Outcomes of Children and Adolescents Admitted With Diabetic Ketoacidosis at Kenyatta National Hospital between February 2013- February 2018

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DECLARATION

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

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DEDICATION

I dedicate this dissertation to my daughter Ella and my son Rianto junior who have been fundamental pillars during this entire process and to Rianto for his unwavering support.

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This study would not have been possible without the efforts of many.

My gratitude goes to the Department of Pediatrics University of Nairobi for allowing this research to take place. The support accorded to me was overwhelming. The lecturers were informative and the criticisms instrumental in shaping this dissertation.

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DEFINITIONS OF TERMS

DKA (diabetic keto-acidosis): state of absolute or relative insulin deficiency. It is a complex metabolic state characterized by hyperglycemia, ketoacidosis, and ketonuria. In this study DKA diagnosis was based on the ISPAD criteria..

- Hyperglycemia [blood glucose (BG) >11mmol/L (≈200 mg/dL)]
- Venous pH < 7.3 or bicarbonate <15mmol/l
- ketonuria > 2 plus and above.

Acute kidney injury: is an abrupt loss of kidney function. In this study AKI was based on the RIFLE criteria of injury, either increase in serum creatinine two times above the baseline levels, or a urine output of less than 0.5ml/kg/hr for 12 hours.

Hyperglycemia: Also known as high blood sugar is a condition in which an excessive amount of glucose circulates in the blood plasma. In this study high blood glucose was defined as a random blood sugar level above 11.1 mmol/l.

Ketonuria: Condition in which ketone bodies (metabolic end-products of fatty acid metabolism) are present in the urine. In this study ketonuria was based on urine deep-stick ketones level of greater than 2 plus.

Metabolic acidosis: an acid-base disorder characterized by a decrease in serum pH and in this study it was considered at a pH of less than 7.35mmHg from an arterial blood sample

Fever: in this study was considered present at a temperature of above 37.5 degrees and was considered to indicate likelihood for infection.
Altered level of consciousness defined in this study as a score of less than A on the AVPU scale.

LIST OF ABBREVIATIONS

DKA	DIABETIC KETOACIDOSIS
ISPAD	INTERNATIONAL SOCIETY for PEDIATRIC and ADOLESCENT DIABETES.
BG	BLOOD GAS
IDF	INTERNAIONAL DIABETES FEDERATION
DM	DIABETES MELLITUS
T1DMM	TYPE 1 DIABETES.
LOS	LENGTH OF STAY
AKI	ACUTE KIDNEY INJURY

ABSTRACT

Diabetic ketoacidosis (DKA) is an acute, major, life-threatening complication that mainly occurs in patients with type 1 diabetes mellitus. Diabetic ketoacidosis (DKA) is the foremost cause of death in children with Diabetes mellitus (DM). Approximately 78000 children are diagnosed with diabetes each year, with a mortality rate of 0.15% - 0.31 % reported in industrialized nations. There is need to understand the DKA mortality rates in non-industrialized countries and associated factors. Recent data from developing countries report cerebral edema, sepsis, shock and renal failure as the main causes of death in DKA.

Objectives: Primary objective: To determine proportion of children aged 0-18 years managed for DKA at KNH who were discharged home.

Study Methods: This was a retrospective study carried out among 159 children (Ages 0– 18 years) admitted with DKA at Kenyatta National Hospital between February 2013 and February 2018. The study site was the central records department at KNH. Inclusion criteria was children aged 0-18 years admitted at KNH with diagnosis of DKA based on the ISPAD guideline biochemical criteria. Exclusion criteria Children with a clinician's diagnosis of DKA but with missing data on some of the diagnostic parameters stated above. Data analysis

Results: Out of 159 files reviewed the median age of 13 years with an IQR of 5, and 57% were females. Most of the participants had either severe DKA (40.9%) or moderate DKA (35.8%). Children discharged home were 93.1% while 6.9% died. The median duration of stay the general pediatric ward, adult ward and ICU was 10, 8 and 5 days respectively. Children who reported a temperature of above 37.5 degrees Celsius during the in-patient period were 88 (55.3%) while 25.7% had either high creatinine or decrease urine output.

Conclusion: 1. 93.1% of the children admitted with DKA were discharged home.

2. The median duration of hospital stay was 8 days which was similar to that reported from previous studies.

3. Factors associated with death among children admitted with DKA were: increased creatinine/ decreased urine output, altered level of consciousness, severe severity of DKA, presence of fever, male gender and lack of HBA1C report in the 6 months preceding admission.

Recommendation1. Need for admission in ICU for close monitoring to reduce mortality and morbidity.

2. There is need to closely monitor children with raised serum creatinine levels and decreased urine output as these are associated with poor clinical outcome in DKA

3. The study did not establish any significant association's between missed insulin doses and poor short term outcomes probably due to the small sample size. Larger studies are required to validate these results.

CHAPTER 1.

INTRODUCTION AND EPIDEMIOLOGY.

Diabetes is a metabolic disease that presents with chronic hyperglycemia resulting from defects in either insulin secretion, insulin function or both (1), The two main types of diabetes are: type 1 diabetes, which is characterized by an absolute deficiency of insulin secretion and type 2 diabetes, which results from resistance to insulin action and inadequate compensatory insulin secretory response (1, 2).Type 1 diabetes mellitus (DM) is a multisystem disease with both biochemical and anatomic/structural consequences (1). It is a chronic disease that affects carbohydrate, fat, and protein metabolism and is caused by lack of insulin, which results from the marked and progressive inability of the pancreas to secrete insulin due to autoimmune destruction of beta cells (3, 4).

Patients, particularly children and teenagers, may present with ketoacidosis as the first manifestation of the disease. (1). Most children in Sub-Saharan Africa present to health facilities with DKA following missed diagnosis of uncomplicated diabetes (5). The main presenting features for a child with type 1 diabetes mellitus is that of complete insulin deficiency, characterized by ketosis and eventually ketoacidosis, these children are therefore entirely dependent on exogenous insulin therapy.

Diabetic ketoacidosis (DKA) has been recognized as the main complication that is a potentially fatal emergency in children and adolescents with type 1 diabetes mellitus (6). DKA presents with a clinical triad of biochemical abnormalities that include hyperglycaemia (1. blood glucose level > 11 mmol/l 2. venous pH of <7.3 or bicarbonate level <15 mmol/L 3. ketonemia with ketonuria). A decrease in serum insulin and imbalance in other glucoregulatory hormones, causes hyperglycaemia, lipolysis and acidosis, which are responsible for development of DKA.

Estimates suggest that 78,000 children below 15 years develop type 1diabetes annually worldwide. (7). Risk factors for progression to DKA include previous infections such as urinary tract infections, pneumonia, pancreatitis, lack of insulin for treatment, non-compliance with treatment protocols, inadequate patient education on management of diabetes, intentional insulin omission and use of other medications that interfere with carbohydrates metabolism. While the true burden of type 1 diabetes in Africa is not known. Estimates propose that diabetes incidence rate will increase by 98% to 28 million patients by 2030, with the frequency of type 1 diabetes similarly expected to increase despite limited epidemiological data (5). Although the true incidence DKA among children in

tropical Africa is also not known it has been approximated that current DKA prevalence of 24% at presentation suggests that many cases are either not reported or are misdiagnosed (7).

DKA is the most common cause of death in children with T1DM, and the most common complication of DKA are cerebral edema, impaired renal function and secondary infections (9, 10). The mortality rate for DKA in children in industrialized countries has declined to 0.15% - 0.31 %.(9, 11). However, in less developed countries, the risk of death from DKA remains high, and children may die before receiving adequate treatment or during treatment (12). Timely recognition of DKA and appropriate subsequent management are important to minimize complications and death.

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CHAPTER 2.

LITERATURE REVIEW:

2.1 Definition of and Outcomes of Diabetic Keto-Acidosis among Pediatric Patients.

Diabetic Keto-acidosis (DKA) is an endocrine emergency which occurs in both newly diagnosed and established type 1 diabetic patient`s due to a reduction in circulating insulin, insulin resistance and increased counter-regulatory hormones. (16,17). DKA presents with a clinical triad which includes hyperglycaemia (blood glucose of greater than 11 mmol) venous pH of less than7.3 or bicarbonate of greater than 15 mmol/L, plus ketonemia and ketonuria. The severity of diabetic ketoacidosis is categorized based on the level acidosis into: Mild: pH of less than 7.3 and/or bicarbonate less than 15 mmol/L, Moderate: pH less than 7.2 and/or bicarbonate less than 10 mmol/L and Severe: pH less than 7.1 and/or bicarbonate less than 5 mmol/L (18).

Estimates suggest that 78,000 children under 15 years develop type 1 diabetes annually worldwide. (6). Up to 80 % of these children present with DKA at first contact, which is associated with both short term risks and long-term consequences (18, 19). The frequency of DKA relative to newly diagnosed diabetes globally varies regionally from between 11% to 67% in Europe (20) to 28.4% in the USA (21). The true incidence of DKA at first presentation in tropical Africa is unknown but has been estimated at 24% (6) suggesting that many cases are either underreported or the diagnosis is missed. While the mortality rate for DKA in children in the industrialized countries has declined to 0.15% - 0.31%.(9, 10) the same cannot be said about less developed countries, where the risk of death from DKA is higher, and many children in this setting die before receiving appropriate treatment (12).

