ASSESSMENT OF ADMISSION PELOD-2 SCORE AS A PREDICTOR OF MORTALITY AT A TERTIARY PAEDIATRIC CRITICAL CARE UNIT IN A LOW-MIDDLE INCOME COUNTRY.

(A RETROSPECTIVE OBSERVATIONAL STUDY)

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DECLARATION

This dissertation is my original work, drafted under the guidance of my supervisors and has not been presented for the award of a degree in any other university. References of work done by others have been cited appropriately.

7/6/2021

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DEDICATION

I would like to dedicate this work to the following people:

- To my husband, **Peter Muasa** for his support and encouragement throughout my course.
- To my sons, **Jasiri Muasa** who has kept me focused even while in my womb, the reason for my being and **Allan Muasa** for his support and love.
- To my late grandfather, **Hon. Nteere Mbogori** and my late grandmother **Jean Mbogori** for always believing in me and encouraging me to be the best in everything I do.
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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

- **AUC –** Area Under Receiver Operating Curve
- **ICU** – Intensive Care Unit
- **KNH** - Kenyatta National Hospital
- **MODS** - Multiple Organ Dysfunction Syndrome
- **PCCU -** Paediatric Critical Care Unit
- **PCPC** - Paediatric Cerebral Performance Category
- **PELOD -** Paediatric Logistic Organ Dysfunction Score
- **PELOD-2 -** Paediatric Logistic Organ Dysfunction Score 2
- **PEMOD -** Paediatric Multiple Organ Dysfunction
- **PEU -** Paediatric Emergency Unit
- **PIM -** Paediatric Index of Mortality
- **POPC** - Paediatric Overall Performance Category
- **PRISM -** Paediatric Risk of Mortality
- **UON -** University of Nairobi

DEFINITION OF TERMS

1. **Paeditaric Logistic Organ Dysfunction 2 (PELOD-2) Score-** It is a descriptive and composite scoring system but can also be used as a prognostic score. It is made up of 5 organ dysfunctions and 10 variables.

2. **WHO defined critical illness** as any severe problem with the airway, breathing or circulation, or acute deterioration of conscious state; includes apnoea, upper airway obstruction, hypoxaemia, central cyanosis, severe respiratory distress, total inability to feed, shock, severe dehydration, active bleeding requiring transfusion, unconsciousness or seizures.

ABSTRACT

Background

Paediatric Logistic Organ Dysfunction 2 (PELOD-2) score is a scoring system that has been used to show that Multiple Organ Dysfunction System is a predictor of duration of Paediatric Critical Care Unit (PCCU) stay, severity of illness and mortality with good validity. No studies have been done in East Africa to assess the relationship between admission PELOD-2 score and mortality and its association with length of PCCU stay.

Broad Objectives:

To assess the relationship between admission PELOD-2 score and mortality and to assess the relationship between admission PELOD-2 score and length of stay in a PCCU in a low-middle income country.

Methodology:

Study design: Retrospective observational study.

Study site/setting: Paediatric Critical Care Unit (PCCU) and main Intensive Care Unit (ICU) at Kenyatta National Hospital.

Study population: Children aged 1 month to 13 years admitted at the PCCU and main ICU at Kenyatta National Hospital.

Study procedure: Data was abstracted from medical records of all patients who met eligibility criteria, from February 2019 to December 2020, until we realized the desired number of patients with the event of interest (100 events(deaths).

Patient's biodata, clinical data, survival data, duration of stay in PCCU and PELOD-2 scores were abstracted from patient files into a predesigned data collection sheet. PELOD-2 scores were calculated from the 10 variables at admission to the PCCU or main ICU.

Data Management and Analysis: Categorical data was summarized using proportions and tabulated with frequency tables. Chi-square test was used to explore any association between the categorical variables. Descriptive statistics such as median and interquatile range were used for continuous variables and Mann Whitney statistics was used to analyse this data.

The assessment of the association between PELOD-2 sore and mortality was determined by carrying out discrimination and calibration tests.

Secondary outcome variable was to compare admission PELOD-2 scores viz a viz length of PCCU stay (LOPS). This data underwent validity testing through discrimination and calibration testing.

Study Utility

PELOD-2 score can be used as a predictor of severity of illness, mortality, length of PCCU stay and functional outcomes. This data will inform resource allocation for better patient care and outcomes.

1.0 INTRODUCTION

1.1 Background

A large number of sick paediatric patients requiring admission to the Paediatric Critical Care Unit (PCCU) usually present with derangements in the functional capacity of 2 or more organs. Multiple Organ Dysfunction Syndrome (MODS) is associated with the development of progressive physiological dysfunction in 2 or more organs. This dysfunction is potentially treatable and reversible [1]. The degree of organ dysfunction can vary from mild to severe. MODS occurs early in paediatric patients who require urgent and emergent care [2]. Various studies have reported that MODS occurs in 11%-57% of children admitted to PCCUs [1, 3, 4]. In a study done by Jose et al they found that 84.6% of the patients had MODS at admission and 56.5% had MODS during their PCCU stay [2, 3].

1.2 Scoring Systems

Critically ill patients are typically characterized by multiple organ dysfunctions. Organ dysfunction scores quantify physiological disturbances in cardiovascular, hepatic, haematologic, renal, pulmonary and central nervous systems. The severity of a physiologic disturbance is estimated by measuring how far apart it is from the normal range [4, 5]. Over the years there has been extensive use of scoring systems in the adult population to determine the severity of illness at baseline and during PCCU stay and to predict mortality [6, 7]. This use of scoring systems has recently been replicated in the paediatric population for morbidity and mortality predictions [5, 6, 8, 9]. These scoring systems have also been correlated with duration of PCCU stay and overall outcomes, therefore it can be used as a quality indicator of care in the PCCU. This estimation of risk of mortality, duration of stay and functional status of patients facilitates informed communication with relatives and colleagues [9]. Scoring systems have great applicability in the assessment of processes of care. These assessments have led to an overall improvement of patient care and outcome.

There are two main types of scoring systems. Composite scoring systems (prognostic scores) and outcome scoring systems [10]. Prognostic scoring systems can predict overall risk of mortality at entry into the PICU. These scores are achieved through assessment of baseline physiologic disturbances at admission. Examples of this category of scoring systems is Paediatric Risk of Mortality (PRISM) score, Paediatric Index of Mortality (PIM) score and Paediatric Logistic Organ Dysfunction (PELOD) score [9, 11, 12]. Outcome scores describe how severe the illness is and therefore the clinical course of the patients during PICU stay. These scores are made up of a group of variables which are obtained from clinical data, physiological data and laboratory data. The data is collected daily from admission and on particular specified days while in the PICU [5]. Examples of these scoring systems are Paediatric Multiple Organ Dysfunction Score (PEMODS), PELOD and Peadiatric Logistic Organ Dysfunction-2(PELOD-2) score [5, 9, 13]. A comparison of PEMOD versus PELOD, showed that PELOD system is best suited to determine the existence of organ dysfunction and the severity level of each organ dysfunction [5, 13]. Therefore, it has been reported to be superior to other scoring systems due to this advantage. PELOD-2 score is an updated and improved version of the PELOD score and has greater validity and utility [5]. In order to be useful in low resource settings, the PELOD-2 score should be accurate, that is, it should have good discrimination and should be reproducible in other settings.

1.3 Validation of scoring systems

The usefulness of a scoring system is determined by its validity [10, 14, 15]. To determine the validity of a scoring system it must undergo discrimination and calibration testing. Discrimination is the ability of a test to differentiate between survivors and non-survivors i.e. patients with outcome versus those without the outcome. This is determined by area under the

receiver operating characteristics curve [10, 14]. The calibration of a score is the measure of correlation between the predicted and actual number of outcomes. The statistical analysis used for this is the Hosmer-Lemeshow goodness-of-fit test [15].

2.0 LITERATURE REVIEW

2.1 PELOD-2 Scoring System

PELOD-2 score stands for Paediatric Logistic Organ Dysfunction - 2 Score. This scoring system evaluates the severity of MODS with good validity [5, 16]. PELOD score was first developed in 1999 then validated in the year 2003. It was later modified in 2013 using data set from 9 university affiliated hospitals in France and Belgium from a study population of approximately 3700 paediatric patients aged >37 weeks and < 18 years, to form an improved version, the PELOD-2 Score [5]. PELOD-2 score is a descriptive and composite score. It is made up of five organ dysfunctions and 10 variables [5]. This updated version incorporates lactatemia and mean arterial pressure but does not contain hepatic dysfunction [5].

It is the most established scoring system used to delineate the severity of illnesses in paediatric patients [5, 17]. In paediatrics, the relationship between the number of organ dysfunctions and mortality is better than the relationship between absence or presence of organ dysfunction and mortality [5]. This is the basis with which the scoring system was established. The score also considers high and low risk of death associated with each organ dysfunction and this forms the basis of weighting of the variables [5, 9]. The variables used in the PELOD-2 score were abstracted from PELOD, Paediatric Multiple Organ Dysfunction (PEMOD) and Sequential Organ Failure Assessement (SOFA) scoring systems. The variables chosen were Glascow Coma Scale (GCS), pupillary size, heart rate, systolic blood pressure, mean arterial pressure, creatinine, blood urea nitrogen (BUN), lactate, partial pressure of

oxygen, P/F ratio, partial pressure of carbon dioxide, mechanical ventilation, white blood cell count, platelet count, liver transaminases, prothrombin time, INR and fibrinogen. The most abnormal value of each variable was recorded at day 1, 2, 5, 8, 12, 16, 28 and discharge. Each of the physiologic dysfunctions were weighted based on its association with death, this was carried out using bivariate logistic regression analysis. Organ dysfunctions with higher prediction of mortality had a higher weighting e.g. neurological and cardiovascular dysfunction. The 10 variables were scored between 0 and 6, and the value furthest from the normal range is recorded. The maximum score for a single organ dysfunction varies from 2-10 depending on the particular organ dysfunction and the highest PELOD-2 score that can be recorded for a patient was determined to be 33 [5].

