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DEPARTMENT OF PAEDIATRICS AND CHILD HEALTH

PREVALENCE AND MANAGEMENT OF SEPTIC SHOCK AMONG CHILDREN ADMITTED AT THE KENYATTA NATIONAL HOSPITAL

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A dissertation submitted in fulfilment for the requirement of the award of Masters of Medicine in Paediatrics and Child health from the University of Nairobi

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DECLARATION

This dissertation thesis is my original work and has not been presented for the award of a degree in any other university

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DEDICATION

To my beloved family- husband (Harish Hirani) and my parents Mr. and Mrs. Vekaria and Hirani, who have been my true inspiration, source of support and encouragement throughout the project.

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LIST OF ABBREVIATIONS

ACCM-American college of critical care medicine

BP-blood pressure

CM- centimetres

ETAT- emergency triage and treatment

GBS- group B streptococci

HIV- Human immunodeficiency virus

Kg- Kilogram

KNH-Kenyatta National Hospital

MAP- mean arterial pressure

Mls-Millilitres

Min.-Minutes

MmHg- millimetre of mercury

Mmol/L- millimoles/litre

NBU- new born unit

NICU-neonatal intensive care unit

PALS-paediatric advanced life support

PEU- paediatric emergency unit

PICU-paediatric intensive care unit

SIRS-systemic inflammatory response syndrome

WHO- world health organization

µg-Micrograms

DEFINITION OF TERMS

1. **SHOCK**- is defined as an acute syndrome that occurs as a result of cardiovascular dysfunction and inability of the circulatory system to provide adequate oxygen and nutrients to meet metabolic demands of vital organs.

2. **INFECTION**-is the invasion of normal sterile fluid/tissue/body cavity by microorganisms

3. **SYSTEMIC INFLAMMATORY RESPONSE SYNDROME**- this is caused by systemic activation of innate immune response regardless of the cause. Clinical criteria require two or more of the following: of which abnormal core temperature or white blood cells must be one of the criteria.
   - Abnormal core temperature<36 degrees or >38.5degrees
   - Abnormal heart rate-tachycardia (>2SD normal for age) or bradycardia (< 10^{th} centile for age).
   - Raised respiratory rate -tachypnoea (>2SD normal for age or mechanical ventilation for acute lung disease)
   - Abnormal white blood cells in circulating blood (above or below normal range for age or >10% immature white cells.)

4. **SEPSIS**-it is a clinical syndrome defined by the presence of both infection and Systemic inflammatory response syndrome.

5. **OLIGURIA**- urine output <0.5ml/kg/hour over six hours.

6. **MODIFIED GLASGOW CHILD'S COMA SCALE**- is used for describing altered mental status; it includes response to voice, motor movements and eye opening for different age groups.

7. **HYPOTENSION**- blood pressure <2SD of the normal lower range for age.

8. **TERM NEWBORN**- defined as baby born ≥37 weeks of gestation up to one month of age. Gestation age was calculated from the last menstrual period by Naegele's rule (Last menstrual period +7/ (for calendar months 1-3 add 9 and for calendar months 4-12 minus 3) /year)

9. **ASPHYXIA**- is defined by WHO as failure to initiate sustained breathing at birth plus an Apgar score less than 7 at 5 minutes.

10. **SEVERE ACUTE MALNUTRITION-** Is defined by World Health Organization as very low weight for height/length (< -3z score of the WHO median growth standards). Mid upper arm circumference of < 11.5 cm, measured over the left upper limb of children less than 5 years.

11. **DIARHOEA-** Acute diarrhoea is defined by ≥3 episodes of loose motion per day.

ABSTRACT

Background

Paediatric septic shock is a major cause of morbidity and mortality in all parts of the world mainly due to acute haemodynamic compromise. Early recognition and early goal directed therapy recommended by Surviving Sepsis Guideline and World Health Organization guidelines have been shown to reduce mortality. Locally the prevalence and outcome of septic shock is unknown. Audit of septic shock management will improve our care for children, improve gaps in knowledge and clinical skills, provide the basis of development of septic shock guidelines and septic shock tool kits for use in emergency care department

Study objective

The primary objectives of this study were to determine the prevalence and to audit the management of septic shock among children aged 0 days to 12 years admitted at the Kenyatta National Hospital. The secondary objective was to determine the outcome of septic shock within 72 hours of admission.

Methods

This was a hospital based longitudinal survey carried out over 2 months (September – October 2016) among children aged 0 days to 12 years admitted at the Kenyatta National Hospital. Consecutive sampling was done and all children who met the inclusion criteria being admitted were enrolled in the study. An informed consent was obtained for all participants enrolled in the study. A standard questionnaire was used for data collection. Data was stored in MS-EXCEL and analysed using STATA 12.

Results

The prevalence of paediatric septic shock among 325 children admitted at KNH was 15.4%, with median age of 4 months (IQR=0.5-9months). Neonates had the highest prevalence 25.6% of septic shock. Odds of being admitted with septic shock reduced with increase in age and no child was diagnosed with septic shock above 60 months of age. Male: female ratio was 1:1.8. All children were admitted with cold shock. Hypotension was present in 56% of the children. Septic shock was recognized in only 56% children by the attending clinician at KNH. All children with

septic shock were in fluid refractory shock. Optimum care was provided as per the surviving Sepsis guidelines in 0%, 6.5% and 20% children at 1st, 24 and 48 hours respectively. The mortality was 70% in 72 hours of admission with 54% dying within first 24 hours. Infants had the highest case fatality of 82.6%. Unavailability of mechanical ventilation in the 1st hour of recognition of shock was associated with high mortality (p value= 0.04). Hypotension on admission was associated with high mortality (p value=0.002).

Conclusion

The prevalence rate of septic shock is 15.4% among children aged 0-12 years admitted at KNH. Septic shock was recognized by the attending clinician 56% of the patients admitted with septic shock. Optimal care as per the Surviving Sepsis Guidelines was a challenge at KNH due to limited intensive care resources and no child received full care in the golden hour. The mortality among children with septic shock was 70% at 72 hours of admission.

Recommendations

Early recognition and management of septic shock requires continues training of health care workers to create awareness and improve care. There is need to include septic shock management guidelines in our local Kenyan paediatric guidelines, to improve management and outcome among children diagnosed with septic shock.

CHAPTER 1: INTRODUCTION

Background

Paediatric septic shock is a subset of sepsis accompanied by cardiovascular and cellular or metabolic dysfunction, with or without hypotension associated with high mortality. Inability of the circulatory system to provide adequate oxygen and nutrients to the vital organs results in cell injury and death. Sepsis is a syndrome of physiologic, pathologic, dysregulated host response and biochemical abnormalities induced by infection, clinically defined by presence of infection (suspected or confirmed) and signs of systemic inflammatory response syndrome. Clinical signs needed to recognize septic shock include signs of sepsis (confirmed or suspected) and altered tissue perfusion. Laboratory parameters have limited role in diagnosing septic shock, hence good knowledge and a high index of suspicion is required in early recognition of septic shock as the diagnosis may easily be missed (1–3).

Septic shock is one of the most dramatic, dynamic and life-threatening condition in critical care and is associated with high mortality. While some research has been done on prevalence and audit of management and outcome in various parts of the world, the epidemiology remains poorly described and no specific patterns are described between developed and developing countries. Guidelines from Surviving Sepsis and World Health Organization have improved recognition and management of shock but mortality still remains high in both developed and developing countries (2,4,5). In Kenya, no studies have been done on septic shock in children, thus the magnitude of the problem is not known.

Early recognition of septic shock is fundamental to improve outcomes, as the pathophysiologic consequences of septic shock are devastating. Trainings done by Emergency triage assessment and treatment plus admission care (ETAT+) and Kenya Paediatric Protocols 2016 Guideline in Kenya do not focus specifically on septic shock but signs of altered perfusion are well described which are applicable in septic shock recognition(6). In developed countries, septic shock tool kits have improved recognition of septic shock in triage.

In an effort to reduce mortality, consensus guidelines emphasize basic principles of goal directed resuscitation ,antimicrobial administration, fluid therapy, vasoactive agent use and other supportive care in septic shock (2,5). Studies done on implementation of guidelines have shown reduction in mortality. A Study done in Bangkok in 2014 showed reduction in mortality from 42% to 19 % after implementation of Surviving sepsis guidelines over 3 years (7).

CHAPTER 2: LITERATURE REVIEW

2.1 Epidemiology

The clinical significance of septic shock cannot be understated. Studies done in various parts of the world have no specific prevalence patterns. There is no difference in the prevalence rate between developed and developing countries as described from literature. Most studies look at prevalence of septic shock among children admitted to paediatric/neonatal intensive care unit. A Study done in Nepal PICU by Basnet et al. over 1 year in children aged between 0 days to 16 years showed a prevalence of 30% of septic shock (8). Another study done in a referral centre in Northern India by Ganjoo et al. on children between 0 days to 12 years admitted showed a prevalence of 2.2% of all admitted children (9). Paulo et al. carried out a study in a hospital in Brazil and found prevalence of septic shock to be 9.8% among all admissions(10). One large study done in Latin America in 2011 showed a prevalence of 19% septic shock among all admission in intensive care in various hospitals (11). The same study compared public versus private hospitals and they found public hospitals had a higher prevalence of 21.5% while private hospitals had 14.1% prevalence of septic shock. In an Indian hospital, a study done on prevalence by Jat et al. found 18.4% septic shock among all admissions to PICU (12). In two hospitals studied in Mexico by Arizaga et. al., the prevalence of neonatal septic shock was 12.7% among all NICU admissions (13). There is paucity of data on prevalence and audit on the management of paediatric septic shock in African countries.

Early recognition of septic shock remains the key to reduction of mortality among children. A study done on missed diagnosis of septic shock on triage in an emergency department showed only 7% of patients were referred with septic shock but the results of the study identified 37% who actually had septic shock that were missed (14).

Audit on early goal directed management have shown marked improvement in mortality after introduction of guidelines. A Study done in Cuba, where they used American College Of Critical Care Medicine (ACCM) guidelines, the mortality in 2003 was 34.6%, dropped to 19% in 2007 and 11.1% in 2010 (15). Implementation of surviving sepsis campaign guidelines by Zambon et al. in 2008, evaluated feasibility of applying guidelines and found that compliance to guidelines reduced mortality from 41% to 16% and reduced length of stay from 9 days to 5 days (16).

Mortality of septic shock remains high worldwide, A prospective observational multi centred study done in Italy PICU showed mortality of 50.8% (17). In Western Germany a mortality of 25% was found among children admitted with septic shock (18). A retrospective study done in Tunisia on neonates identified 40 neonates with septic shock over 8 years with a mortality of 19.1% (19).

Challenges in resource limited areas where availability of PICU/NICU, equipment, staff and training may hinder implementation of international Surviving Sepsis Guidelines and WHO Guidelines but an evaluation on the improvement of septic shock has not been done as yet in our setup (2,5). A study done in African hospitals showed that only 67% of the Surviving Sepsis guideline can be implemented in African hospitals and only 1.4% of low and middle income African hospitals can fully implement Surviving Sepsis Guideline (20).

2.2 Aetiology

Various studies have been done to isolate organisms responsible for sepsis and eventually septic shock. The causative organisms can be bacteria, virus and fungi. In children, the organisms differ by local geography, age and medical co-morbidities such as immunosuppression from malignancies, malnutrition and human immunodeficiency virus infection. Overcrowding and poor vaccination coverage also increases the risk of infection and septic shock (21).

The causative organisms include a wide variety of gram positive and gram-negative bacteria. In neonates presenting with septic shock the most common bacteria include coagulase negative staphylococcus, group B streptococci and enteric gram-negative rods and anaerobes. A study done by Paulo in 2001 showed 58% neonates progressed to septic shock from group B streptococci infection (22). Viral–bacterial co-infection occurs in up to 34% of cases of severe pneumonia that can cause septic shock, resulting in a higher likelihood of respiratory failure and septic shock (23).

2.3 Pathophysiology

In the normal physiological state, delivery of oxygen is key for a cell to undergo aerobic metabolism and produce adequate energy to meet the metabolic demands of the body. Oxygen delivery to the cell is determined by the cardiac output and oxygen content. This can be summarized by the formula below:

Oxygen delivery = CO x $[(Hb \times 1.36 \times sa0_2) + (0.003 \times pa0_2)]$

Where:
CO-cardiac output
Hb-haemoglobin
$sa0_2$- oxygen saturation
$pa0_2$-partial pressure of oxygen.

Cardiac output is the amount of blood the heart pumps in 1 minute and is determined by the heart rate and stroke volume. Stroke volume depends on preload, afterload and contractility of the heart. Preload is the degree of myocardial distension prior to shortening and largely depends on the amount of ventricular filling. After load is the resistance against which the ventricles must act in order to eject blood, and is largely dependent on the arterial blood pressure and vascular tone(24).

In septic shock microbial products of bacteria and virus trigger an immune response(25). These products trigger the beginning of a cellular activation of macrophages, monocytes and neutrophils. These interact with endothelial cells by numerous pathogen recognition receptors and release cytokines (25). Prostaglandins that cause fever, elastase and superoxide further damage the endothelium.

Vascular injury causes tissue ischemia and global tissue hypoxia that accompanies septic shock. Failure to deliver oxygen is as a result of hypotension, cardiac dysfunction, reduced red cell deformability , microvascular thrombosis and mitochondrial damage (26). Nitric oxide released by the endothelial cells, causes vasodilatation by reducing the venous tone. This causes reduction in blood pressure where the diastolic pressure is more affected giving a wide pulse pressure.

Septic shock is a classic example of distributive shock in which there is predominant circulatory maldistribution of fluid. This is associated with peripheral vasodilation, arterial and capillary shunting. Maldistribution of fluids causes inadequate circulatory body volume and in turn causes peripheral vasoconstriction later in the pathophysiology of septic shock.

In septic shock, the body increases heart rate to compensate to improve oxygen delivery. There is activation of sympathetic nervous system in an attempt to compensate by increasing the venous tone.

Children have limited cardiac reserve, they are not able to double the heart rate unlike adults because there is not enough time for diastolic filling. Therefore, a predominant response to a decreasing cardiac output is vasoconstriction. This may affect the pulse oximeter reading of oxygen saturation. The continued increase in vasoconstriction is detrimental as it further impairs cardiac output leading to cardiac failure and death. This elevated systemic vascular resistance makes hypotension a late sign in paediatric septic shock (27).

In neonates, sepsis induced acidosis and hypoxia increase pulmonary artery pressures causing persistent pulmonary hypertension in the neonate. Hence neonates can present with cardiac failure, tricuspid regurgitation and hepatomegaly (27).

When oxygen does not reach the organs, features of shock are seen. In the central nervous system hypoxia causes altered mental state. Hypoperfusion to the kidneys cause oliguria.

Hyperglycaemia occurs commonly in septic shock and is thought to be caused by peripheral resistance to insulin and increased gluconeogenesis (28). Hyperglycaemia causes endothelial dysfunction by impairing phagocytic function of neutrophils and macrophages and is associated with higher mortality (29). Children may also present with hypoglycaemia due to high glucose needs and low glycogen stores resulting in neurological sequalae. A Study done by Losek et al. found that 44% patients with septic shock get hypoglycaemia (30).