A study was conducted at G. B. Pant Children hospital Srinagar in India between December 2012 and November 2014 looking at clinical outcomes for children admitted with DKA. Among Children aged ≤ 15 years with DKA enrolled in the study; 31 (70%) patients were males and 13(29.5%) were females mortality in this study was noted to be at 2.2% (22). Another study whose main aim was to investigate the complications of DKA in hospitalized patients was conducted in Namazi hospital, Shiraz, Iran with a total patient population of 224. In this study it was revealed that the mortality rate was at 1.7% (23).

Mbugua et al conducted a prospective cross-sectional study at KNH in 2005. The patients recruited in this study were those admitted in the medical wards. The sample size constituted 48 patients with type 2 diabetes who had DKA. Of the 48 patients 29.8% percent of the patients enrolled in the study

died within 48 hours of hospitalization. The major precipitating factors of DKA in this study were missed insulin injections and infections (24). Cerebral edema, sepsis, shock and renal failure contribute to high mortality in DKA (25). Poorly managed DKA in children below the age of 5 years is often associated with cerebral oedema which has a reported overall frequency for both newly diagnosed and established cases of approximately 0.7% in the United Kingdom (1,15) approximately 2% in Australia (Bui et al. 2002) and approximately 0.9% in North America (Glaser et al. 2001) (1). Neither the incidence nor prevalence of cerebral edema in African children who develop DKA is not known as many of them end up dying undiagnosed or develop unrecognizable, non-reversible neurological complications (1,5). It might not be as surprising as such that the incidence or the prevalence of cerebral oedema in African children who develop DKA is not known. Many of them end up dying undiagnosed or develop unrecognizable, non-reversible neurological complications (1,5). A consensus statement on diabetic ketoacidosis in children and adolescents done by David B. Dunger et al in 2003 reported a mortality rate of approximately 21% to 24% in children with DKA who developed cerebral oedema accounting for the bulk of DKA deaths and a high rate of invariable neurologic morbidity (13, 14, 15). Edge et al reported that cerebral oedema among 69 reviews of children with DKA between the ages 0-12 years of age was responsible for 0.46% - 4.66% mortalities and was the leading cause of mortality related to DKA. DKA was also noted to relate with impaired cognitive functions, such as short term memory and long term intelligence (26). Overall, cerebral edema accounts for approximately 60–90% of all childhood deaths related to diabetic-ketoacidosis. (28).

Renal failure has been largely recognized to be an important risk factor for increase in mortality in DKA by multivariate analysis in various studies from south India and around the globe (30). Acute renal failure though it might not be common in children with DKA, has a high mortality rate. Intrinsic renal failure in diabetic keto-acidosis is reported to occur in 11.5% of children from South India, with associated case fatality reports varying from 40% to 72% (25). A medical records review of all children admitted with DKA was conducted in British Colombia children`s hospital, from 2008 to 2013 by Hursh et al. The main objective was to determine the proportion of children hospitalized for DKA who developed AKI. The study revealed that of the 165 children hospitalized for DKA, 64.2% developed AKI. Stage 1 A was reported in 34.9%, stage 2 was noted in 45.3%, stage 3 was seen in 19.8% and two children required hemodialysis (29).

Acute kidney injury in DKA is concerning because it is associated with increased morbidity and mortality as well as increased risk of development of chronic renal disease, a finding that is especially relevant among children who are already at risk for diabetic nephropathy (29, 30). Renal

function in DKA could be deranged in various ways, one being that where there may be no previous impaired renal function and in this type kidney function may be returned to normal by correction of dehydration. This type is commonly encountered in DKA. The other type is where renal function gradually deteriorates for a variable period in time probably due to reversible renal ischemia (25).

2.2 Length of Hospital Stay and Associated Risk Factors

Although research indicates that intensive diabetes management reduces the risk of acute and chronic complications of type 1 diabetes, medical expenditures for its complications remain substantial. Short-term complications from type 1 diabetes represent one of the most potentially preventable causes of hospitalization in children, accounting for $67 million in hospital costs per year (31, 35). Inpatient facility care for diabetic ketoacidosis (DKA) is a potentially life-threatening but largely preventable complication in diabetes (36), and it is associated with significant health care utilization and expenditure (37, 38).

The repercussions of a failed public healthcare delivery systems in the African continent have negatively impacted on the overall management of patients (especially children) with DKA in particular and diabetes (5). For instance a Sudanese study, outlined that only 10% of children with diabetes were put in an in-patient care facility not even at the time of diagnosis but when they later developed severe hyperglycaemia or DKA (1, 32).

DKA admissions associated length of hospital stay has declined over the last two decades currently reaching to an acceptable length of hospital stay, with very little capacity for any further decline in the length of hospital stay. Focus being shifted towards reducing the general number of hospital admissions rather than trying to reduce further the number of days spent in an in-patient care facility (39*).* Historically, studies from the UK and USA have reported an average length of hospital stay to be approximately 6.1 to 6.9 days (40, 41). In the United States of America, reported in the years from 1988 through 2009, the average length of hospital stay of DKA patients as the first-time diagnosis declined by around 2.3 days (from 5.7 to 3.4 days) (42, 43).

Studies have implied that diabetic-ketoacidosis associated hospital admission is greatly associated with significant rise in medical costs. In Indiana, the direct medical care expenses associated with DKA admissions amounted to about 28.1% of the direct medical care expenses for the group of patients with diabetes type 1 who had been hospitalized. Hospitalized patients with DKA experience a longer hospital stay than non-DKA patients (44).

In a study conducted at a tertiary care facility in Pakistan. A total of 88 pediatric patients with DKA who were reviewed retrospectively. The mean age of the particular group of children was 7.5 ± 3.6 years. The mean duration of symptoms was approximately 3.2 ± 2.7 days which described the average number of days spent in the hospital (12).

In comparison to a study conducted in Ethiopia, which was a chart review of 151 patients admitted with a diagnosis of DKA ages between 15-84 years. Out of a total of the 151 DKA patients admitted during the given study period, more than two thirds (68.9%) patients had type 1 diabetes. Around 71(47%), of the patients had long hospital stay (stayed in the hospital for more than 7 days) ranging from 1 day to 59 days (45*).* Reasons for longer hospital in this particular study were related to DKA management set up, DKA management protocol, and patient characteristics.

Kenya`s focus is currently on communicable disease and most of the health care funding is diverted to communicable diseases neglecting non- communicable ones like diabetes. Lack of constant provision of insulin and blood sugar monitoring equipments, as this are largely considered as expensive drugs in Kenya. (46, 47)

According to the Kenya national diabetic strategy 2010- 2015, the scourge of diabetes is ravaging our country affecting the lives of our people, mainly the economically active groups resulting in a decrease in the output put of the country's labor force and consequently reducing the Gross Domestic Product (GDP). This has been compounded by a rapid increase in the prevalence of risk factors for diabetes and other chronic non-communicable diseases. If the disease is not tackled, it will hinder the attainment of the Millennium Development Goals (MDGs) or SDGs and realization of the Vision 2030 (46).

Diabetes and other non-communicable disease are now a threat to national development as they often result in long standing complications that are usually very costly to treat. Similarly these diseases are long standing and if not managed well can be fatal. They progressively drain the strength and resources of an individual rendering them unproductive and poor (46).

However steps have been made and a technical Working Group was established under the auspices of the Division of Non-communicable Diseases (DNCD) to develop this strategy based on evidence based prevention and control strategies for diabetes mellitus. This strategic framework will guide the funding, planning, organization, provision and monitoring and evaluation of services for people with or at risk of diabetes. It will consolidate and improve the quality and coverage of diabetes care services in Kenya.

The National Diabetes Strategy (NDS) proposes a framework and implementation options based on the overall goal of preventing or delaying the development of diabetes in the Kenyan population, improvement of the quality of life through reduction of complications and premature mortality in people with diabetes (46). It also places more emphasis on the need for more research towards better treatment, prevention and control methods for diabetes. There is a high proportion of undiagnosed cases of diabetes that end up with irreversible complications imposing a huge economic burden to the individual, family, community and in the health care system. The country has severe shortage/limited resources to take care of the extra burden of diabetes.

In areas where resources such health workers exist, they are not adequately trained and equipped to effectively manage diabetes and its complications. In addition, many of the existing health facilities in the country lack the capacity for early detection of diabetes as routine screening for high blood sugar is not often done (46).

Understanding the determinants of length of hospital stay in children with DKA is of great importance as multiple factors are likely to have contributed to the decrease of mean duration of length of hospital stay in more developed nations like America, hence reduction in hospitals general expenditures. These overall compounding factors lead to an increase in the incidence of DKA as not proper or timely management of patients is instituted. Therefore increasing the overall risk of complications, overall admissions and finally the duration of hospital stay. (48)

Infections complicating diabetic-ketoacidosis is much more common in developing nations, than the developed world counter-parts. While the role that infections play in complications of diabetic-ketoacidosis like: shock, cerebral edema, renal failure and death have been largely under studied. (48). Infections has been noted to be the second commonest cause of deaths in diabetic patients with DKA in the greater sub- Saharan Africa region (1). Diabetic children who develop DKA therefore continue to be at an increased risk of death secondary to infections as compared to those without infections. (1)

Generally malaria is among the top-most cause of childhood mortality in tropical Africa, and its manifestations such as metabolic acidosis, mental confusion to coma, hypoglycemia, vomiting, diarrhea, anemia, during the pathogenesis of the disease how it affects a child with diabetes and how it affects his/her prognosis remains to be unknown same implying to one who suffers DKA. The above mentioned symptoms greatly are similar to those encountered in patients with DKA making diagnosis and ultimately the overall clinical management more demanding and unfavorable. (1)

Infections are reported to accelerate the development of DKA in 32% of diabetic patients in the globe (5). Bacterial infections accounting to (51%) viral infections accounting for (49%) and *M.* tuberculosis (2%) infections: this being the most common among others (49).