2.2 PELOD-2 score correlation with mortality

PELOD-2 score is the most established scoring system used to delineate the severity of illnesses in paediatric patients. This evaluation of several organ dysfunctions helps to predict risk of mortality, duration of hospital stay and functional outcomes of patients [6, 8, 11]. Mortality rates of approximately 6% have been reported in patients admitted in the paediatric intensive care unit (PICU) versus 20% mortality reported for their adult ICU counterparts [6, 7, 8]. Mortality rates from MODS has been reported to be as high as 54%- 91% and is therefore a more frequent occurrence than death [3, 6]. Most of the deaths in the PICU are related to MODS, this is reported as a 97-100% occurrence [3]. A study done by Wilkinson et al on outcome of paediatric patients with MODS showed that mortality was 54% for patients with MODS and only 0.3% for patients without MODS [7]. He also reported that the probability of death increased as the number of failing organs increased, 1% for 1 organ, 11% for 2 organs, 50% for 3 organs and 75% for 4 organs. A study by Ana Lila found that variables significantly associated with mortality were abnormal pupillary reflexes, acidosis,

BUN, and WBC count. Abnormal pupillary reflexes had nine times risk of mortality, whereas acidosis had three times risk of mortality. Deranged BUN (odds ratio [OR]: 1.03) and WBC count (OR: 1.02) were directly related to mortality [18].

A multicenter study done by Leclerc et al in Europe reported that day 1 PELOD-2 score of patients with infection was highly predictive of mortality [11]. In the same study he reported that a patient with a day 1 PELOD-2 Score of $\geq$8 is predicted to have an overall risk of mortality of $\geq$ 9.3% in children with sepsis [11].

These findings are similar to a study done by El-Nawawy et al in Alexandria University PICU in Egypt comparing the performance of PELOD versus PELOD-2 in a developing country. The study revealed that patients with 5 organ dysfunctions contributing to the PELOD-2 score had up to 80% mortality while patients with 0-2 organ dysfunctions contributing to the PELOD-2 score had only 2% mortality [19].

2.3 PELOD-2 score association with duration of paediatric critical care unit stay

The average length of stay for paediatric patients in the PCCU varies from 3-10 days [4, 20, 21]. A study done by Kaur et al to assess if PRISM 3 score is a predictor of length of hospital stay and mortality reported that the average length of stay in their PICU was 10 days [20]. Length of hospital stay has been reported to be longer for children with MODS [8, 22]. Typpo et al reported that patients with MODS on day 1 had a longer mean PICU stay of 3.6 days versus 1.3 days. A linear regression analysis performed showed that each organ dysfunction was independently associated with length of hospital stay. He also reported that a higher number of organ dysfunction is directly correlated with length of PICU stay [8].

2.4 Scoring system association with outcome scores

Paediatric Overall Performance Category (POPC) and Paediatric Cerebral Performance Category (PCPC) scores are outcome scores that assess the global function and cognitive function of patients. These scores were developed by D. Fiser to easily measure and quantify morbidity after a child's critical illness or injury [23]. The scores are collected at the time of admission and discharge from PCCU. The scores have a grading of 1-6, where 1-normal function, 2- Mild dysfunction, 3- Moderate dysfunction with impairment of competitive function at school, 4- Severe functional impairment, 5- Persistent vegetative or comatose state, 6- Brain death [23, 24].

The functional outcomes of patients with MODS lies mostly between the moderate to severe dysfunction group [8, 22, 24, 25]. This correlates with a study done by Volakli et al on functional outcome following PICU care which showed that 21% of patients on discharge had intact cerebral function and only 0.7% had normal overall performance [24]. In a study done by Typpo et al, patients with MODS had a higher baseline POPC and PCPC scores. They were also noted to have worse change in POPC and PCPC score from PICU admission to discharge. The type and number of organ dysfunctions was associated with higher outcome scores. POPC and PCPC scores of greater than 3 were observed in patients with MODS versus scores of 1or 2 for patients with less than or equal to 1 organ dysfunction [8].

It is therefore possible to predict morbidity or mortality by using the maximum PELOD-2 score during critical illness [5, 25]. Organ dysfunction scores have great applicability in clinical trials and also in evaluation of the quality of processes of care of patients in the PCCU [7, 26].

3.0 STUDY JUSTIFICATION AND UTILITY

PELOD 2 score was developed and validated in 2013 by Leteurtre et al [5]. It was developed as a predictor of mortality due to its higher prevalence [5, 6]. Due to this high prevalence, the use of PELOD-2 score as a variable and a predictor of mortality would be of great utility in clinical trials by reducing the sample size required for mortality outcome studies. This is because reported mortality rates tend to be much lower in paediatrics as compared to adults [6, 8] and therefore a larger sample size would be required for these studies.

It has been used in a number of studies in developed countries to show that MODS is a predictor of severity of illness and therefore mortality [6, 16, 27]. PELOD-2 score has also been used similarly to correlate MODS with length of PICU stay and functional outcomes and is therefore also a quality indicator in the PICU [8]. A study done by Leclerc et al revealed that the overall risk of mortality increased to $\geq$ 9.3% when one had an admission PELOD-2 score $\geq$ 8 in children with suspected infection [11].

Few studies have been done in low-middle income countries [19, 28] and none in East Africa to evaluate the relationship between admission PELOD-2 score and mortality and also its association with length of PCCU stay.

There is a probability of reporting higher admission PELOD-2 scores in developing countries as compared to developed countries. This is likely because patients in developing countries tend to be sicker than those in developed countries [3, 28, 29]. This is as a result of higher prevalence of malnutrition which correlates with reduced immunity and increased likelihood of MODS [3, 30]. Other factors that may contribute to higher admission PELOD-2 scores are poor sanitation and overcrowding which are associated with increased rates of communicable

diseases and severity of illness. Notably, low patient-clinician ratio, poor health seeking behaviors resulting from low social economic status and poor access to tertiary health care facilities lead to patients presenting to hospital late in the illness with significant MODS [30].

Higher admission PELOD-2 scores are also likely to be reported due to fewer resources in PICU (staff, equipment and drugs) and delays in treatment [31]. Therefore, this allows for evaluation of standardized care processes.

The duration of PCCU stay is likely to be longer in patients in developing countries in comparison to patients in developed countries, this is due to higher admission PELOD-2 scores in developing countries and therefore greater degree of severity of illness [28, 31]. It is also likely to be longer for patients with similar admission PELOD-2 scores to their developed country counterparts due to effect of patient load, fewer resources for treatment and delays in treatment in developing countries [31].

Patients in developing countries are also likely to have worse functional outcomes due to similar constraints mentioned above.

4.0 RESEARCH QUESTION

Does a high admission PELOD-2 score correlate with increased likelihood of mortality in critically ill children aged 1 month-13 years in a tertiary paediatric critical care unit in a low-middle income country?

4.1 Null Hypothesis

There is no difference in mortality rates between children with high and low admission PELOD-2 scores in a tertiary paediatric critical care unit in a low-middle income country.

4.2 Main Objective

1. To assess the relationship between admission PELOD-2 score and mortality in a tertiary paediatric critical care unit in a low-middle income country.

4.3 Secondary Objective

1. To assess the relationship between admission PELOD-2 score and length of stay in a tertiary paediatric critical care unit in a low-middle income country.

5.0 RESEARCH METHODOLOGY

5.1 Study Design

Retrospective observational study.

5.2 Study Area

The study was carried out at the Paediatric Critical Care Unit (PCCU) and main ICU at the Kenyatta National Hospital. This is a level 6 teaching and referral hospital, located in Dagorreti North constituency, Nairobi county, Kenya. The hospital receives patients from all over the country with the main catchment area being Nairobi county due to easier accessibility to the hospital.

The hospital has a bed capacity of 1800. The total bed capacity of the 4 paediatric wards is 240 beds. The PCCU has a 6-bed capacity and the main Intensive Care Unit (ICU) has a 21-bed capacity. The age of admission to the general paeditric ward in Kenyatta National Hospital is 0 days to 13 years and to the PCCU is 1 month to 13 years.

The average monthly admission of paediatric patients is estimated at 450 children in the general paediatric wards and 20 in the PCCU and main ICU that is an annual admission of approximately 240 patients in the Critical Care Unit. The monthly mortality rate is about 50% in the PICU and therefore the estimated mortality is around 120 patients per annum. The

PCCU is run by 2 paediatric intensivists, 5 paediatric critical care and emergency fellows (1st and 2nd years), 2 paediatric residents, 1 medical officer per shift, 4 nurses per shift, 1 nutritionist and 2 physiotherapists/occupational therapists. The main ICU is run mainly by the anaesthesia residents and anaesthetists. The paediatric team form the PCCU normally reviews all paediatric patients admitted in main ICU.

Critically-ill paediatric patients are received through Paediatric Emergency Unit (PEU) where they are triaged and receive initial emergency care. Following which they are admitted to the paediatric critical care unit or main ICU or acute rooms in the wards.

