participants had a consolidation on chest radiograph in our study at 76%. This was higher than the KNH study that found 19.3% of patients with consolidations. This may be explained by the fact that patients in my study were purely medical patients with chest symptoms while KNH study had a different population who included head injury patients that could have had respiratory failure due to depression of central drive rather than lung parenchymal injury.

The mean severity of illness score, SAPS II score in this study was 27 with a median estimated mortality of 7.2 (2.9, 15.3). This indicated that our patients were severely ill at recruitment and explains the actual mortality rate that was found of 23%. Therefore, most of these patients with respiratory failure require to be managed in ICU with early oxygenation by an appropriate mode of oxygen delivery to reduce on the worst outcome. This score was slightly lower than the median found by Franca et al, 2011 of 37 (27-48), which could be due to the fact that Franca et al selected ICU patients who had multiple organ failures at the time of recruitment hence a higher severity of illness score. This was also lower than what R. Scala et al, 2004 found a mean Acute Physiologic and Chronic Health Evaluation II score (APACHE II) of 59 who recruited ICU patients as well.

Only a few participants received mechanical ventilation at 3.75% with the rest receiving oxygen by mask or nasal prongs at 71.4% or no oxygenation at 24.9%, however at least 23% of patients needed mechanical ventilation based on the severity of illness and were unable to get it. This could be due to the limited ICU beds in the setting where this study was conducted. In a US study by M.S. Stefan et al., 2013, 49.7% received mechanical ventilation with intubation and mechanical ventilation

(IMV) being 42.1% and non - invasive ventilation (NIV) 10.1%. In our setting no patient received non - invasive ventilation.

In this study out of the participants that survived at 30 days only 41.9% had full recovery and 58.1% had residual respiratory failure. This was higher than KNH study (Mativa et al., 2009) where 32.5% had full recovery while 2.4% had residual respiratory failure.

The mean length of hospital stay was 11.0 (7.0, 18.0 IQR), compared to M.S. Stefan et al., 2013 who found 7.8 -7.1 days in 2001 and 2009 respectively. Franca S.A. et al., 2011 found that patients with ARF had a longer ICU (median, 16 vs 3 days; P b .001) and hospital (median, 27 vs 15 days; P b. 001) length of stay than those without ARF. The difference could be due to the fact that the mortality at KNH study was at 65.1% meaning they had more severely ill patients.

We found the mean cost of treatment per patient to be USD 348 (222, 529) with a range of USD 61– USD 8,504. This is very high in our setting considering that the average income of Kenyans is low with a per capita income of USD 810 (USD 2.20 per day) compared to the Africa or the World averages of USD 1700 & 10,000 respectively according to world bank estimates. At least 36% Kenyans live below the poverty line (World Bank Group, 2018). This is however lower compared to a study in the US that found an increase in total hospital costs out of respiratory failure treatment from USD 30.1 billion to USD 54.3 billion between 2001 and 2009 in the US with mean cost per case USD 15,900, (M. S. Stefan, MD, 2013). This is possibly due to the fact that the patients in this study were mostly managed in ICU since ICU space is much more readily available in the US than in Kenya. We also note that the cost in the

patients in this study was mainly for medical ward admission since only 3.7% out of 23% who required mechanical ventilation received it in an ICU setting, therefore the

Cost of care could have been higher had they all been managed in ICU.

There was no association between gender and mortality in this study with a p = 0.210. Age was also not associated with respiratory failure or mortality (p = 0.133) in this study contrary to what other studies have found. Behrendt et al., 2000 found ARF incidence increased markedly with age, resulting in an 88-fold difference in risk between the youngest and oldest age groups. In a study by Franca S.A. et al., 2011, patients who developed ARF were older with a median of 63 years compared to those without respiratory failure at 53 years P = .005). Additionally, non survivors of ARF in this comparison study were older (median, 62 vs 49 years; P b .001).

Cardiovascular disease had an inverse association with mortality with a p value of <0.015 meaning that other factors were responsible for death in patients with cardiovascular disease. COPD however had a positive associated with mortality with a p value of <0.043. Additionally, HIV was associated with mortality in this study with a p value of <0.023. This was similar to Franca et al., 2011, who found an association between HIV and mortality with a p value of 6% vs 2%; P = .001. Hematological diseases, solid malignancy was not associated with mortality in our study unlike the study by Franca S.A. et al., 2011, where non survivors more frequently had a history of hematologic malignancy (7% vs 1%; P b .001) or cancer.