Complications of streptococcus infections, herpes simplex or mycobacterium tuberculosis may trigger meningeal infections with common symptoms of inter-cranial infiltrations such as pyrexia, headache, altered mentation from simple irritability, confusion up to loss of consciousness (5). Precipitating those symptoms of cerebral oedema as well as overlapping with the same leading to an increase the general morbidity and mortality of these patients with DKA.

A study conducted at the pediatric intensive care unit (PICU) of Institute of Child Health and Hospital for Children, Chennai, India, whose main aim was to identify the role of infections in children with DKA (48). The study was conducted among 118 admissions of DKA from a pediatric tertiary care Institute where they had identified infections as a significant risk factor for severe metabolic derangements, complications and contributed to poor outcomes in children with DKA. Fever was encountered in 61 children at presentation. 34 of the 71 children reported to have had a fever had an infection while 27 out of the 71 children without fever as a presentation had no infection (48).

However infections were identified in 47 children. Infections were highly associated with severe persistent acidosis, higher base deficit, higher osmolarity at 6 hours, longer duration of insulin infusion, longer hospital stay, hypoglycemic episodes and complications like shock, cerebral edema and renal failure. (48, 49).

Conceptual framework

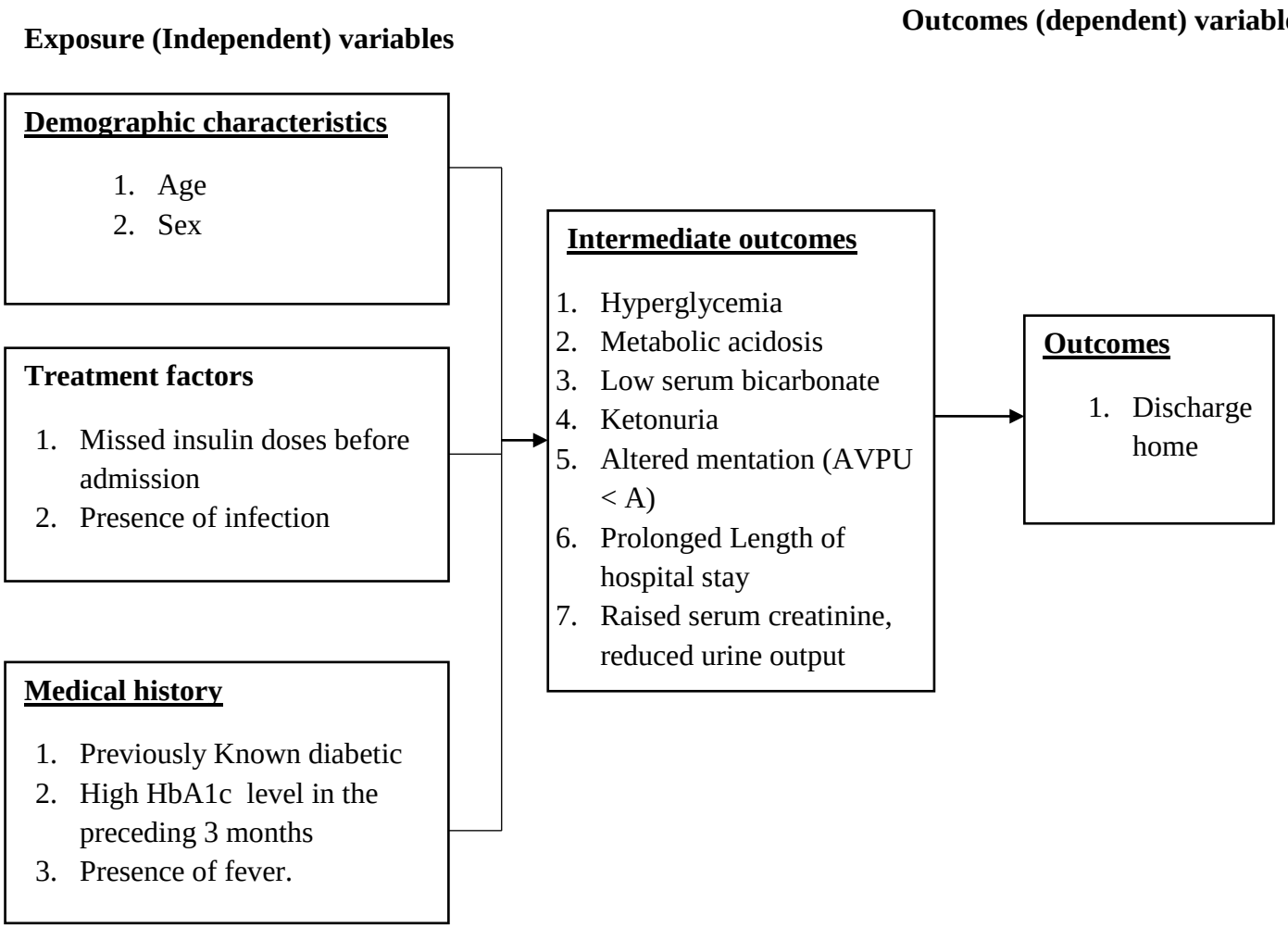

Figure 1: Conceptual Framework

CHAPTER 3.

3.1 STUDY JUSTIFICATION AND UTILITY.

Children with T1DM are frequently poorly managed especially when they develop DKA. Healthcare workers need to be aware of the high mortality and morbidity risk associated with DKA as well the related factors in children. Currently there are very few studies conducted in Kenya that have looked at complications and outcomes of DKA among Kenyan children. For a diabetic child who develops DKA several factors will ultimately influence the outcome of their treatment. These factors include DKA severity, fever, creatinine levels, reduced urine output, altered level of consciousness, missed insulin doses prior to admission and HBA1c levels. The aim of this study was to determine what proportion of children admitted with DKA are discharged home and subsequently assess for patient factors associated with mortality among children with DKA. This information would guide clinicians on better implementation of available treatment and follow up protocols so as to minimize the occurrence of poor outcomes in this group.

Identifying factors associated with long hospital stay provides a window for efficient utilization of hospital resources through modification of these factors. Results will also assist health care workers to better understand the effect of hospital stay on the quality of these children's lives. Finally estimating the proportions of children, who are discharged home alive will provide useful information on local trends on outcomes of DKA management and allow for institution of proper holistic care plans that will reduce mortality in these groups of children.

3.2 STUDY QUESTION:

How many children admitted with diabetic ketoacidosis at Kenyatta National Hospital are discharged home?

3.3 STUDY OBJECTIVES

Primary objective: To determine proportion of children aged 0-18 years managed for DKA at KNH who are discharged home.

Secondary bjectives:

1. To describe the average length of hospital stay for children admitted with DKA at KNH.
2. To describe factors associated with discharge among children admitted with DKA (DKA severity, altered level of consciousness, increased serum creatinine/ decreased urine output, presence/absence of fever, previously diagnosis versus newly diagnosed, HBA1c not done within preceding 6 months, and missed insulin doses prior to admission).

CHAPTER 4.

METHODOLOGY

4.1 Study Design

This was a retrospective study to describe clinical outcomes of children managed for DKA at KNH over a 5 year period (February 2013- February 2018) as well as to describe factors associated with mortality.

4.2 Study Location

Kenyatta National Hospital is the largest national referral facility in Kenya and is affiliated to the University Of Nairobi College Of Health Sciences as a teaching hospital. KNH bed capacity is approximately 1800. However bed occupancy is between 200-300% at any given time. There are 4 pediatric wards that admit 600- 800 children every month. Children aged 12 years and below are admitted in the pediatric wards. Approximately 4 and 2 children are admitted in the pediatric and adolescent wards respectively every month.

Diabetic children are seen in two diabetic clinics. Those under the aged 12 years and below are seen at the pediatric diabetic clinics, run by 3 pediatric endocrinologists and pediatric registrars. Those above 12 are seen at the adolescents diabetic clinics run by physicians. This study was carried out at the KNH central records department over a 3 month period between 1st January and 1st March 2019 where medical records of 159 children admitted with DKA were reviewed.

4.3 Study Population

Children aged 0-18 years admitted with DKA at KNH between February 2013 and February 2018. Children aged 12 years and below were admitted in the pediatric wards and those above 13 years were admitted in the medical wards. The study targeted a total population of 150 children admitted with diagnosis of DKA within the period of study.

4.4 Inclusion Criteria

Children aged 0-18 years admitted at KNH with diagnosis of DKA based on all the biochemical criteria as per the ISPAD guidelines during the period between February 2013 and February 2018.

- Hyperglycemia [random blood glucose (BG) >11mmol/L (≈200 mg/dL)].
- Arterial blood pH < 7.3 or bicarbonate <15mmol/l.
- ketonuria > 2 Plus in urine sample.

4.5 Exclusion Criteria

- Children with a clinician's diagnosis of DKA but with missing data on some of the diagnostic parameters stated above.