5.3 Study Duration

Patients were recruited over a period of approximately 2 years, from 1st of February 2019 to 31st December 2020.

5.4 Study Population

Children aged 1 month to 13 years admitted at the paediatric CCU and main ICU at Kenyatta National Hospital.

5.4.1 Inclusion Criteria

Eligibility criteria for inclusion into the study is:

1. Critically ill children aged 1 month to 13 years admitted in the PCCU and main ICU

5.4.2 Exclusion Criteria

The following children were excluded:

1. Children < 1 month and >13 years.

5.4.3 Case Definitions

PELOD-2 Score

PELOD-2 score is a composite and descriptive score. It is made up of five organ dysfunctions and 10 variables [11]. The organ dysfunctions are neurological, cardiovascular, renal, respiratory and haematologic. The 10 variables are Glasgow Coma Score (GCS) and pupillary reaction in neurologic, lactatemia and mean arterial pressure in cardiovascular, creatinine in renal, partial pressure of oxygen (Pao2), partial pressure of carbon dioxide (Paco2) and invasive ventilation in respiratory and WBC count and platelets in haematologic [Appendix 8.2]. Each variable has a score of 0-6, depending on level of severity. The maximum score that can be assigned to a given variable is 10 and the highest PELOD-2 score that can be recorded for a patient is 33.

Critical Illness

As defined by the WHO, "Critical illness is any severe problem with the airway, breathing or circulation, or acute deterioration of conscious state; includes apnoea, upper airway obstruction, hypoxaemia, central cyanosis, severe respiratory distress, total inability to feed, shock, severe dehydration, active bleeding requiring transfusion, unconsciousness or seizures" [32].

5.5 Sample Size

This being a validation study, and following guidelines by Gary et al that requires validation studies of prognostic scores to have a minimum number of 100 primary events [33] (that is deaths in our study). We sampled medical files of the eligible patients as many as possible until this requirement was met. The number of paediatric deaths that occur in critical care

units at KNH is approximately 120 per annum. We would therefore require to sample files for at least 12 months to be able to achieve the 100 events(deaths) of interest.

5.6 Sampling Method

We consecutively sampled and abstracted data of all medical records of patients aged 1 month -13 years admitted to the PCCU or main ICU between February 2019 and December 2020 until we realized the desired number of patients with the event of interest (100 events of interest, that is, 100 deaths).

5.7 Training Procedures

We recruited two research assistants who collected the data from the patient files and also inputed this data into the REDcap electronic database. The basic qualification of the assistants was nurses working in the critical care units at KNH. We conducted a 3-day training which focused on accurate data collection and stepwise data entry into REDcap electronic database. This enabled us to minimize errors of data entry and therefore ensured data quality was maintained.

5.8 Study Procedure

We consecutively sampled and abstracted data of all medical records of patients aged 1 month -13 years admitted to the PCCU or main ICU between February 2019 and December 2020, until we realized the desired number of patients with the event of interest (100 events of interest, that is, 100 deaths).

Data was abstracted from these patient files into a customized data capture tool designed in the non-proprietary Research Electronic Data Capture (REDCap) platform by the trained

research assistants [Appendix 8.1]. The principal investigator double checked the entries made on the REDcap platform and identified omissions and errors and corrected them after verification from the files and data capture tool. The predesigned REDcap contained patient's biodata that is the study identification number, ICU location, age and sex. It also contained the clinical data which entailed the date of admisssion, date of discharge, number of days in the PCCU or main ICU, primary and secondary admission and discharge diagnosis, admission PELOD 2 score and its' variables, number of days on mechanical ventilation, vasopressor use and survival or mortality data [Appendix 8.1].

The admission PELOD-2 scores had been calculated for all paediatric patients at entry into the PCCU and main ICU at KNH from February 2019 following the commencement of the Peadiatric Emergency and Critical Care Fellowship in January 2019. This data was collected using the PELOD-2 score forms and these forms were available in the patient files [Appendix 8.2]. Admission PELOD-2 scores were calculated from the 10 variables at admission to the PCCU or main ICU. It is made up of five organ dysfunctions and 10 variables [Appendix 8.2]. The organ dysfunctions are neurological, cardiovascular, renal, respiratory and haematologic. The 10 variables are Glasgow Coma Score (GCS) and pupillary reaction in neurologic, lactatemia and mean arterial pressure in cardiovascular, creatinine in renal, partial pressure of oxygen (Pao2), partial pressure of carbon dioxide (Paco2) and invasive ventilation in respiratory and WBC count and platelets in haematologic [Appendix 8.2]. Each variable was given a score of 0-6, depending on level of severity of the dysfunction. If a variable was not measured, it was considered normal. If the patient was sedated the GCS before sedation was used. The pupillary reaction was not assessed if the dilatation was iatrogenic. While assessing the cardiovascular dysfunction, the value when the patient was calm and not agitated was the one that was recorded and used. The maximum score that was

assigned to a given variable was 10 and the highest PELOD-2 score that was recorded for a patient was 33.

5.9 Study Variables

Explanatory and outcome variables were assessed. Explanatory variable consisted of the patient's biodata and their clinical attributes (Appendix 8.1).

The explanatory variables were divided into categorical and continuous variables. Categorical variables that were analyzed were sex, admission and discharge diagnosis, mortality or survival data, presence of accidental extubations and any vasopressor use.

The continuous variables that were assessed were age of the patient, number of PCCU or main ICU days, number of days on mechanical ventilation and admission PELOD-2 scores and its' variables.

The outcome variables that were assessed were the association between admission PELOD-2 score and mortality and the association between admission PELOD-2 score and length of PCCU stay.

5.10 Study tools

The data was collected on predesigned collection sheets [Appendix 8.1]. The PELOD-2 scores were calculated using the PELOD-2 score forms [Appendix 2].

6.0 DATA COLLECTION, MANAGEMENT AND ANALYSIS

Biodata and clinical attributes of the patients were abstracted from medical records from PCCU and main ICU paediatric patients. This data was collected on predesigned collection sheets. Before entry into REDcap the data collection forms were reviewed by another research assistant to reduce data collection errors. This information was then transferred in a secure password-protected electronic database (REDCap).

Categorical data was summarized using proportions and tabulated with frequency tables. Chi-square test was used to explore any association between the categorical variables. Descriptive statistics such as median and interquatile range were used for continuous variables and Mann Whitney statistics was used to analyse this data.

It was expected that medical files would not have 100% documentation of the data required by the study. We therefore used multiple imputation to address missingness of the data using chained equations under the assumption of missing at random (MAR). The simulation error was minimized by using 50 imputations with 100 iterations. We then assessed convergence of the imputation model by inspecting marginal distribution of both imputed and observed values. We also undertook a sensitivity analyses to investigate the validity of the MAR assumption in our data using pattern mixture models.

Primary outcome variable was divided between mortality group and survival group. The assessment of the association between admission PELOD-2 sore and mortality was determined by carrying out discrimination and calibration tests. Discrimination was determined by using Area Under the Receiver Operating Curve (AUC) characteristics (with 95%CI) to differentiate the survivors from the non-survivors.

Calibration of the score was calculated using Hosmer-Lemeshow chi square test. Acceptable calibration p value = $\geq$ 0.05. The Logit (mortality) and probability of death: {Logit (mortality) = – 6.61 + 0.47 × PELOD-2 score; Probability of death = 1/ (1 + exp [– logit(mortality)])}, was calculated for each patient and calibration was then carried out to determine association between predicted death and actual death.

Secondary outcome variable was to compare admission PELOD-2 scores viz a viz length of PCCU or main ICU stay (LOPS). The length of PCCU or main ICU stay was divided into two groups, short PCCU stay (4 days) vs long PCCU stay ($\geq$ 5 days). The number of days was chosen based on evidence form PELOD-2 study that reported the mean number of days in PCCU to be 3-4 days [4]. This data underwent validity testing through discrimination and calibration testing. Discriminant power of the score to length of PCCU stay was estimated using Area Under the Receiver Operating Curve (AUC) characteristics (with 95%CI). Calibration was done to determine what we predicted (higher admission PELOD-2 scores is associated with longer PCCU or main ICU stay) was in fact what was observed. This was assessed using Hosmer-Lemeshow chi square test. This was carried out in the survivors and non- survivors' group.

7.0 ETHICAL CONSIDERATIONS

The study was conducted after getting ethical approval from the Kenyatta National Hospital/ University of Nairobi – Ethics Research Committee.

Informed Consent

Being a retrospective study, we requested for waiver of informed consent to study participation since it was very difficult to locate the guardians and there may have been negative consequences to obtaining informed consent from guardians of deceased patients.

Confidentiality

Strict confidentiality was observed for the entire duration of the study period, held in trust by the principal investigator, research personnel and study institution. The study participants were given study identification numbers and no personal identification data was recorded. This study identification numbers were not shared with any 3rd party without formal authorization by KNH/UON ethics committee.

Risks

No experimental drugs or procedures were employed in this study.

Benefits

The study will provide a better understanding of association of admission PELOD-2 score and mortality and admission PELOD-2 score and length of PCCU stay in a developing country. This will aid in the evaluation of the different levels of care processes and improve communication with caregivers and fellow doctors. The overall benefit being improvement of patient care and outcome.

8.0 STUDY LIMITATIONS

The study utilized data from one center- Kenyatta National Hospital. While this is a regional referral hospital, generalizability of our study findings is limited and might not be applicable to all hospital, including private hospitals.