Other characteristics associated with mortality in our study included a high white cell count and SAPS II score with p values of <0.01 &< 0.0001 respectively. This was similar to Franca et al., 2011 who found that non survivors had a greater severity of illness at ICU admission, as evaluated by the SAPS II (median, 44 vs 30; P b .001),

APS (median, 26 vs 18; P b .001), and LODS (median, 5 vs 3; P b .001) scores compared to survivors of ARF. The presence of infection, chronic renal failure or liver cirrhosis, the presence of circulatory shock on ICU admission was associated with mortality according to Vincent J.et al., 2002. Our study however found no association between mortality and renal chronic renal failure.

Lastyly, the landscape of respiratory failure has greatly evolved over the course of reporting on the findings of this study since it is a major cause of respiratory failure. Therefore, further studies are required to enumerate the prevalence and the course of respiratory failure in the setting of Covid-19 pandemic.

STRENGTHS

Arterial blood gas analysis which is the gold standard used to diagnose respiratory failure was used in recruitment of patients with respiratory failure.

A Prospective study design was employed where patients were followed up for 30 days and this is a very good study design for outcome studies.

LIMITATIONS

It was difficult to establish whether the CRF outcome was as a result of the current admission or was present even before admission since patients were recruited at first encounter.

The distinction between acute and chronic hypoxemic respiratory failure cannot readily be made on the basis of arterial blood gases since chronic respiratory failure develops over days to weeks while acute respiratory failure develops over hours to a few days.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

This study shows that there is a high burden of respiratory failure in MTRH with a high morbidity and mortality. Hypoxemic respiratory failure was the commonest type and most participants had a consolidation on chest radiograph. A high SAPS II score was associated with mortality and a significant proportion of the participants did not get supplemental oxygen while only a small number got mechanical ventilation.

6.2 Recommendations

There is need to improve capacity to diagnose respiratory failure in MTRH by performing arterial blood gas analysis for patients with low oxygen saturations to enable early intervention. There is also need to perform severity of illness scores like SAPS II score to predict mortality, enhance the capacity and access to oxygen therapy in the medical wards for patients with respiratory failure and create awareness on the role of none invasive mechanical ventilation (NIV) in order to increase its utilization.

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APPENDICES

APPENDIX A: QUESTIONNAIRE

THE BURDEN OF RESPIRATORY FAILURE AMONG PATIENTS ADMITTED IN THE MEDICAL WARDS AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA

PATIENT ID.....

DEMOGRAPHIC DATA (Tick in the box where appropriate.)

AGE .....

GENDER MALE ☐ FEMALE ☐

RACE BLACK ☐ WHITE ☐ ☐

ASIAN

OCCUPATION .....

LEVEL OF EDUCATION PRIMARY ☐ SECONDARY ☐ ☐

TERTIARY

II. CLINICAL CHARACTERISTICS (Tick in the box if symptom is present)

COUGH ☐ CHEST PAIN ☐ DYSPNEA ☐

CYANOSIS ☐ SAPS II SCORE ☐

DOCUMENTED DIAGNOSIS ..... COMORBIDITY .....

BASELINE LABORATORY FINDINGS

UEC'S

UREA ..... CREATITININE .....

POTASSIUM ..... SODIUM .....

CBC

WBC..... HGB .....PLT.....

ARTERIAL BLOOD GAS

PH ..... HCO3 .....

PO2 ..... PCO2 .....

TREATMENT OPTIONS

VENTILATION OPTION NONE ☐ OXYGEN BY MASK ☐

NPPV ☐ INTUBATION & MV ☐

APPENDIX B: OUTCOMES FORM.
PATIENT ID.....

COST OF TREATMENT ksh .....

OUTCOME AT 30 DAYS

DEAD ☐ ALIVE ☐

COUGH ..... CHEST PAIN .....

DYSPNEA ..... CYANOSIS .....

SPO2 .....

ALIVE WITH FULL RECOVERY ☐

ALIVE WITH CHRONIC RESPIRATORY FAILURE ☐

APPENDIX C: DEFINITION OF VARAIBLES

Clinical characteristics refer to the symptoms, signs of respiratory failure and severity of illness as measured by Simplified Acute Physiologic Score II (SAPS II).