2.4 Management of septic shock

The optimal management of paediatric septic shock patients includes early recognition of inadequate tissue perfusion and its timely correction in an effort to prevent anaerobic metabolism, acidosis, and cellular death. Guidelines used for management of septic shock include Surviving Sepsis, 2014 and WHO 2016 guidelines (2,5). The Surviving Sepsis Guidelines gained its recognition from the study done by Rivers et al. in 2001 which utilized a goal directed approach for septic shock and showed 16% reduction in mortality (31). It was updated for children in 2014 for children and it describes a timely order of stepwise interventions that need to be done especially in the first one hour. The major limitation to the guidelines is unavailability of PICU/NICU in resource limited countries. WHO 2016 Guideline describes the fluid management in septic shock for resource limited countries which is different from the Surviving sepsis guideline.

Diagnosis of septic shock.

Since septic shock is largely a clinical diagnosis, laboratory data are of limited utility in establishing the diagnosis. Paediatric septic shock is recognized in a child with suspected sepsis, signs of SIRS and abnormal perfusion.

These signs include temperature abnormality (hyperthermia or hypothermia), tachypnoea or tachycardia, altered mental state and features of warm/cold shock as listed in table 1 (2,32). Early in the disease features of warm shock are seen and as the disease progresses features of cold shock are seen (33).

Recognition of septic shock requires a high index of suspicion with good knowledge and clinical skills for evaluation.

Table 1:Signs of warm and cold shock

WARM SHOCK (early/hyperdynamic phase)	COLD SHOCK (late/hypodynamic/decompensated phase)
Warm flushed peripheries	Cold mottled peripheries
Capillary refill <1 second	Capillary refill >2 seconds
Bounding pulse	Weak/thready/absent pulse

Oxygen therapy

Within the 1st hour of recognition of septic shock in children, active cardiorespiratory resuscitation is needed, this includes, maintenance of airway and this remains the fundamental principle of septic shock, high flow oxygen is immediately started with venturi masks, non-rebreathing masks or nasal cannula as per WHO guidelines even in the absence of respiratory distress or hypoxemia (5). If adequate oxygenation is not achieved, bag valve ventilation should be started and early intubation and mechanical ventilation may support cardiac output by reducing work of breathing and reduce oxygen consumption by sedation (34). Glasgow coma scale of < 8, severe metabolic acidosis (increased compensatory respiratory rate due to tissue hypoxia) or respiratory failure requires intubation (35).

Intravenous fluid therapy

Once an intravenous access is obtained, fluids at 10ml/kg in neonates and children 20mls/kg is given as a bolus (Surviving Sepsis Guidelines) or over 30 minutes to one hour (WHO revised guideline in 2016). Crystalloids such as Ringers lactate are used as per the WHO 2016 and Surviving Sepsis Guidelines (2,5). As the fluids are delivered signs of improvement (normalization of perfusion and blood pressure) or deterioration (hepatomegaly, rales due to pulmonary oedema) are monitored with fluid administration (36). WHO revised 2016 guidelines used results on fluid management from the FEAST trial, that showed increased mortality after rapid fluid boluses (37). In this study fluid boluses were audited as per the Surviving Sepsis Guideline since the healthcare workers have not been trained on the WHO guidelines of fluid management.

Urine monitoring

Urine monitoring must be measured in all patients with a target of urine >0.5mls/kg/hour with the ongoing fluid resuscitation in children and >1ml/kg/hour in neonates. An indwelling urinary catheter, urine collection bag, container or weighing diapers are used to measure urine. The time and amount of each voiding episode should be recorded (3).

Blood sugar monitoring

In septic shock, the patient may get hypoglycaemia (blood sugar <2.2mmol/l), hence it should be monitored and promptly treated with 10% dextrose containing fluids at 2 mls/kg bolus in neonates and 5mls/kg bolus in children (38). Inversely some patients may get hyperglycaemia which needs to be monitored and maintained ≤10mmol/L (2). Hyperglycemia may need correction with insulin infusion when RBS>10mmol/l as recommended by the Surviving Sepsis guideline (2).

Antibiotic therapy

Antibiotics should be given with in the first hour of recognition of septic shock. Delays in antibiotic have shown to increase morbidity and mortality (39). The choice of empirical antibiotics depends on complex issues related to patient's history including drug intolerance, recent receipt of antibiotics (< 3 months), setting (home/hospital), local susceptibility patterns and drug resistance patterns (2). Initial empiric therapy includes one or more drugs that have activity against all microbial and that penetrate in adequate concentration in to the tissues and broad-spectrum monotherapy is preferred.

Calcium monitoring

Serum ionized calcium levels are frequently low (<1mmol/l) in septic shock and this contributes to myocardial dysfunction and reduces vascular tone (40). A study done by Buysse et al. in 2001 showed hypocalcaemia (<1mmol/l) was present in 68 % of the enrolled patients (40). Replacement should be directed to correct to normalize ionized calcium levels with 10% calcium gluconate at 0.5-1ml/kg intravenous given slowly (2).

PICU/NICU care for refractory shock

Presence of signs of poor perfusion and hypotension following fluid therapy for intravascular volume repletion is recognized as fluid refractory shock and warrants vasoactive therapy. Vasopressors improve perfusion pressure and cardiac output through an increase in mean arterial

pressure. They also improve cardiac preload and increase cardiac output by reducing venous compliance and augmenting venous return. The aim is to maintain a target MAP depending on the age of the child (41). Dopamine is considered the first line vasopressor at 5-10µg/kg/min given by the peripheral line. At this dose dopamine acts an ionotropic agent. In the very young children (<6 months) insensitivity to dopamine has been documented which is thought to be due to lack of development of the full component of sympathetic vesicles upon which the dopamine acts to release norepinephrine (42). Children with septic shock more often have myocardial dysfunction and low cardiac output, hence an inotrope dobutamine at 10µg/kg/min may be added (2). At threshold levels of dobutamine it is an effective ionotropic agent with minimal chronotropic effect.

If in one hour of fluid and dopamine/dobutamine therapy and the patient has signs of poor perfusion and hypotension, this is recognized as fluid refractory, dopamine/dobutamine resistant shock. This requires insertion of a central line and vasoactive agent administration. Cold shock requires epinephrine at 0.05-0.3µg/kg/min. Epinephrine(adrenaline) is an adrenergic agonist with potent ionotropic and chronotropic effects thus increases heart rate and improves myocardial contractility. Management of warm shock requires norepinephrine at 0.05-0.3µg/kg/min to increase peripheral vascular resistance (2).

Begin hydrocortisone at 50mg/m^2/24hours if the child has catecholamine resistant septic shock and is at risk for adrenal insufficiency (in prior history of steroid use). Although evidence is lacking regarding the best method to identify adrenal insufficiency in children with refractory septic shock, assessment of adrenal status (either baseline serum cortisol or adrenocorticotropin hormone stimulation testing) is advised prior to corticosteroid administration (43).

Blood requirement

Blood transfusion may be needed in patients with a low haemoglobin levels. Oxygen delivery is one of the goals of supportive care and this is achieved by increasing the haemoglobin. Studies show haemoglobin levels >7g/dl may be safe for haemodynamically stable children with septic shock while haemoglobin >10g/dl are targeted for haemodynamically unstable patients (2).

Lactate monitoring

Patients in septic shock develop increased anionic gap metabolic acidosis from lactic acid production as a result of anaerobic metabolism. Blood lactate levels should be measured on admission and repeated thereafter to follow up. Elevated lactate levels ≥4 Mmol/L have been associated with higher morbidity and mortality (2,12).

Other supportive care

Other advanced supportive care with extracorporeal membrane oxygenation are recommended for refractory shock which reduces mortality but these are not available in resource limited regions (2).

2.5 Outcome

The outcome of septic shock in children is influenced by the time of recognition of septic shock and the time of initiation and goal directed management provided. Mortality remains high in the first three days of onset of sepsis and septic shock from an initial predominance of hyper inflammatory phase (cytokine storm) of the immune response (44). Hence early recognition and goal directed therapy has shown to improve outcomes and reduce mortality of septic shock (31). Severe metabolic acidosis and low arterial systolic blood pressure have been associated with poor outcomes in the first few days of diagnosis (18). A study done by Makhija et al. A study done in New Delhi among children more than one month age (mean of 4 months) showed a 32% prevalence of septic shock and the mortality within 4 days (average 2.15 days) of 70% (45).

2.6 Study justification and utility

Septic shock is associated with high mortality. The diagnosis of septic shock is based on clinical signs and this requires a high index of suspicion and good knowledge as many times it may go unrecognized. If it is recognized late in the decompensated state, where it is irreversible it is associated with high mortality, hence early recognition has shown to improve outcomes of septic shock.

Use of international guidelines such as Surviving Sepsis Guidelines have shown reduction of mortality and improvement in recognition of septic shock in the early stages of shock. The guideline recommends timely early goal directed therapy to improve outcome of septic shock.

Locally the prevalence and outcome of septic shock is not known. Kenya Paediatric Protocols revised in 2016 focusses on hypovolemic shock and not septic shock. Being the first audit in the African region, the research on audit of septic shock will provide valuable information to improve our care for children, correct errors, improve gaps in knowledge and skills among children diagnosed with septic shock.

Analyses of septic shock management practices in KNH will provide the basis of development of septic shock guidelines, policies and septic shock tool kits for use in emergency care departments. The information obtained will further guide us on staff training on early recognition and appropriate management of septic shock. The study will provide baseline data in prevalence, management and outcome to help in formulating hypothesis further research on septic shock.

CHAPTER 3: RESEARCH QUESTIONS AND OBJECTIVES

3.1 Research questions

1. What is the prevalence of septic shock among children aged 0 days to 12 years admitted at Kenyatta National Hospital?
2. How is septic shock being managed in 72 hours of recognition of septic shock among children aged 0 days to 12 years admitted at KNH?
3. What is the outcome of septic shock at 72 hours among children aged 0 days to 12 years admitted at KNH?

3.2 Objectives

3.2.1 Primary objectives:

1. To determine the prevalence of septic shock among children aged 0 days to 12 years admitted at Kenyatta National Hospital.
2. To audit the management of septic shock among children aged 0 days to 12 years at 1st, 24 and 48 hours of admission at KNH.

3.2.2 Secondary objective:

1. To determine the outcome of septic shock at 72 hours among children aged 0 days to 12 years admitted at KNH.

CHAPTER 4: RESEARCH METHODOLOGY

4.1 Study design

This was a hospital based longitudinal survey.

4.2 Study period

The study was carried out over a period of 2 months (September – October 2016).

4.3 Study site

Paediatric emergency unit, paediatric wards, paediatric intensive care unit and new born unit at the Kenyatta National Hospital (KNH) were sites used for data collection in the study. KNH is a national teaching and referral hospital located 4 kilometres away from the Central Business District in the capital city of Kenya, Nairobi. The hospital serves both children and adults from all over the country and neighbouring countries. Children aged 0 days to 12 years are admitted in the paediatric section of the hospital. There are 4 paediatric wards with a total bed capacity of 240, 5 PICU beds and 45 cots and incubators in the new born unit.

Each paediatric ward has an acute room, where all the very sick children are managed awaiting Paediatric or neonatal intensive care unit (PICU/NICU) bed availability. Neonates past 1 day of life from home or a referral facility are admitted to the general paediatric wards instead of new born unit(NBU). Laboratory support remains a challenge at KNH.

The average admission of children aged 0 days -12 years per month is estimated at 450 children in the general paediatric wards and 250 neonates in the new born unit. Most children are admitted from the paediatric emergency unit where postgraduate paediatric resident students' triage, initiate the emergency care of sick children at all times and admits to wards/NBU/PICU/NICU.

4.4 Study population

Children aged 0 days (term neonate ≥37 weeks) to 12 years admitted at the Kenyatta National Hospital paediatric wards/NBU/PICU.

4.4.1 Inclusion criteria

Participants meeting all the following inclusion criteria were included in the study:

1) Children aged 0 days (term neonates (≥37weeks)) to 12 years.
2) Children admitted to KNH Paediatric wards/PICU/NBU

4.4.2 Exclusion criteria

Participants meeting any of the following exclusion criteria were excluded from the study:

1) Trauma, burn and post-surgical patients.
2) Anaphylaxis reaction from drug/insect bite/other allergens
3) Known Cardiac disease patients
4) Known Chronic renal failure
5) Liver failure
6) Neonates with birth asphyxia
7) Severe acute malnutrition (WHZ < -3z)
8) Diarrhea.

4.5 Study tool

A standardized questionnaire was used for collecting data from the enrolled participants- Appendix 17.4. The questionnaire was pretested in paediatric emergency unit among children being admitted at the KNH. The questionnaire included:

- The patient's demographic data
- Focused clinical exam was done as per the questionnaire to recognize septic shock namely temperature, respiratory rate, heart rate, capillary refill time, extremity temperature gradient, radial pulse characteristics, level of consciousness, blood pressure and oxygen saturation.
- An audit on the management at admission, at 1st, 24 hours and 48 hours
- Outcome (survived/died) within 72 hours was recorded.

4.6 Study personnel

1. Principle investigator- was the supervisor in charge of the research team. The role was to ensure proper required procedures and data recording was done in the questionnaire for all enrolled participants. Ensured all materials needed were available and all data collected was entered in to computer every 72 hours.
2. Research assistants- three research assistants (clinical officers) assisted in data collection data under supervision. The research assistants aided in recognition of septic shock at admission and audit of septic shock management. They received training for one day on standard ways of doing required procedures for the study as per the questionnaire and given operational procedure manual. They were informed on the purpose of the study. All study definitions were provided to them.

4.7 Study outcome

1. Prevalence of septic shock among children aged 0-12 years admitted to the KNH paediatric wards/NBU/PICU.
2. Audit on the management provided to children with septic shock aged 0-12 years of age at KNH paediatric wards/PICU/NBU at 1st, 24 and 48 hours.
3. Outcome of children diagnosed with septic shock at 72 hours (survive/die) of admission.

4.8 Sample size determination

The Sample Size was determined using Fischer's Formula for Sample Size Determination in Prevalence studies:

$$m = \frac{z^2\, p(1-p)}{d^2} = \frac{1.96^2 \times\ 0.3\ \times 0.7}{0.05^2} = \mathbf{323}$$

- m = calculated Sample Size
- z = Normal standard deviation taken with a 95% Confidence Interval; set at 1.96.
- p = Expected prevalence of septic shock admitted, estimated as 30% per *Basnet et al'* s study carried out in Nepal(8)
- d = Study precision taken as 5%.

A study sample of 325 was taken.

4.9 Sampling

Consecutive screening and enrolment of all children meeting the inclusion criteria was done till the desired sample size of 325 was reached. This took 2 months to collect all the data.

4.10 Case definition of septic shock

1. **Suspected sepsis** (suspected infection with SIRS) manifested by:
    a) Abnormal core temperature: >38.5 °C or <36 °C.
    With one or both of the following SIRS signs (b or c)
    b) Tachycardia (age dependent)
    c) tachypnoea (age dependent)

    AND

2. Signs of altered perfusion (all signs have to be present)
    a) Reduced or altered consciousness(GCS)
    b) Capillary refill time - >2second or <1 second
    c) Pulse- weak, thready, absent or bounding.
    d) Extremities-cold, mottled or flushed.