This being a retrospective study we are likely to encounter issues of missing data which will probably affect our results. To address these issues, we used multiple imputation during data analysis and management.

9.0 RESULTS

9.1 Baseline Characteristics of Patients included in the Study

Between the months of 1st of February 2019 to 31st December 2020, the total number of patients included in the study were 236. The median age for the study population was 11 months, interquartile range (IQR) of (6, 36). Males comprised a total of 63.06% of patients. The primary reasons for paediatric critical care unit (PCCU) admission were pneumonia (33.3%), septic shock (21.4%) and meningitis (14.3%) (Table 1) (Figure 1).

The total percentage of patients who received mechanical ventilation was 89%. The median length of PCCU stay was 5 days. The mortality rate was 50.8% and the median admission PELOD-2 score was 9, IQR (6,12) (Table 1).

Table 1: Baseline Characteristics of Patients

Total number of patients	**236**
Age (Median, IQR)	**11(6, 36) months**
Sex (Male) (%)	**63.06%**
Primary reasons for PICU admission (3 top reasons) (%)	**1. Pneumonia (33.3%)** **2. Septic shock (21.4%)** **3. Meningitis (14.3%)**
Mechanical Ventilation (%)	**212(89%)**
Length of CCU stay (Median, IQR)	**5(2, 9) days**
Mortality rate (%)	**116(50.8%)**
Admission PELOD-2 score (Median, IQR)	**9(6, 12)**

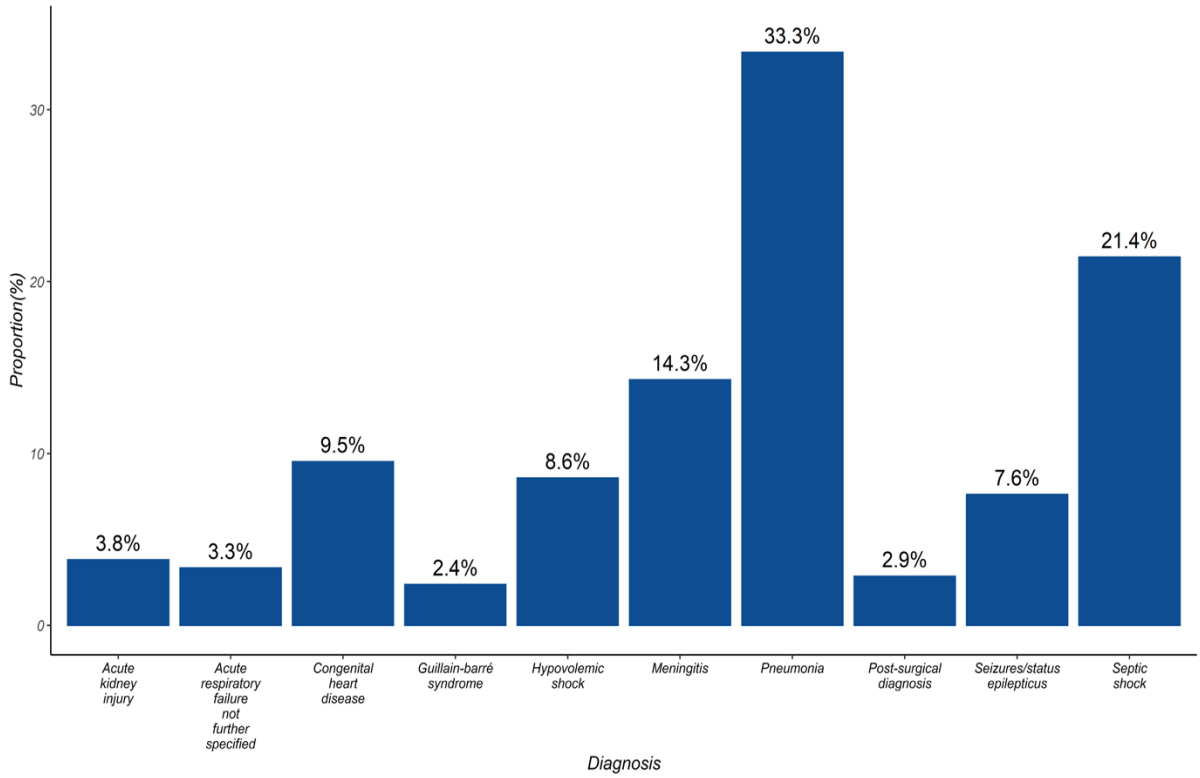

Figure 1: Bar Graph showing the percentage distribution of primary admission diagnosis

9.2 Test of Independence between the Survivors and Non-Survivors

The median age of survivors was 17 months versus 9 months for non-survivors and this age was statistically significant, p value of approximately (<0.01). The admission PELOD-2 score was higher in the non-survivors, median score of 11, IQR (8, 15) versus a median score of 8, IQR (5, 9) in the survivors, p value of approximately (<0.01) (Table 2, Figure 2).

Table 2: Comparison of Key Characteristics between the Survivors and Non- Survivors group.

	Survivors	**Non-Survivors**	**P value**
Age in month (Median, IQR)	**17(7, 48)**	**9(5, 23)**	**9.589e-05 (<0.01)**
Admission PELOD-2 score (Median,IQR)	**8 (5, 9)**	**11(8,15)**	**2.184e-15(< 0.01)**
Length of PCCU stay in days (Median, IQR)	**7 (4, 11)**	**3(1,6)**	**0.01648**

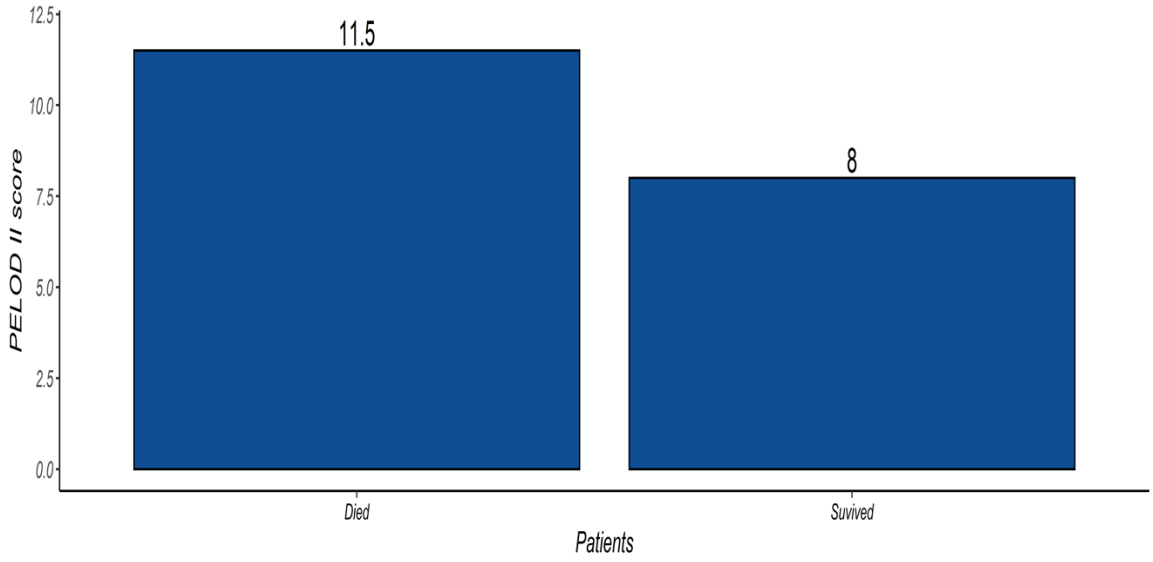

Figure 2: Bar graph showing median admission PELOD-2 score for Non-survivors and Survivors

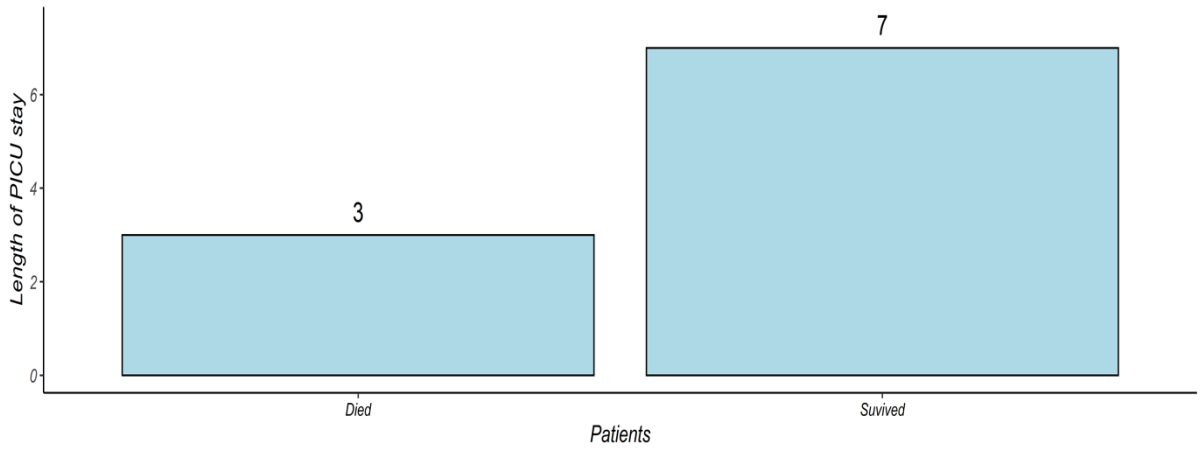

Figure 3: Bar Graph showing median length of PCCU stay for Non-Survivors and Survivors

9.3 Relationship between admission PELOD-2 score and Mortality

The admission PELOD-2 score was noted to be directly proportional to mortality. An increase in the admission PELOD-2 score was associated with an increase in percentage mortality. An admission PELOD-2 score of < 8 was associated with a mortality of between (0-35%) and a score of > 8 was associated with a mortality rate of (46-100%). Admission PELOD-2 scores of > 17 were associated with 100% mortality (Figure 4).