Dyspnoea is defined by American Thoracic Society as a term used to characterize a subjective experience of breathing discomfort that is comprised of qualitatively distinct sensations that vary in intensity. The experience derives from interactions among multiple physiological, psychological, social, and environmental factors, and may induce secondary physiological and behavioral responses, (Parshall MB, et al., 2012)

Cyanosis: is defined by American Thoracic Society as a bluish-purple discoloration of the tissues due to an increased concentration of deoxygenated hemoglobin in the capillary bed, results from a variety of conditions, many of which are life-threatening [1]. It is most easily appreciated in the lips, nail beds, earlobes, mucous membranes, and locations where the skin is thin, (Parshall MB, et al., 2012).

Documented Diagnosis in this study refers to the primary illness found by the physicians after evaluation that is the primary reason for admission.

Comorbidity in this study refers to other secondary or chronic illness that the patient might have in addition to the primary illness that may not be the main reason for admission.

Laboratory characteristics include:

Hematological characteristics which refer to the complete blood count also known as a full blood count (FBC), that is a set of medical laboratory tests that provide information about the cells in a person's blood. The CBC indicates the counts

of white blood cells, red blood cells and platelets, the concentration of hemoglobin, and the hematocrit (the volume percentage of red blood cells).

Arterial Blood Gas Analysis is a biochemical test that measures the the amounts of arterial gases, such as oxygen and carbon dioxide by assessing the blood gas tension values of the arterial partial pressure of oxygen (PaO2), and the arterial partial pressure of carbon dioxide (PaCO2), and the blood's pH.

Biochemical findings refer to Urea, Electrolytes and Creatinine which are used to estimate kidney function by calculating the glomerular filtration rate.

Laboratory Normal Reference Ranges.

VARIABLE	REFERENCE	UNITS
UREA	0-8.3	mmol/l
POTASSIUM	3.5-5.1	mmol/l
CREATININE	44-80	µmol/l
SODIUM	136-145	mmol/l
WBC	5.2-12.4	103µl
PLATELET	130-400	103/µl
HGB	12-18	g/dl
RBC	(4.2-5.4)	106/µl
PH	7.35-7.45	-
PAO2	>80	mmHg
PACO2	35-45	mmHg
HCO3	22-29	mEq/L

Chest X-ray: A **chest radiograph**, called a **chest X-ray** (**CXR**), or **chest film**, is a projection radiograph of the chest used to diagnose conditions affecting the chest, its contents, and nearby structures. The X rays done in this study were in a posterior anterior (PA) view.

The Oxygenation mode in this study represents the mode of treatment for the respiratory failure which was either: None meaning no form of oxygen was given to

the patient, oxygen by masks or nasal prongs, invasive mechanical ventilation by intubation (IMV) and non-invasive mechanical ventilation (NIV).

Outcomes in this study include:

Full recovery: is complete recovery with absence of cough, dyspnea, chest pain or cyanosis and an SPO2 of or more than 92% on pulse oximetry at 30 days.

Chronic respiratory failure: is the presence of cough, dyspnea, chest pain or cyanosis with an SPO2 less than 92% on pulse oximetry at 30 days.

Mortality is death from all causes during the admission at or before 30 days.

Cost of treatment is the cumulative medical bills that the patient accrues during the admission due to respiratory failure.

Length of hospital stay is the total number of 24 - hour days that the patient spends in the medical ward under active care due to respiratory failure until discharge or death or 30 days whichever is earlier.

APPENDIX D: LABORATORY PROCEDURE

BLOOD GAS ANALYSIS

Arterial blood was obtained from an artery in the wrist (radial artery), arm, groin (femoral artery), or pre-existing arterial line. The injection site was sterilized with an antiseptic like chlorhexidine. Once an artery is located, a needle with a heparinized syringe was inserted into the artery and blood drawn into the heparinized syringe. After the needle was removed, a bandage was put over the puncture wound. Blood drawn was placed in a container with an ice pack and delivered the MTRH biochemistry laboratory where it was analysed using the RAPID point 500 arterial blood gas machine in the MTRH laboratory. All samples were analysed within 10 minutes of the procedure to ensure an accurate test result. The results were then recorded in a specially designed laboratory results form for analysis.