The vital signs were age dependent as shown in table 2. Surviving Sepsis Guidelines and WHO 2016 guidelines define abnormal respiratory rate and heart rate above the 95^{th} percentile and abnormal systolic blood pressure below the 5^{th} percentile.(2,5)**.** Blood pressure is a late sign in paediatric septic shock and is not included in the case definition however it was measured to describe its association with mortality in our enrolled children. Reduced or altered level of consciousness was assessed using GCS as shown in figure 1.

Table 2: Age dependent vital signs reference values.

Age	Heart rate/Minute		Respiratory Rate/Minute	Systolic BP (MmHg)
	Tachycardia	Bradycardia		
0 days-1 week	>180	<100	>50	<60
>1week-1month	>180	<100	>40	<70
>1month-1 year	>180	<90	>34	<70+ (2 x age in years)
>1year-5years	>140	NA	>22	<70+ (2 x age in years)
>5years-12years	>130	NA	>18	<90

PEDIATRIC GLASGOW COMA SCALE (PGCS)				
	> 1 Year		**< 1 Year**	**Score**
EYE OPENING	Spontaneously		Spontaneously	4
	To verbal command		To shout	3
	To pain		To pain	2
	No response		No response	1
MOTOR RESPONSE	Obeys		Spontaneous	6
	Localizes pain		Localizes pain	5
	Flexion-withdrawal		Flexion-withdrawal	4
	Flexion-abnormal (decorticate rigidity)		Flexion-abnormal (decorticate rigidity)	3
	Extension (decerebrate rigidity)		Extension (decerebrate rigidity)	2
	No response		No response	1
	> 5 Years	**2-5 Years**	**0-23 months**	
VERBAL RESPONSE	Oriented	Appropriate words/phrases	Smiles/coos appropriately	5
	Disoriented/confused	Inappropriate words	Cries and is consolable	4
	Inappropriate words	Persistent cries and screams	Persistent inappropriate crying and/or screaming	3
	Incomprehensible sounds	Grunts	Grunts, agitated, and restless	2
	No response	No response	No response	1
TOTAL PEDIATRIC GLASGOW COMA SCORE (3-15):				

Figure 1:Paediatric modified Glasgow coma scale.

4.11 Guideline on audit criteria of management of septic shock

Table 3 shows guide on measured variable with the audit criteria used in the study from recognition of shock, 1st, 24 and 48 hours of management of septic shock.

Table 3:Guideline on audit criteria of management of septic shock.

Audit variable	**Audit criteria**
Recognition of septic shock on admission	Recognized or not recognized (as per case definition section 4.10) Record not documented clinical signs needed for shock recognition
Oxygen	Administered or not regardless of oxygen saturation
Intravenous fluids	Appropriate 2 boluses (10-20mls/kg/hour) and fluid type given in the 1st hour of management
Blood sugar	Measured or not. Hypoglycemia(<2.2mmol/l) corrected. Hyperglycemia (>10mmol/l) corrected after 1 hour of diagnosis of septic shock with insulin infusion 0.05-0.1 regular insulin/kg/hour infusion.
Antibiotics	Received all doses, reasons for missed doses.
Serum calcium	Measured or not. Children with <1mmol/l
Blood lactate	Measured or not. Children with ≥4mmol/l
Urine monitoring	Monitoring initiated on admission, for neonates with urine output <1ml/kg/hour and children <0.5mls/kg/hour audit dialysis availability
Blood and blood products	Needed for Hb<10g/dl and availability
PICU/NICU	Availability at 1st, 24 and 48 hours of diagnosis of septic shock.
Vasoactive use	Type used and availability in septic shock at 1st, 24 and 48 hours of diagnosis of septic shock.

4.12 Patient recruitment procedure

Patients who met the inclusion criteria on admission were recruited in to the study. Those who met the exclusion criteria were excluded.

The study patient was enrolled in to the study after the child was triaged and admitted by the admitting clinician at the paediatric emergency unit or new born unit and after the guardian signed consent or consent and assent for above 8 years of age (for those able to sign).

The parent/guardian was explained on the study, its benefits to the child and risks regarding the study in English or Kiswahili. Explaining that the child would be examined during the study to recognize septic shock and if present, the primary clinician will immediately be alerted if diagnosis of septic shock was missed by them (for ethical reasons) made the parent/guardian keen to be enrolled in the study. The parent/guardian was assured, this is a minimal risk study and it would not delay the management of their child.

Once the patient was enrolled into the study, demographic data was recorded on the questionnaire. This included study identity number, age, sex, and if they were referred from any health facility.

A focused clinical exam was performed (after the clinician completed his /her focused examination) and recorded in the questionnaire. This included recording of temperature, heart rate, respiratory rate, Oxygen saturation, pulse character, temperature gradient of extremities, capillary refill time, consciousness level and blood pressure. The recordings were then compared to the normal for age reference values as shown in table 2 and figure 1. The procedure done was as described below:

1. Temperature recording-rectal core temperature was taken by a digital thermometer. This was cleaned with alcohol swabs after each use.
2. Heart rate was counted for one minute using a digital timer.
3. Pulse character-was defined as weak/thready/absent, normal or bounding pulse felt at the radial artery pulse in any wrist.
4. Respiratory rate- was counted for one minute using digital timer and recorded
5. Oxygen saturation was measured using a pulse oximeter over the index/middle finger of any hand.

6. Limb extremities of upper and lower limb were examined from distal to proximal to identify cold or warm peripheries.
7. Capillary refill time- The palmar aspect of the thumb/toe was pressed for 5 seconds measured by a digital watch and released and the time taken for refill was recorded in seconds.
8. The consciousness level was assessed by the Glasgow coma scale as shown in figure 1 (46).
9. Blood pressure- the American heart association guidelines 2005 on blood pressure measurements was used. The correct size of cuff as shown in table 4 was used.

Table 4:Blood pressure cuff sizes for different age groups.

AGE	RECOMMENDED CUFF SIZE
Neonate	4*8 cm
Infant	6*12cm
Children	9*18cm

The analogue sphygmomanometer was inflated at least 30mmHg above the point at which the radial pulse disappears, then deflate at 2-3mmHg/second and read. Two readings were taken one minute apart and an average blood pressure was recorded.

Once the patient was examined and met the criteria of septic shock as per the case definition, the primary clinician was immediately alerted to continue with the care on septic shock if septic shock was not recognized (documented) by the attending clinician. The clinical signs of septic shock missed by the attending clinicians were recorded. An audit was then performed on the children with septic shock as per the questionnaire.

Audit of the management at 1st hour of admission, 24 hours, 48 hours and the outcome within 72 hours was recorded in the questionnaire (appendix V). The audit included:

1) Initial audit of management at admission at 1st hour of recognition of septic shock.

   a) Oxygen if administered was recorded.

   b) Intravenous fluid therapy- amount of fluid per kilogram per bolus given, type of fluid and number of boluses given in one hour was recorded from the participant's file, fluid chart and treatment sheet

c) Blood sugar, lactate levels and serum calcium levels if done were recorded from the participant's file.

d) Antibiotic administration-initiation time of antibiotics from the arrival time to PEU/NBU was recorded from the participant's file, treatment sheet or nursing Cardex. If blood cultures were done was recorded and if not done the reason was recorded from the file and nursing cardex. The choise of antibiotic was recorded from the treatment sheet.

e) Urine monitoring- if urine collector or catheter was inserted for urine monitoring was recorded from the participant's file.

f) In fluid refractory shock - availability of PICU/NICU care was recorded. For those admitted to PICU/NICU, vasoactive agent used (dopamine/ norepinephrine/ epinephrine) and mechanical ventilation need, availability and reason for ventilation was recorded from the participant's file and treatment sheet.

2) Subsequent Audit of management at 24 hours and 48 hours was done as described below.

a. Temperature, respiratory rate, pulse rate, pulse character, blood pressure, limb extremities temperature gradient, capillary refill and oxygen saturation was recorded from the participant's file and clinical signs chart.

b. Blood sugar, calcium levels and lactate levels measured was recorded from the participant's file.

c. Antibiotic administration- from the treatment sheet the frequency of antibiotics administered and if they missed any dose was recorded at 24 and 48 hours. The reason for missing the dose was recorded from the treatment sheet and the patient's file or nursing cardex.

d. Urine output- if it was continuously monitored was recorded from the participant's file and fluid charts. The amount of urine collected per hour was calculated and recorded. If dialysis was done for children urine output <0.5mls/kg/hour or neonates with urine output <1ml/kg/hour was recorded.

e. Blood transfusion requirement and availability was recorded as per the participant's file.

f. Availability of PICU/NICU was recorded as per the documentation in the participant's file.

g. Those in PICU/NICU- vasoactive medication ongoing was noted and those on mechanical ventilation was recorded. The reason for mechanical ventilation was recorded as per the patient's file.

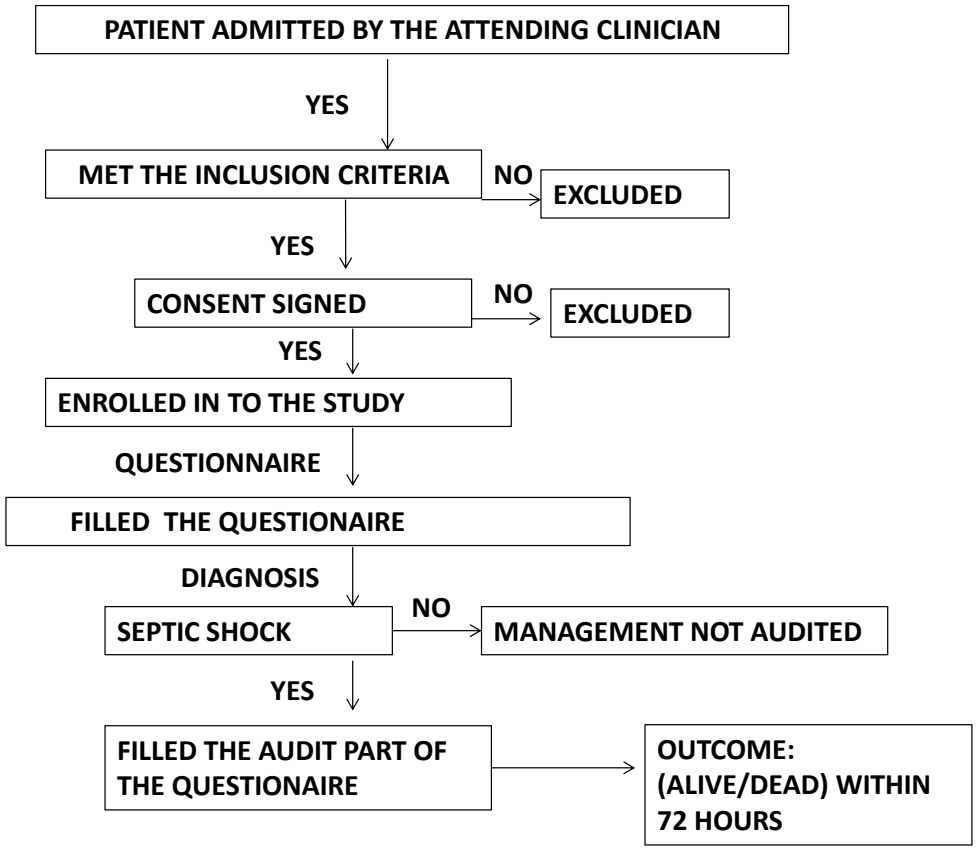
3) Outcome in 72 hours was recorded in the questionnaire.

   a) The enrolled patient was identified as alive or dead.

   b) The time of death in hours from the time of admission was recorded.

   c) The parents/guardians of the children who died during the study were provided with information and counseling by the principal investigator.

Figure 2:Study flow chart



4.13 Data collection, management and analysis

Data collection

Following selection of study subjects, data was collected from identified children whose parents/guardian consent using a pretested questionnaire as described in study tool (appendix V).

Data management

Collected data was recorded in the computer storage program MS-EXCEL at the end of 72 hours of follow up of the enrolled participant. Data verification was done manually by proof reading. The data is stored confidentially preventing inappropriate use of data by use of passwords. Data is and will be protected throughout the data lifecycle from creation to destruction and prevent unauthorized sharing. The stored data is only available with the principal investigator.

Data analysis

Data analysis was carried out using STATA 12 software. Means with standard deviations was calculated for normal distribution and skewed data was expressed in terms of medians with interquartile ranges (IQR). Frequency and percentages were calculated for categorical variables. Tests of association between the outcome variable (septic shock) and independent variables such as age, gender, and blood pressure was carried out by chi-square test, student t-test and logistic binary regression for normally distributed data. Where distribution was skewed a Mann Whitney U tests was performed. Statistical significance was set at a p-value less than 0.05. Audit data was compared to surviving Sepsis Guideline as described in section 4.11 on septic shock management with outcome at 1st, 24 and 48 hours and 72 hours being the end point, since there are no Kenyan guidelines on management of paediatric septic shock. Bivariate analysis using chi-square test was carried out for each of the parameters collected.

4.14 Control of bias and errors

1. **Measurement bias**- the questionnaire was pretested to reduce bias, ensuring the questions are sensitive enough to detect what might be important difference in the variable of interest. Training of the research assistance on the data collection procedure reduced bias.
2. **Sampling bias**- only those who met the eligibility criteria were included.
3. **Instrument error**- thermometer, sphygmomanometer, pulse oximeter and digital timer were checked daily to ensure correct data measurements
4. **Information bias**- each assistant was familiarized with the study and the questionnaire. They received a copy of study definition of terminologies guide to ensure uniform interpretation of terms. A standard operational procedure manual was given to each assistant to ensure even way of carrying the required procedures for the study. The principal investigator assessed the responses given to the questionnaire on daily basis to oversee data entry to ensure validity of collected data.

4.15 Ethical consideration

1. A full explanation of the study was given to the parent/guardian and obtain written consent in English or Kiswahili signed by the parent/guardian or an assent by the child aged 8-12 years to participate in the study, if they were able to.

2. All patient information has been handled with strict confidentiality. All electronic databases are password protected with the principal investigator.

3. The study procedures did not include any interventions that extend beyond the routine clinical assessment required for all admitted children. The interview and clinical exam were deferred for all children requiring emergency intervention and the principal investigator was providing active support for children requiring emergency care including basic and advanced life support as required. The principal investigator was further providing information and counseling for caregivers throughout the management and those who died during the study period. The primary clinician would there after take over the death procedures as per the hospital protocols.

4. The KNH Ethics Research Committee gave approval to carry out the study at KNH (P228/03/2016).

5. The Overall study findings have been availed to the specialists and staff, thereby contributing to the improvement of care delivered to this subset of children.

CHAPTER 5: RESULTS

SOCIODEMOGRAPHIC CHARACTERISTIC OF STUDY POPULATION

A total of 325 children aged 0 days to 12 years admitted were enrolled in the study. The median age was 8 (IQR 1.3 – 26) months. Infants comprised the highest proportions of admissions enrolled in the study. Table 5 shows 78(24%) children were < 1 month, 110(33.9%) were between 1 – 11 months, 96(29.5%) were 12 – 59 months and 41 (12.6%) were ≥60 months.

Out of the total children 191(58.9%) were female and 134(44.3%) were male. Female children were higher than the male participants. Children admitted as referral from other health facilities were 234 (72%) and 91 (28%) were admitted from home. As expected referred children from other health facilities were higher in number as KNH is a tertiary hospital.