4.6 Study Outcomes

- Proportion of children with DKA discharged home.
- Proportion of children who had altered consciousness
- Proportion of children with increased creatinine (> 2 times above normal levels) or decreased urine output <0.5mls/kg/hr for 12 hours.
- Average length of hospital stay.
- Factors associated with death among children with DKA (presence of fever, newly diagnosed compared to previously diagnosed, missed insulin doses prior to current admission, HBA1c level in the 6 months preceding current admission, male gender, and DKA severity).

4.7 Sample Size Determination

The study used Fisher's formula for sample size determination as below:

$$n = \frac{z^2 p\ (1-p)}{d^2}$$

Where,

n = Desired sample size

Z = Value from standard normal distribution corresponding to desired confidence level (Z=1.96 for 95% CI)

P = which was 70% proportion of children with DKA that we estimate will be discharged home based on study by Mbugua et al conducted in the adolescent wards that reported the same percentage. estimated patients admitted in the adolescent ward and managed for DKA at KNH (24).

d = desired precision (0.05)

$$n_o = \frac{1.96^2 0.70\ (1 - 0.70)}{0.05^2} = 322$$

Medical records were reviewed for the last 5 years and data from medical records estimated there would be a total of 30 admissions of children with DKA every year giving a total target population of 150 children. The sample size after adjustment for finite populations less than 10,000 is:

$$n = \frac{n_0}{1 + \frac{n_0 - 1}{N}} = \frac{322}{1 + \frac{322 - 1}{150}} = 103$$

Hence a sample size of 103 medical records of children admitted with diagnosis of DKA.

4.8 Sampling Procedure

A list of all admitted DKA patients was generated by reviewing admission records of children for the 5 year period under consideration. Files were retrieved from KNH central registry and identification of patient records that met the inclusion criteria was done. The eligibility criterion was files with all ISPAD biochemical criteria for DKA documented. Consecutive sampling was done to select 159 files that were then recruited into the study. The missing files and those that did not meet the inclusion criteria were excluded.

4.9 Data Collection Methods

4.9.1 Data collection tools/ instruments.

A structured questionnaire (Appendix 1) was used to collect data on patients' demographic characteristics, medical history and DKA-specific information.

4.9.2 Data Collection

Data collection was conducted by the investigator assisted by two research assistants, who were trained clinical officer interns. The research assistants were trained by the investigator on DKA ISPAD criteria identification, identification of children with raised serum creatinine and reduced urine output, identification of altered level of consciousness, filling of the structured questionnaire, data collection methods and ethical concerns. Medical records of patients (0-18 years) with DKA admitted to the KNH pediatric and adult wards were traced and drawn from records department.

KNH file tracing protocol was used to trace, retrieve and re-file all the patients' files within the central records unit. Relevant data was abstracted from the files and information entered into a structured questionnaire. The data that was captured included patient demographics, presenting symptoms, precipitating causes of DKA, biochemical profiles (blood glucose, urine ketone, urine output, serum creatinine levels and serum bicarbonate levels), presence of neurological signs and fever and length of hospital stay. Records of patients admitted multiple times during the specified study period for DKA were only reviewed once and the most recent admission data recorded.

4.10 Study variables

Independent variables:

1. Severity of DKA.
2. Fever.
3. Creatinine levels, reduced urine output.
4. Altered level of consciousness.
5. HBA1c levels.
6. Missed insulin doses prior to admission.

Dependent variable

1. Discharge home.

4.11 Data Management and Analysis

Coded data was entered and analyzed in SPSS version 22.0 statistical software. Baseline descriptive summary patient characteristics were summarized and presented in form of frequency tables, histograms, pie charts and bar graphs. Categorical variables were presented in form of percentages and means or medians were presented for continuous variables. Proportion of children who were discharged home , had altered level of consciousness, had either increased serum creatinine or decreased urine output were calculated and presented as percentages with 95% confidence intervals. The average length of hospital stay was presented as a median and inter-quartile range (IQR). Presence of fever, newly diagnosed compared to previously diagnosis, effect of gender, HBA1c done in the preceding 6 months, DKA severity, presence of altered level of consciousness during in-patient period, increased creatinine/decreased urine output and missed insulin doses prior to current

admission were tested for association with the primary outcome measure, discharge home using chi square test. Tests of association were conducted at 5% significance level (p value < 0.05).

4.12 Control of errors and bias.

1. A clearly defined case definition was used to ensure only children with DKA were recruited into the study.
2. Use of a standard data abstraction tool to ensure data is abstracted in a uniform manner from files.

4.13 Study limitations

This being a retrospective record review, missing data especially on the exposure factors was a limitation in testing for associations. The investigator tried to ensure data abstraction was as complete as possible and the cases with missing data were included during analysis to ascertain the level of bias due to missing information. The investigator could also not make definite conclusions on associations between exposure variables and outcomes of interest based on the fact that the sample size was inadequate to test for these associations

4.14 Ethical considerations

1. Approval was sought from Kenyatta National Hospital and University of Nairobi ethics research committee to collect and analyze data as part of thesis dissertation. Copies of the protocol, were presented to the above named committee for written approval prior to commencement of the study.
2. Permission was sought from the KNH administration to review patient records.
3. To ensure patient confidentiality was maintained, no names were recorded in the data abstraction tool and the data abstracted was only available to the principal investigator, and was kept under lock and key.

4.15 Dissemination of Study Findings

The results of the study will be:

1. Presented to KNH (paediatric endocrinology unit), adult endocrinology unit and UON DPCH through a formal meeting where a copy of the same will be provided.
2. Presented in pediatric medical conferences.
3. Submitted for publication in a peer reviewed journal.

4. Availed to the Ministry of health - department of non-communicable diseases as part of sensitization on treatment outcomes of children with DKA type 1 diabetes.

CHAPTER 5.

RESULTS

5.1 Introduction

The purpose of this study was to establish outcomes and associated correlates among children admitted with DKA at KNH. The study included children who met the ISPAD criteria on DKA: Blood glucose level > 11mmol/L; Venous pH < 7.3mmol/L or Bicarbonate < 15mmol/L and Ketonuria > 2 plus in urine sample.

This was a retrospective study which reviewed medical records of 159 children admitted with DKA over a period of 3 months in the past 5 years. All children recruited met all the eligibility criteria and therefore qualified for further analyses.

5.2 Bio-Data

The median age of children in this study is 13 years with inter-quartile range (IQR) of 5. The study found out 90 (56.6%) of the children were admitted in the medical wards while 69 (43.4%) were admitted in the pediatric wards.

5.2.1 Gender of children

The study found 91 (57.2%) of the children were females and 68 (42.8%) males. The summary of these findings are presented in the table below.

Table 1: Distribution of DKA patients by Gender

	Medical wards		Pediatric wards		Total	
	n	%	n	%	n	%
Female	51	56.7	40	58.0	91	57.2
Male	39	43.3	29	42.0	68	42.8
Total	90	100	69	100	159	100

5.3 Medical History

5.3.1 Children's admission history

The results revealed 30 (18.9%) of the children admitted with DKA were referrals, 25 (15.7%) were direct admissions to KNH while for the majority 104 (65.4%) it was not documented whether they were referrals or not. Of the 30 children referred 66.6% of them had the referring facility indicated while 33.4% did not. This data is summarized in the table below.

Table 2: Admission history of children with DKA

		Medical wards		**Pediatric wards**		**Total**	
Study characteristic		n	%	n	%	n	%
Referral histories of children (n= 159)	Referred to KNH	9	10.0	21	30.4	30	**18.9**
	Self-referrals	13	14.4	12	17.4	25	**15.7**
	Not indicated whether they were referred or not	68	75.5	36	52.2	104	**65.4**
	Total	90	100	69	100	159	**100**
Referring facility (n=30)	Indicated	4	44.4	16	76.2	20	**66.6**
	Not indicated	5	55.6	5	23.8	10	**33.4**
	Total	9	100	21	100	30	**100**

5.3.2 Previous versus new diagnosis of diabetes

Diabetes treatment history

The study found that out of 159 children admitted with DKA, 103 (64.8%) had a previous diagnosis with diabetes (prior to current admission) and 56 (35.2%) were newly diagnosed during the current admission. Newly diagnosed children in the pediatric and medical wards were 40.6% and 31.1% respectively. Among previously diagnosed children, 88 (85.4%) were on mixtard insulin, 11 (10.7%) were on (lantus+ short acting insulin) and for 4 (3.9%) children their records did not indicate the type of insulin they were on. Results also revealed that 26.2% of previously diagnosed children had a record of having missed insulin doses prior to admission. The summary of these findings are presented on the table below.

Table 3: Diabetes treatment history of children

Treatment characteristic		**Medical wards**		**Pediatric ward**		**Total**	
		n	%	n	%	n	%
Time of diabetes diagnosis in relation to current admission (n=159)	Previously diagnosed	62	68.9	41	59.4	103	**64.8**
	Newly diagnosed	28	31.1	28	40.6	56	**35.2**
	Total	90	100	69	100	159	**100**
Type of Insulin treatment prior to current admission (previously diagnosed n=103)	Mixtard	55	88.7	33	80.5	88	**85.4**
	Lantus + short acting insulin	6	9.7	5	12.2	11	**10.7**
	Missing record	1	1.6	3	7.3	4	**3.9**
	Total	62	100	41	100	103	**100**
Missed insulin doses prior to current admission (n=103)	Yes	19	30.6	8	19.5	27	**26.2**
	No	43	69.4	33	80.5	76	**72.8**
	Total	62	100	41	100	103	**100**

Data on HbA1c testing

It was found that out of 159 children recruited into the study, only 37 (23.3%) had a record having done a HbA1c level within the 6 months preceding admission. The mean value of HbA1c for children in adult wards was 11.52% while those in pediatric wards had a mean of 11.48%. Overall mean value of HbA1c was 11.48%.