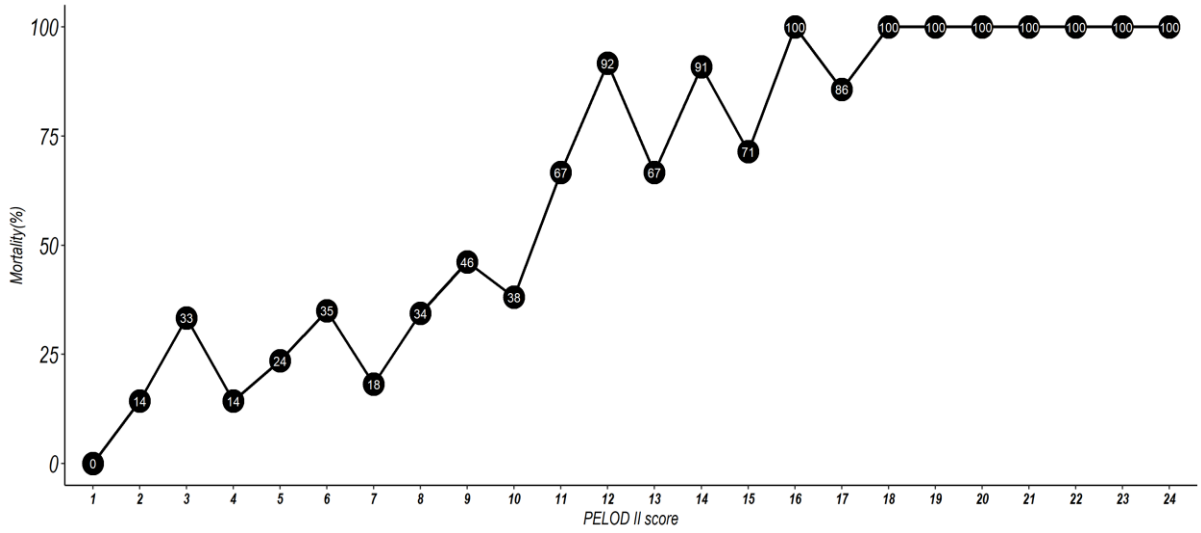

Figure 4: Line graph showing the relationship between admission PELOD-2 score and Mortality.

9.4 Discrimination and Calibration of PELOD-2 score for Mortality

The discriminatory ability of admission PELOD-2 for mortality using area under the receiver operating curve (AUC) (with 95% CI) was 0.63(0.575-0.685) (Figure 5).

The calibration of the score for mortality calculated using the Hosmer- Lemeshow chi square test was p value = 0.782 (Figure 6).

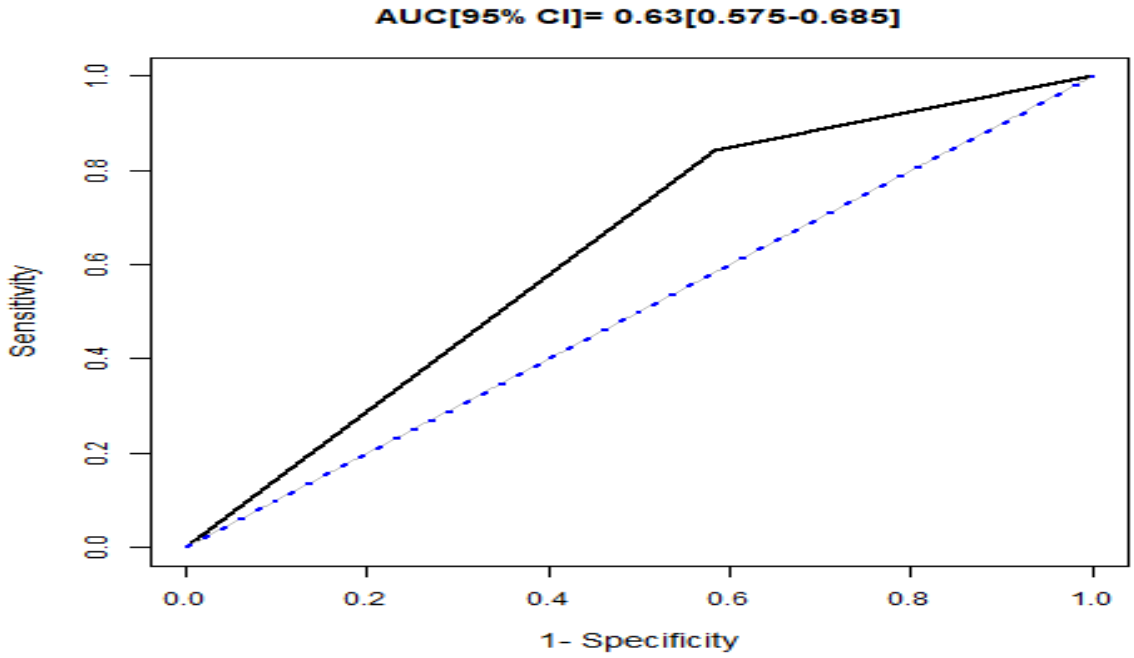

Figure 5: Area Under Receiver Operating Curve showing the discriminatory ability for admission PELOD-2 for mortality with 95% CI

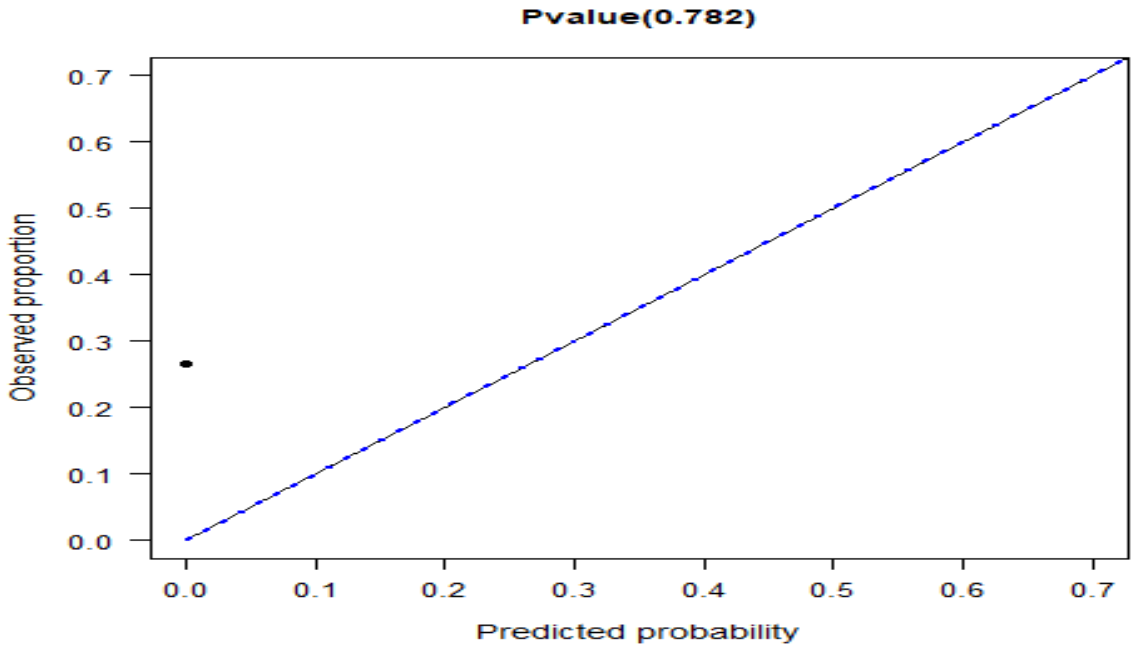

Figure 6: Calibration Plot for admission PELOD-2 score in determining those who died and the predicted deaths.

9.5 Relationship between admission PELOD-2 score and Length of Paediatric Critical Care Unit Stay.

The admission PELOD-2 score had a wide variation with the length of paediatric critical care unit stay (LOPS). The patients with an admission PELOD-2 score of <6 had an average LOPS of 4 -5 days, while those with an admission PELOD-2 score of 7-13 had an average stay of 7 days and patients with scores of > 13 had an average length of stay of 2 days (Figure 7).