Table 5: Socio- demographic data for patients recruited in the study.

Variable	**Characteristic**	**Frequency (N=325)**
Age (Months)	< 1	78 (24.0)
	1 – 11	110 (33.9)
	12 – 59	96 (29.5)
	≥60	41 (12.6)
Sex	Female	191 (58.7)
	Male	134 (41.3)
Referred from Another Hospital	No	91 (28.0)
	Yes	234 (72.0)

PREVALENCE OF SEPTIC SHOCK

Septic shock was diagnosed in 50 children out of the 325 admitted children giving a prevalence of 15.4% (95% CI 11.8 – 19.8) as shown in figure 3. Among those admitted with septic shock median age was 4 months (IQR 0.5 – 9.0).

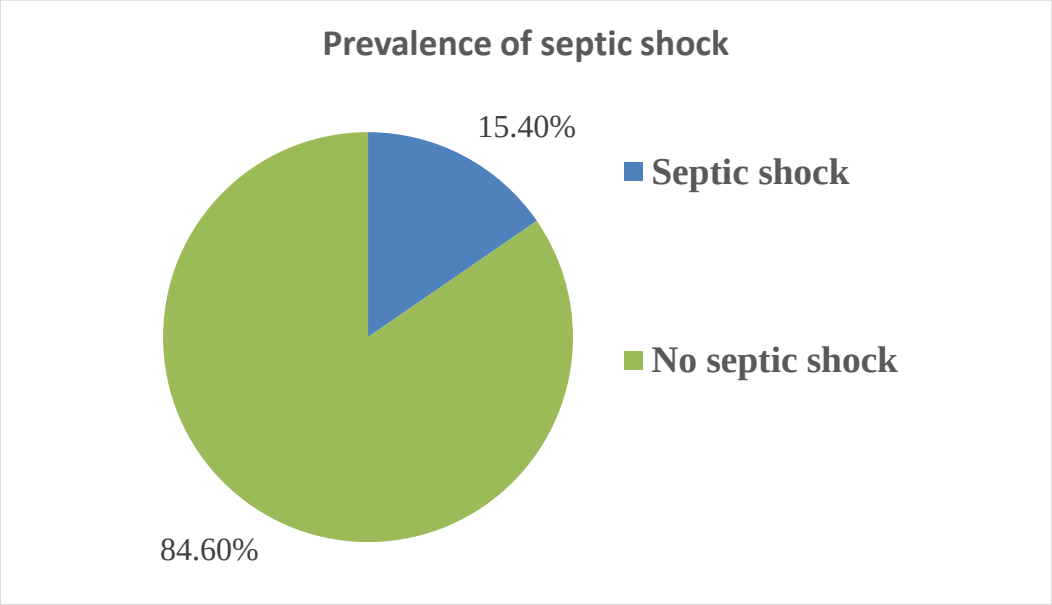


Figure 3:Prevalence of septic shock

Neonates and infants had the highest proportion of septic shock as shown in figure 4.

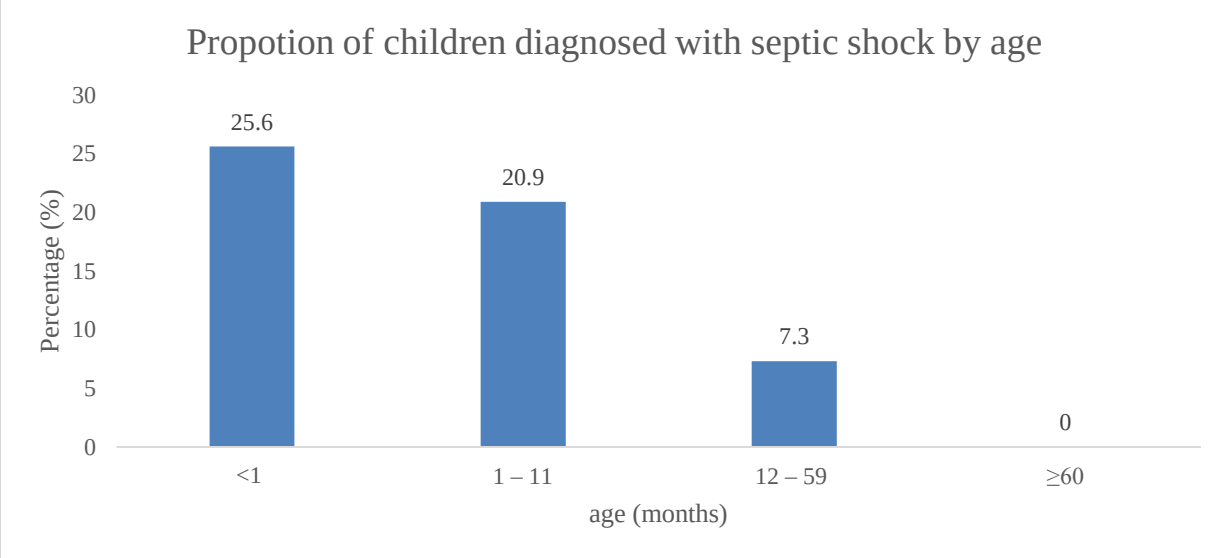


Figure 4:Propotion of children diagnosed with septic shock by age.

Sex distribution of septic shock.

From the 50 children diagnosed with septic shock, 32 (64%) were female and 18 (36%) were male children. This gives a male: female ratio of 1:1.8.

Association of septic shock with demographic variables.

The odds of being admitted with septic shock decreased with increase in age. Odds ratio was computed using 12 – 59 months as the reference age group as shown in Table 6. The odds of admitting children with septic shock were higher in those referred from another facility (3.28; 95%CI 1.35 – 8.0) as compared to those not referred with p value 0.009, and this was statistically significant.

Table 6:Association of demographic variables with septic shock

Variable	Characteristic	Septic shock (n=50)	No septic shock (n=275)	Odds ratio (95% CI)	P Value
Age (Months)	<1	20	58	4.38 (1.74 – 11.0)	0.002
	1 To 11	23	87	3.36 (1.37 – 8.24)	0.008
	12 – 59	7	89	Reference	
	0	0	41	-	-
Sex	Male	36	134	1.61 (0.95 – 2.71)	0.08
	Female	32	191	Reference	
Referral	Yes	44	190	3.28 (1.35 – 8.0)	0.009
	No	6	85	Reference	

INITIAL CLINICAL SIGNS OF CHILDREN DIAGNOSED WITH SEPTIC SHOCK

The measured and assessed clinical signs of initial recognition of septic shock was done by the investigator using the case definition as described in section 4.10. All children admitted had an abnormal rectal temperature. High temperature(>38.5^0C) was found in 34(68%) and low(<36^0C) in 16(32%) children. Either respiratory rate or heart rate change was considered as a sign of SIRS. Normal respiratory rate was seen in 11 (22%) children with septic shock and 39(78%) had a higher respiratory rate for the age. Normal heart rate was recorded in 4(8%) and high in 46(92%) children.

All 50 children with diagnosis of septic shock had cold extremities. In radial pulse characteristics, 37(74%) cases had weak/thready pulse volume while 13(26%) had absent radial pulse. Capillary refill time was > 2seconds in all the 50 children. The GCS was < 15 in all the 50 children. These results show that all children admitted were in cold shock.

Blood pressure was found to be normal in 22(44%) and low in 28(56%) children. Measured oxygen saturation by pulse oximeter of <90% was recorded in 44(88%) and ≥ 90% in 6 (12%) children.

AUDIT OF THE MANAGEMENT OF SEPTIC SHOCK

The Surviving Sepsis Guideline was used for the audit criteria of measured variables as described in section 4.11. An audited variable not documented was assumed to be not done or measured.

1. AUDIT ON RECOGNITION OF SEPTIC SHOCK

The case definition as described in section 4.10 was used for auditing the missed signs of septic shock by the attending clinician. Among 50 children diagnosed with septic shock, only 28 (56%) cases were recognized on admission by the attending health clinician at KNH. Septic shock was recognized (documented diagnosis of septic shock on the referral note) from other public hospitals (for those that were referred) in 5(11.36%) of 44 referred children with septic shock. Table 7 shows capillary refill time measurement was the most missed clinical sign by the attending clinician on admission at KNH. Documentation of ‘not alert’ was assumed to have low GCS. Oxygen saturation was measured in 40 of 50(80%) and blood pressure was measured in 10 of 50(5%) children with septic shock.

Table 7: Clinical signs not documented by the attending clinician, required to recognize septic shock.

Signs	Missed clinical signs (n=50)	Percentage (%)
Capillary refill	14	28.0
Radial pulse characteristics	13	26.0
Temperature gradient	12	24.0
Altered consciousness	6	12.0
Respiratory rate/heart rate	4	8.0
Temperature	1	2.0

2. AUDIT AT THE 1ST HOUR OF RECOGNITION OF SEPTIC SHOCK

No child received optimum care as per the audit guideline (section 4.11) in the first hour of care of septic shock. Figure 5 shows parameters that were monitored for 50 children in the 1st hour of recognition of septic shock. The variables audited are described below:

Oxygen- was given to all the 50(100%) children diagnosed with septic shock.

Blood sugar - was measured in 49(98%) children.

Antibiotics- No child received antibiotics in the 1st 5 minutes as recommended by the surviving sepsis guideline, 44(88.0%) received antibiotics between 5 to 60 minutes and 6(12.0%) received antibiotics after 60 minutes.

Blood culture was taken in 12(24%) children prior to antibiotic administration. The reason for not doing blood cultures were: not ordered by the attending clinician in 8(21.05%) and no blood culture bottle available in 30(78.95%) of the children.

Blood lactate- was measured in 23(46.0%).

Serum calcium levels – was measured in 4(8.0%).

Urine monitoring- was done in 40 (80.0%). Among these children, urine catheter was placed in 21(52.5%) and urine collector was used in 19(47.5%) children.

Blood – was required in 24(48%) whose haemoglobin was <10g/dl.

PICU/NICU care was available in 0% and was needed in all the 50(100%) children in fluid refractory shock. Mechanical ventilation was needed in 42(84.0%) and none received mechanical ventilation in the 1st hour.

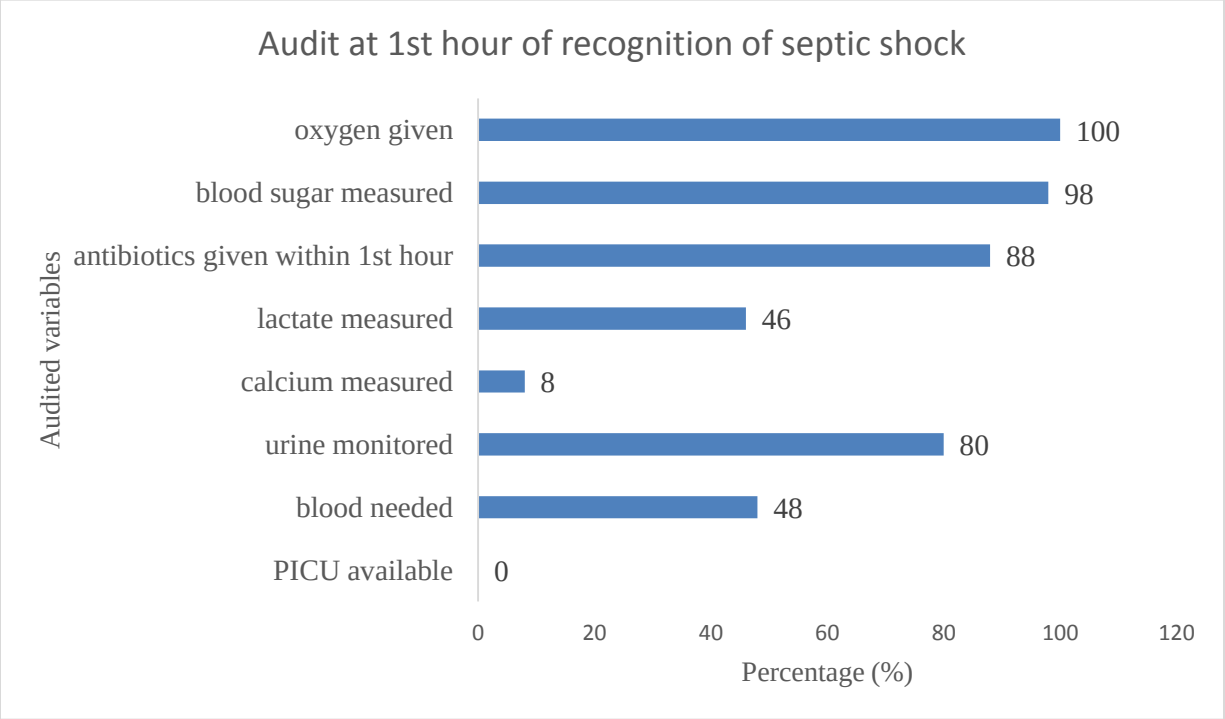


Figure 5:Audit of management at 1st hour after recognition of septic shock.

The results and the interventions among those done of the audited parameters are as shown in table 8.

Blood sugar: Hypoglycemia (<2.2mmol/l) was found in 19(38.88%) of 48 children and corrected appropriately in 18(94.7%). Hyperglycemia (>10mmol/l) was seen in 20(40.8%).

Intravenous fluids: Appropriate fluid choice (ringers lactate) and volume (2 boluses) fluid were received by 33 children (66.0 %).

Antibiotics: Optimal empirical antibiotic treatment for septic shock was given at appropriate in 49(98%) of the prescribed antibiotics by the clinician. Crystalline penicillin, gentamycin, ceftriaxone, ceftazidime, vancomycin, amikacin, meropenem and flucloxacillin were the antibiotic used. The guideline recommends that antibiotic use depends on local studies on organisms and resistance patterns. Currently there are no local guidelines antibiotic use in septic shock hence the antibiotic use cannot be compared.

Blood: was needed for 24(48%) in children with Hb,10g/dl but only available for 3(12.5%)

Serum calcium: no child had calcium<1.0mmol/l

Lactate: 12(52%) children had lactate levels >4mmo/l

V***asoactive agents*** were not used for any child in the 1st hour of septic shock.

Mechanical ventilation: was needed in 42(84%) and not available for any child. Reasons for mechanical ventilation need were GCS<8 in 22(52.4%) for airway support, severe metabolic acidosis with GCS<8 in 18(42.8%) and respiratory failure with GCS< 8 in 2(4.8%).

Table 8: Audit of interventions of septic shock at 1st hour after recognition of septic shock.

Variable	**Results among those measured**	**At 1st hour**		
		Frequency (%)	**Intervention**	
			Done	**n (%)**
Blood sugar	<2.2mmol/l	19(38.9)	Corrected	18(94.7)
	>10mmol/l	20(40.8)	-	-
Intravenous fluids 10-20mls/kg/bolus	2 boluses (appropriate)	33(66)	-	-
	0 bolus	1(2)		
	1 bolus	12(24)	-	-
	3 boluses	4(8)	-	-
Antibiotics	Appropriate dose	49(98)	-	-
	Mono therapy	32 (64)	-	-
	Dual therapy	17 (34)	-	-
	Triple therapy	1(2)	-	-
Blood	Needed (Hb <10g/dl)	24(48)	Available	3(12.5)
Vasoactive agent (fluid refractory shock)	Needed	50(100)	Available	0(0)
Mechanical ventilation	Needed	42(84.0)	Available	0(0)

3. AUDIT OF MANAGEMENT OF SEPTIC SHOCK AT 24 AND 48 HOURS.

Clinical signs audited at 24 and 48 hours of septic shock

The clinical signs measured (temperature, capillary refill time, oxygen saturation and blood pressure) and assessed (respiratory rate, heart rate, extremities, radial pulse characteristics and GCS) were recorded from the patient's records who were alive at 24 and 48 hours.