These results are presented in the bar graph below.

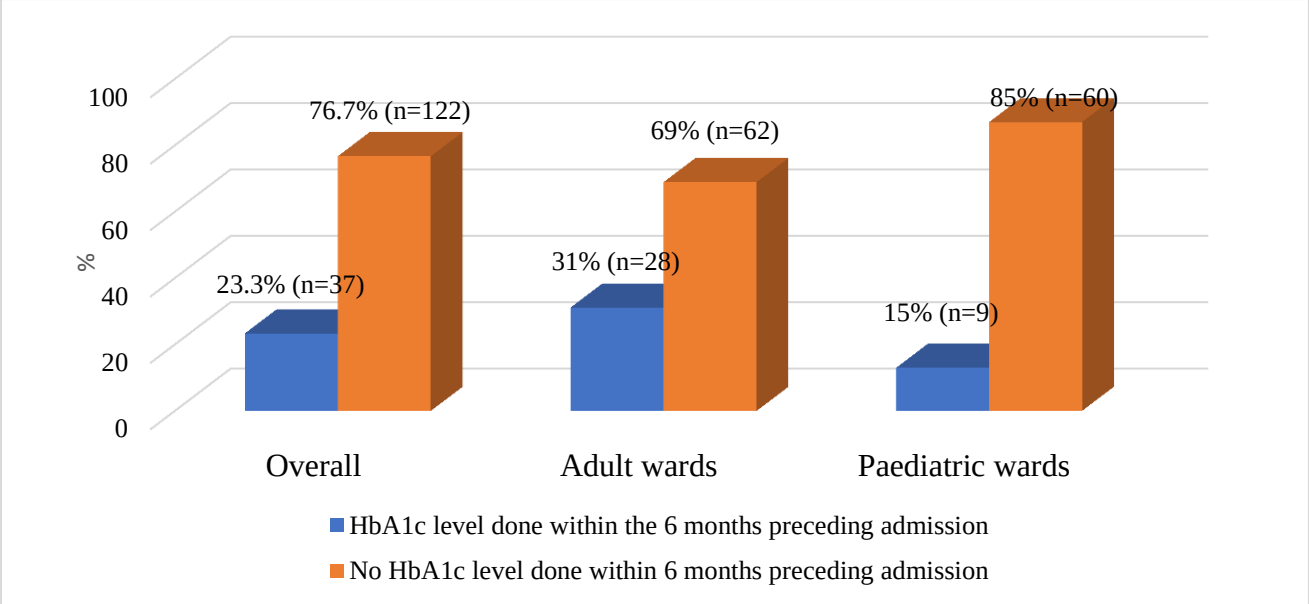

Figure 2: Bar graph showing data on HBA1c records of children admitted with DKA

Among the 37 records (HbA1c level done within the 6 months preceding admission) the mean HBA1c level was 11.48% which is above the recommended 8% level that would indicate good sugar control. Only 6 (16.2%) of the 37 children had HbA1c below 8% indicating good sugar control while 31 (83.8%) had HbA1c above 8%.

These results are presented in the pie charts below.

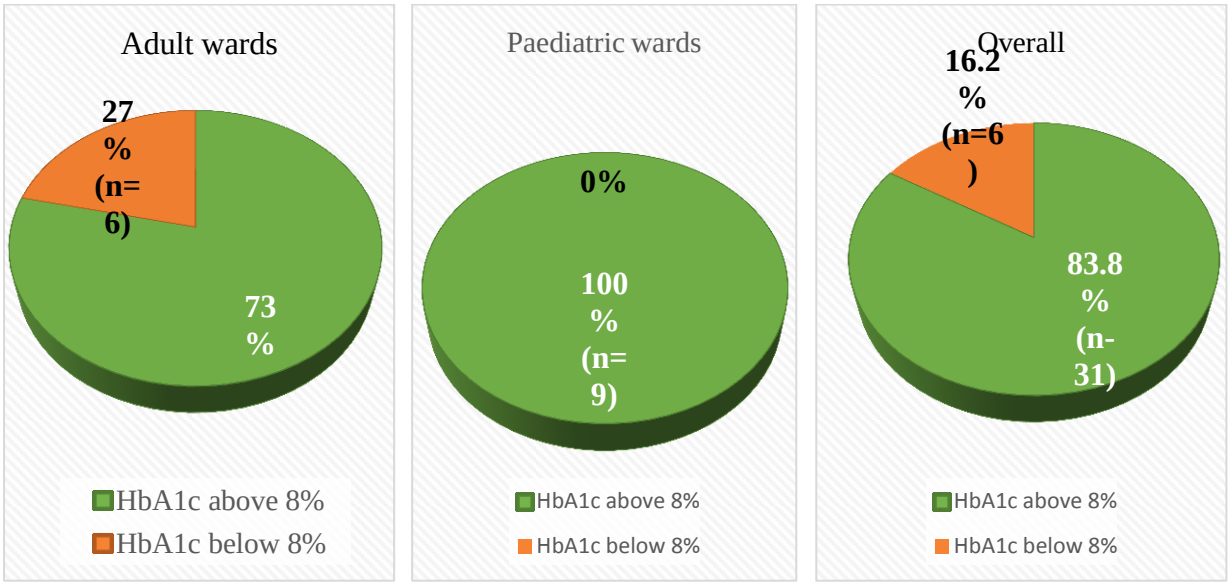

Figure 3: HbA1c levels indicting sugar control

Data on follow up clinics for previously diagnosed children

The study found out of the 103 children previously diagnosed with diabetes, 16 (15.5%) were on regular follow up within diabetes clinics at various facilities while for 74% records did not indicate whether they were on follow up or not. The minority 9.7% of the children were not on follow up.

Of the 16 (15.5%) children on follow up, 10 were on follow up at the KNH diabetic clinic constituting 62.5% of children on follow up.

These results are summarized in the table below.

Table 4: History on follow up for children previously diagnosed with daibetes

		medical wards		**Pediatric**		**Overall**	
		n	%	n	%	n	%
Previously diagnosed (n-103)	**On follow up**	12	19.4	13	31.7	16	15.5
	Not on follow up	6	9.6	9	22	10	9.7
	Missing records	44	71.0	19	46.3	77	74.8
	Total	62	100	41	100	103	100
Point of follow up (n-16)	**Follow up at various facilities**	1	16.7	1	10.0	2	12.5
	At KNH	3	50.0	7	70.0	10	62.5
	Follow up facility not indicated	2	33.3	2	20.0	4	25.0
	Total	6	100	10	100	16	100

5.3.3 Severity of DKA

Results revealed that out of the 159 children admitted with DKA 65 (40.9%) had severe DKA, 57 (35.8%) had moderate DKA and 37 (23.3%) had mild DKA. In the adult wards, 41.1% had severe DKA while in pediatric ward 42% had severe DKA. The results are presented in the pie charts below.

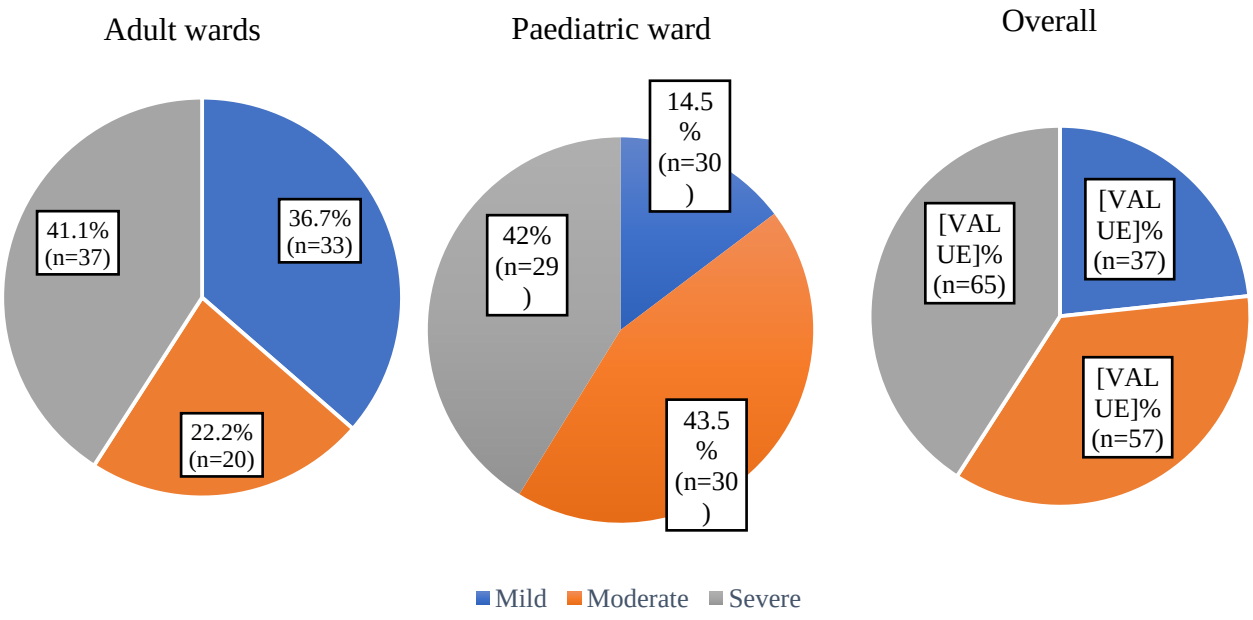

Figure 4: Severity of DKA

5.3.4 Presence of fever

The study also established that out of the 159 children admitted with DKA in KNH 88(55.3%) of children had temperature readings above 37.5 degrees Celsius at some point during the inpatient stay. Of the remaining 68(42.8%) had normal temperatures while 3 (1.9%) did not have any temperature readings documented in the records. In this study a high temperature above 37.5 degree Celsius was considered to indicate possible infection.