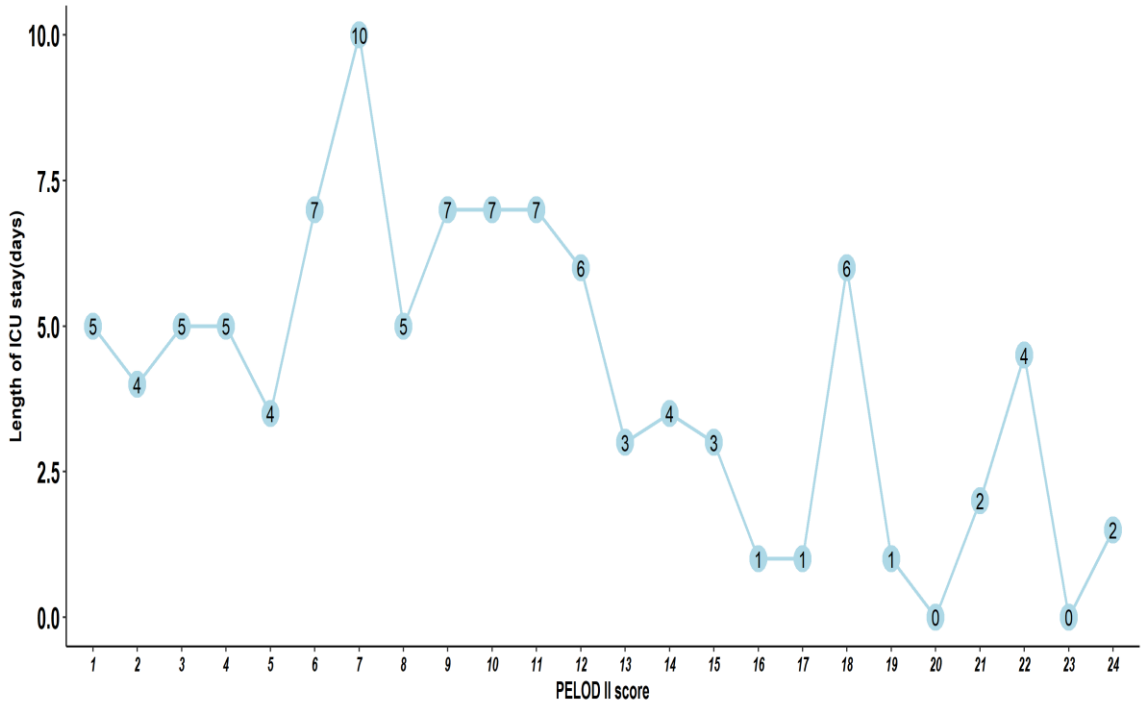

Figure 7: Line graph showing the relationship between admission PELOD-2 score and length of PCCU stay.

9.6 Discrimination and Calibration of admission PELOD-2 score for Length of Paediatric Critical Care Unit Stay.

The discriminatory ability of admission PELOD-2 for length of PCCU stay using area under the receiver operating curve (AUC) (with 95% CI) was 0.512(0.454-0.570) (Figure 8).

The calibration of the score for length of PCCU stay calculated using the Hosmer- Lemeshow chi square test was p value = 0.90 (Figure 9).

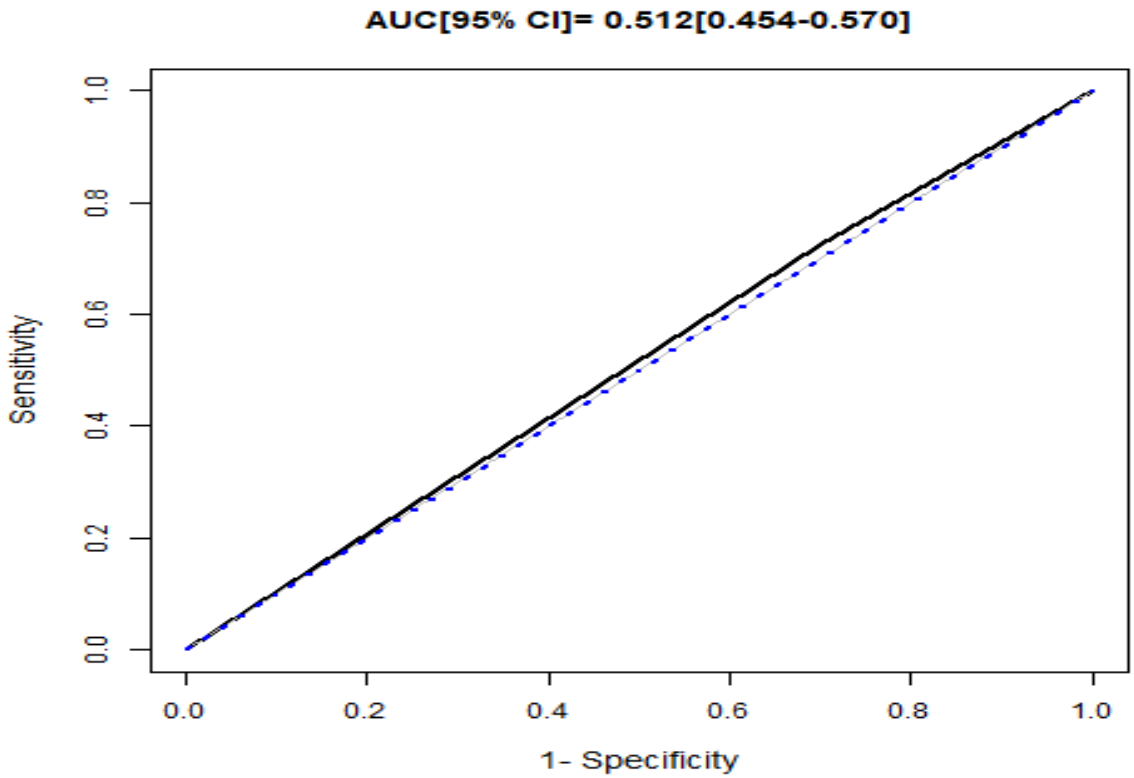

Figure 8: Area Under Receiver Operating Curve showing the discriminatory ability for admission PELOD-2 score for length of PCCU stay with 95%CI.

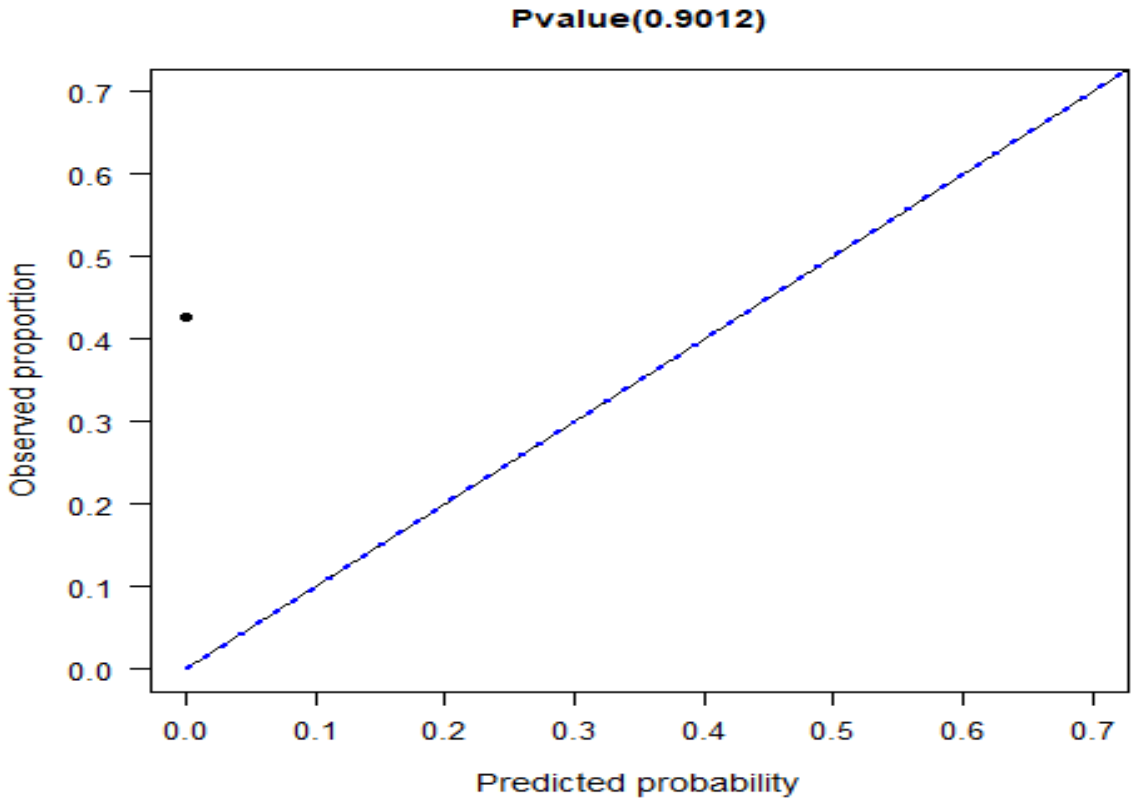

Figure 9: Calibration Plot for admission PELOD-2 score in determining those who had longer PCCU stay and those predicted to have longer PCCU stay

10.0 DISCUSSION

Multiple organ dysfunction refers to derangements in the functional capacity of 2 or more organs. It is the most common cause of death reported in the peadiatric critical care unit (PCCU). PCCU mortality correlates with the number and degree of organ dysfunction and therefore with PELOD-2 score. In this retrospective cohort study, admission PELOD-2 scores, survival or mortality data, biodata and clinical data were abstracted from files of 236 patients admitted to the PCCU at Kenyatta National Hospital, a level 6 teaching and referral hospital located in Nairobi county, Kenya.

The median age of all patients admitted in the unit was 11 months (IQR = 6, 36 months). The survivors had a median age of 17 months and the non-survivors had a median age of 9 months and this difference was statistically significant. We postulate that the higher mortality in infants is due to late presentation as it is harder to detect illness in infants and therefore they present with greater severity of illness. We also attribute it to the fact that infants tend to have lower immunity and therefore faster physical deterioration.