At 24 hours 31(62%) children were alive and all clinical signs of abnormal perfusion was measured/assessed in 26 (83.9%) children. At 48 hours 20(40%) children were alive and all clinical signs of abnormal perfusion was measured/assessed in 14 (70%) children. Figure 6 shows the clinical signs audited at 24 and 48 hours. Records of clinical signs at 24 and 48 hours were used for audit in this study.

clinical signs at 24 hours- temperature, respiratory rate and heart rate was measured in all 31 (100%) children. Radial pulse characteristics was assessed in 28(90.3%). Extremities were assessed in 26(83.9%). Capillary refill time was measured in 27(87.1%). GCS was measured in 29(93.6%). Oxygen saturation was measured in 28(90.3%). Blood pressure was only measured in 6(19.35%).

Clinical signs at 48 hours – temperature was measured in 19(95%) of 20 children. Respiratory rate and heart rate was assessed in all 20(100%). Radial pulse characteristics was measured in 19(95%). Extremities were assessed in 19(95%). Capillary refill time was measured in 15(75%). GCS was assessed in 18(90%). Oxygen saturation was measured in 16(80%). Blood pressure was only measured in 4(20%) children.

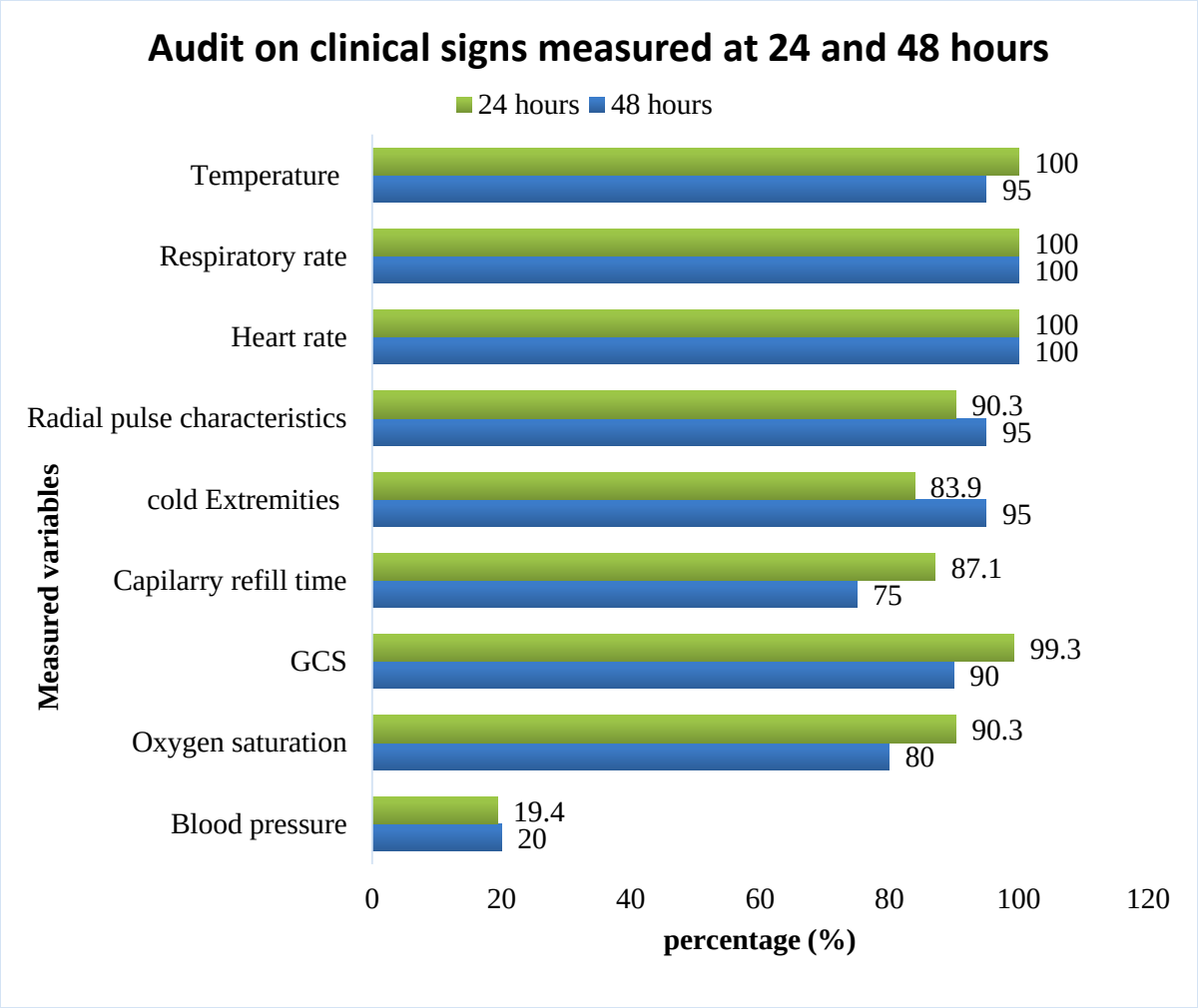


Figure 6: Audit of clinical signs at 24 and 48 hours of septic shock

At 24 and 48 hours, all alive children had at least one sign of abnormal perfusion hence all the alive children (for those whose signs of altered perfusion were measured) were still in septic shock. The results of the clinical signs are as shown in table 9. The measured variables were compared with table1 and figure 1(section 4.10)

Table 9:Clinical signs audited at 24 and 48 hours of septic shock

Sign	Audit at 24 hours			Audit at 48 hours		
	Measured (%)(n=31)	**Normal**	**Abnormal**	**Measured (%) (n=20)**	**Normal (%)**	**Abnormal (%)**
Temperature	31(100.0)	14(45.2)	17(54.8)	19(95.0)	12 (63.2)	7 (36.8)
Respiratory rate	31(100.0)	15(48.4)	16(51.6)	20(100.0)	16(80.0)	4(20.0)
heart rate	31(100.0)	19(61.3)	12(38.7)	20(100.0)	14(70.0)	6(30.0)
Radial pulse	28(90.3)	5(17.9)	23(82.1)	19(95.0)	9(47.4)	10(52.6)
Temperature gradient	26(83.9)	7(26.9)	19(73.1)	19(95.0)	13 (68.4)	6(31.6)
Capillary refill time	27(87.1)	2(7.4)	25(92.6)	15(75.0)	5(33.3)	10(66.7)
GCS	29(93.6)	0(0)	29(100.0)	18(90.0)	0(0)	18(100)
Oxygen saturation	28(90.3)	18(64.3)	10(35.7)	16(80.0)	9(56.3)	7(43.8)
Blood pressure	6(19.35)	3(50.0)	3(50.0)	4(20.0%)	2(50.0)	2(50.0)

Audit on management of septic shock at 24 and 48 hours.

Each element of care in septic shock was audited in reference to the surviving sepsis guidelines. Optimum care as per the guideline was only given to 2(6.5%) of 31 alive children at 24 hours and 4(20%) of 20 alive children at 48 hours

Audit on the measured variables at 24 and 48 hours.

Figure 7 shows the audited measured variables at 24 and 48 hours of diagnosis.

At 24 hours – Urine output was measured in 25(80.6%) of 31 children. Full dose of appropriate antibiotics as prescribed by the attending clinician was received in 25(80.65%). Blood was needed in 21(67.7%). Blood sugar, lactate and calcium was measured in 24(77.4%), 10(32.3%) and 5(50%) respectively. PICU/NICU was needed in all the children as they were still in septic shock. Mechanical ventilation was needed in 24(77.4%).

At 48 hours –urine output was measured in 18(90%) of 20children. Full dose of appropriate antibiotics was received in 19(95%). Blood was needed in 14(70%). Blood sugar, lactate and calcium was measured in 15(75%), 7(35%) and 4(20%) respectively. PICU/NICU was needed in all the children as they were still in septic shock. Mechanical ventilation was needed in 14(70.0%).

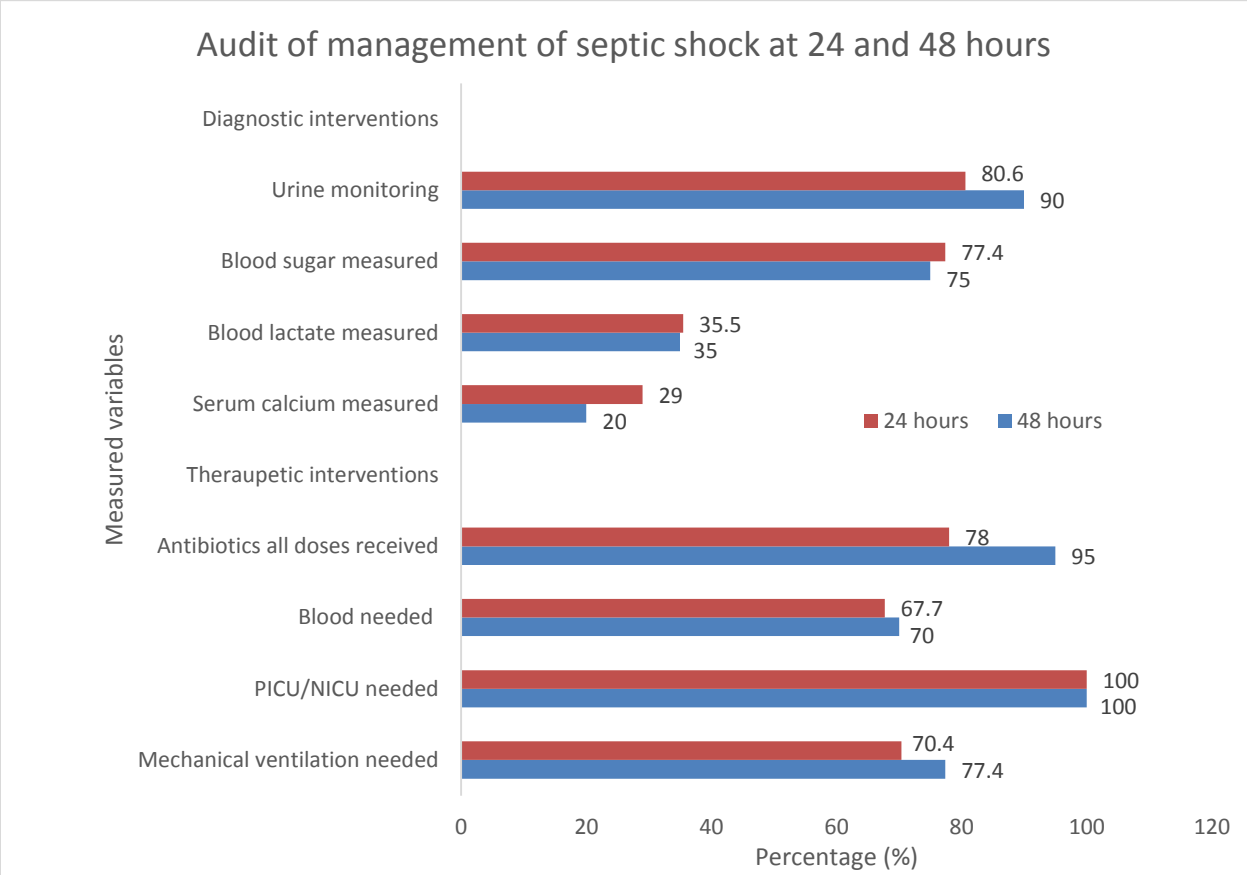


Figure 7:Audit of management of septic shock at 24 and 48 hours.

Audit on the results and interventions done of the measured variables

The results and interventions audited for the measured elements of care at 24 and 48 hours are described below. The interventions audited as per the guideline were requested by the attending clinician and documented in the file. The availability of the intervention is a shown in table 10.

At 24 hours – 10(40%) of 25 cases had reduced urine output. Appropriate antibiotics dose was not given in 6(19.3%) children due to lack of IV access, which was fixed in 5(83.3%) children before the next dose. Antibiotics were changed in 7(22.6%). Blood was only available for 2(9.5%). Hypoglycemia was corrected in all children and insulin was used in 1(10%) of 10 cases with hyperglycemia >10mmol/l. No child had calcium <1.0mmol/l and blood lactate>4mmol/l was seen in 5(50%) of 10 children. PICU/NICU was available in 2(6.5%) of 31 children. Most children 24(77.4%) required mechanical ventilation to maintain airway (GCS<8) and overall mechanical ventilation available in only 2(8.33%) of 24 children. Dopamine was used for one child while norepinephrine, epinephrine and hydrocortisone were not used in any child.

At 48 hours – 2(11.1%) of 18 children had reduced urine output. Appropriate antibiotics dose was not given 1(5%) child due to lack of IV access, which was fixed before the next dose. Antibiotics were changed in 1(5%) child. Blood was available for 3(21.4%). insulin was used in 1(10%) with hyperglycemia >10mmol/l. No child had calcium<1.0mmol/l and blood lactate>4mmol/l was seen in 2(28.6%) of 7 children. PICU/NICU was available in 4(20.0%). Most children 14(70.0%) required mechanical ventilation to maintain airway (GCS<8) and overall mechanical ventilation available in only 24(28.6%). Dopamine was used for 3(15.0%) of 20 children while norepinephrine, epinephrine and hydrocortisone were not used in any child

Table 10: Audit of interventions at 24 and 48 hours of septic shock.

Variable	Results among those measured		At 24 hours (alive=31)			At 48 hours (alive=20)		
			frequency (%)	Intervention		frequency (%)	Intervention	
				done	n (%)		Done	n (%)
Urine output	< 0.5mls/kg/hr		10(40.0)	Dialysis	0(0)	2(11.1)	Dialysis	1(50)
	≥0.5mls/kg/hr		15(60.0)	-	-	16(88.9)	-	
Antibiotic	Received all doses		25(80.7)	-	-	19(95.0)	-	
	Missed Dose	1	4(66.7)	IV access fixed	5(83.3)	1(100.0)	IV access fixed	1(100)
		2	2(33.3)			0		
	Antibiotics changed		7(22.6)	-		1(5.0)	-	
Blood	Needed		21(67.7)	Available	2(9.5)	14(70.0)	Available	3(21.4)
Blood sugar	<2.2mmol/l		2(8.3)	Corrected	2(100)	0	-	-
	>10mmol/l		10 (76.9)	Insulin	1(10)	6(85.7)	Insulin	1(16.7)
PICU/NICU	Needed		31(100.0)	available	2(6.5)	20(100.0)	Available	4(20.0)
Vasoactive agent	Needed		31(100.0)	Dopamine	1(3.2)	20(100.0)	Dopamine	3(15.0)
Mechanical ventilation	GCS<8		24(77.4)	Available	2(8.3)	14(70.0)	Available	4(28.6)

OUT COME OF SEPTIC SHOCK IN 72 HOURS

The overall mortality among 50 children with septic shock followed up for 72 hours was 35(70.0%). Median time of death was 14 hours and the mode was 6 hours.