UEC'S AND CBC

Venous blood was obtained from the cubital fossa or the femoral vein in the inguinal region following the aseptic technique explained above, then it was placed in a red top vacutainer for the UEC'S and purple top vacutainer for the CBC. Both samples were then delivered to and analysed in the MTRH biochemistry and hematology laboratories respectively. The UEC'S were analysed using the Cobas Integra 400+ machine and the results recorded in a specially designed laboratory results form for further analysis.

APPENDIX E: BUDGET

ITEM	Unit	COST
Research assistant	2 *3*10,000	60,000
Phlebotomist	1*3*10,000	30,000
ABG'S	381*700	266,700
Chest Xray	381 *700	266,700
Miscellaneous	1 *20,000	20,000
Total		643,400

APPENDIX F: TIME SCHEDULE

Activity	**Commencement Date**	**Completion Date**
Proposal Development	March 2017	June 2017
Proposal Writing	July 2017	September 2017
IREC Approval	October 2017	December 2017
Research Data collection	June 2018	September 2018
Data Analysis	October 2018	March 2019
Thesis Writing	April 2019	September 2019
Departmental Thesis Defense	October 2019	
Thesis Defense	December 2020	

APPENDIX G: CONSENT FORM.

PREAMBLE

I am Dr. Daisy Korir, a medical practitioner registered by the Kenya Medical Practitioners and Dentists Board. I am pursuing my Master's degree in Internal Medicine at Moi University. I am conducting a research on The Burden of Respiratory Failure among Patients admitted in the Medical Wards at Moi Teaching and Referral Hospital, Eldoret, Kenya.

I would like to enrol you into my study which entails taking a sample of your blood for laboratory measurements of blood count, kidney functions and oxygenation of blood and also taking a chest X-ray.

Before participating in this research, it is important that you read and understand the information contained in this form. The information provided here will help you decide whether you wish to participate in this study. In case you need to make any clarifications, please address these concerns to myself or my research assistants, who will be able to answer them. Kindly do not sign this form until you are sure you understand the information in this form.

PURPOSE OF THE RESEARCH:

Respiratory failure is a disease of inadequate function of the lungs in its main two functions of taking oxygen into the body and removing carbon dioxide a waste product out of the body. This study aims to assess how many of the patients with low oxygen in their blood actually have respiratory failure and what else they present with to help in future plans of the best treatment of this condition at our hospital.

DESCRIPTION OF THE RESEARCH:

This study will entail collection of basic demographic data such as age, sex. A questionnaire will then be administered by the research assistant/ PI inquiring about information such as any existing chronic illnesses and other conditions the patient may be suffering from at the moment of participation in the study or in the past. A measurement of your blood count, kidney function and lung function will be done by drawing blood from your vein and artery and thereby a chest X ray will done to evaluate the lungs.

BENEFITS

There will be **NO** direct benefits to you by participating in this study and there will be no money or gifts offered for participation. However the knowledge obtained in this study will generate useful knowledge in the management respiratory failure in our hospital and beyond.

HARMS.

This study poses minimal risk to you. There might be slight pain and discomfort while obtaining blood specimen but this pain or discomfort will wear off after some minutes.

ALTERNATIVES TO PARTICIPATION:

You do not need to participate in this study to receive treatment for your condition. If you choose not to participate, you will still receive the standard treatment for respiratory failure offered by MTRH hospital.

COSTS TO PARTICIPATION

There are no costs to you should you decide to participate in this study since the cost of the chest x-ray and laboratory tests will be paid by researcher. So it's a free activity.

PARTICIPATION AND WITHDRAWAL:

Participation in research is voluntary. You may refuse to participate or answer any questions, or withdraw from the study at any time. If you choose not to participate, your care will not be interrupted. If you choose to withdraw from the study, the data you provided up to the point of termination (withdrawal) and information about your health status may still be used for analysis.

CONSENT FORM.

STUDY TITLE: THE BURDEN OF RESPIRATORY FAILURE AMONG PATIENTS ADMITTED IN THE MEDICAL WARDS AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA.

