EFFECTS OF THE FIRST 72 HOURS OF POSITIVE FLUID BALANCE ON THE DEVELOPMENT OF ACUTE KIDNEY INJURY AND MORTALITY IN PATIENTS WITH SEPTIC SHOCK. (A RETROSPECTIVE COHORT STUDY)

PRINCIPLE INVESTIGATOR:
DR. FADHILA SHABANI TEKKA
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DEPARTMENT OF PAEDIATRICS AND CHILD HEALTH

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DECLARATION

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

Signature:  **Date:** 04/07/2022

Dr. Fadhila Shabani Tekka, MD, Mmed

CERTIFICATE OF SUPERVISION

This dissertation has been submitted for examination with our approval as supervisors:

Signature: .....  **Date:** 8th July 2022

Dr. Bhupi Reel, M.D

Lecturer,Paediatric Intensivist, Department of Pediatrics and Child Health, Facultyof Health Sciences, University of Nairobi

Signature .....  **Date:** 10 – September 2022

Dr. Rashmi Kumar, M.D

Lecturer, Paediatric Intensivist, Department of Pediatrics and Child Health, Faculty of Health Sciences, University of Nairobi.

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ABBREVIATIONS

AKI: Acute kidney injury

ANP: Atrial Natriuretic Peptide

ARDS: Acute Respiratory Distress Syndrome

BP: Blood Pressure

BUN: Blood Urea Nitrogen

CHD: Congenital Heart Disease

CHD: Chronic Kidney Disease

ECF: Extracellular Fluid

FEAST: Fluid Expansion As Supportive Therapy

GFR: Glomerular Filtration Rate

ICF: Intracellular Fluid

ICU: Intensive Care Unit

IF: Interstitial Fluid

KDIGO: Kidney Disease: Improving Global Outcome

KNH: Kenyatta National Hospital

MAP: Mean Arterial Pressure

PELOD: Pediatric Logistic Organ Dysfunction

PICU: Pediatric Intensive Care Unit

PR: Pulse Rate

PRIFLE: Pediatric Risk, Injury, Failure, Loss, End Stage Renal Disease

RAAS: Renin Angiotensin Aldosterone System

RR: Respiratory Rate

Scvo2: Central Venous Oxygen Saturation

SPO2: Saturation Partial Pressure of Oxygen

T: Temperature

UON: University of Nairobi

WHO: World Health Organization

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DEFINITION OF TERMS

Sepsis: Life threatening organ dysfunction secondary to dysregulated immune response to infection(1)

Septic shock: Defined as severe sepsis with evidence of cardiovascular system dysfunction in which there are underlying circulatory and cellular/ metabolic abnormalities(1).

Shock: A state of inadequate tissue perfusion causing inadequate oxygen delivery to meet cellular metabolic needs and oxygen utilization or a combination of both.

Fluid bolus: Volume of fluid given over a defined period of time. For example, giving 10-20mls/kg of fluid over a period of 30 minutes.

Fluid overload: Volume overload can be viewed in either absolute or relative terms. Absolute volume balance refers to the cumulative total volume input minus the total volume output over a given period. Relative volume balance is defined as the absolute volume balance (in liters) divided by the patient's body weight (in kilograms) and is expressed as per cent volume (or fluid) balance.

Positive fluid balance: refers to a net fluid accumulation.

Negative fluid balance: refers to a net fluid deficit.

Fluid overload percent: The total fluid input in 24hrs - total fluid output in 24hrs (MLS)/weight at admission (kilograms)*100.

Daily input: calculated as the sum of total parenteral/enteral fluids, medications, blood and blood products.

Daily output: Calculated as the sum of daily urine output and other body fluids output [drains, naso/orogastric aspirates].

Daily fluid balance: daily difference in all intakes and all outputs, which exclude insensible losses.

ABSTRACT

Background:

Septic shock is defined as severe sepsis with evidence of cardiovascular system dysfunction. A state of shock causes inadequate tissue perfusion that leads into inadequate oxygen delivery to meet cellular metabolic needs. Appropriate fluid management is compulsory for the restoration of adequate cardiac output, tissue perfusion and restoration of organs function. However, excess fluid can be fatal and has been linked to multiple organ dysfunction, increased length of hospital stay, ventilator dependence as well as increased mortality. KNH PICU has a high mortality rate of septic shock in the first 72 hours of admission. We intend to determine whether the excessive fluid administration contributes to this mortality.

Objective:

To determine the effects of fluid balance in the first 72 hours of septic shock in children admitted to the KNH PICU.

Justification and Utility:

The results from this study will help assess how fluid management in critically ill PICU patients with septic shock may affect early mortality and organ dysfunction. This study will provide data to aid in developing an ideal fluid management strategy that may help reduce organ dysfunction and mortality in pediatric patients presenting with septic shock. Given the high numbers of patients with septic shock and their high rate of mortality in the KNH PICU, future PICU patients will benefit from the results of this study.

Methodology:

Study design: Retrospective study.

Study site/ setting: Kenyatta National Hospital Paediatric Intensive Care Unit.

Study population: Paediatric patients (1-12 years) admitted with septic shock.

Study procedure: Patients admitted with septic shock will be retrospectively identified over the past 2 years (from January 2019 to December 2020) and recorded and from them 162 patients' numbers will be randomly selected. Using the selected numbers, the files will be selected from the medical records department and data collected and documented on an excel spreadsheet for data analysis.

Data analysis and management: Data management will be done in Microsoft Excel 2016 data entry sheet. The data will be exported into IBM SPSS version 23 for statistical analysis. The demographic data will be put into percentages and continuous variables into means or medians. The relationship between fluid overload and outcome variables will be examined using bivariate and multivariate analyses. The significance of association and strength of the relationship between variables will be explained using p-values, odds ratios and confidence intervals. The study findings will be presented using tables and graphs

CHAPTER 1: INTRODUCTION AND BACKGROUND

Sepsis is a multiorgan failure secondary to dysregulated host response to infection, which may range from over exaggerated to no response especially in the immune compromised individuals(1)(2). Recognizing sepsis early is the mainstay of successful treatment and reducing the mortality in these patients. Late recognition and treatment of sepsis is more likely to progress into severe sepsis and hence septic shock.

Septic shock is defined as sepsis with the evidence of cardiovascular system dysfunction(3). As per World Health Organization (WHO) definition, there should be a presence of cold extremities, poor capillary refill of more than 3 seconds and weak peripheral pulses to be defined as septic shock.

A successful management of septic shock involves rapid recognition, antibiotics for source control, fluid management, inotropic and vasopressor support, oxygen delivery, nutritional support and electrolyte management. Adequate amount of fluid resuscitation in septic shock in children, especially in our setting, remains controversial.

Despite its significance in the management of septic shock, aggressive fluid resuscitation has been shown to increase mortality. In a large multicenter Randomized controlled trial that was done is sub- Saharan Africa (FEAST trial), fluid boluses in patients with septic shock were shown to increase mortality(4). Therefore, current guidelines, recommend restriction of fluid boluses especially in the settings with no intensive care units. In the current surviving sepsis campaign, up to 60mls/kg of fluid boluses can be given in patients with septic shock in the settings with intensive care units. However, if intensive care is not available, fluid boluses should be limited to 40mls/kg in hypotensive patients and no boluses are recommended in the absence of hypotension with fluid resuscitation limited to maintenance fluids only(5).

In spite of the above guidelines, mortality secondary to septic shock have been high and accounts for up to 50% especially in the resource limited settings(5). In a study done in KNH, mortality was even higher at 70% in the first 72 hours(6). In an attempt to identify whether fluid management in our unit contributes to this high mortality rate, I intend to focus on the quantity of fluid management on the outcome of patients with septic shock.