Half of the children enrolled with septic shock died within 24 hours. Children who died in ≤24 hours were 19(54.3%), those that died between >24 to ≤48 hours were 11(31.4%) and those who died between >48 to ≤72 hours were 5(14.3%).

At 72 hours, infants had the highest proportion of mortality 19(54.29%), followed by neonates 11(31.3%) and 12 – 59 months 5(14.3%).

0ut of the 35 children who died 22(62.86%) were female and 13(37.14%) were male.

From the referred children 29(85.3%) of 34 children died and all 6 children who were not referred died.

Case fatality of septic shock

The case fatality of septic shock in 72 hours is shown in figure 9. The case fatality of < 1 month was 55.0%, 1 – 11 months was 82.6 % and 12 – 59 months was 71.4 %.

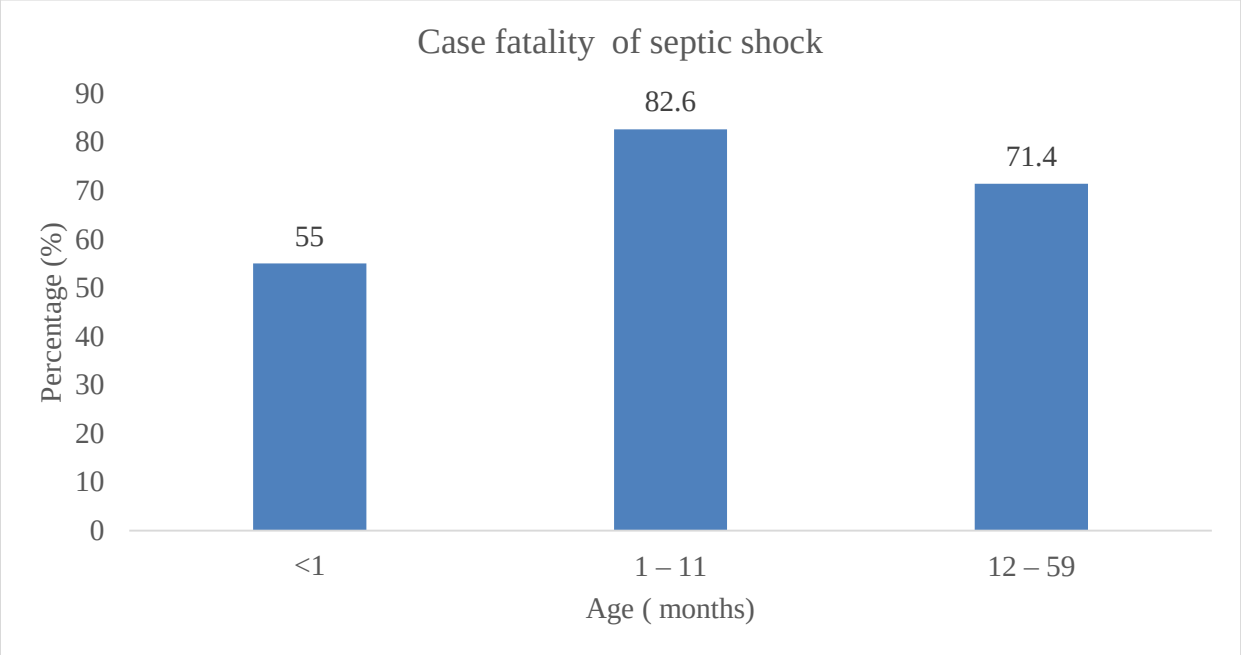


Figure 8:Age distribution and Case fatality in 72 hours of septic shock

Association of mortality with demographic and measured variables.

Time of death, age, sex was not significantly associated with mortality but admission as a referral from another hospital was significant as shown in table 11. Infants have a higher odds ratio of dying as compared to 12 – 59 months but this was not statistically significant. The odds of dying within the first 24 hours was high as compared to >48 – ≤72 hours but not statistically significant.

Table 11:Association of Mortality of demographic variables with septic shock at 72 hours.

Variable	Characteristic	Frequency		Odds ratio (95%CI)	P value
		Died	Alive		
Time	≤ 24	19	31	1.83 (0.58 – 5.88)	0.71
	>24 – ≤ 48	11	20	1.65 (0.47 – 5.77)	0.83
	>48 – ≤ 72	5	15	Reference	
Age (months)	<1	11	20	0.77 (0.20 – 3.00)	0.30
	1 – 11	19	23	1.16 (0.32 – 4.24)	0.43
	12 – 59	5	7	Reference	
Sex	Female	22	10	0.85 (0.24 – 3.02)	0.79
	Male	13	5	Reference	
Referral	Yes	29	5	2.89 (1.16 – 7.20)	0.02
	No	6	0	Reference	

Association of mortality with measured variables

Measured variables during initial recognition and management were analysed using odds ratio to mortality as shown in table 12. Low blood pressure and unavailability of mechanical ventilation was significantly associated with mortality.

Table 12:Association of mortality with measured variables on admission with septic shock.

Variable	Characteristic	Frequency		Odds ratio (95%CI)	P value
		Died	Alive		
Blood pressure	Low	25	3	10.0 (2.31 – 43.16)	<0.01
	Normal	10	12	Reference	
Mechanical ventilator	Needed	32	10	5.33 (1.08 – 26.36)	0.04
	Not needed	3	5	Reference	

CHAPTER 6: DISCUSSION

This study was set out to determine the prevalence, audit the management and determine the outcome in 72 hours of paediatric septic shock at the Kenyatta National Hospital over a period of 2 months. To our knowledge this is the first study on septic shock in children in our region. The prevalence of paediatric septic shock among 325 children admitted at KNH was 15.4%, which is higher than other similar studies done globally. Study done by Ganjoo et al, at a referral centre in Northern India of children aged (0 - 12years) diagnosed with septic shock showed prevalence of 2.2% of all admitted children (9). The prevalence of septic shock may have been higher in our study partly because three quarter of children studied were referrals from another hospital, where there may have been a delay in recognition of septic shock or transfer to KNH for better management of the condition.

The male: female ratio was 1:1.8 in our study while in some studies males were found to have higher proportion of septic shock. Study done by Bindle et al in 2003 found male: female ratio as 2:1, While a study done by Giatte et al. in 2011 found almost equal male: female ratio before implementation of septic shock guideline and higher female ratio after implementation of the guideline (47,48). Male gender has been associated with high mortality in sepsis and since most of our children were referrals from other public facilities, they may have died at the peripheral hospitals where shock may not have been recognized and promptly transferred to KNH. The study population was not systematically selected hence it is difficult to assess reason for high female proportion of septic shock.

In this study, a quarter of neonates admitted had septic shock which is much higher than other similar studies done but admitted to NICU. Study by Arizaga et al. in two hospitals in Mexico prevalence of neonatal shock admitted to NICU was found in 12.7% of all neonatal admissions (13). The reasons for high neonatal prevalence were not explored but may be due to delay in recognition of septic shock and early transfer, poor health seeking behaviour and maternal education before discharge on neonatal danger signs.

Infants comprised the highest number of admissions and diagnosis of septic shock. A study by Giatte Larsan et al. done in 2011 showed infants had the highest prevalence of septic shock (48). This can be explained by the low immune state of the infants which predisposes them to sepsis(49). The median age of septic shock was 4 months in this study while the median age was

6 months (excluded neonates) in a study done by Larsen et al in 2011 (48). Our results in this study shows, the diagnosis of septic shock reduces with increasing age. In our study, no child was diagnosed with septic shock above 5 years of age, hence our main focus should be on children under 5 years of age.

Septic shock was only recognized in 56% of the cases by the attending clinician on admission and missed in 44%. The recognition of septic shock is lower than a study done by Raina et al in 2002, which showed septic shock was recognized in 79% of the patients after use of guideline(50). An adherence to PALS guidelines done by Paul et al. in 2012 showed a similar 79% of recognition of septic shock after the guidelines were used (50). Only 11.4% cases had septic shock recognized from other public health facilities and referred to KNH for further management. Lack of awareness and training on recognition of septic shock, availability of local septic shock guidelines and toolkit for use in emergency unit may be hindrance factors in recognition of septic shock in children.

Recognition of shock was based on clinical signs of suspected sepsis, SIRS and signs of hypoperfusion as per Surviving Sepsis 2014 and WHO 2016 Guidelines(2,5). All children admitted with septic shock were found to be in cold shock, this suggests children were being diagnosed late in to the illness (33). Similar studies show cold shock is commoner in children such as in a study done by Khilani et al. and Brierley et al. (35,51). Hypotension is usually seen late in paediatric septic shock and this was found in 56% of septic shock children. Elevated systemic vascular resistance makes hypotension a late sign of septic shock in children.

From this study, management of septic shock is a big challenge at KNH just like many other public hospitals in developing countries. Using the Survival Sepsis 2014 and WHO 2016 Guidelines, not all the steps on management were followed in the initial first hour of management of septic shock (2,5). The individual monitored variables ranged from 0 % (PICU/NICU availability) to 100% (oxygen administration). All patients in this study were in fluid refractory shock and none of them received ionotropic and PICU or NICU care in the first one hour. The reasons behind inadequate management of septic shock were not fully explored in this study, but the following reasons were noted. Lack of knowledge on septic shock management, blood products unavailability when needed, inadequate laboratory support, staff shortages, unavailability of infusion pumps to give vasopressors in emergency departments,

monitors, PICU/NICU and unavailability of local septic shock tool kits and guidelines. This is a major limitation in resource limited countries globally. Khilani et al. reported similar findings in 2010(35). Since this is the first study on paediatric septic shock in Kenya, our results cannot be compared to any other study locally, but studies done in other parts of the world shows improvement in management steps of septic shock after educating health workers and implementation of guidelines. One such study done in Utah by Gitte et al showed improvement in compliance to individual care element after use of guidelines(48). A study done by Paul et al. in 2012 showed all steps were not followed of individual care variables even in the presence of guidelines. The adherence to fluid management and inotrope use in the first hour was at 35 %. Antibiotics were given in 78% of all children (50). Hence training of health care workers on septic shock remains critical.

The initial 72 hours are critical in the management of septic shock and individual optimum care shows improvement in survival(31,44). In the continuation of septic shock care at 24 and 48 hours, clinical signs were recorded in a range of 19-100%. Inappropriate care given at 24 hours was considered inappropriate at 48 hours. Blood pressure was only done in 19.4% children at 24 hours and 20% at 48 hours. This can be explained by lack of proper cuffs in the wards and lack of knowledge on care of septic shock. Very few children received optimum care at 24 and 48 hours. A study done in Cuba by Cartaya et al, showed even after implementation of guidelines, the steps in management were not fully followed appropriately (15). KNH has limited intensive care resources in terms of PICU/NICU availability, hence only few children manage to receive this care. All children alive at 24 and 48 hours whose clinical signs were measured still had signs of septic shock. This means the very sick children died earlier hence the number of living children were less at 48hours. There is no similar study to compare 24 and 48 hours of audit of septic shock as most studies focus on the 1st one hour which is the golden hour in septic shock.

The mortality within 72 hours of septic shock in this study was 70%. Most studies look at mortality of children admitted with septic shock in PICU/NICU but our mortality rate is for children in the wards as most of our children with septic shock were managed in the wards due to unavailability of PICU/NICU beds. A study done by Makhija et al. in New Delhi found mortality at 70 % in 4 days follow up (45). Study done by Desy et al. in Indonesia shows mortality of 88.2% with an average stay of 4 days relating to delay in recognition of septic shock, lack of PICU infrastructure, understaffing and limited access to health care (4). An Indian study done by

Kaur et al. in Haryana shows mortality of 50.8% children(52). The high mortality in our study was due to unavailability of early intensive care, delay in recognition, delay in transfer from other public health facilities to KNH, lack of knowledge on septic shock and unavailability of local guidelines for use in limited resource setting, but in this study, we did not evaluate the reasons of high septic shock mortality.

Mortality was highest in the first 24 hours of admission of septic shock (54%). Children who were referred from other public hospitals and diagnosed with septic shock on admission at KNH were significantly associated with high mortality. This high mortality may be due to late referrals as all children presented with cold shock and unavailability of PICU/NICU care at KNH in the first hour of recognition of septic shock.

In this study mortality in 72 hours is not significantly predicted individually by age of the child with septic shock, sex and duration of stay in the hospital. Similar results were found in an Indian study done in Haryana by Kaur et al.(52). Infants had the highest case fatality in our study. Other studies done by Larsen et al. shows similar results but Cartaya et al. found infant mortality was low in a Cuban PICU(15,48).

Hypotension was independently significantly associated with high mortality in 72 hours and a study done by Cartaya et al. found similar findings(15). Children diagnosed with septic shock and needed ventilator care regardless of the reason was significantly associated with high mortality. From this audit, no child received mechanical ventilator care at the 1st hour of management. This can be explained by unavailability of PICU/NICU beds at KNH due to limited intensive care resources.

Strengths

This was a study done in one hospital and the results may not be generalizable but, it is among the first study in Africa to document on the prevalence, audit on management of paediatric septic shock and outcome in 72 hours,

The findings of this study provide valuable information for improving recognition and management of septic shock. This is possible by aiding identification of knowledge gaps.

This study carried out over 72hours, provided a relative quick way in obtaining information on prevalence, management and outcome of septic shock.

Limitation

Poor documentation may have affected the results on audit of management provided to the children with septic shock.

Accuracy of clinical observation of the clinical signs audited may be different between individual health workers affecting the accuracy of audit data.

The investigator assisted in resuscitation when required (due to ethical reasons) and this may have affected the accuracy of audit data.

It is difficult to determine whether high rates of mortality were a result of inadequate access to PICU/NICU care or due to late referral.

CHAPTER 7: CONCLUSION, RECOMMENDATION AND CONFLICT OF INTEREST

7.1 Conclusion

The prevalence rate of septic shock is 15.4% among children aged 0 – 12 years admitted at KNH. Septic shock was recognized by the attending clinician at KNH in only about half of the patients admitted with septic shock. Optimal care as per the Surviving Sepsis Guidelines is a challenge at KNH due to limited intensive care resources. Appropriate care was provided in 0%, 6.5% and 20% at 1st, 24, 48 hours respectively. The mortality among children with septic shock is high at 70% in 72 hours of diagnosis of septic shock.

7.2 Recommendations

1. Early recognition and management of septic shock requires continues training of health care workers to create awareness and improve care.
2. There is need to include septic shock management guidelines in our local Kenyan paediatric guidelines, to improve management and outcome among children diagnosed with septic shock.

7.3 Conflict of interest

There was no conflict of interest.