The research study has been explained to me, and my questions have been answered to my satisfaction. I have been informed of the alternatives to participation in this study. I have the right not to participate and the right to withdraw without affecting the quality of my medical care at MTRH. The potential harms and benefits of participating in this research study have also been explained to me and I have been

told that I have not waived my legal rights nor released the investigators or involved institution from their legal and professional responsibilities.

I know that I may ask now, or in the future, any questions I have about the study. I have been told that records relating to me and my care will be kept confidential and that no information will be disclosed without my permission to unauthorized persons unless required by law. I have been given sufficient time to read the above information.

_____ _____ _____

Name of Participant Signature of Participant Date/Time

I have explained to the above Participant the nature and purpose, the potential benefits, and possible risks associated with participation in this research study. I have answered all questions that have been raised.

_____ _____ _____

Name of Person Obtaining Consent Signature of Person Obtaining Consent Date/Time

I am the Principal Investigator responsible for the conduct of this study at MTRH and I have delegated the explanation of this study to this participant to _____ (Name of person conducting the consent discussion).

_____ _____ _____

Name of Investigator Signature of Investigator Date

This study has been approved by the Institutional Research and Ethics Committee (IREC) of Moi University/Moi Teaching and Referral Hospital.

For further clarifications please contact IREC using the address below.

The Chairman IREC,

Moi Teaching and Referral Hospital,

PO Box 3, Eldoret. Tel: 33471/2/3

My cell phone number is: 0721791364

B. KISWAHILI

Jina langu ni Daktari Daisy Korir. Nimehitimu udaktari na nimesajiliwa na bodi ya madaktari ya Kenya (Kenya Medical Practitioners and Dentists Board). Mimi ni msomi wa shahada ya pili (Masters) ya udaktari katika chuo kikuu cha Moi. Ninafanya utafiti kuhusu utepetevu wa mapafu kwa kazi yake ya kupitisha hewa safi kwa mwili na kuondoa hewa chafu kutoka mwilini.

Katika utafiti huu, sampuli ya damu itatolewa kwa minajili ya uchunguzi katika maabara kuhesabu damu, kuchunguza kazi ya figo na kuchunguza kazi ya mapafu kupitia kwa picha ya Xray.

Matokeo yatasalimishwa na kuwekwa siri. Utapata matibabu bila kubaguliwa na bila kuzingatia uweko wako katika uchunguzi huu.

Hakuna madhara yeyote yatakayokufikia kwa kuwepo kwako kwenye utafiti huu. Hakuna malipo yoyote itakayahitajika kutoka kwako ili kuwepo kwenye utafiti huu.

Uchunguzi huu umehidhinishwa na kamati ya kusimamia utafiti (Institutional Research and Ethics Committee-IREC) katika chuo kikuu cha Moi na hospitali yarufaa ya Moi

Iwapo unahitaji maelezo zaidi tafadhali wasilianana IREC kwa kutumia anwani ifuatayo.

Mwenyekiti IREC,

Moi Teaching and Referral Hospital,

S. L. P. 3, Eldoret. Simu: 33471/2/3

Nambari yangu ya simu ya rununu ni: 0721791364.

HIDHINI YAKO :

Walio na miaka 18 na zaidi

Nimeelezwa kwamba ninashiriki katika utafiti wa kuchunguza utepetevu wa mapafu

Kwa kazi yake. Mchunguzi amenihakikishia kuwa matibabu yangu yataendelea bila hitilafu bila kuzingatia kushiriki kwangu katika utafiti huu. Aidha nafahamu kuwa hamna gharama kwangu katika utafiti huu na hamna madhara kwangu.

Sahihi: _____ Jina: _____ Tarehe: _____

APPENDIX H: ASSENT

PREAMBLE

INFORMATION SHEET

This informed assent form is for participants aged between 14 and 17 years who are admitted in the MTRH medical wards and who we are inviting to participate in the research on The Burden of Respiratory Failure among Patients Admitted in the Medical Wards at Moi Teaching and Referral Hospital, Eldoret, Kenya.

I am Dr. Daisy Korir, a medical practitioner registered by the Kenya Medical Practitioners and Dentists Board. I am pursuing my Master's degree in Internal Medicine at Moi University. I am conducting a research on The Burden of Respiratory Failure among Patients Admitted in the Medical Wards at Moi Teaching and Referral Hospital, Eldoret, Kenya.