Positive fluid balance has been shown to increase the mortality and hospital length of stay in septic shock patients(7)(8)(9)(10). Not only does it cause increase in mortality but also excess fluid has been shown to increase the development of acute kidney injury (AKI) in the patients with septic shock(11). This study aims at investigating whether abnormal fluid balance is a contributor to the high rate of mortality in our Pediatric Intensive Care Unit (PICU)

CHAPTER 2: LITERATURE REVIEW

2.1 Physiology of body fluids

The human body consists of 75% by mass of fluids in infants which decreases to about 50%-60% in adults. The body fluids are distributed in two main compartments, of which 40% of body weight are intracellular (ICF) and 20% extracellular (ECF). The ECF compartment is further divided into intravascular consisting of 5%, and interstitial fluid (IF) consisting of 12% of body weight(12). Different compartments have different concentrations of electrolytes: ICF

has high concentrations of potassium, phosphate, magnesium and proteins, while ECF has high concentrations of sodium, chloride and proteins. Within the extracellular compartment the IF has lower concentration of proteins compared to plasma. Fluids are in constant motion from one compartment to the other depending on the osmolality (number of particles of solute per little of fluid) of the compartment which alters the starling forces (oncotic pressure and hydrostatic pressures) responsible for the movement of fluids(13).

2.2 Fluid therapy in septic shock

Fluid resuscitation in septic shock is a prerequisite for the survival of patients. It aims to correct the hypovolemia that was caused by vasodilation, capillary leak secondary to inflammation, as well as replacement of other fluid loses due to for example diarrhea, vomiting that frequently accompany pediatric illnesses. Maintain adequate preload (the amount of ventricular stretch at the end of diastole) with adequate fluid resuscitation improves cardiac output and helps restore organs perfusion. The earlier the stabilization of the patient, the better the outcome. Rivers et al, in their study on early goal-directed therapy in the management of sepsis and septic shock which aimed at early identifying and managing cardiovascular collapse, had both short term and long-term benefits where one of them was lower mortality in patients who were managed with resuscitation bundle that focused on achieving hemodynamic optimization within the first six hours of attendance that included early fluid resuscitation to achieve a Central Venous Pressure of 8-12 mmHg, Vasopressor support to achieve MAPs of >65% and vasodilators for MAPs above 90 mmHg and RBC transfusion to achieve a hematocrit of at least 30%. For patients whom hemodynamic stabilization could not be achieved received mechanical ventilation and sedatives(14).

According to the current surviving sepsis campaign guidelines, fluid resuscitation should begin immediately together with other managements like antibiotic therapy(5). The amount of fluids depends on the patients' presentation and the availability of intensive care services in the facility. In settings with no intensive care units nor advanced support, fluid boluses are discouraged in patients with no hypotension as they have been shown to increase mortality

according to the FEAST trial(4). These patients should receive maintenance fluids only. For those with septic shock and hypotension and no ICU services, fluid boluses should be limited to 40ml/kg in the first hour (given as aliquots of 10-20mls/kg). In settings that do offer intensive care and advanced support, fluid boluses can be given up to 40-60mls/kg in one hour (10-20mls/kg per bolus). Fluid boluses in all settings should be titrated to clinical markers of cardiac output that include heart rate, urine output, capillary refill time, blood pressure and level of consciousness. Fluids should be stopped with development of any signs of fluid overload such as new or worsening hepatomegaly or pulmonary edema(15).

Various hemodynamic indices are monitored when giving fluids in patients with septic shock. Mean Arterial Pressure (MAP) should be maintained in a normal range for age which is between 5^{th} percentile for age and below 90^{th} percentile for age. Advanced hemodynamic monitoring like systemic vascular resistance or central venous oxygen saturation (Scvo2), cardiac output/cardiac index when available can be used and should be maintained in their normal ranges. Bed side clinical signs of cold and warm shock like peripheral temperature gradient, peripheral pulses and capillary refill time alone are no longer recommended because of their observed no correlation with advanced monitoring and many patients who showed to have warm shock were found to have cardiovascular dysfunction(16)(17)Serial lactate levels can be followed in guiding the success of cardiovascular resuscitation(15). These indices can help avoid fluid overload and determine when to hold further fluid resuscitation and start other management strategies such as inotropic support in case of fluid refractory shock.

2.3 Pathophysiology of fluid overload

The abnormalities of fluid balance in the body are due to either fluid excess (fluid overload) or fluid deficit (dehydration). Fluid overload may be caused by the pathologic states such as heart failure where decrease in cardiac pump function decreases the perfusion of the kidneys and hence activates neuro-hormonal mechanisms (RAAS pathway) that cause retention of sodium

and fluid in the body. Similarly, liver disease that causes decrease in albumin production leads to decrease in oncotic pressure with extravasation of fluids into the interstitial compartment, intravascular fluid depletion, and hence poor renal perfusion and again activation of neuro-hormonal (RAAS pathway) with net fluid retention. Renal disease can also impair its ability to filter excess fluids from the body. Fluid overload can also be induced iatrogenically. Fluid resuscitation has always been a way to restore the intravascular volume and hence restore organ perfusion especially in patients with shock. When this fluid is given in excess, fluid overload can occur. In patients with septic shock, both pathologic or iatrogenic causes can contribute to a positive fluid balance. This research study will focus on positive fluid balance as well as negative fluid balance.

2.4 Effects of fluid overload in different body systems

Despite the fact that fluid is necessary for the restoration of cardiac output and ensuring proper organ perfusion, excess fluid has been shown to increase the risk of multiorgan dysfunction and end organ damage which translates into increased hospital length of stay and hospital mortality. In Acute respiratory distress syndrome (ARDS), alveolar flooding is the pathognomonic feature of the disease. This is due to an increase in the pulmonary arterial hydrostatic pressure and increased permeability of the alveolar- capillary membrane. Alveolar flooding renders surfactant inactive and even changes its composition. All these factors cause impairment in gas exchange and lead to hypoxemic respiratory failure(18). Giving the right amount of fluids in these patients will allow proper tissue perfusion and minimize further alveolar flooding and increase chances for the survival of these patients. Negative fluid balance has been shown to increase survival and reduce the mortality in patients with ARDS(19) (20).

Sepsis can lead significant myocardial depression secondary to inflammatory cytokines. Despite normal total cardiac output, significant reduction in both stroke volume and ejection fraction have been observed(21). Major factors that cause myocardial dysfunction are decreased contractility and decreased myocardial compliance(22)(23)(24)(25). Myocardial

depression impairs cardiac output, leading to arterial under filling and reduction of the effective circulating blood volume. The latter causes baroreceptor sympathetic activation and stimulation of neuro-hormonal mechanisms (RAAS) that causes further retention of fluids and acts as a vicious cycle. As a consequence, the end diastolic volume index is increased and further impairs the filling and contractility of the heart(26).

CNS dysfunction in patients with sepsis is multifactorial and includes increased microglial activation, changes in the neurotransmission process, dysfunction of the blood brain barrier and decreased brain perfusion secondary to immune processes(27). However fluid overload has also been associated with prolonged delirium and coma days in patients with sepsis(28).

Movement of fluids across the capillary membrane depends on the balance between capillary hydrostatic and capillary oncotic pressures, but the permeability of the membrane also plays a key role. Increase in capillary hydrostatic and decrease in capillary oncotic pressures, with increase in capillary permeability cause increase in fluid filtration across the capillary membrane. The vascular endothelium is covered by the endothelial glycocalyx, which is carbohydrate-rich later. Any damage in the endothelial glycocalyx causes an increase in the vessel leakiness and hence filtration across the membrane. Endothelial glycocalyx can be damaged by inflammatory markers, hyperglycemia, Atrial Natriuretic Peptide (ANP) and can be damaged through ischemia- reperfusion injuries. Fluid overload has been shown to contribute to the development of AKI in sepsis due to various factors: reperfusion of the previously hypo-perfused kidneys causes injury to the renal glycocalyx, leading to fluid leakage, interstitial edema, decrease in intravascular volume with associated decreased renal perfusion pressure and hence development of AKI. Interstitial edema also leads to decreased diffusion of oxygen across the tissues, to impairment of lymphatic drainage, and further progression the organ failure. The effects of interstitial edema are more severe in the kidneys due to the presence of the renal capsule limiting its distensibility. Fluid overload also causes stretch of the atria with release of the ANP. This leads to destruction of the endothelial glycocalyx and increases interstitial edema and its effects as explained previously(29).