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APPENDIX I Study time line

ACTIVITY	NOV 2016	JAN-FEB	APR-JUL	AUG	SEP- OCT	NOV- DEC	JAN -MAY 2017	JUNE
Research concept								
Proposal development								
ethical review.								
Pretesting questionnaire								
Data collection								
Data analysis								
Thesis writing								
Thesis submission								

APPENDIX II: Budget

Category	**Remarks**		**Units**	**Unit Cost (Kshs)**	**Total Cost (Kshs)**
Proposal development	Printing draft		3	700	2100
	Proposal photocopies		10	250	2500
Data collection	Questionnaire	printing	1	90	90
		photocopying	350	27	9450
	Consent and assent forms	Printing	1	25	25
		Photocopying	350	15	5250
	Stationery packages (pens, file, staple, paper punch, folder)		2	1000	2000
	Research assistants		3	20000	60000
Equipment	Alcohol swabs		350	5	3500
	Thermometer		1	350	350
	Digital timer		1	500	500
	Pulse oximeter		1	5500	5500
	Sphygmomanometer		1	15000	15000
Data analysis	Statistician		1	30000	30000
Poster	Printing		1	2000	2000
Thesis write up	Printing thesis		10	1000	10000
	Final thesis binding		7	500	3500
Contingency funds					20000
Total					**171,765**

APPENDIX III: Consent form

Consent information document in English

Date: _____

Study Title: **PREVALENCE AND MANAGEMENT OF SEPTIC SHOCK AMONG CHILDREN ADMITTED AT THE KENYATTA NATIONAL HOSPITAL**

Introduction:

I am a postgraduate student at the University of Nairobi, pursuing studies leading to specialisation in Paediatrics and Child Health. I wish to request for your permission, for your child to participate in a study that will form part of my degree work. The study will involve requesting you to allow me examine your child for septic shock and an audit of the management if he/she has septic shock for 48 hours. This will be recorded and analysed for research purposes only.

Purpose of the study:

The purpose of this study is to determine the prevalence and to audit the management of septic shock among children aged 0 days to 12 years admitted at the Kenyatta National Hospital and determine the outcome within 72 hours of admission. The information gathered will help in improving knowledge on management of children with septic shock.

Investigator: Dr. Varsha V. Hirani

Paediatric resident, university of Nairobi

P. O. Box 39259-00623. Nairobi

Mobile: 0735360831

Lead supervisor: Dr Rashmi Kumar

Consultant critical care paediatrician, University of Nairobi.

P. O. Box 49872

Mobile: 0733733505

KNH- UON ERC secretariat

Telephone: 2726300 extension 44355

Kenyatta National hospital

Nairobi

Background:

Paediatric septic shock is a major cause of morbidity and mortality in all parts of the world mainly due to acute haemodynamic compromise. Early recognition and early goal directed therapy has been associated with improved outcomes. Early recognition is fundamental as the pathophysiologic consequences of septic shock are devastating.

Study Procedures:

Children aged 0 days to 12 years will be included in the study. The enrolled participant being admitted to KNH paediatric wards/ PICU/NBU after obtaining an informed consent or assent will undergo a focused clinical exam to diagnose septic shock. Children diagnosed with septic shock will undergo audit on their management from time of diagnosis to 48 hours. The data will be filled in the questionnaire. The outcome of the patient will be recorded within 72 hours.

Benefits:

An audit of the management will help in appropriate care of your child. If the diagnosis of septic shock was missed the clinician will be alerted. The results of the research will also be used by the healthcare providers in to help improve the care we provide to hospitalized children.

Risks:

There will be no harm or risks anticipated to your child during the study. There will be no invasive procedures carried out in the study that may harm your child.

Voluntariness:

The study will be fully voluntary. There will be no financial rewards to your child for participating in this study. One is free to participate or withdraw from the study at any point. Refusal to participate will not affect the management of your child in any way.

Confidentiality:

The information obtained about your child will be kept in strict confidence. No specific information regarding your child will be released to any person without your written permission. We will, however, discuss general overall findings regarding all children assessed but nothing specific will be discussed regarding your child's condition. Your child's study identity number will be used for follow up in the wards/PICU/NBU for 72 hours and will not be revealed to anyone.

Problems or Questions:

If you ever have any questions about the study or about the use of the results you can contact the principal investigator, Dr. Varsha V. Hirani by calling on 0735360831

If you have any questions on your rights as a research participant, you can contact the Kenyatta National Hospital Ethics and Research Committee by calling 2726300 extension 44355.

Consent form

PREVALENCE AND MANAGEMENT OF SEPTIC SHOCK AMONG CHILDREN ADMITTED AT THE KENYATTA NATIONAL HOSPITAL

Investigator: Dr. Varsha V. Hirani

Paediatric resident, university of Nairobi

P. O. Box 39259-00623. Nairobi

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Lead supervisor: Dr Rashmi Kumar

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Kenyatta National hospital

Nairobi

I _____having received adequate information regarding the study research, benefits and risks hereby AGREE / DISAGREE (Cross out the appropriate) to participate in the study with my child. I understand that our participation is fully voluntary and that I am free to withdraw at any time. I have been given adequate opportunity to ask questions and seek clarification on the study and these have been addressed satisfactorily.

Parents/Guardian's Signature: _____Date_____

I _____ declare that I have adequately explained to the above participant; the study procedure, benefits and risks and given him /her time to ask questions and seek clarification regarding the study. I have answered all the questions raised to the best of my ability.

Investigator's Signature_____Date_____

FOMU LA KUTOA IDHINI YA KUSHIRIKI KATIKA UTAFITI

Tarehe_____

Kichwa cha Utafiti:

KIWANGO CHA MAAMBIKIZI NA USIMAMIZI YA UGONJWA WA SEPTIC SHOCK KATI YA WATOTO WANAYOLAZWA KWENYE HOSPITALI KUU YA KENYATTA.

Kutambuliza Kwanza:

Mimi ni mwanafunzi uzamili yeneye chuo kikuu ya Nairobi, na soma utalam ya watoto. Na penda kuomba ruhusa kama mtoto yako anaweza kuchunguzwa kwa hii utafiti, ni vile inatakikana kwa masomo yangu. Utafiti huu ita kuhushisha nipewe ruhusa kuchunguza ugonjwa wa septic shock kwa mtoto wako. Mtoto akipatikana na ugonjwa wa septic shock nita fuatilia matibabu anayopewa kwa saa 72. Habari nitazipata ita angaliwa na kutumiwa kwa utafiti peke yake.

Lengo wa utafiti:

Lengo la utafiti huu ni kuchunguza usamimizi wa ugonjwa wa septic shock kati ya watoto umri 0-12 umri na matibabu wanaopata kwenye hospitali kuu ya Kenyatta. Utafiti huu uta chunguza usamimizi kwa watoto walikosewa ku pimwa Ugonjwa wa septic shock na matokeo kwa saa ya 72 kutoka mtoto alazwe hospitali. Habari kutoka uatfiit huu ita tumiwa kuongeza elimu kutibu watoto wanapimwa na ugonjwa wa septic shock.

Mtafiti Mkuu:

Daktari Varsha Hirani,

mwanafunzi wa shahada kuu ya matibabu maalum ya watoto, Chuo Kikuu cha Nairobi.

Nambari ya posta: 39259-00623

simu: 0735360831

Msamizi Mkuu:

Daktari Rashmi Kumar

Matibabu ya watoto, chuo Kikuu cha Nairobi.

Nambari ya Posta:49872

Simu: 0733733505

KNH-UON ERC secretariat,

Simu: 2726300 extension 44355

Nairobi

Habari muhimu

Ugonjwa wa septic shock kwa watoto ni sababu kubwa ya magonjwa and kifo. Hiyo ni kwa sababu ina haribu gafla wile mwili ina fanya kazi. Ikipatikana mapema na matibau ikianzishwa kwa haraka, matokeo inakuwa mzuri. Kutambuliwa mapema ni muhimu sana vile matokeo ya ugonjwa wa septic shock ni mbaya sana.

Utaratibu wa utafiti

Watoto wenye umri siku sufuri mpaka mwaka kumi na mbili watakuwa kwa utafiliti huu. Wale watoto wata lazwa kwa ward/PICU/NBU na wazazi/watoto juu ya mwaka nane wame piga ishara, wata angaliwa kama wakona ugonjwa wa septic shock. watoto wakipatikana na ugonjwa wa septic shock, ukaguzi utafanyiwa kutaoka saa huu mpaka saa 48. Matokeo ya ugonjwa wa septic shock ita andikiwa ndani ya saa 72.

Faida ya Utafiti huu:

Ukaguzi ya maambikizi itawasaidia kupata huduma sahihi kwa mtoto wako. Utafiti huu pia utatumikana wasika dau wa secta ya afya ili kuhakikisha huduma bora zimetolewa kwa watoto ambao wamelazwa hospitalini.

Athari ya Utafiti huu:

Hakutakuwa na athari zozote wakati utafiti huu utakapotumika kwa motto wako. Hakuna vamizi taratibu itatumiwa kwa hii utafiti yenye ita letea athari kwa mtoto wako

Kushiriki Utafiti:

Kushiriki utafiti huu ni kwa hiari yako mwenyewe. Hakuna fedha utapewa kushiriki kwa hii utafiti. Una haki ya kukataa kushiriki au hata kujiondoa kutoka utafiti huu wakati wowote. Kukataa kushiriki au kujiondoa kwako hakutaadhiri huduma zitakazotolewa kwako au kwa mtoto wako.

Usiri wa habari za utafiti

Tutaajibika kulinda habari zote tutakozopata kuhusu mtoto wako wakati na baada ya utafiti huu ili kuhakikisha habari hizo ni siri ya hali ya juu kati yetu na wewe. Hakuna watu au idara zozote zitakazopata habari hizo bila ya idhini yako. Hata hivyo tutaongelea mambo kwa ujumla kulingana na utafiti wa watoto wote na hakuna kitu kitazungumziwa kuhusu afya ya mtoto wako peke yake. Nambari ya utafiti zitatumika kwa ajilia kufuatilia mtoto wako kwa wodi/PICU/NBU kwa saa 72 na hazita tangazwa kwa mtu yoyote.

Matatizo au maswali

Kama ukona maswali yoyote juu ya hii utafiti ama matokeo yah ii utafiti una weza kuwasiliana na mtafiti mkuu wa hii utafiti daktari Varsha V. Hirani na kupiga simu nambari 0735360831

Ukiwa na maswali yoyote juu ya haki yako kama mshiriki yah ii utafiti unaweza kuwasiliana na kamati ya hospitali kuu ya maadili na utafiti kwa kupiga nambari 2726300 ugani 44355

FOMU LA KUTOA IDHINI YA KUSHIRIKI KATIKA UTAFITI

KIWANGO CHA MAAMBIKIZI NA USIMAMIZI YA UGONJWA WA SEPTIC SHOCK KATI YA WATOTO WANAYOLAZWA KWENYE HOSPITALI KUU YA KENYATTA.

Mtafiti Mkuu: Daktari Varsha Hirani,

mwanafunzi wa shahada kuu ya matibabu maalum ya watoto, Chuo Kikuu cha Nairobi.

Nambari ya posta: 39259-00623

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Msamizi Mkuu: Daktari Rashmi Kumar

Matibabu ya watoto, chuo Kikuu cha Nairobi.

Nambari ya Posta: 49872

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Nairobi

Mimi_____kuwa nime pokea habari kuhusu utafiti hii, faida and athari kukubaliana/ kukataza (kata jibu sahihi) kushiriki kwa utafiti hii. Naelewa kushiriki ni kikamilifu hiari na naweza kujiondoa saa yoyote. Nipepatiwa mda wa kutosha kuuliza maswali na kupata ufafanuzi kwa utafiti hii na hizi zote zime shugulikiwa.

Sahihi ya mzazi/mlezi_____ Tarehe_____

Mimi_____natangaza nime eleza ya kutosha kwa mshiriki hapo juu, utatatibu ya utafiti, faida na athari. Nimepea mda wa kuuliza maswali na kupata ufafanuzi kuu yah ii utafiti. Nime jibu maswali yote kwa uwezo yangu.

Sahihi ya mtafiti/mtafiti msaidizi_____ Tarehe_____

APPENDIX IV: Assent form

In English

STUDY TITLE: PREVALENCE AND MANAGEMENT OF SEPTIC SHOCK AMONG CHILDREN ADMITTED TO KENYATTA NATIONAL HOSPITAL

Investigator: Dr. Varsha V. Hirani

Paediatric resident, university of Nairobi

P. O. Box 39259-00623. Nairobi

Mobile: 0735360831

Lead supervisor: Dr Rashmi Kumar

Consultant critical care paediatrician, University of Nairobi.

P. O. Box 49872

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KNH- UON ERC secretariat Telephone: 2726300 extension 44355

Kenyatta National hospital

Nairobi.

Why are we doing this study?

We are doing a study to know, how many children get admitted with septic shock and how they are being treated at Kenyatta National Hospital.

Why are you being asked to participate in the study?

You are being asked to participate in this study and to allow us examine you for septic shock and to know how you will be managed.

What will happen during this study?

You will be examined (no injections or any blood will be taken) which will take a few minutes but if found to have septic shock you will be followed for 3 days.

What are the good things that will happen in this study?

The study will benefit you in prompt diagnosis and management if found to have septic shock.

What are the problems that may happen in the study?

There will be no risk to you if you participate.

Who will be told the findings we learn about in this study?

No one will know about your findings and will be used for this study only.

Will you get any money or gifts from this study?

You will not get any gifts/ money for participating in this study.

Who should you ask if you have any questions?

You will ask Dr. Varsha Hirani at any time during the study.

What if you change your mind?

If you change your mind to leave the study no one will be upset or angry with you and your doctor will continue treating you.

If you don't want to be in the study, don't sign this paper. No one will be upset with you if you don't sign.

If you sign this paper it means you have read and understood the above information, and agree to participate in this study.

Your signature_____Date_____

Signature of person obtaining assent_____Date_____

Printed Name of Person Obtaining assent_____

FOMU LA ASSENT

Kichwa cha Utafiti:

KIWANGO CHA MAAMBIKIZI NA USIMAMIZI YA UGONJWA WA SEPTIC SHOCK KATI YA WATOTO WANAYOLAZWA KWENYE HOSPITALI KUU YA KENYATTA.

Mtafiti Mkuu: Daktari Varsha Hirani,

mwanafunzi wa shahada kuu ya matibabu maalum ya watoto, Chuo Kikuu cha Nairobi.

Nambari ya posta: 39259-00623

simu: 0735360831

Msamizi Mkuu: Daktari Rashmi Kumar

Matibabu ya watoto, chuo Kikuu cha Nairobi.

Nambari ya Posta: 49872

Simu: 0733733505

KNH-UON ERC secretariat- Simu: 2726300 extension 44355

Nairobi.

Kwa nini tuna fanya utafiti huu?

Tunafanya utafiti kuangalia watoto wangapi wana lazwa na ugonjwa wa septic shock, na vile wanatibiwa kwenye hospitali kuu ya Kenyatta.

Kwa nini una ulizwa kushiriki kwa huu utafiti?

Wewe unaulizwa kushiriki kwa huu utafiti na kupeya ruhusa ya kuchunguza.

Nini ita fanyika kwa huu urafiti?

Kwa huu utafiti uta chunguzwa (hakuna shindano au damu ita tolewa) kwa dakika kadha. Kama ukipatikanan na ugonjwa wa septic shock, utafuatiliwa siku tatu.

Nini vizuri zitafanyika kwa huu utafiti?

Ukipatikana na ugonjwa wa septic shock, itatibiwa mapema

Shida gani inayaweza tokea kwa huu utafiti kwako?

Hakuna madhara utaya pata kwa huu utafiti.

Nani atamwambiwa matokeo tutayapata kwa huu utafiti?

Hakuna mtuu atayejua matokeo yako na ita tumiwa kwa utafiti peke yake.