I would like to enrol you into my study which entails taking a sample of your blood for laboratory measurements of blood count, kidney functions and oxygenation of blood and also taking a chest X- ray.

Before participating in this research, it is important that you read and understand the information contained in this form. The information provided here will help you decide whether you wish to participate in this study. If you agree to take part in the study, your parents will also have to give permission. Should you not want to take part in the research, you will not be forced, even if your parents have agreed.

In case you need to make any clarifications, please address these concerns to myself or my research assistants, who will be able to answer them. Kindly do not sign this form until you are sure you understand the information in this form.

PURPOSE OF THE RESEARCH:

Respiratory failure is a disease of inadequate function of the lungs in its main two functions of taking oxygen into the body and removing carbon dioxide; a waste product out of the body. This study aims to assess how many of the patients with low oxygen in their blood actually have respiratory failure and what else they present with to help in future plans of the best treatment of this condition at our hospital.

DESCRIPTION OF THE RESEARCH:

This study will entail collection of basic demographic data such as age, sex. A questionnaire will then be administered by the research assistant/ PI inquiring about information such as any existing chronic illnesses and other conditions the patient may be suffering from at the moment of participation in the study or in the past. A

measurement of your blood count, kidney function and lung function will be done by drawing blood from your vein and artery and thereby a chest X ray will done to evaluate the lungs.

BENEFITS

There will be **NO** direct benefits to you by participating in this study and there will be no money or gifts offered for participation. However the knowledge obtained in this study will generate useful knowledge in the management respiratory failure in our hospital and beyond.

HARMS.

This study poses minimal risk to you. There might be slight pain and discomfort while obtaining blood specimen but this pain or discomfort will wear off after some minutes.

ALTERNATIVES TO PARTICIPATION

You do not need to participate in this study to receive treatment for your condition. If you choose not to participate, you will still receive the standard treatment for respiratory failure offered by MTRH hospital.

COSTS TO PARTICIPATION

There are no costs to you should you decide to participate in this study since the cost of the chest xray and laboratory tests will be paid by researcher. So it's a free activity.

PARTICIPATION AND WITHDRAWAL

Participation in research is voluntary. You may refuse to participate or answer any questions, or withdraw from the study at any time. If you choose not to participate, your care will not be interrupted. If you choose to withdraw from the study, the data you provided up to the point of termination (withdrawal) and information about your health status may still be used for analysis.

CERTIFICATE OF ASSENT

STUDY TITLE: The Burden of Respiratory Failure among Patients Admitted in the Medical Wards at Moi Teaching and Referral Hospital, Eldoret, Kenya.

The research study has been explained to me, and my questions have been answered to my satisfaction. I have been informed of the alternatives to participation in this study. I have the right not to participate and the right to withdraw without affecting the quality of my medical care at MTRH. The potential harms and benefits of participating in this research study have also been explained to me and I have been

told that I have not waived my legal rights nor released the investigators or involved institution from their legal and professional responsibilities.

I know that I may ask now, or in the future, any questions I have about the study. I have been told that records relating to me and my care will be kept confidential and that no information will be disclosed without my permission to unauthorized persons unless required by law. I have been given sufficient time to read the above information.

I agree to take part in the study.

OR

I do not wish to take part in the study and I have <u>not</u> signed the assent below._____ (initialed by child/minor)

<u>Only if child assents:</u>

_____ _____ _____

Name of Participant Signature or initials Date/Time

I agree to take part in the study.

OR

I do not wish to take part in the study and I have <u>not</u> signed the assent below._____ (initialed by child/minor)

Print name of child _____

Signature of child: _____

Date _____

<u>If illiterate:</u>

I have witnessed the accurate reading of the assent form to the child, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness (not a parent) _____

Signature of witness _____

Date _____

Day/month/year

PRINT

I have explained to the above Participant the nature and purpose, the potential benefits, and possible risks associated with participation in this research study. I have answered all questions that have been raised.

_____ _____

_____

Name of Person Obtaining Signature of Person Obtaining

Date/Time

Assent Assent

I am the Principal Investigator responsible for the conduct of this study at MTRH and I have delegated the explanation of this study to this participant to _____ (Name of person conducting the consent discussion).