The primary reason for admission in our cohort was pneumonia at 33.3% followed by septic shock at 21.4 % and Meningitis at 14.3%. This is similar to a study done by Thukral et al in India that showed that majority of the case load of patients admitted to the PCCU had medical issues as opposed to surgical which comprise the majority of the case load in developed countries [6, 28]. This was a likely contributor to the high mortality of 50.8% seen in our study.

In our study, 89% of the patients required mechanical ventilation. This is higher than reported in most studies. A study done by Leteurtre et al reported 52.5% use of mechanical ventilation [6] while that by Gonclaves reported 68.5% use of mechanical ventilation [21]. This shows that our patients had greater severity of illness compared to those in the developed countries.

PELOD 2 score was developed and validated in 2013 by Leteurtre et al [5]. It has been used in a number of studies in developed countries to show that MODS is a predictor of severity of illness and therefore mortality [6, 16, 27]. Day 1 PELOD-2 score was also shown to be a significant prognostic factor in this study [6]. In our study we reported a median admission PELOD-2 score of 9, IQR (6, 12). This PELOD-2 score is higher than that reported in developed countries, that is a median PELOD-2 score of 4 IQR (2-6) for survivors and 12

IQR (8-18) for non-survivors reported in a study population of 9 university affiliated PICUs in Europe [6]. There is however a similarity in the PELOD-2 scores reported in developing countries such as that reported in India by Thukral, a high mean PELOD-2 score of 16 [28]. We postulate that our high admission PELOD-2 scores can be attributed to the fact that we are the biggest referral hospital and therefore we receive patients with greater severity of illness. The patients also tend to have a number of organ dysfunctions due to delays in access to health care secondary to their low socioeconomic status. Most of our patients are also malnourished and therefore have lower immunity and this contributes to their faster physical deterioration.

We reported a mortality rate of 50.8%. This score is similar to that reported in other developing countries, that is 50% [19] and significantly higher than in developed countries that report a rate of 6.1% [6]. There are several factors that contribute to this, majority of our patients have medical conditions as opposed to surgical conditions and therefore present with a higher number of organ dysfunctions. The high case load with limited bed space and resources to manage the patients admitted also contribute to rapid deterioration and patient morbidity and mortality.

The study's primary objective was to assess the relationship between admission PELOD-2 score and mortality in a tertiary PCCU in a low middle-income country. This was achieved by comparing the admission PELOD-2 scores and the mortalities for each of these scores. The assessment of the association between admission PELOD-2 sore and mortality was then determined by carrying out discrimination and calibration tests. Discrimination was determined by using Area Under the Receiver Operating Curve (AUC) characteristics (with 95%CI) to differentiate the survivors from the non-survivors.

Calibration of the score was calculated using Hosmer-Lemeshow chi square test. Acceptable calibration p value = $\geq$ 0.05. The Logit (mortality) and probability of death: {Logit (mortality) = – 6.61 + 0.47 × PELOD-2 score; Probability of death = 1/ (1 + exp [– logit(mortality)])}, was calculated for each patient and calibration was then carried out to determine association between predicted death and actual death.

In this study, the admission PELOD-2 score was noted to be directly proportional to mortality. An increase in the admission PELOD-2 score was associated with an increase in percentage mortality. An admission PELOD-2 score of < 8 was associated with a mortality of between (0-35%) and a score of > 8 was associated with a mortality rate of (46-100%). This is in contrast to a study done by Leclerc at al in 9 university affiliated universities in Europe that showed that patients with day 1 PELOD-2 scores of > 8 had an overall risk of mortality of 9% [11]. Admission PELOD-2 scores of > 17 were associated with 100% mortality in our study.

The discriminatory capacity of admission PELOD-2 for mortality using area under the receiver operating curve (AUC) (with 95% CI) was acceptable at 0.63(0.575-0.685). Studies in developed countries have shown higher discrimination of the score for mortality, 0.75 – 0.89 [6]. We postulate that the reason why the discriminatory power was acceptable and not excellent even though we had a good correlation between admission PELOD-2 score and mortality, was because of our small data set, in addition we also reported high mortality percentages in patients with low admission PELOD-2 scores (this was due to socio-economic reasons mentioned earlier).

The calibration of the score for mortality calculated using the Hosmer- Lemeshow chi square test was good, p value = 0.782.

The secondary outcome was to assess the relationship between admission PELOD-2 score and length of stay in a tertiary paediatric critical care unit in a low-middle income country. We reported a median PCCU stay of 5 days IQR (2-9 days). This is similar to both populations in developed and developing countries that report a median PCCU stay of an average of 2-4 days [5, 6, 19].

In our study admission PELOD-2 score had a wide variation with the length of paediatric critical care unit stay (LOPS). The patients with an admission PELOD-2 score of <6 had an average LOPS of 4 -5 days, while those with an admission PELOD-2 score of 7-13 had an average stay of 7 days and patients with scores of > 13 had an average length of stay of 2 days. Patients with very high admission PELOD-2 scores had greater severity of illness and died within 24 – 48 hours.

The discriminatory ability of the admission PELOD-2 score for length of Paediatric CCU stay using area under the receiver operating curve (AUC) (with 95% CI) was acceptable at 0.512(0.454-0.570). This could be attributed short duration of stay secondary to death in patients with higher admission PELOD-2 scores.

The calibration of the score for length of Paediatric CCU stay calculated using the Hosmer-Lemeshow chi square test was good, p value = 0.90.

The strengths of the study were that it is the first study in East and Central Africa to evaluate the relationship between admission PELOD-2 score and mortality and admission PELOD-2

score and length of PCCU stay. These results are therefore likely to be generalizable to low middle-income countries with similar constraint. The study also had acceptable discrimination and calibration.

Limitations in this study were that it was a retrospective study and therefore had missing data. We however corrected for this using multiple imputation method during data analysis and management.

The study was a single center study comprising a small data set and this likely affected the internal validity of the study. Collection of data of only admission PELOD-2 scores likely underestimated the incidence of MODS throughout the PCCU stay.

11.0 CONCLUSION

Patients with MODS and therefore higher admission PELOD-2 scores had higher mortalities and higher average length of PCCU stay.

Patients in our study had higher mortalities for lower admission PELOD-2 scores due to presence of a higher case load, with limited bed space and resources to manage these patients leading to their rapid deterioration.

The patients with very high admission PELOD-2 scores (>13) had shorter PCCU length of stay due to greater severity of illness leading to mortality in 24-72 hours.

12.0 RECOMMENDATIONS

The admission PELOD-2 score should be used as a tool to help identify ideal patients to admit in our PCCU. This would allow for better resource allocation and better patient outcomes, especially in our unit which has limited bed space.

This tool should also be used to advocate for better resource allocation to reduce mortality especially in patients with lower admission PELOD-2 scores and this would therefore increase the quality, efficiency and effectiveness of our PCCU and others in the country.

A multicenter study using daily PELOD-2 scores over an 8-day period should be carried out to further assess response to intervention and subsequently evaluate quality of care and complex systems of care in our PCCU.

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14.0 APPENDICES

Appendix 14.1: Predesigned admission PELOD-2 study data collection sheets

Instructions: Tick all that apply.

Confidential

FPECC Outcomes

Record ID	_____
Patient ICU location:	◯ PICU ◯ Adult ICU ◯ Other
Patient age in:	◯ Months (please select if under 2 years) ◯ Years (please select if 24 months or older)
Patient age in months:	_____
Patient age in years:	_____
Patient sex:	◯ Male ◯ Female

Hospital / PICU Admission and Discharge	
Date of hospital admission:	_____
Please check if hospital admission date is unknown:	☐ Hospital admit date unknown
Date of PICU admission:	_____
Please check if PICU admission date is unknown:	☐ PICU admit date unknown
Date of PICU discharge:	_____
Please check if PICU discharge date is unknown:	☐ PICU admit discharge unknown
Number of days in the ICU	_____
Date of hospital discharge:	_____
Please check if hospital discharge date is unknown:	☐ Hospital discharge date unknown

Diagnoses	
Primary PICU admission diagnosis:	◯ Sepsis ◯ Septic shock ◯ Hypovolemic shock ◯ Undifferentiated shock ◯ Pneumonia ◯ ARDS ◯ Bronchiolitis ◯ Acute respiratory failure not further specified ◯ Malaria ◯ Meningitis ◯ Encephalitis ◯ Gastroenteritis ◯ Anemia ◯ Hemorrhage ◯ Sickle cell disease ◯ Severe acute malnutrition ◯ Seizures/status epilepticus ◯ Post-surgical diagnosis ◯ Congenital heart disease ◯ Acute kidney injury ◯ Multi-organ dysfunction syndrome ◯ Dehydration ◯ Malnutrition ◯ Guillain-Barré Syndrome ◯ Tuberculosis ◯ HIV ◯ Brain tumor ◯ Poisoning ◯ Traumatic Brain Injury ◯ Other ◯ Unknown
Please specify post-surgical diagnosis	_____
Please specify type of congenital heart disease	_____
Please specify other diagnosis	_____