Elevated temperature was seen in 60.9% of the children admitted in pediatric wards and in 51.1% of children admitted in adult wards. The summary is presented in the bar graph below.

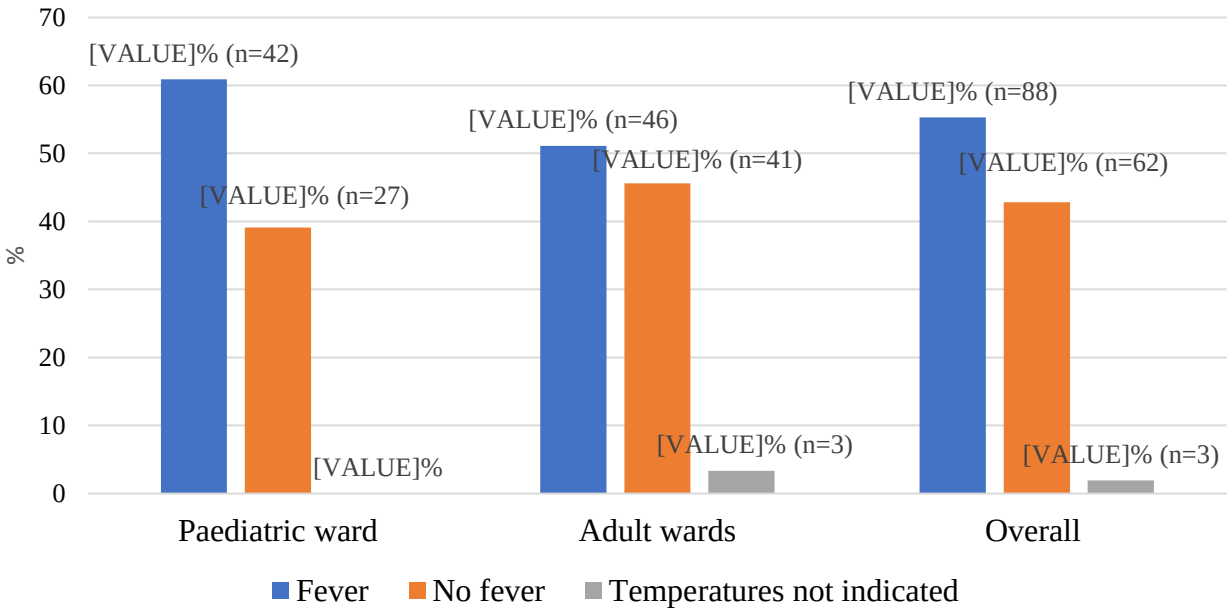

Figure 5: Presence on infection

5.4 OUTCOME MEASURES

5.4.1 Proportion of children aged 0-18 years managed for DKA at KNH who were discharged home

The primary objective of this study was to establish the proportion of children aged 0-18 years managed for DKA at KNH and discharged home. Out of the total sample of 159 children with DKA recruited, 148 (93.1%) were discharged home while 11 (6.9%) died. In adult wards, 86 (95.6%) of children were discharged home and 4 (4.4%) died while in pediatric wards 62 (89.9%) were discharged home and 7 (10.1%) died. The summary of these findings is presented in the pie charts below.

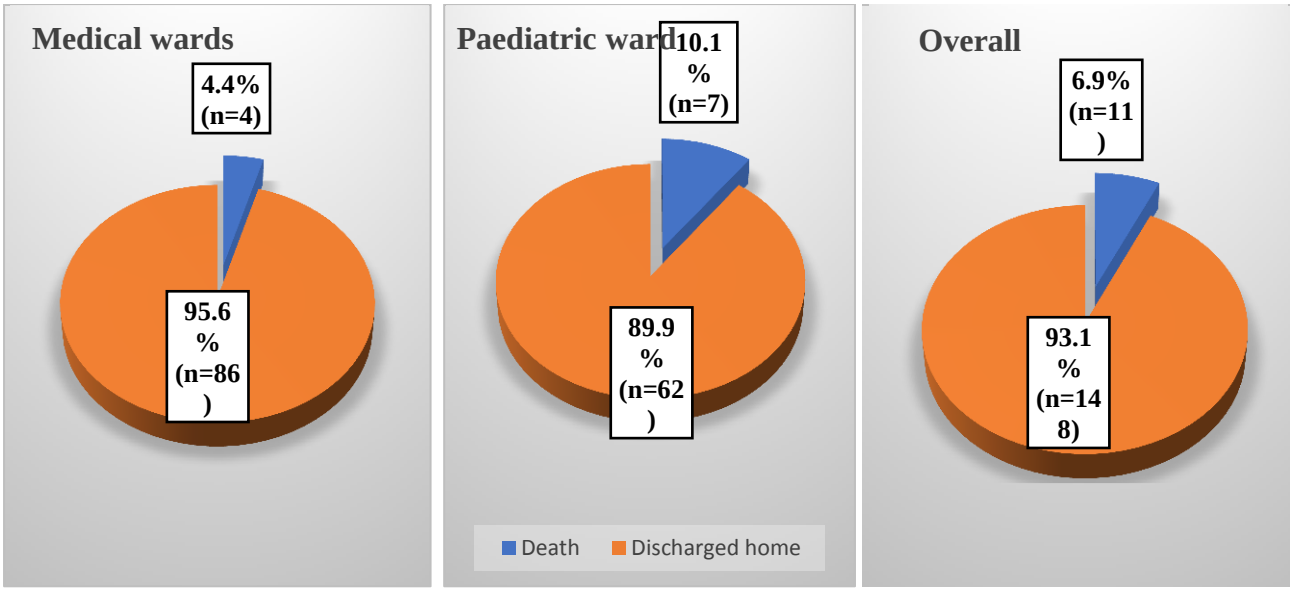

Figure 6: Proportion of children discharged home.

5.4.2 Creatinine and urine outputs levels of children

At some point during the in-patient period 29(18.2%) children had high serum creatinine while 12(7.5%) had either anuria or reduced urine output of less than 0.5ml/kg/hr for ≥ 12 hours. These findings are summarized in the table below.

Table 5: Raised creatinine above baseline and decreased urine output during inpatient stay

Characteristic	Medical ward		Pediatric ward		Overall	
	n	%	n	%	n	%
Serum creatinine levels raised > 2 times above the baseline level	19	21.1	10	14.5	29	18.2
Anuria or reduced urine output of less than 0.5ml/kg/hr for 12 hours	8	8.9	4	5.8	12	7.5
Normal kidney function	63	70	55	79.7	118	74.3
Total	90	100	69	100	159	100

5.4.3 Children who reported altered level of consciousness during the admission period

The study found that 76 (47.8%) children had signs of altered level of consciousness while 80 (50.3%) had normal level of consciousness at some point during the in-patient period. However these findings had also resolved at the time of discharge. These findings are reflected in the bar chart below.

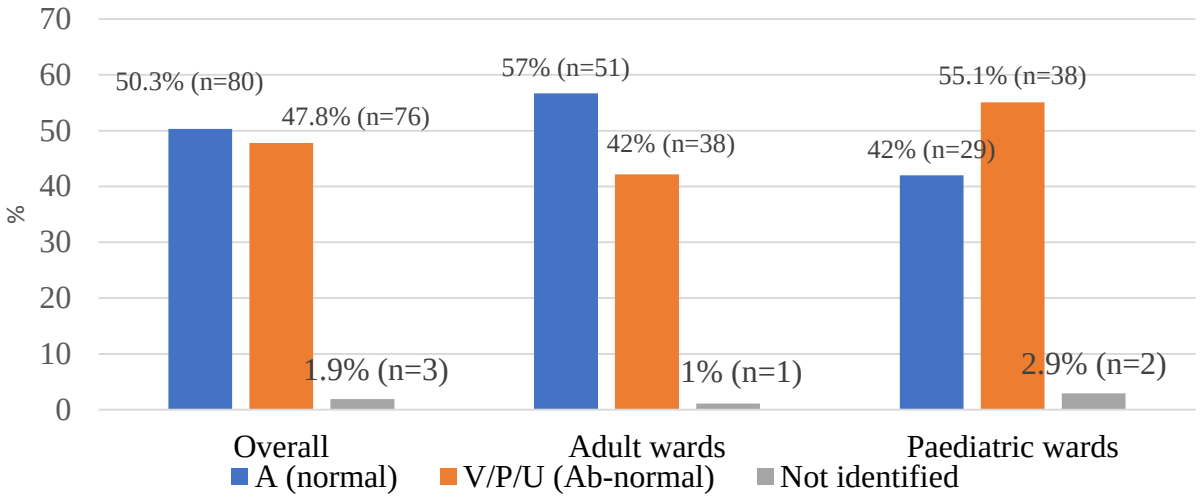

Figure 7: Assessment of Children's level of consciousness based on the AVPU scale.