_____ _____

_____

Name of Investigator Signature of Investigator Date

Parent/Guardian has signed an informed consent ___Yes ___No _____ (initialed by researcher/assistant)

This study has been approved by the Institutional Research and Ethics Committee (IREC) of Moi University/Moi Teaching and Referral Hospital.

For further clarifications please contact IREC using the address below.

The Chairman IREC,

Moi Teaching and Referral Hospital,

PO Box 3, Eldoret. Tel: 33471/2/3

My cell phone number is: 0721791364

APPENDIX I: SAPS II SCORE CALCULATOR

The Simplified Acute Physiology Score (SAPS II) is a severity score and mortality estimation tool developed from a large sample of medical and surgical patients in North America and Europe. The study analyzed a total of 12,997 patients from 137 medical, surgical, or mixed intensive care units in 12 countries from 9/30/1991 to 12/27/1991, (Le Gall JR, 1993). It is used to evaluate health status or severity of disease for critically ill patients and predict mortality.

THE SAPS II SCORE CALCULATOR

Use the *worst* value for each physiological variable within the past 24 hours.

Age _____ years

Vitals

Heart rate _____ bpm

Systolic BP _____ mmHg

Temp _____ C or F

Glasgow coma score _____

Oxygenation

Mechanical ventilation or CPAP ◉ Yes ○ No

PaO_2 _____

FiO_2 _____ %

Renal

Urine output _____ mL

BUN _____

Chemistry

Sodium _____ mEq/L

Potassium _____ mEq/L

Bicarbonate _____ mEq/L

Bilirubin _____

Other

WBC _____ x 10^9/L

Chronic diseases

- ☐ Metastatic cancer
- ☐ Hematologic malignancy
- ☐ AIDS

Type of admission

Mortality prediction:

Mortality	SAPS II Score
10%	29 pts
25%	40 pts
50%	52 pts
75%	64 pts
90%	77 pts

APPENDIX J: IREC APPROVAL

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET

Reference: IREC/2017/172
Approval Number: 0002023

25th January, 2018

Dr. Daisy Korir,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
25 JAN 2018
APPROVED
P. O. Box 4606 - 30100 ELDORET

Dear Dr. Korir,

RE: FORMAL APPROVAL

The Institutional Research and Ethics Committee has reviewed your research proposal titled:-

"Respiratory Failure in Moi Teaching and Referral Hospital Eldoret Kenya: The Burden and 30 Day Outcome".

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 2023*** on 25th January, 2018. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 24th January, 2019. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

DR. S. NYABERA
DEPUTY-CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc CEO - MTRH Dean - SOP Dean - SOM
Principal - CHS Dean - SON Dean - SOD

APPENDIX K: HOSPITAL APPROVAL (MTRH)

An ISO 9001:2015 Certified Hospital

MOI TEACHING AND REFERRAL HOSPITAL

Telephone:(+254)053-2033471/2/3/4
Mobile: 722-201277/0722-209795/0734-600461/0734-683361
Fax: 053-2061749
Email: ceo@mtrh.go.ke/directorsofficemtrh@gmail.com

Nandi Road
P.O. Box 3 – 30100
ELDORET, KENYA

Ref: ELD/MTRH/R&P/10/2/V.2/2010

30th January, 2018

Dr. Daisy Korir,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:-

"Respiratory Failure in Moi Teaching and Referral Hospital Eldoret Kenya: The Burden and 30 Day Outcome".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

DR. WILSON K. ARUASA, *MBS*
CHIEF EXECUTIVE OFFICER
MOI TEACHING AND REFERRAL HOSPITAL

cc - DCEO, (CS)
- Director of Nursing Services (DNS)
- HOD, HRISM

APPENDIX L: BLOOD GAS ANALYSIS STANDARD OPERATING PROCEDURE

MOI TEACHING AND REFERRAL HOSPITAL

LABORATORY DEPARTMENT

SOP Title:	**PROCEDURE FOR OPERATION AND MAINTENANCE OF RAPID POINT 500 SYSTEM (B.G.A MACHINE)**

Document No.	**Revision No.**	**Effective Date:**
MTRH/LAB/PRC/4004	**00**	

	Name, Title	**Signature, Date**
Author		

	Name, Title	**Signature, Date**
Reviewed by:		

	Name, Title	**Signature, Date**
Approved by:		

Copy No.	Discontinuation date:

1. PURPOSE/INTRODUCTION:

Designed to meet the challanges of point-of care settings,RAPID POINT 500 Blood Gas systems deliver fast,accurate and comprehensive test results in 60 seconds.It is flexible,easy to use and helps the cliniciansto focus and improve patient care without reliability or maintainance worries.