2.5 Effects of Negative fluid balance

Negative fluid balance occurs when the total fluid output exceeds the total input. Lower circulating volumes cause poor tissue perfusion and multiple organs failure. This happens when the patient is in shock or severely dehydrated but having negative fluid balance does not mean the former two. Not many studies have been done on the effects of negative fluid balance in the body systems. A retrospective pilot study by Alsous et al found 30% of ICU admitted patients to have negative fluid balance. In their study, negative fluid balance in any of the first three days of ICU admission was shown to improve survival and reduce the mortality in patients admitted with septic shock(30). Study by Bellomo et al found that, a negative fluid balance was associated with improved clinical outcome by increasing renal replacement free days(31). Collins et al found that, negative fluid balance reduces the days of ICU admission as well as 28-day mortality(32). Though many of these studies compared negative to positive fluid balance and neither compared negative fluid balance to even fluid balance, there are much more promising results in a side of negative fluid balance compared to positive fluid balance. From literature search, no study has found a harmful effect of negative fluid balance as compared to positive fluid balance. More randomized controlled studies need to be done that will compare negative fluid balance and even fluid balance so as to find the effects of negative fluid balance.

2.6 Acute kidney injury and septic shock

Acute kidney injury (AKI) is a sudden loss of kidney function that results in a decrease in glomerular filtration rate (GFR), retention of urea and other nitrogenous wastes, improper regulation of extracellular fluid volume and other electrolytes in the body. Duan et al found the incidence of AKI in septic shock to be greater that 40% (30). Causes of AKI can be pre-renal, renal and post renal. In septic shock, various risk factors for AKI have been studied including hypovolemia and poor kidney perfusion which are most common, but also hematologic/ immunologic comorbidities, malignancies, chronic kidney diseases, abdominal

infection, elevated hospital admission illness severity, systolic blood pressure of less than 5th percentage for age.

In patients with shock, decreased circulatory volume causes stimulation of baroreceptors and osmoreceptors leading to activation of a cascade of events that causes renal vasoconstriction and hence decreased GFR, increased proximal tubular sodium and water reabsorption and increased collecting duct sodium reabsorption. All of these effects result in decreased in fractional excretion of sodium and increased antidiuretic hormone release which again lead to increased collecting duct water reabsorption and reduced urine output. The medical team's response usually is to restore the circulating volume with fluid resuscitation. Excessive fluid resuscitation has been shown to be an independent risk factor for the pathogenesis of AKI(33) and other studies have shown fluid overload to be a negative predictor for recovery of renal function(34). Multiple causes for the negative impact of fluid overload on kidney function have been described. They include the following: Destruction of the endothelial glycocalyx and reperfusion injuries as explained above. Other etiologies include micro vascular dysfunction in sepsis and septic shock causing heterogeneous abnormalities in renal blood flow where some capillaries are under perfused while others have normal or abnormally high blood flow. Administration of excess fluid can cause or exacerbate this heterogeneity in renal blood flow. Therefore, although fluid therapy can normalize renal arterial flow, it can cause abnormal circulation in the renal cortex, resulting in a pattern of hypoxic areas next to normoxic areas. Hypoxia then leads to renal oxygen extraction dysfunction and production of reactive oxygen species that can further contribute to kidney injury(35).

There are various criteria that are used to define AKI. These include the Kidney Disease Improving Global Outcome (KDIGO) criteria and pediatric Risk Injury Failure Loss End stage renal disease (pRIFLE) criteria. Due to data availability, KDIGO criteria will be used to define AKI in this study. KDIGO criteria use serum creatinine values and urine output to define AKI as shown in the table below.

Table 1: **KDIGO criteria for staging AKI**(36)

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline OR ≥0.3 mg/dL rise increase	<0.5 mL/kg/h for 6–12 h
2	2.0–2.9 times baseline	<0.5 mL/kg/h for ≥12 h
3	3.0 times baseline OR Increase to ≥4.0 mg/dL (>18 yr of age) OR Decrease in eGFR <35 mL/ min/1.73m^2 (<18 yr of age) OR Initiation of renal replacement therapy	≤0.3 mL/kg/h for ≥24 h OR Anuria for ≥12 h

Solution: Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group—KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl. 2012;2:1–138.

Abbreviations: eGFR, estimated glomerular filtration rate.

2.7 Study Justification

Sepsis is a life-threatening condition and is the common pathway to many infectious illnesses worldwide which can lead to septic shock especially in children. More than 1.2 million cases of childhood sepsis have been reported per year worldwide(37). Though sepsis and septic shock are common worldwide, the burden of disease and case fatality rate have been more severe in resource limited settings especially in Africa(38). Kenya is no different from other African countries. In a study done by Vekaria-Hirani et al at the Kenyatta National Hospital, the prevalence of septic shock was 15.4% and the mortality was 70% at 72 hours of admission. Infants case fatality rate was as high as 82.6%. Lack of mechanical ventilation and presence of

hypotension were associated with high mortality. It was also noted that, the level of care (Example fluid management) was not at the level of surviving sepsis campaign guideline of 2012(39). Despite the availability of currently more resources such as ventilator support in the intensive care unit, mortality remains high in patients admitted to PICU with septic shock. Fluid therapy being a common intervention and an available resource to all our patients at all times, it is important to ensure its proper use. Since fluid overload has been shown to increase mortality in patients admitted with septic shock, investigating it's the role and potential contribution to the risk of mortality in our PICU patients at KNH is important.

As discussed above, fluid overload affects multiple organs. This study will focus on the kidneys and the frequency of AKI in patients with septic shock which has been a common encounter in our setting.

In this study therefore, I intend to find out whether fluid overload is one of the key culprits for the high mortality and organ dysfunction in patients admitted with septic shock at the KNH-PICU. Through this study, information on the correct fluid therapy will be obtained to help inform proper clinical guidelines for fluid management as a step towards reducing mortality in our PICU.

CHAPTER 3: RESEARCH QUESTION AND OBJECTIVES

3.1 Research Question

Does positive fluid balance or negative fluid balance contribute to the increase in mortality and the development of acute kidney injury in pediatric patients with septic shock?

3.2 Null hypothesis

Fluid balance has no effect on mortality and the development of AKI in pediatric patients with septic shock.

3.3 Broad Objective

To determine the effects of positive fluid balance in pediatric patients presenting with septic shock.

3.4 Specific Objectives

- ✓ To determine the proportion of patients admitted with septic shock that had positive fluid balance.
- ✓ To determine the prevalence of AKI in patients with septic shock
- ✓ To determine the relationship between positive fluid balance and the prevalence of AKI in patients with septic shock
- ✓ To determine the effects of fluid balance and AKI on mortality

CHAPTER 4: METHODOLOGY

4.1 Study design

This was a retrospective cohort study.

4.2 Study population

Pediatric patients aged 1-12 years admitted in the KNH-PICU with septic shock.

4.3 Study site

Data were obtained from the files of the patients who were admitted at Pediatric Intensive care unit of Kenyatta National Hospital (KNH-PICU).

4.4 Study period

Data collection was done for 2 months for completion of this study.

4.5 Sample size calculation

The following formula will be used:

Sample size = Z^2 P(1-P)/ d^2

Where

Z = Z statistic for 95% level of confidence = 1.96

P = Expected proportion in population who had fluid overload based on the previous study

d = margin of error = 5%

Using the study done by Martinez- Garsia et al, "Fluid balance and acute kidney injury in septic shock". The reason I chose this study is because it had the same design and aim of investigating the effect of fluid overload in the pediatric patients admitted in their pediatric ICU.

Therefore:

Sample size = $1.96^2 \times 0.12(1-0.12)/0.05^2$

Sample size is **162 patients**

4.6 Study variables

Independent variable

- ✓ Septic shock

Dependent variables

- ✓ Fluid overload
- ✓ Acute kidney injury
- ✓ Mortality

4.7 Eligibility criteria

Inclusion criteria

- ✓ Pediatric patients (1mo-12 years) admitted to KNH PICU
- ✓ Diagnosis of septic shock (as per WHO definition)

Exclusion criteria

- ✓ Patients with chronic illnesses that affect fluid input such as CHD, CKD
- ✓ <1mo and >12 years
- ✓ Patents who did not meet all the three criteria of shock as per WHO

4.8 Recruitment and study procedure

From the PICU admission book, patients who had septic shock from January 2019 to December 2020 were recorded and their identification numbers were written. 162 identification numbers were documented and presented to the medical record department for the file extraction. From the files all the required details were obtained.