5.4.4 Outcomes of children with high creatinine or decreased urine output and altered level of consciousness during the admission period

Children with raised serum creatinine were 9, in this group 5 died. Those who had a reduced urine output were 12, in this category 4 died. Children with altered level of consciousness were 76 those who died in this group were 9 .These findings are summarized in the table below.

Table 6: Outcomes of children with high creatinine/decreased urine output and altered level of consciousness during the admission period

		Medical ward		**Pediatric ward**		**Overall**	
		Discharged Home	Died	Discharged Home	Died	Discharged Home	Died
Serum creatinine levels raised > 2 times above the baseline level		17	2	7	3	24	5
Anuria or reduced urine output of less than 0.5ml/kg/hr for 12 hours		6	2	2	2	8	4
Normal kidney function		63	0	53	2	116	2
Total		86	4	62	7	148	11
Altered level of consciousness	A/V/P/U<A	34	4	33	5	67	9
	A(normal)	51	0	27	2	78	2
	Not identified	1	0	2	0	3	0
Total		86	4	62	7	148	11

5.5 Average length of hospital stay for children admitted with DKA at KNH

One secondary objective was to establish the average length of hospital stay for children admitted with DKA at KNH. The overall median duration of hospital stay was 8 days with an inter-quartile range of 8, the median number of days children admitted in the pediatric and Main ICU was 5 with an inter-quartile range of 4 and 5 respectively, and median number of days in the adult and pediatric wards was 10 and 8 days with an inter-quartile range of 8 and 5.5 respectively. The summary statistics are presented in table 7 below.

Table 7: Duration of hospital stay

Ward	Median length of hospital stay	IQR
Pediatric ward	10	8
Adult Medical ward	8	5.5
Pediatric ICU	5	4
Main ICU	5	7
Overall duration of hospital stay	8	8

5.6 Factors associated with discharge home among children admitted with DKA.

To describe factors associated with death among children with DKA, the study looked for associations between the exposure variables like severity of DKA, age, gender, presence of fever at any time during the in-patient period, previous diagnosis of diabetes, type of insulin child was on, missed insulin doses prior to current admission, HBA1c level in the preceding 6 months and death Associations between these exposure variables and the outcome were tested using chi-square test of independence and where the cells had numbers less than 5, Fischer's exact test was applied. Odds ratios with 95% CIs were calculated to identify presence of significant associations.

From the results children admitted to the adult wards had higher odds of being discharged home (OR 2.427; 95% CI: 0.681-8.653; p=0.0503) as compared to those in pediatric ward. The results revealed children with HbA1C of >8% had a lower likelihood of death (OR: 0.1, 95% CI: 0.0021-1.6201, $p<0.05$) as compared to those whose HbA1C was <8% which contrary to literature however, this is because only 37 (23.3%) of the total sample had HbA1C done.

Children with serum creatinine levels raised > 2 times above the baseline level were 5.833 times more likely to die (AOR 5.833; 95% CI: 1.604-21.213; $p<0.05$) while those who had anuria or reduced urine output of less than 0.5ml/kg/hr for 12 hours or longer were 9 times more likely to die (AOR 9; 95% CI: 2.173-37.279; $p<0.05$). However the confidence intervals were very wide due the small sample size.

Children who were females compared to males had 2 times higher odds of dying (AOR 2.088; 95% CI: 0.533-8.186; $p<0.05$). Children with normal level of consciousness were less likely to die as compared to those with altered level of consciousness based on the AVPU scale (AOR 0.191; 95% CI: 0.04-0.914; $p<0.05$). It was that established that children with fever were 1.383 times more likely to die (AOR 1.383; 95% CI: 0.388-4.931; $p<0.05$) compared to those with no fever.

Children with severe DKA had highest odds of dying (OR: 4.6, 95% CI: 1.8-15.2, $p<0.05$) while children with moderate DKA had higher odds of death as compared to those children with mild DKA (OR: 3.3, 95% CI: 1.4-13.8, $p<0.05$).

This study did not establish any significant association between ward of admission, type of insulin the child was on, missed insulin doses prior to current admission and death outcomes.

The summary of these findings is presented in table below.

Table 8: Association between patient characteristics and discharge home.

Study characteristic			Death	
		n	AOR (95% CI)	p-value
Age in years	>12	90	0.412 (.116-1.469)	0.0503
	<=12	69	Reference category	
Type of insulin the child is on	Mixtard	88	0.864 (0.096-7.767)	0.864
	Lantus + short acting insulin	11	Reference category	
Missed insulin doses	Yes	27	1.087 (0.206-0.922)	0.922
	No	75	Reference category	
HBA1c <8% in the preceding 6 months	>8%	31	**0.1 (0.0021-1.6201)**	**0.028**
	<8%	6	Reference category	
Serum creatinine levels raised > 2 times above normal level	Yes	29	**5.833 (1.604-21.213)**	**0.007**
	No	130	Reference category	
Anuria or reduced urine output of less than 0.5ml/kg/hr for 12 hours	Yes	12	**9.0 (2.173-37.279)**	**0.002**
	No	140	Reference category	
Sex	Female	91	**2.088 (0.533-8.186)**	**0.021**
	Male	68	Reference category	
Level of Consciousness	A	80	**0.191 (0.04-0.914)**	**0.002**
	<A	76	Reference category	
Temperature above 37.5 degrees Celsius	Fever	88	**1.383 (0.388-4.931)**	**0.046**
	No fever	68	Reference category	
DKA severity	Mild	37	Reference category	
	Moderate	57	**3.3 (1.4-13.8)**	**0.010**
	Severe	65	**4.6 (1.8-15.2)**	**0.000**

*all p value are based on fisher's exact tests because all cells had expected count less than 5.

CHAPTER 6:

6.1 DISCUSSION

This study revealed that out of the 159 children admitted with DKA, 93.1% of these children were discharged home while 6.9% of them died. The mortality rate of 6.9% in this study was lower when compared to a study conducted in KNH adult wards. Mbugua et al conducted a prospective cross-sectional study at KNH among patients admitted in the adult wards with DKA. Twenty nine point eight percent (29.8%) of the patients died within 48 hours of hospitalization. In that study the major precipitating factors of DKA were missed insulin injections and infections. (24)). Our rate was higher as compared to a different study that was conducted at G. B. Pant Children hospital Srinagar in India between December 2012 and November 2014 among Children aged ≤ 15 years with DKA; reported Mortality rate of at 2.2%. (22). Studies from developed countries have reported mortality rate ranges between 0.15% - 0.31 %.(9, 10). This high mortality rate may be attributed to the fact that majority of the children who died either had altered level of consciousness or high serum creatinine/ reduced urine output. Of the children admitted in the adult wards 95.6% were discharged home while 4.4% died and of those admitted in the pediatric wards 89.9% were discharged home and 10.1% died. Generally pediatric wards had a higher mortality as compared to the adult wards. On further analysis study revealed that children admitted in adult wards had lower odds of experiencing death as compared to those admitted in the pediatric wards (AOR 0.421; 95% CI: 0.116-1.469; p<=0.05). These findings can be attributed to the fact that most of the children admitted in the adult wards had better sugar control as compared to those admitted in pediatric wards. Based on the HbA1c records majority of the children admitted in the pediatric wards had HbA1c of more than 8% indicating poor control.

This study revealed that out of the 159 children who were admitted with DKA, 24.7% (41) had either raised serum creatinine levels greater than 2 times the baseline or a reduced urine output of less than 0.5ml/kg/hr in 12 hours. On further analysis the study revealed that children with serum creatinine levels raised > 2 times above the baseline level were 5.833 times more likely to die (AOR 5.833; 95% CI: 1.604-21.213; p<0.05) while those who had anuria or reduced urine output of less than 0.5ml/kg/hr for 12 hours were 9 times likelihood of experiencing death (AOR 9; 95% CI: 2.173-37.279; p<0.05). Renal failure has been largely recognized to be an independent risk factor for increased mortality in DKA by multivariate analysis in various studies conducted in India and other parts of the world (30). Intrinsic renal failure in diabetic keto-acidosis was reported to have occurred

in 11.5% of children with DKA in South India, with case fatality reports varying from 40% to 72% (25). The AKI rate of 24.7% from our study was however a lower rate as compared to a similar study conducted in British Colombia that revealed 64.2% of the children developed AKI (29). In the same study it was reported that with severe acidosis and profound volume depletion children were at an increased risk of severe acute kidney injury. This study in British Columbia had limitations for example; no child had a baseline creatinine value. All children were considered healthy based on an approximation of height and an estimated glomerular filtration rate of 120 mL/min/1.73m^2. The researchers also did more conservative analyses using an eGFR of 90 mL/min/1.73m^2, the lower limit of normal kidney function. These findings can explain the higher percentage of children with AKI in that study**.** In DKA, high blood glucose levels can lead to increased urination and volume depletion, hence contributing to renal injury. AKI in our study may be attributed to poor fluid management during the initial stages of DKA management which could result from failure by healthcare providers to adhere to ISPAD guidelines. Acute kidney injury is concerning because it is associated with increased morbidity and mortality as well as increased risk of development of chronic renal disease, a finding that is especially relevant among children who are already at risk for diabetic nephropathy.