Secondary PICU admission diagnoses:	☐ Sepsis ☐ Septic shock ☐ Hypovolemic shock ☐ Undifferentiated Shock ☐ Pneumonia ☐ ARDS ☐ Bronchiolitis ☐ Acute respiratory failure not further specified ☐ Malaria ☐ Meningitis ☐ Encephalitis ☐ Gastroenteritis ☐ Anemia ☐ Hemorrhage ☐ Sickle cell disease ☐ Severe acute malnutrition ☐ Seizures/status epilepticus ☐ Post-surgical diagnosis ☐ Congenital heart disease ☐ Acute kidney injury ☐ Multi-organ dysfunction syndrome ☐ Dehydration ☐ Malnutrition ☐ Guillain-Barré Syndrome ☐ Tuberculosis ☐ HIV ☐ Brain tumor ☐ Poisoning ☐ Traumatic Brain Injury ☐ Other ☐ None ☐ Unknown
Please specify post-surgical diagnosis	_____
Please specify type of congenital heart disease	_____
Please specify other diagnosis	_____
Please specify type of malnutrition:	◯ Severe acute malnutrition ◯ Moderate malnutrition ◯ Mild malnutrition ◯ Other
Please specify type of tuberculosis:	◯ Pulmonary TB ◯ TB meningitis ◯ Disseminated TB
Please specify type of brain tumor:	_____
Please specify type of poisoning:	_____

Primary PICU discharge diagnosis:	◯ Sepsis ◯ Septic shock ◯ Hypovolemic shock ◯ Undifferentiated Shock ◯ Pneumonia ◯ ARDS ◯ Bronchiolitis ◯ Acute respiratory failure not further specified ◯ Malaria ◯ Meningitis ◯ Encephalitis ◯ Gastroenteritis ◯ Anemia ◯ Hemorrhage ◯ Sickle cell disease ◯ Severe acute malnutrition ◯ Seizures/status epilepticus ◯ Post-surgical diagnosis ◯ Congenital heart disease ◯ Acute kidney injury ◯ Multi-organ dysfunction syndrome ◯ Dehydration ◯ Malnutrition ◯ Guillain-Barré Syndrome ◯ Tuberculosis ◯ HIV ◯ Brain tumor ◯ Poisoning ◯ Traumatic Brain Injury ◯ Other ◯ Unknown
Please specify type of congenital heart disease	_____
Please specify post-surgical diagnosis	_____
Please specify other diagnosis	_____

Secondary PICU discharge diagnoses:	☐ Sepsis ☐ Septic shock ☐ Hypovolemic shock ☐ Undifferentiated Shock ☐ Pneumonia ☐ ARDS ☐ Bronchiolitis ☐ Acute respiratory failure not further specified ☐ Malaria ☐ Meningitis ☐ Encephalitis ☐ Gastroenteritis ☐ Anemia ☐ Hemorrhage ☐ Sickle cell disease ☐ Severe acute malnutrition ☐ Seizures/status epilepticus ☐ Post-surgical diagnosis ☐ Congenital heart disease ☐ Acute kidney injury ☐ Multi-organ dysfunction syndrome ☐ Dehydration ☐ Malnutrition ☐ Guillain-Barré Syndrome ☐ Tuberculosis ☐ HIV ☐ Brain tumor ☐ Poisoning ☐ Traumatic Brain Injury ☐ Other ☐ None ☐ Unknown
Please specify type of congenital heart disease	_____
Please specify post-surgical diagnosis	_____
Please specify other diagnosis	_____
Please specify type of malnutrition:	◯ Severe acute malnutrition ◯ Moderate malnutrition ◯ Mild malnutrition ◯ Other
Please specify type of tuberculosis:	◯ Pulmonary TB ◯ TB meningitis ◯ Disseminated TB
Please specify type of brain tumor:	_____
Please specify type of poisoning:	_____

PIM2	
Admission PIM2 score:	_____
Please check if PIM2 score is unavailable:	☐ Not Available

PELOD	
Admission PELOD score:	_____
Please check if PELOD score is unavailable:	☐ Not Available
Mean Arterial Pressure (lowest value):	_____
Lactatemia (mmol/L) (enter highest value):	_____
PaO2/FiO2 ratio (please enter lowest value of ratio for measures taken at the same time):	_____
PaCO2 (mmHg)(highest value):	_____
Was patient on mechanical ventilation?	◯ Yes ◯ No ◯ Not available
Glasgow Coma Scale (GCS)(lowest value):	◯ 1 ◯ 2 ◯ 3 ◯ 4 ◯ 5 ◯ 6 ◯ 7 ◯ 8 ◯ 9 ◯ 10 ◯ 11 ◯ 12 ◯ 13 ◯ 14 ◯ 15 ◯ Unknown
Admission AVPU	◯ A ◯ V ◯ P ◯ U ◯ not available
Pupillary Reaction:	◯ Both Reactive ◯ Both Fixed ◯ Unknown

WBC (lowest value):	_____
Platelets (lowest value):	_____
Creatinine (highest value):	_____

Ventilator Days

Number of days on ventilator:	_____
Please check if days on ventilator is unavailable:	☐ Not Available

Accidental Extubations

Number of accidental extubations during ICU stay:	_____
Please check if number of accidental extubations is unavailable:	☐ Not Available

Vasopressors

On vasopressors during ICU stay:	◯ Yes ◯ No ◯ Unknown

Survival to discharge

Survival to PICU discharge:	◯ Yes ◯ No ◯ Unknown
Survival to hospital discharge:	◯ Yes ◯ No ◯ Unknown

PCPC/POPC

PCPC Score at pre-ICU admission	◯ 1-Normal ◯ 2-Mild Disability ◯ 3-Moderate Disability ◯ 4-Severe Disability ◯ 5-Coma or Vegetative State ◯ 6-Brain Death ◯ Not available

PCPC Score at hospital discharge:	◯ 1-Normal ◯ 2-Mild Disability ◯ 3-Moderate Disability ◯ 4-Severe Disability ◯ 5-Coma or Vegetative State ◯ 6-Brain Death ◯ Not available
POPC Score at pre-ICU admission	◯ 1-Good Overall ◯ 2-Mild Overall Disability ◯ 3-Moderate Overall Disability ◯ 4-Severe Overall Disability ◯ 5-Coma or Vegetative State ◯ 6-Brain Death ◯ Not available
POPC Score at hospital discharge:	◯ 1-Good Overall ◯ 2-Mild Overall Disability ◯ 3-Moderate Overall Disability ◯ 4-Severe Overall Disability ◯ 5-Coma or Vegetative State ◯ 6-Brain Death ◯ Not available
Other Comments:	

Appendix 14.2: PELOD-2 scoring forms

Organ Dysfunctions and Variables[a]	Points by Severity Levels						
	0	1	2	3	4	5	6
Neurologic[b]							
Glasgow Coma Score	≥ 11	5–10			3–4		
Pupillary reaction	Both reactive					Both fixed	
Cardiovascular[c]							
Lactatemia (mmol/L)	< 5.0	5.0–10.9			≥ 11.0		
Mean arterial pressure (mm Hg)							
0 to < 1 mo	≥ 46		31–45	17–30			≤ 16
1–11 mo	≥ 55		39–54	25–38			≤ 24
12–23 mo	≥ 60		44–59	31–43			≤ 30
24–59 mo	≥ 62		46–61	32–44			≤ 31
60–143 mo	≥ 65		49–64	36–48			≤ 35
≥ 144 mo	≥ 67		52–66	38–51			≤ 37
Renal							
Creatinine (µmoL/L)							
0 to < 1 mo	≤ 69		≥ 70				
1–11 mo	≤ 22		≥ 23				
12–23 mo	≤ 34		≥ 35				
24–59 mo	≤ 50		≥ 51				
60–143 mo	≤ 58		≥ 59				
≥ 144 mo	≤ 92		≥ 93				
Respiratory[d]							
Pao_2 (mm Hg)/Fio_2	≥ 61		≤ 60				
$Paco_2$ (mm Hg)	≤ 58	59–94		≥ 95			
Invasive ventilation	No			Yes			
Hematologic							
WBC count (× 10^9/L)	> 2		≤ 2				
Platelets (× 10^9/L)	≥ 142	77–141	≤ 76				

[a]All variables must be collected, but measurements can be done only if justified by the patient's clinical status. If a variable is not measured, it should be considered normal. If a variable is measured more than once in 24 hr, the worst value is used in calculating the score. Fio_2: fraction of inspired oxygen.

[b]Neurologic dysfunction: Glasgow Coma Score: use the lowest value. If the patient is sedated, record the estimated Glasgow Coma Score before sedation. Assess only patients with known or suspected acute central nervous system disease. Pupillary reactions: nonreactive pupils must be > 3 mm. Do not assess after iatrogenic pupillary dilatation.

[c]Cardiovascular dysfunction: Heart rate and mean arterial pressure: do not assess during crying or iatrogenic agitation.

[d]Respiratory dysfunction: Pao_2: use arterial measurement only. Pao_2/Fio_2 ratio is considered normal in children with cyanotic heart disease. $Paco_2$ can be measured from arterial, capillary, or venous samples. Invasive ventilation: the use of mask ventilation is not considered invasive ventilation.

Logit (mortality) = −6.61 + 0.47 × PELOD-2 score.

Probability of death = 1/(1 + exp [−logit(mortality)]).

Appendix 14.3: GANTT chart

	July	Aug	Sep	Oct	Nov	Dec	Jan	Feb	March	April
Proposal Development										
ERC approval										
Data Collection										
Data Analysis										
Results Presentation										
Final Report										

Appendix 14.4: Study Budget

Item	Cost (Kshs)	
Printing and photocopy	15,000	
Research assistants	30,000	
Statistician	150,000	
ERC processing fee	2,000	
Contingency fund (10% of budget)	19,500	
Total	**216,500**	

Appendix 14.5: Ethical Approval Letter from KNH-UON ERC