From the files, the following were recorded; Patients' demographic data (age, sex, weight on admission), admission date, diagnoses, vitals on admission (BP, PR, RR, T, SPO2, MAP) on admission, mechanical ventilation use, days on mechanical ventilation, Inotropic support, days on Inotropic support, serum creatinine on days 1,2 and 3 of admission, blood urea nitrogen (BUN) on days 1, 2 and 3 of admission, fluid input and output on days 1,2 and 3 of admission, types of fluid given, patients' outcome (discharge or death), discharge date and length of PICU

stay. Patients' severity of illness and risk of mortality on admission were assessed using the Pediatric Logistic Organ dysfunction (PELOD) and the PIM 2 scores.

Measurement tools

- ✓ PELOD score chart

4.9 Outcome

The primary outcome was the proportion of patients with septic shock who had positive fluid balance in their first three days of PICU admission. Secondary outcomes included the effects of positive fluid balance on mortality, hospital stay and presence of AKI in patients with septic shock.

4.10 Data management and Analysis

Data management was done in Microsoft Excel 2016. After data entry and cleaning, data were exported into IBM SPSS version 23 for statistical analysis. The study population will be described by summarizing demographic data into percentages and continuous variables into means or medians. The relationship between fluid overload and outcome variables was examined using bivariate [chi -squared tests for categorical data i.e. association between overload and mortality] and multivariate analyses [logistic regression] for mortality, controlling for confounders such as age, renal comorbidity, gender, nutritional status and severity of illness at admission. The significance of association and strength of the relationship between variables were explained using p-values, odds ratios and confidence intervals. The study findings were presented using tables and graphs

4.11 Ethical consideration.

Permission to carry out the study was sought from KNH/UON Research and Ethics committee. There was no use of names or subject identifiers. All the study findings were availed to the KNH Ethics and Research Committee and the UON department of pediatrics. Data collection proceeded after obtaining a formal permission from KNH Research and Programs department.

4.12 Study strength and limitations:

The results from this study will help determine the current state of fluid management in our PICU patients, and will help inform if we are following Surviving Sepsis Campaign Guidelines in managing our patients with septic shock. This study may help optimize our clinical practices and formulate local PICU fluid guidelines for the successful management of our patients.

Study results and conclusions were limited given that this is a single center, retrospective, non-randomized study. Clinical data was incomplete and determination of fluid resuscitation prior to patient arrival to KNH was limited. Also, as stated above development of AKI and mortality of critically ill children are multi-factorial and inferences based on fluid balance alone therefore limited.

CHAPTER 5: RESULTS

Demographic characteristics

This study had a sample size of 162. The total number of patients whose files while accessed was 124 giving a response rate 76.5% which is sufficient as Fincham J. 2008 suggest that a 60% response rate is sufficient. The table below represents the demographic characteristics of the total number of patients whose files were accessed.

The minimum age among the children was 1.25 months while the oldest child had 48 months. The median age was 9 months with an interquartile range of 6 months. 55.3% (n = 68) of the children were between 1-9 months, 41.5% (n = 51) were between 10-18 months while only 3.2% (n = 5) were 19 months and above. Of the total number of patients, 45.5% (n = 56) were males while 54.5% (n = 68) were females.

The median length of hospital stay was 5 days with an interquartile range of 10 days. 58.5% (n = 72) of the patients died while 41.4% (n = 52) survived.

Table 2: Demographic and clinical characteristics

Variable	**Categories**	**Frequency** N=124	**Percentage**
Children's characteristics			
Age **(median = 9.0 months, IQR = 6.0 months)**			
Age category	1-9 months	68	55.3

	10-18 months	51	41.5
	19 months and above	5	3.2
Sex	Male	56	45.5
	Female	68	54.5
Clinical findings			
Days of hospital stay (**Median = 5 days, IQR = 10 days)**			
Mortality:	Died Survived	72 52	58.5 41.5

Out of the 124 files that were accessed, 98 of them had complete patient's information and they were retained in the study. The demographic and clinical information is shown on the table below.

Of these patients, the youngest was 1.5 months while the oldest was 26 months with a median of 8 months and an interquartile range of 5.0 months. 62.2% (n = 61) were between 1 and 9 months while 36.8% (n = 36) were between 10-18 months. 55.1% (n = 54) were females while 44.9% (n = 44) were males.

In terms of PICU stay, the maximum stay was 47 days while minimum stay was 1 day. The median length of stay was 6.5 days with an interquartile range of 10 days. Those children who survived PICU were 51% (n = 50) while 49% (n = 48) died. 87.5% (n = 84) had fluid overload while 12.5% (n = 12) did not have fluid overload.

On development of acute kidney injury, 98% (n = 96) had AKI while 2% (n = 2) did not have AKI. Acute kidney injury was also classified in to stages where by 11.7% (n =9) of the children had stage 1 Aki, 32.5% (n = 25) had stage 2 while 55.8% (n =43) had stage 3 acute kidney injuries. The mean PELOD score at admission was 9.5 with a standard deviation of 3.0.

Table 3: Demographic and clinical characteristics 2

Variable	**Categories**	**Frequency N=98**	**Percentage**
Children's characteristics			
Age **(median = 8.0 months, IQR = 5.0 months)**			

Age category	1-9 months	61	62.2
	10-18 months	36	36.8
	>= 19 months	1	1.0
Sex	Male	44	44.9
	Female	54	55.1
Clinical findings			
Days in PICU (**Median = 6.5 days, IQR = 10 days)**			
Survived:	No Yes	50 48	51 49
Fluid overload:	Yes No	84 12	87.5 12.5
Acute kidney injury: Yes No	Yes No	96 2	98 2
Stages of AKI: Stage 1 Stage 2 Stage 3	Stage1 Stage 2 Stage3	9 25 43	11.7 32.5 55.8
PELOD score (**Mean = 9.5, SD = 3.0**)			

Age of the participants in terms of gender

For the different age categories of the participants, 33.0% of those between ages 1-9 months were females while 30.0% were females. 22.0% of those between ages 10-18 months were females while 14.0% were males.

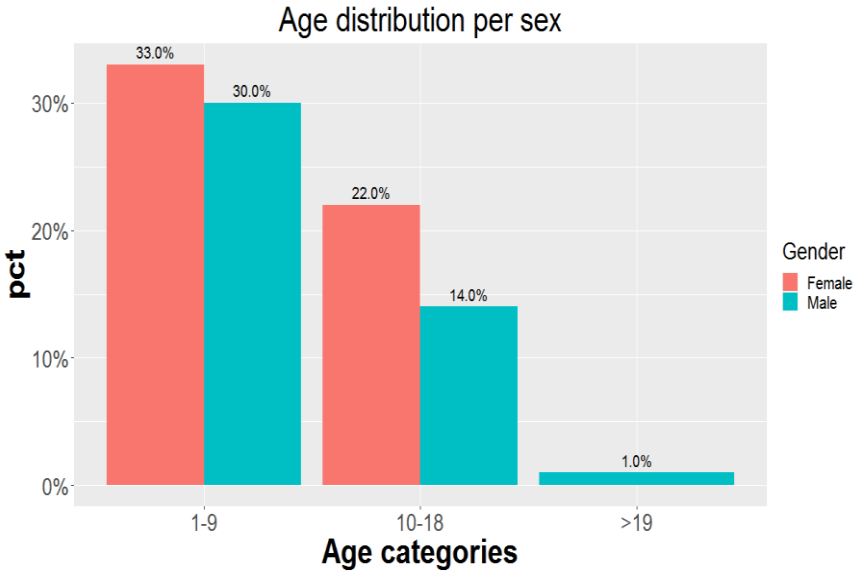

Figure 1: Age distribution per sex

Age distribution and fluid overload

In terms of fluid overload, 57% of the children between ages 1-9 months had fluid overload while 5% did not. 29% of those between ages 10-18 months had fluid overload while 7% did not have fluid overload.