Out of the 159 children admitted with DKA. It was established that 76 (47.8%) children had signs of altered level of consciousness based on the AVPU scale of less than A while 80 (50.3%) had normal level of consciousness during the in-patient stay. Fifty five percent (55.1%) of the children admitted in the pediatric ward had altered mentation compared to those in the adult where 44.1% had altered level of consciousness. On further analysis the study revealed that children with normal level of consciousness AVPU of A were less likely to die as compared to those with an AVPU of less than A (AOR 0.191; 95% CI: 0.04-0.914; p<0.05). Cerebral oedema may present with altered level of consciousness and contributes to approximately 20-25% of mortality in children with DKA (22). While this study did not look particularly at presence of cerebral edema, altered level of consciousness may indicate presence of cerebral edema which is often associated with poor prognosis.

The percentage of children who experienced CNS involvement in this study is much higher as compared to the reports on other studies. Known serious complications of unmanaged DKA in children below the age of 5 years including cerebral oedema have been reported to occur in approximately 0.7% of children with DKA in the United Kingdom (1,15), 2% in Australia (Bui et al. 2002) and approximately 0.9% in North America (Glaser et al. 2001) (1). Another population based

study by Dunger et al in which all cases of cerebral oedema in England, Scotland, and Wales were reported through the British pediatric Surveillance Unit between October 1995 and September 1998,documented a mortality rate of approximately 21% to 24% among children with DKA accounting for the bulk of deaths in that setting (13, 14, 15). Edge et al reported that cerebral oedema among 69 reviews of children with DKA between the ages 0-12 years of age was responsible for 0.46% - 4.66% mortalities (26).Overall, cerebral edema accounts for approximately 60–90% of all childhood deaths related to diabetic-ketoacidosis. (28). The high number of children who experienced altered mental status in our study correlated with the severity of the disease as the study revealed that majority of the children (40.9%) with AVPU < A had severe DKA.

In this study the results established that 88 (55.3%) of the 159 children admitted with DKA had temperature above 37.5 degrees an indicator of infection. On further analysis results revealed that, children with temperature above 37.5 degrees Celsius were 3.069 times more likely to die (AOR 3.069; 95% CI 1.596-5.901; $p<0.05$) compared to those with normal temperature. A study conducted at the pediatric intensive care unit (PICU) of Institute of Child Health and Hospital for Children, Chennai, India, among 118 admissions of DKA from a pediatric tertiary care Institute identified infections as a significant risk factor for severe metabolic derangements and contributed to poor outcomes in children with DKA (48). Diabetic children with DKA therefore continue to be at an increased risk of death secondary to infections as compared to those without infections. (1)

Among the 37 records with (HbA1c level done within the 6 months preceding admission) the mean HBA1c level was 11.48% which is above the recommended 8% level. Only 6 (16.2%) of the 37 children had HbA1c below 8% indicating good sugar control. While 31 (83.6%) had HbA1c above 8%. Children with HbA1C value >8% had a less likelihood of experiencing death as compared to those whose HbA1C value was <8% (OR: 0.1, 95% CI: 0.0021-1.6201, $p<0.05$). This is contrary to what is seen in literature and can be attributed to the small sample we have (seeing we only had 37 records of values of HbA1C available). The group of children with HBA1c levels done in the previous 6 months was likely to be those on regular follow-up and insulin which may explain the lower risk for death. In this study out of the 159 children admitted with DKA 40.9% (65) had severe DKA and children in this category had a 4.6 times higher likelihood of death (OR: 4.6, CI: 1.8-15.2, $p<0.05$) compared to children with mild DKA. Those with moderate DKA constituted 35.7% (57) of the total number of children and had a 3.3 times higher likelihood of developing dying as compared to those children with mild DKA (OR: 3.3, CI:1.4-13.8, $p<0.05$). With severe DKA the risk of

developing complications are higher due to associated metabolic derangements' increased ketosis, profound dehydration and deranged kidney function.

Although previous studies may have established an association between age, missed insulin doses prior to admission, type of insulin and gender, our study did not find a similar association and this could be explained by the fact that the sample size was small and larger studies would be required to confirm these associations.

The median duration of hospital stay was 8 days, and that of pediatric and medical wards was 8 and 10 days respectively. These findings were similar to the duration of hospital stay reported in previous studies. This study also found children admitted to the ICU were 15.762 times more likely to die compared with those not admitted to the ICU and long-stay of children in the hospital had 2.8 higher odds of death compared to those who stayed fewer days. This can be attributed to the fact that children admitted to ICU are those with severe DKA and are also the ones with higher likelihood of death. majority of the children with severe DKA will also require longer period of hospitalization. The findings are comparable to a study conducted in Ethiopia, which was a chart review of 151 patients admitted with DKA. Around 71(47%), of the patients had long hospital stay (stayed in the hospital for more than 7 days), with a range of 1 day to 59 days. (45). Reasons for longer hospital stay in that particular study were related to DKA management set up, DKA management protocol, and patient characteristics. However in our study the investigator could not ascertain whether the duration of hospital stay was due to severity of DKA, complications of DKA or financial limitations.

6.2 STUDY LIMITATION.

The study did not have adequate sample size to establish if there were any significant associations between children's age, the type of insulin the child was ~~is~~ on, missed insulin doses, receiving medication prior to admission, and death. Larger studies are needed to assess for associations between these factors and treatment outcomes in children with DKA.

CHAPTER 7

CONCLUSION

1. In this study 93.1% of the children admitted with DKA were discharged home.

2. The median length of hospital stay for children was 8 days

3. Factors independently associated with discharge home were: normal serum creatinine, normal urine output, normal level of consciousness , mild and HBA1c done in the 6 months preceding admission.

7.1 Recommendations

1. There need for closer ICU care for Children with moderate and severe DKA for close monitoring to ensure better clinical outcomes
2. There is need to closely monitor children with raised serum creatinine levels and decreased urine output as these are associated with poor clinical outcome in DKA
3. The study did not establish any significant association's between missed insulin doses and poor short term outcomes probably due to the small sample size. Larger studies are required to validate these results. We need to think through how to rephrase this recommendation.

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APPENDIX 1: DATA ABSTRACTION TOOL.

OUTCOMES AND CORRELATES OF DIABETIC KETOACIDOSIS AMONG CHILDREN ADMITTED WITH DIABETIC KETOACIDOSIS AT KENYATTA NATIONAL HOSPITAL

The principle investigator: Dr. Sophie Musoma

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Biodata

Unique ID……..

Date of assessment……

Age (yrs)? _____

Sex: Male ☐ Female ☐

2.Obligate criteria for diagnosis of DKA

	Yes	No
Blood glucose level > 11mmol/L	☐	☐
Venous pH < 7.3mmol/L or Bicarbonate < 15mmol/L	☐	☐
Ketonuria > 2 plus in urine sample	☐	☐

3. Medical history.

Children admission history

a) Referral. (If yes, origin_____)
b) Direct admission to KNH

Is the child a known diabetic? Yes ☐ No ☐

What type of insulin is the child on

a) mixtard
b) Lantus + short acting insulin.

i. if the answer above is yes, were they on any medication prior to admission?

Yes ☐ No ☐

if yes was there any record of any missed insulin doses prior to admission ?

Yes ☐ No ☐

ii. Was there a record of the latest HBA1C ?

Previously diagnosed:

a) On follow up
b) (If yes, indicate point of follow up _____)
c) Not on follow up

Severity of DKA

	MILD	MODERARE	SEVERE
ARTERIAL Ph	7.25-7.30	7.0-7.24	<7.00
bicarbonate	15-18	10-14	<10

3. Correlates of DKA.

a) was there any previous diagnosis of renal failure prior to current admission?

Yes ☐ No ☐

If above answer is no:

i) Was the serum creatinine levels raised more than 2 times above the baseline level (based on RIFLE criteria on AKI)?

Yes ☐ No ☐

ii) Was there record of anuria or reduced urine output of less than 0.5ml/kg/hr for 12 hours.

Yes ☐ No ☐

b) Indication of any signs of CNS involvement. (answer yes or no)

ii) level of consciousness based on AVPU scale. A ☐ V ☐ P ☐ U ☐

presence of infection.

c) Temperature above 37.5 degrees Celsius? Yes ☐ no ☐

4. Clinical outcomes of DKA.

a) what were the outcomes of DKA?

I. Death ☐
II. Survival ☐

b) What was the duration of hospital stay ?_____(days)

i. Number of days admitted in pediatric ICU?_____
ii. Number of days in general pediatric wards?_____

APPENDIX II: TIME FRAME

The following is the expected time frame of the study process:

Number	Activity	Estimated Time
1.	Development of Proposal and presentation	January to February 2018
2.	Proposal Submission for ethical approval	October 2018
3.	Proposal resubmission for ethical approval	January 2019
4.	Data Collection	January2019- February 2019
5.	Data Analysis	February 2018
6.	Thesis Writing	February –March 2019
7.	Poster Presentation	March 2019
8.	Thesis Submission	April 2019

APPENDIX III: STUDY BUDGET

The following is the estimated budget cost for the study.

Category	**Remarks**	**Units**	**Unit Cost**	**Total (Ksh.)**
Proposal Development	Printing drafts	1000 pages	5	5000
	Proposal copies	8 copies	1000	8000
Data Collection	Stationery pack (Pens, paper etc)	400	50	20000
	Research Assistants	20 weeks	2000 X 2	80000
Data Entry	Data Clerk	1	7000	7000
Data Analysis	Statistician	1	35000	35000
Thesis Write up	Printing drafts	1000 pages	5	5000
	Printing Thesis	10 copies	1500	15000
Contingency fund				
Total				**175,000**