Je' utapata zawadi au pesa yoyote kutoka huu utafiti?

Hakuna zawadi au pesa uta fata kushiriki kwa utafiti huu.

Ukiwa na maswali uta uliza nani?

Ukiwa na maswali yote, uliza daktari Varsha Hirani.

Je' ukibadilisha mawazo yako itakuwaje?

Uki badilisha mawazo yako, ukitoka hakuna mtu ataye kasirika na daktari yako ataendelea na matibabu.

Kama hutaki kushiriki usitie sahihi kwenye karatasi hili. Kukataa kushiriki ni sawa nahakuna atakaye kasirika ukikataa.

Ukitiasahihi kwenye karatasi hili, unakubali kushiriki katika utafiti huu.

Sahihi lako_____ Tarehe _____

Sahihi la muombaidhini _____ Tarehe_____

Jina la muombaidhini _____

APPENDIX V: Questionnaire

STUDY TITLE

PREVALENCE AND MANAGEEMNT OF SEPTIC SHOCK AMONG CHILDREN ADMITTED AT THE KENYATTA NATIONAL HOSPITAL.

(A) DEMOGRAPHIC DATA

1. Study identity number: _____
2. Date of admission: date_____month___ year____
3. Date of data collection: date_____month____year_____
4. Time of admission: _____AM / PM (circle the appropriate)
5. Date of birth: date____month____year____
6. Age: days_____ months____years_____
7. Gender: female____ male____ (tick the appropriate)
8. Is the child a referral from another health facility? (Tick the appropriate)

   (1)Yes_____ (2) No _____

9. Weight of the child_____Kg.
10. In which unit is the child admitted
    1) Ward_____ Specify which ward_____
    2) Paediatric intensive care unit_____
    3) New born unit____

FOCUSED CLINICAL EXAMINATION ON ADMISSION:

TABLE A: Fill in the obtained values during examination in column 1. Compare the obtained values with table 1 and figure 1 to TICK (√) column 2 or 3 appropriately.

	COLUMN 1	COLUMN 2	COLUMN 3	SIGNS MISSED BY CLINICIAN
SIGNS	UNIT	NORMAL	ABNORMAL	
11. Core rectal temperature	^{0}centigrade	0)	1) Low	
			2) High	
12. Respiratory rate	/minute	0)	1) low	
			2) High	
13. Oxygen saturation (pulse oximetry)	%	0)	1) <90%	
			2) ≥90%	
14. Pulse rate	/minute	0)	1) Low	
			2) High	
15. Radial Pulse characteristic	--	0)	1)bounding	
			2)Weak/thready/absent	
16. Extremities	--	0)	1)Warm and flushed	
			2)Cold and mottled	
17. Capillary refill	seconds	0)1-2 seconds	1) <1 second	
			2) >2 seconds	
18. Mental state	GCS /15	0)	1)GCS< 15	
19. Blood pressure	/ Mm/Hg	0)	1) Low	

DIAGNOSIS OF SEPTIC SHOCK

20. Septic shock diagnosis (must have abnormal signs 11. With 12. or 14. and abnormal signs 15-18. - from TABLE A)
    1) Present_____ (If patient has septic shock is present proceed to audit part of the questionnaire)
    2) Absent_____

21) recognized by clinician (tick the appropriate)

1) Yes____ 2) No____

AUDIT ON THE MANAGEMENT

INITIAL AUDIT ON MANAGEMENT OF SEPTIC SHOCK

21. Was oxygen support given? (tick the appropriate)
    1) Yes_____
    2) No_____

22. Blood sugar
    1) Was blood sugar measured?
        i. Yes_____ (if yes proceed to b)
        ii. No____
    2) What was the random blood sugar? _____mmol/litre (if < 2.2mmol/l proceed to c).
    3) Was hypoglycaemia corrected?
        iii. Yes_____ amount of 10% dextrose given? _____mls/kg
        iv. No_____

23. Fluid therapy
    1) What amount of fluid was given during initial resuscitation? _____mls/kg
    2) Number of fluid bolus given? _____

24. antibiotic administration
    1) State the time of 1st dose of antibiotic given _____AM /PM (circle the appropriate)
    2) Blood culture done_____ if not done tick the reason
        i. Not ordered by attending clinician ____
        ii. no culture bottle available_____
    3) What antibiotics were administered?
        i. _____
        ii. _____
        iii. _____

25. Blood lactate levels

1) Was blood lactate levels done?
    i. Yes_____ measured value ____mmol/l
    ii. No_____

26. Serum calcium levels

1) Was calcium measured? (tick the appropriate):
    i. Yes_____ (if calcium is ≤1.1mmol/l go to 2)
    ii. No_____
2) Was hypocalcaemia corrected?
    i. Yes_____
    ii. No_____

27. Urine monitoring

1) Was urine monitoring instituted? (tick the appropriate)
    i. Yes_____ (if yes go to b)
    ii. No_____
2) What method was used? (tick the appropriate)
    i. Urine catheter_____
    ii. Urine collector_____
    iii. Weighing of diaper_____

28. Blood

1) Was blood required (tick the appropriate)
    i. Yes_____ (if yes go to b)
    ii. No_____
2) Was it available?
    i. Yes____
    ii. No____

29. Fluid refractory shock (presence of signs of hypoperfusion after 2 boluses of fluids)

1) Was PICU/NICU available at that moment? (tick the appropriate)
    i. Yes_____ (if yes proceed to question 10)
    ii. No_____

30. PICU/NICU care

1) Vasoactive agent use
    i. What vasoactive agent was used?
        1. Dopamine_____dosage_____µg/kg/min.
        2. Norepinephrine_____dosage_____µg/kg/min.
        3. Epinephrine_____dosage_____µg/kg/min.
        4. Hydrocortisone_____dosage_____mg/kg.

2) Mechanical ventilation needed? (tick the appropriate)
    i. No_____
    ii. Yes_____ (if yes go to 1 and 2)
        1. Is it available?
            1) Yes___
            2) No_____
        2. Why was it needed? (tick the appropriate)
            1) GCS≤8_____
            2) Metabolic acidosis_____
            3) Respiratory failure_____

AUDIT ON THE MANAGEEMNT AT 24 AND 48 HOURS AFTER INITIAL RESCUSITATION

TABLE B: Fill in the signs done by the attending clinician at 24 hours and 48 hours appropriately and fill column 1 (if not done state **not done** in column 1). Compare obtained values with table 1 and figure 1 to TICK (√) column 2 or 3 appropriately.

	AUDIT AT 24 HOURS			**AUDIT AT 48 HOURS**		
	COLUMNS			COLUMNS		
	1	2	3	1	2	3
SIGNS	UNIT	N.	ABNORMAL	UNIT	N.	ABNORMAL
31. 32. Core rectal temperature	____^{0}C	1)	2)Low 3)high	_____^{0}C	1)	2)Low 3)High
33. Respiratory rate	/minute	1)	2)low 3)High	____/minute	1)	2)Low 3)High
34. Oxygen saturation	%	1)	2)<90% 3)≥90%	%	1)	2)<90% 3)≥90%
35. Heart rate	____/minute	1)	2)Low 3)High	____/minute	1)	2)Low 3)High
36. Radial Pulse characteristic	--	1)	2)bounding 3)Weak/thready/absent	--	1)	2)bounding 3)Weak/thready/absent
37. Extremities	--	1)	2)Warm and flushed 3)Cold and mottled	--	1)	2)Warm and flushed 3)Cold and mottled
38. Capillary refill	____seconds	1)	2)<1 second 3)>2 seconds	____seconds	1)	2) <1 second 3)>2 seconds
39. Blood pressure	____ /____ MmHg	1)	2)low	____ /____ MmHg	1)	2)Low
40. Mental state	GCS____/15	1)	2)GCS< 15	GCS ____/15	1)	2)GCS< 15

KEY: - N- normal

AUDIT ON THE MANAGEMENT AT 24 HOURS AND 48 HOURS

Table C: Tick appropriately as required and fill in the measured values where applicable

MANAGEMENT	**AUDIT AT 24 HOURS**	**AUDIT AT 48 HOURS**
41. URINE OUTPUT	1)YES_____ What Amount of urine was measured? i.<0.5mls/hour___Dialysis____ ii.>0.5mls/hour____	1)YES_____ What amount of urine was measured? i.<0.5mls/hour___Dialysis____ ii.>0.5mls/hour____
	2)NO_____	2)NO_____
42. ANTIBIOTICS	Did the Patient receive all doses? 1)YES_____	Did the Patient receive all doses? 1)YES_____
	2)NO_____ 1. How many doses were missed? _____out of_____doses in 24 hours 2. What was the reason for missing the required doses? i) No IV access_____ ii) Medicine not available_____ iii) Missed by health worker___ iv)Other reasons_____ 3.Were antibiotics changed? i)No_____ ii)Yes_____ (go to 4.) 4.What antibiotics were given _____ _____	2)NO_____ 1. How many doses were missed? _____out of_____doses in 24 hours 2. What was the reason for missing the required doses? i) No IV access_____ ii) Medicine not available_____ iii) Missed by health worker___ iv)Other reasons_____ 3.Were antibiotics changed? i)No_____ ii)Yes_____ (go to 4.) 4.What antibiotics were given? _____ _____

MANAGEMENT	**AT 24 HOURS**	**AT 48 HOURS**
43. BLOOD REQUIREMENT	Was blood required? 1)YES_____ 1. Was blood available? i.Yes____amount_____mls/Kg ii.No_____	Was blood required? 1)YES_____ 1. Was blood available? i.Yes____amount_____mls/Kg ii.No_____
	2) NO_____	2) NO_____
44. BLOOD SUGAR	Was blood sugar measured? 1)YES____ 1.Measured value_____Mmol/L	Was blood sugar measured? 2)Yes____ 1.Measured value_____Mmol/L
	2) NO_____	2)NO_____
45. BLOOD LACTATE	Was blood lactate done? 1)YES_____ 1.measured value_____Mmol/l	Was blood lactate done? 1)YES_____ 1.measured value_____Mmol/l
	2) NO_____	2) NO_____
46. SERUM CALCIUM	Was serum calcium levels measured? 1)YES_____ 1.Was serum calcium ≤1.1mmol/l corrected? i.Yes____ ii. No_____	Was serum calcium levels measured? 1)YES_____ 1.Was serum calcium ≤1.1mmol/l corrected? i.Yes____ ii. No_____
	2) NO_____	2) NO_____

MANAGEMENT	**AT 24 HOURS**	**AT 48 HOURS**
47. PICU/NICU AVAILABILITY AND CARE	Was PICU/NICU available? 1)NO_____ 2)YES_____ (go to A, B, C)	Was PICU/NICU available? 1)NO_____ 2)YES_____
	A) What vasoactive agent was used? i.Dopamine_____ dosage_____µg/kg/min. ii.Norepinephrine_____ Dosage_____µg/kg/min. iii.Epinephrine_____ dosage_____µg/kg/min. iv.Hydrocortisone_____ dosage_____mg/kg	A) What vasoactive agent was used? i.Dopamine_____ dosage_____µg/kg/min. ii.Norepinephrine_____ Dosage_____µg/kg/min. iii.Epinephrine_____ dosage_____µg/kg/min. iv.Hydrocortisone_____ dosage_____mg/kg
	B) Was Mechanical ventilation needed? 1)NO_____ 2) YES_____ reason? 1.GCS≤8_____ 2.Metabolic acidosis_____ 3.Respiratory failure_____	B) Was Mechanical ventilation needed? 1)NO_____ 2) YES_____ reason? 1.GCS≤8_____ 2.Metabolic acidosis_____ 3.Respiratory failure_____
	C) Was ventilator available? 1)Yes_____ 2) No_____	C) Was ventilator available? 1)Yes_____ 2) No_____

OUTCOME OF SEPTIC SHOCK WITHIN 72 HOURS (tick the appropriate)

48. Outcome

1) Alive_____
2) Dead_____ Exact hours of death from time of admission_____hours.
   i. ≤24 hours_____
   ii. >24 hours - ≤ 48 hours_____
   iii. >48 hours - ≤ 72 hours_____

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KENYATTA NATIONAL HOSPITAL RECEIVED 16 JUN 2016 KNH/UoN-ERC P.O. Box 20723-00202 NRB.

KENYATTA NATIONAL HOSPITAL APPROVED 16 JUN 2016 KNH/UoN-ERC P.O. Box 20723-00202 NRB.

Ref: KNH-ERC/A/211

16th June, 2016

Dr.Varsha Vekaria Hirani
Reg.No.H58/74546/2014
Dept. of Paediatrics and Child Health
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Hirani

REVISED RESEARCH PROPOSAL- PREVALENCE AND MANAGEMENT OF SEPTIC SHOCK AMONG CHILDREN ADMITTED AT THE KENYATTA NATIONAL HOSPITAL (P228/03/2016)

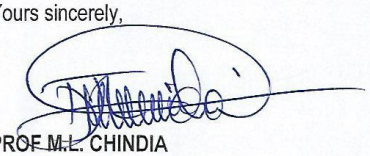
This is to inform you that the KNH- UoN Ethics & Research Committee (KNH-UoN ERC) has reviewed and **approved** your above proposal. The approval period is from 16th June 2016 – 15th June 2017.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH-UoN ERC before implementation.
c) Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
f) Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
g) Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

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

Yours sincerely,



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

c.c. The Principal, College of Health Sciences, UoN
The Deputy Director, CS, KNH
The Assistant Director, Health Information, KNH
The Chair, KNH- UoN ERC
The Dean, School of Medicine, UoN
The Chair, Dept.of Paediatrics and Child Health,UoN
Supervisors: Prof. Ezekiel Wafula, Dr.Rashmi Kumar, Prof.Rachel Musoke

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Study Registration Certificate

1. Name of the Principal Investigator/Researcher
   DR. VARSHA VEKARIA HIRANI
2. Email address: Verg830@gmail.com Tel No. 0735360831
3. Contact person (if different from PI).....
4. Email address: ..... Tel No. .....
5. Study Title
   PREVALENCE AND MANAGEMENT OF SEPTIC SHOCK AMONG CHILDREN ADMITTED AT THE KENYATTA NATIONAL HOSPITAL (PAEDIATRICS)
6. Department where the study will be conducted KENYATTA NATIONAL HOSPITAL
   (Please attach copy of Abstract)
7. Endorsed by Research Coordinator of the Department where the study will be conducted.
   Name: Dr. R. Kumar Signature ..... Date 27/6/16
8. Endorsed by Head of Department where study will be conducted.
   Name: Dr. Inwani Signature ..... Date 24/6/16
9. KNH UoN Ethics Research Committee approved study number P228/03/2016
   (Please attach copy of ERC approval)
10. I DR. VARSHA VEKARIA-HIRANI commit to submit a report of my study findings to the Department where the study will be conducted and to the Department of Research and Programs.
    Signature ..... Date 23/6/2016
11. Study Registration number (Dept/Number/Year) Paediatrics / 59 / 2016
    (To be completed by Research and Programs Department)
12. Research and Program Stamp

KENYATTA NATIONAL HOSPITAL H.O.D. RESEARCH & PROGRAMS 27 P.O. Box 20723 NAIROBI

All studies conducted at Kenyatta National Hospital **must** be registered with the Department of Research and Programs and investigators **must commit** to share results with the hospital.