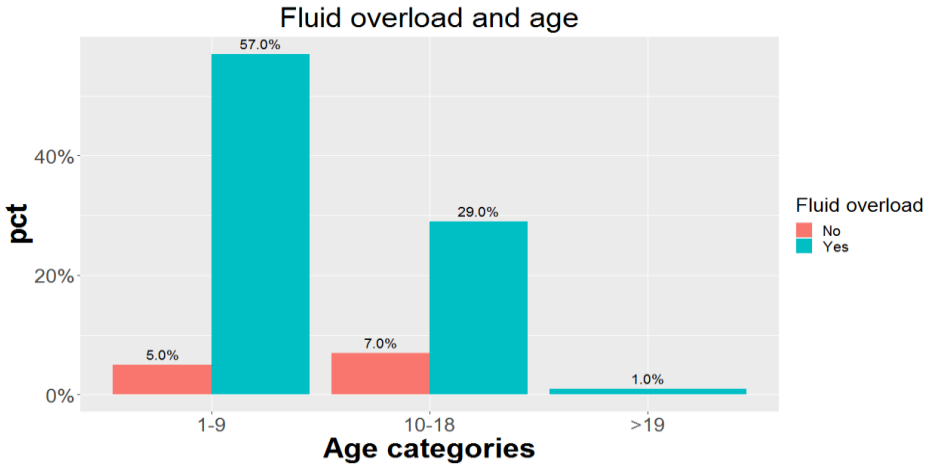

Figure2: Fluid overload according to age

Fluid overload per gender

Under fluid overload per gender, 48.0% of female children had fluid overload while 7.0% of the children did not have fluid overload. Among the males, 40.0% had fluid overload while 5.0% did not have fluid overload.

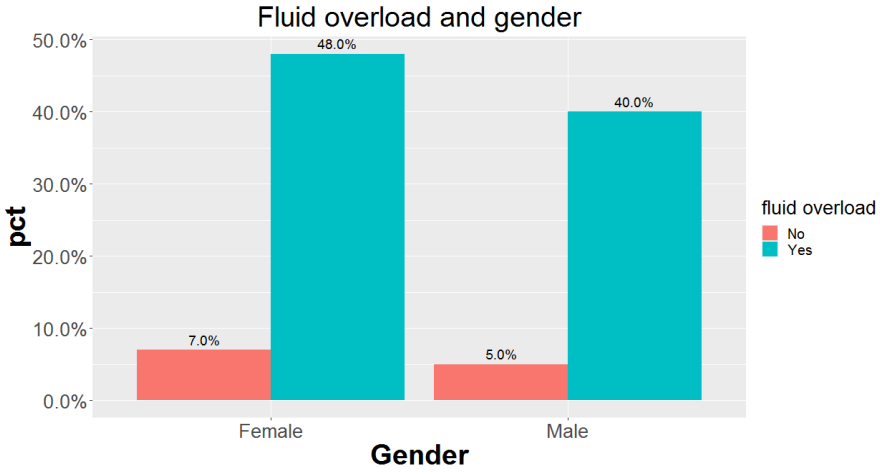

Figure 3: Fluid overload according to gender

Gender distribution and mortality

In terms mortality per gender, 34.0% of the females died while 21.0% did not. Among the males, 30.0% survived while 15.0% of them died.

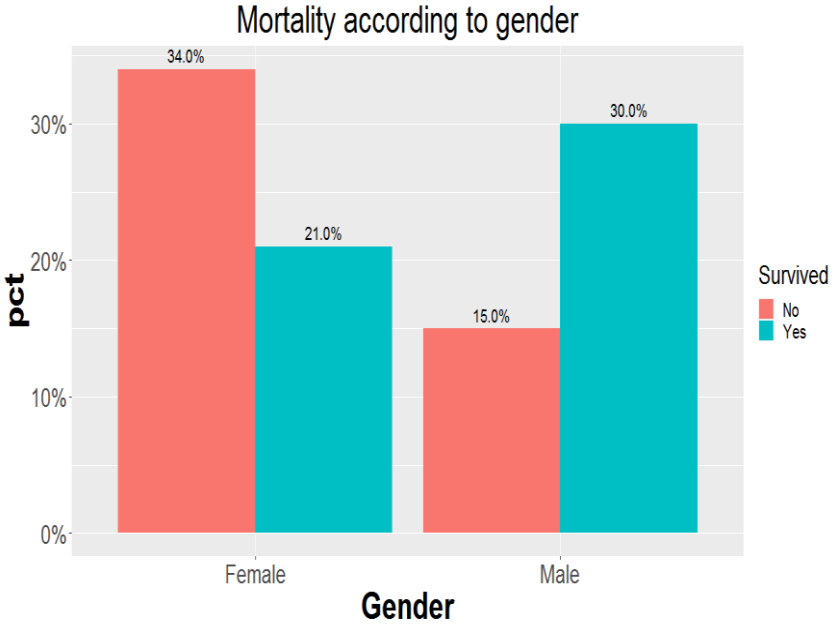

Figure4: Mortality in the two genders

Age distribution in terms of mortality

Among the participants who were between ages 1-9 months, 36.0% survived while 27.0% died. 21.0% of those between 10-18 months died while 15.0% survived.

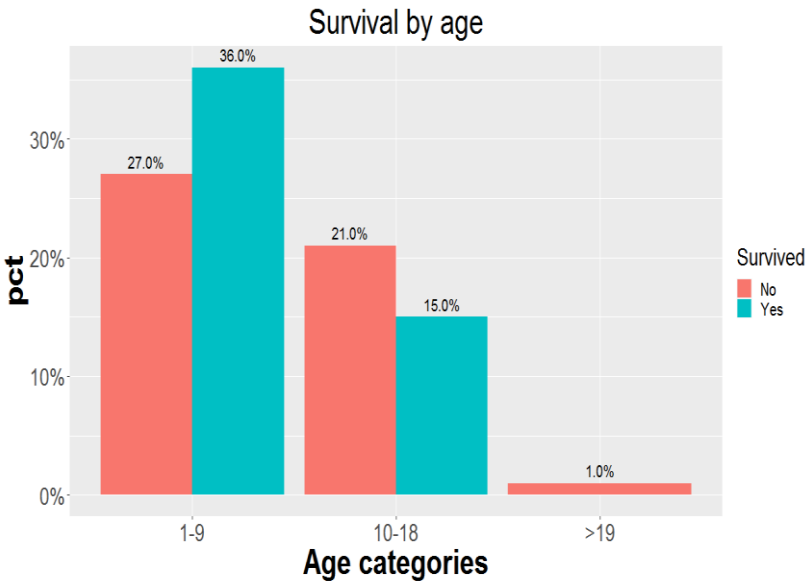

Figure5: Showing mortality according to age

✓ **Objective1: To determine the prevalence of patients admitted with septic shock that had fluid overload.**

The prevalence of children with fluid overload was 88%. The proportion of those with overload together with 95% confidence interval was 0.88 (0.79, 0.93).

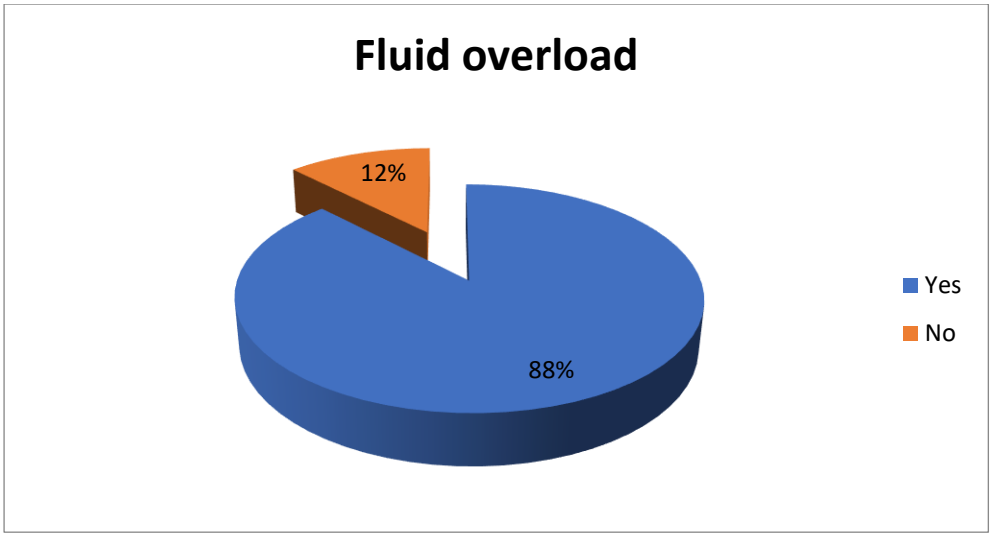

Figure6: Prevalence of fluid overload

Objective2: To determine the prevalence of AKI in patients with septic shock

The study participants were divided in to two age groups i.e. those with one year and below and those above one year. To determine whether a patient had AKI or not, upper limits of age specific creatinine levels were used to assign acute kidney injury status.