2. SCOPE / RESPONSIBILITY:

2.1. This document applies to MTRH laboratory sections which carryout this procedure.

2.2. It is the responsibility of the section in charge to ensure training and adherence to this sop is done.

2.3. It is the responsibility of the technical staff to ensure they read understand and adhere to this sop.

3. DEFINITIONS AND ABBREVIATIONS:

3.1. ABBREVIATIONS

3.1.1. SOP	Standard Operating Procedure
3.1.2. MTRH	Moi Teaching and Referral Hospital
3.1.3. N/A	Not Applicable
3.1.4. Doc. No.	Document Number
3.1.5. P-o-c	Point of care
3.1.6. QC	Quality Control
3.1.7. Na+	Sodium
3.1.8. K+	Potassium
3.1.9. Cl-	Chloride
4.1.10 (tHb)	Total hemoglobin
4.1.11 PH	Potential of hydrogen

3.2. DEFINITIONS:

3.2.1. **Potentiometry**-Is the technology that measures the difference in potential between two electrodes in a solution without applied current.

3.2.2. **Amperometry**-Involves applying voltage to an electrode and then measuring the current generated.

3.2.3. **Conductance**-Is the readiness with which a conducting substance transmits electrical current

4. SPECIMEN:

Recommended Specimens	**Collection Notes**	**Pre-Analytical Processing**
Whole oxygenated blood is recommended or use and it's collected from the Radial artery or the phemoral artery.	A 2ml syringe is heparinised by flushing it with commercial sodium heparin then corked using a new needle. Remove air bubbles from the syringe then palpate the artery of use and pierce at between 45 to60	Identify the patient to be done for the Blood gases. Prepare the syringes to be used. Have an alcohol swab and an ice pack for transportation of the sample When doing gases for patients away from the I.C.U

	degrees directional to the arteries. Brick red sample will enter the syringe with pressure.	

5. EQUIPMENT / SUPPLIES/ REAGENTS:

Equipment	Supplies	Reagents
-Rapid Point 500 B.G.A Machine	- syringes -Sodium heparin -gloves -needles. -ice pack -Gauze -cool box -cotton wool -70%alcohol.	-Reagent cartridge -Wash cartridge

6. SAFETY PRECAUTIONS

6.1. Make sure that conscious patients are immobilized before drawing the samples.

6.2. Avoid pricking yourself while pulsating and pricking the patient's artery.

6.3. Do not spill blood on your body while drawing the sample.

6.4. Apply pressure on the site of the prick after drawing the sample and strap it to avoid hematoma and excessive bleeding of the patient.

7. METHODOLOGY:

7.1. TEST PRINCIPLE

RAPID Point 500 systems use measurement technology that is based on electrochemical phenomena. Electrochemistry involves the measurement of current voltage in an electrochemical cell. The consists of two or more electrodes that interact with a chemical and that are connected to an electrical system. It uses potentiometry, amperometry and conductance to measure the concentration of analyte in the sample.

7.2. PROCEDURES:

7.2.1. Enter the password

7.2.2. mix the sample thoroughly by rolling the syringe between your palms and gently inverting it several times to

7.2.3. Introduce sample into the sample port and select start button.

7.2.4. When prompted, remove the sample syringe from the sample port and select continue.

7.2.5. Enter patient's demographic information and select continue.

7.2.6. Print the results.

7.3. PROCEDURE NOTES

8. QUALITY CONTROL

Done at 3 levels of independent quality control solutions

8.1. QUALITY CONTROL MATERIALS.

Rapid Point 500 QC cartridge.

9. CALIBRATOR

N/A.

9.1. CALIBRATION

N/A

10. APPENDICES:

- **10.1.** SOP Readership log.
- **10.1.** Document Change History
- **10.2.** Rapid Point 500 system Daily maintenance log

11. REFERENCE

- **11.1.** Wikipedia.
- **11.2.** TUV
- **11.3.** -CSA
- **11.4.** IEC/EN 61010-1
- **11.5.** RapidPoint 500 User manual.