Out of the 98 children, 87.8% (n = 86) children were less than one year old while 12.2% (n = 12) were above one year old. Of those that were below one year, 97.7% (n = 84) had AKI while 2.3% (n = 2) did not have AKI. All the children that were above one year old had acute kidney injury.

Of the 98 study participants, 98% (n = 96) had AKI while 2% (n = 2) did not have AKI. The proportion of children who had AKI with 95% confidence interval was 0.98 (0.92, 1.00).

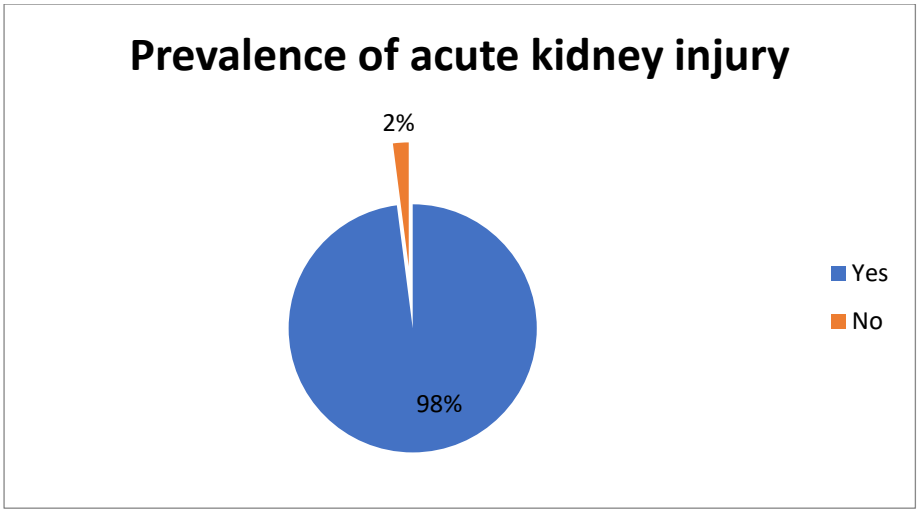

Figure 7: Prevalence of acute kidney injury

Association between fluid overload and AKI

The bar chart below shows that 86% of the children who had fluid overload developed acute kidney injury while 1% did not. Of those who did not have fluid overload, 11% developed AKI while 1% did not.

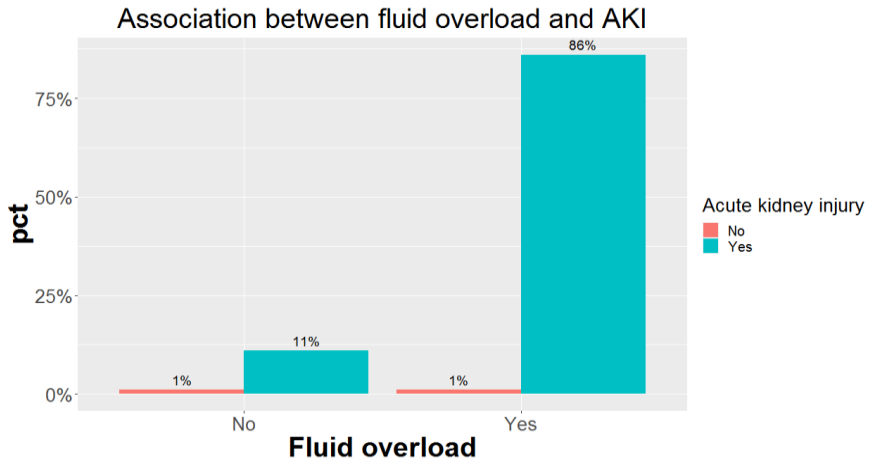

Figure 8: Bar graph showing relationship between fluid overload and AKI

Effect of fluid overload on mortality

Of the total patients with fluid overload, 47.0% of them died while 41.0% did not die. 3.0% of those without overload died while 9.0% did not die.

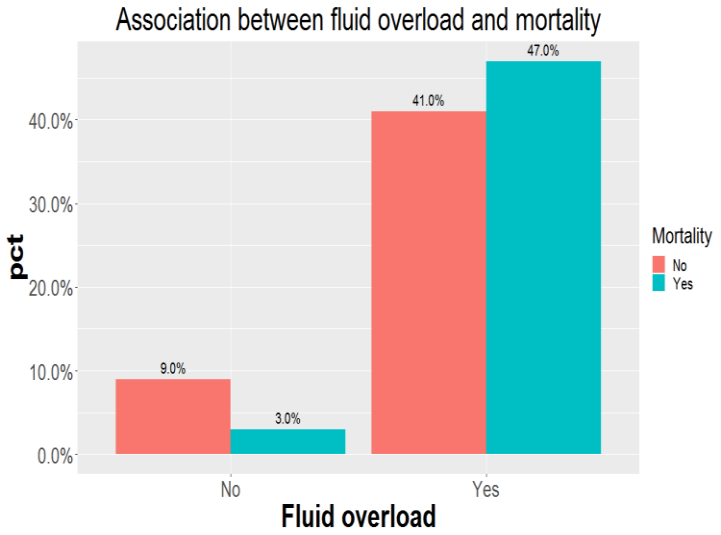

Figure 9: Bar graph showing relationship between fluid overload and mortality

Association between AKI stages and mortality

The bar graph below shows that mortality generally increased with higher stages of AKI. The number of children who died in the third stage of AKI was 37.0% followed by 15.0% in the second stage while 6.0% died in the first stage.

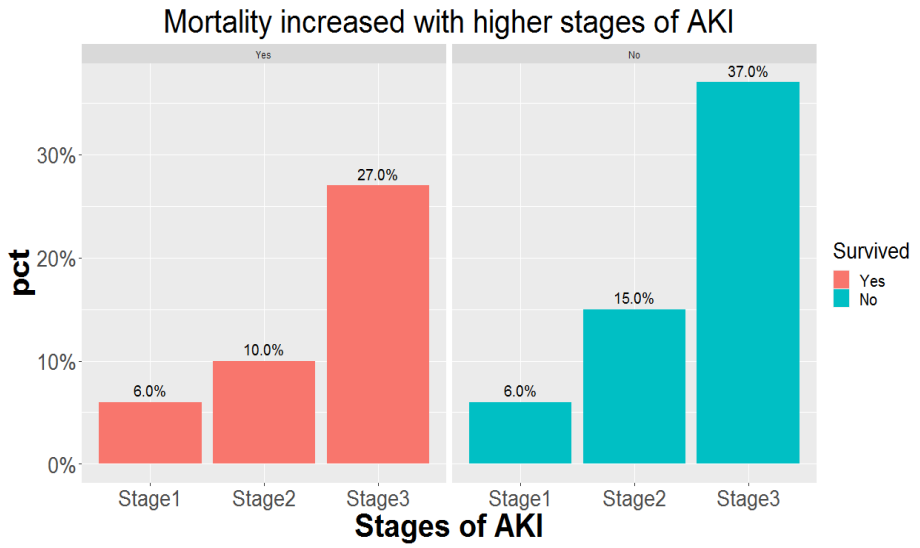

Figure 10: Bar graph of mortality and AKI stages

Association between fluid overload and acute kidney injury

From the bar graph below, it is clear that majority of those who had fluid overload were those with stage 3 of acute renal failure at 58.0% followed by stage 2 at 24.0% while those with stage 1 acute kidney injury were only 11.0%.

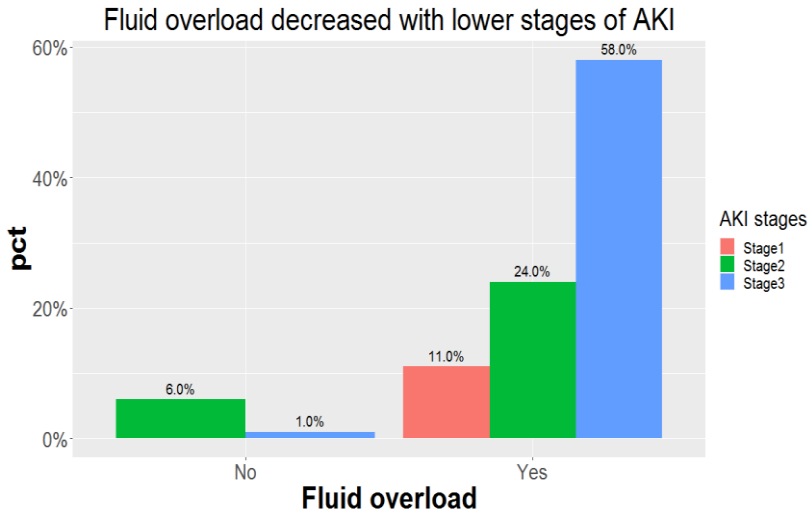

Figure 11: Bar graph showing relationship between fluid overload and AKI

Table3: Factors associated with mortality, AKI, stages of AKI and ventilator days

Inferential statistics

Table 4: Inferential statistic, Bivariate analysis

Factors associated with mortality				
Variable	**Survived N = 98**		**Crude OR (95% CI)**	**P-value**
	Yes	No		
AKI: No Yes	0 50	2 46	NA	0.24
Fluid overload: No Yes	9 39	3 45	3.46 (0.88, 13.69)	0.12

Inotropic use: No Yes	19 31	14 34	 1.48 (0.64,3.46)	0.48
PELOD score: <=10 >10	36 14	31 17	 1.41 (0.60, 3.32)	0.57
AKI stages: Stage1 Stage 2 Stage 3	5 13 26	4 12 22	 1.15 (0.25, 5.33) 1.06 (0.25, 4.230	0.98

Factors associated with AKI

Variables	**Acute kidney injury N = 98**		**Crude OR (95% CI)**	**P-value**
	Yes	No		

Fluid overload: No Yes	11 83	1 1		0.13 (0.01, 2.27)	0.24
Inotropic use: No Yes	32 64	1 1		0.5 (0.03,8.26)	1.00
	Stage 1	Stage 2	Stage 3		
Fluid overload: No Yes	9 0	5 19	1 46	NA	0.02

Factors associated with ventilator days

Variable	Ventilator days	**Crude OR (95% CI)**	P-value
Inotropic use	NA	1.47 (1.19, 1.83)	0.01

Factors associated with mortality

Interpretations of p-values

Using P-values, AKI, fluid overload, inotropic use, PELOD-2 score and AKI stages were not statistically significantly associated with mortality as their p-values are more that 0.05 at 95% confidence level. To determine whether these factors had any effect on mortality, we use odds ratios.

Interpretation of odds ratios

Fluid overload

The odds ratio of fluid overload and mortality is 3.46 (0.88, 13.69). Inside the bracket is the 95% confidence interval which includes one hence indicating no statistically significant association between fluid overload and mortality. Despite there being no association, fluid overload has an effect on mortality as the children got fluid overload are 3.46 times more likely to die as compared to the children who did not fluid overload.

Inotropic support

The children who were on inotropic support were 48% more likely to die compared to those who were not on inotropic support.

Stages of AKI

In terms of odds ratios, a child who had stage 2 acute kidney injury was 15% more likely to die as compared to a child in stage 1 acute kidney injury. On the other hand, a child who had stage 3 acute kidney injury was 6% more likely to die compared to a child who was in stage 1 acute kidney injury.

PELOD score

On PELOD score, a child with a PELOD score of more than 10 was 41% more likely to die compared to a child who had a PELOD score of 10 and below.

Factors associated with AKI

The p-values for inotropic use and fluid overload are more than 0.05 at 95% confidence level which indicate that these two factors are not statistically significantly associated with the development of acute kidney injury. On the other hand, the p-value for the association

between fluid overload and acute kidney injury at 95% confidence level is 0.02 indicating that there is a significant statistical association between fluid overload and the stages of AKI.

Interpretation of odds ratios

The same conclusion can be drawn from the 95% confidence intervals for odds ratios for these two variables which include one meaning there is no statistically significant association. Nevertheless, the odds ratios themselves indicate that these two variables have some effect on the development of AKI.

The children who had fluid overload were 87% less likely to develop acute kidney injury compared to those who did not get fluid overload.

The children who were put on inotropic support were 50% less likely to develop acute kidney injury compared to those who were not put on inotropic support.

Factors associated with ventilator days

Here, we will look at the effect of inotropic use on ventilator days. The p-value of 0.01 at 95% confidence level is less than 0.05 indicating that inotropic use is statistically significant in its association with ventilator days. This is supported by the confidence interval of odds ratio of 0.55 to 0.84 which does not include one in the range hence significant statistical association.

When it comes to the odds ratio itself, the children who were on inotropic support are likely to spend 47%% more days on mechanical ventilation compared to those who were not on inotropic support.

Multivariable analysis

Table 5: Factors associated with mortality, AKI and ventilator days.

Factors associated with mortality	

Variable	**Survived N = 98**		**Adjusted OR (95% CI)**	**P-value**
	Yes	No		
AKI: No	0	2	NA	0.24
Yes	50	46		
Fluid overload: No	9	3		0.21
Yes	39	45	3.43 (0.52, 29.95)	
Inotropic use: No	19	14		
Yes	31	34	2.71 (0.98,8.41)	0.06
PELOD score: <=10	36	31		
>10	14	17	1.39 (0.51, 3.86)	0.52
AKI stages: Stage1	5	4		
Stage 2	13	12	1.47 (0.28, 8.06)	0.65
Stage 3	26	22	1.35(0.31, 6.29)	0.69

Factors associated with AKI				
Variables	**Acute kidney injury N = 98**		**Adjusted OR (95% CI)**	**P-value**
	Yes	No		
Fluid overload: No	11	1		0.21
Yes	83	1	0.13 (0.04, 4.24)	
Inotropic use: No	32	1		0.95
Yes	64	1	0.91 (0.03,29.95)	

Factors associated with mortality

Interpretations of p-values

Using P-values, AKI, PELOD-2 score, AKI stages and fluid overload were not associated with mortality even after adjusting for other factors as their p-values are more that 0.05 at

95% confidence level. On the other hand, inotropic use had a p-value of 0.05 hence it is statistically significantly associated with mortality after adjusting for other variables.

Interpretation of odds ratios

Fluid overload

Holding all the other factors constant

The odds ratio of association between fluid overload and mortality is 3.43 (0.52, 29.95). Inside the bracket is the confidence interval at 95% confidence level which includes one hence indicating that there is no statistical significance in association between fluid overload and mortality. The odds ratio of 3.43 means that the children who received fluid overload were 3.43 times more likely to die compared to those who did not get fluid overload.

Inotropic support

Holding all the other factors constant

The children who were on inotropic support were 2.71times more likely to die as compared to those who were not on inotropic support. The confidence interval of the odds ratio at 95% confidence level is 0.98 to 8.13. This interval includes one hence the association between inotropic support and mortality is not statistically significant.

PELOD-2 score

Holding all the other factors constant

The odds ratio for PELOD score is 1.39. This indicates that the children who had a PELOD score of above 10 were 39% more likely to die compared to those who had a PELOD score of 10 and below.

Stages of AKI

Holding all the other factors constant

A child being at stage 2 of AKI is 47% more likely to die compared to a child who is in stage 1 of AKI. Equally, a child who is in stage 3 of AKI is 35% more likely to die compared to a child who is in stage 1 of acute kidney injury.

Using the 95% confidence intervals for odds ratios, stage 2 (0.28, 8.06) and stage 3 (0.31, 6.29), there is no statistical significance in association between stage 2 and 3 of AKI and mortality as the two confidence intervals include 1.

Factors associated with AKI

Holding inotropic use constant;

The p-value for fluid overload 0.21 is more than 0.05 at 95% confidence level indicating that there is no statistically significant association between fluid overload and development of acute kidney injury.

Holding fluid overload constant

The p-value for inotropic use 0.95 is more than 0.05 at 95% confidence level indicating that there is no statistically significant association between inotropic use and development of acute kidney injury.

Interpretation of odds ratios

Fluid overload

Holding inotropic use constant

The children who got fluid overload were 87% less likely to develop AKI compared to those who did not get fluid overload. Despite fluid overload having an effect on development of acute kidney injury, the association is not statistically significant since the confidence interval for adds ratio (0.04, 4.24) includes one.

Inotropic use

Holding fluid overload constant

The children who were on inotropic support were 9% less likely to develop AKI as compared to those who were not on inotropic support. The confidence interval is 0.03 to 29.95 indicating that there was no statistically significant association between inotropic use and development of acute kidney injury.

CHAPTER 6: DISCUSSION

In this study, the association between fluid overload and unfavorable outcome were explored. We had a response rate of 76.5% which was sufficient as Fincham J. 2008 suggest that 60% response rate is sufficient. The association between fluid overload and mortality was not significant with a p value of 0.12 and odds ratio, 3.46 (0.88- 13.69). This finding was different from similar studies that have been done previously, for example, in a retrospective study done by Wachiraporn et al of 1048 patients, they found increased mortality in patients with first 72 hours positive fluid balance, odds ratio (95% CI) 3.04 (1.9–4.48) }. Another study done by Neyra et al which was a retrospective cohort of 2632 patients, they found out that, for Every 1-L increase in cumulative fluid balance at 72 hours of ICU admission was independently associated with hospital mortality in all patients (adjusted odds ratio, 1.06 [95% CI] 1.04-1.08; $p < 0.001$). In a study done by Martinez – Garcia et al, they found out that, mortality was significantly associated with positive fluid balance of >9% with (OR 4.3, 95% CI 1.6-11.7; p=0.003).

The relationship between fluid overload and AKI was not significant with a p value of 0.24 and, OR (95% CI), 0.13 (0.01 – 2.27). Though the association between the two was not significant, fluid overload was significantly associated with different stages of AKI. (p= 0.02). In a study done by Wang et al, they found an increased in severity of AKI with increased in fluid overload similar to our study, though they also found a significant association between fluid overload and AKI where fluid overload was significantly higher in the AKI group and was an independent risk factor for AKI (odds ratio, OR 4.508, 95% confidence interval, CI 2.9–7.01, $p < 0.001$).

Lack of similarity of the results finding between this study and other studies done before could be attributed by the small sample size we had compared to the comparing studies. Furthermore, we did not have a good number of control subjects as more than 80 % of patients had fluid overload and 98% had features of AKI.

This study was not without limitations, Lack complete data from the files that necessitated to have a smaller sample size was the biggest of all which necessitates to have prospective study that can give a clear picture of the problem and possible formulation of proper guidelines for

the proper fluid management. Some patients do present with features of AKI at presentation, therefore fluid overload might not be the contributing factor for AKI. And AKI might be among the organ dysfunction that occur in septic shock. Small number of control data might be one of the small setbacks which might have contributed to the major unreliable results that we had.

CONCLUSION

From this study, 88% of patients admitted with septic shock got fluid overload. The prevalence of AKI in patients admitted with septic shock was 98%. The relationship between fluid overload and AKI was not significant though fluid overload was significantly associated with the severity of AKI. Fluid overload had no significant association with mortality. While many studies had shown a significant association between fluid overload and its outcomes, this study did not show any. The differences in the results from the previous studies might have been contributed by the small number of sample size compared to the previous studies, small number of the control subjects since almost all the patients had fluid overload. There is a need for a large Randomized control study with a reasonable number of control subjects to be compared to those with fluid overload so as to have a clear picture on the intensity of the problem of fluid overload and its outcomes.

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APPENDICES

Table 6: Data collection sheet

		Patient 1	Patient 2	Patient 3
Patient ID				
Age				
Sex				
Admission weight				
Admission Date				
Discharge date				
Number of days in PICU				
Vitals on Admission	BP			
	RR			
	Temperature			
	PR			
	MAP			
PaO2 on admission				
PaCO2 on admission				
Lactate level on admission				
GCS on admission				
Pupillary reaction on admission				
WBC on admission				
Platelets on Admission				
MV use				
Days on MV				
Inotropic Use				
Days of Inotropic use				
S. creatinine	Day 1			
	Day 2			
	Day 3			
BUN	Day 1			
	Day 2			
	Day 3			

Total Fluid Input	Day 1			
	Day 2			
	Day 3			
Total Fluid Output	Day 1			
	Day 2			
	Day 3			
Patient Outcome	discharged/death			
PELOD score on admission				
PIM score on admission				

Table 7: PELOD score chart

Table I - Pediatric Logistic Organ Dysfunction Score - (PELOD-2)[6]

Organ dysfunctions and variables	**Points by severity level**						
	0	**1**	**2**	**3**	**4**	**5**	**6**
Neurologic							
• Glasgow coma score	≥11	5-10			3-4		
• Pupillary reaction	Both reactive					Both fixed	
Cardiovascular							
• Lactatemia (mmol/L)	<5.0	5.0-10.9			≥11.0		
• Mean arterial pressure (mmHg) (months)							
0-<1	≥ 46		31-45	17-30			≤ 16
1-11	≥ 55		39-54	25-28			≤ 24
12-23	≥ 60		44-59	31-43			≤ 30
24-59	≥ 62		46-61	32-44			≤ 31
60-143	≥ 65		49-64	36-48			≤ 35
≥144	≥ 67		52-66	38-51			≤ 37
Renal							
• Creatinine (µmol/L) (months)							
0-<1	≥ 69		≥ 70				
1-11	≥ 22		≥ 23				
12-23	≥ 34		≥ 35				
24-59	≥ 50		≥ 51				
60-143	≥ 58		≥ 59				
≥144	≥ 92		≥ 93				
Respiratory							
• PaO_2 (mmHg)/FiO_2	≥ 61		≤ 60				
• $PacO_2$ (mmHg)	≥ 58	59-94		≥ 95			
• Invasive ventilation	No			Yes			
Hematologic							
• WBC Count (x10^9/L)	>2		≤ 2				
• Platelet (x10^9/L)	≥142	77-141	≤ 76				

KENYATTA NATIONAL HOSPITAL
P.O. BOX 20723, 00202 Nairobi

Tel.: 2726300/2726450/2726550
Fax: 2725272
Email: knhadmin@knh.or.ke

Ref: KNH/PAEDS-HOD/48 Vol.II

Date: 13th October 2021

Dr. Fadhila Shabani Tekka
Department of Paediatrics and Child Health
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Tekka

RE: AUTHORITY TO COLLECT DATA IN PAEDIATRICS DEPARTMENT

Following approval of your Research proposal by the KNH/UON-Ethics & Research Committee and subsequent filing of the Study Registration Certificate, this is to inform you that authority has been granted to collect data in ***Paediatrics Department***, on your study titled ***"Effects of the first 72 hours of positive fluid balance on the development of acute kidney injury and mortality in patients with septic shock.***

Kindly liaise with the Senior Assistant Chief Nurse, Paediatrics for facilitation.

You will also be required to submit a report of your study findings to the office of the undersigned after completion of your study.

HOD OFFICE

Dr. Bill Kigathi
AG. Head of Department, Paediatrics

Cc. SACN, Paediatrics
ACN Incharge, PICU

UNIVERSITY OF NAIROBI
FACULTY OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/369

8th October, 2021

Dr. Fadhila Shabani Tekka
Reg. No.H16/37142/ 2020
(Pediatric Emergency and Critical Care Fellow)
Dept.of Paediatrics and Child Health
Faculty of Health Sciences
University of Nairobi

KENYATTA NATIONAL HOSPITAL APPROVED 08 OCT 2021 KNH/UoN-ERC P.O. Box 20723-00202 NAIROBI

Dear Dr. Tekka

RESEARCH PROPOSAL: EFFECTS OF THE FIRST 72 HOURS OF POSITIVE FLUID BALANCE ON THE DEVELOPMENT OF ACUTE KIDNEY INJURY AND MORTALITY IN PATIENTS WITH SEPTIC SHOCK (A RETROSPECTIVE COHORT STUDY) (P409/05/2021)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH-UoN ERC) has reviewed and approved your above research proposal. The approval period is 8th October 2021 – 7th October 2022.

This approval is subject to compliance with the following requirements:

i. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
ii. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
iii. 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.
iv. 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.
v. Clearance for export of biological specimens must be obtained from KNH- UoNERC for each batch of shipment.
vi. 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).
vii. 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.

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 Senior Director, CS, KNH
The Chair, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Medicine, UoN
The Chair, Dept.of Diagnostic Imaging & Radiation Medicine, UoN
Supervisors: Dr. Nelson Mukora Kimani, ,Dept. of Diagnostic Imaging and Radiation Medicine, UoN
Dr. Eunice Omamo, Dept.of Diagnostic Radiology, KNH

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