PREVALENCE OF HYPOGLYCEMIA AMONG CHILDREN ADMITTED AT KENYATTA NATIONAL HOSPITAL.

A research proposal submitted in partial fulfillment for the degree of Master of Medicine in Paediatrics and Child Health at the University on Nairobi.

By: DR JOAN ARWA ONGARE

MB.Ch.B - UON

H58/63735/2010

2014

DECLARATION

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

Dr. Joan Arwa Ong'are

M.B.Ch.B (University of Nairobi)

Signed…… Date …….

This dissertation proposal has been presented with full approval of supervisors.

Dr. Daniel Njai

Consultant Paediatrician

Senior Lecturer, Department of Paediatrics and Child Health

University of Nairobi.

Signed …… Date ……

Dr. Ahmed Laving

Consultant Paediatrician / Gastroenterologist

Lecturer, Department of Paediatrics and Child Health

University of Nairobi.

Signed ..... Date .....

TABLE OF CONTENTS

ACKNOWLEDGEMENTS

I wish to express my sincere gratitude to:

- My supervisors, Dr Daniel Njai and Dr Ahmed Laving for their support, patience, very helpful input and guidance throughout the study.
- My research assistant, Mr Edwin Osewe for his unwavering support and hard work put into data collection.
- All the babies and their caregivers who participated in the study process for their patience and co-operation.
- The staff at the pediatric filter clinic: the nurses, doctors on call during the study period and support staff for their help and input throughout the study process.

DEDICATION

I dedicate this book to my entire family for their support throughout the study period.

LIST OF FIGURES

LIST OF TABLES

ABBREVIATIONS

EGP - Endogenous Glucose Production

PEM - Protein Energy Malnutrition

PFC - Pediatric Filter Clinic

KNH - Kenyatta National Hospital

WHO - World Health Organization

RBS - Random Blood Sugar

ETAT - Emergency Triage and Treatment

DEFINITIONS

Level of consciousness: **A-** Alert

V- Child responding to verbal stimulation.

P- Child responding to pain stimulation.

U- Unresponsive child.

Diarrhoea – The passage of 3 or more loose or liquid stools per day, or more frequently than is normal for the child.

Convulsion – Uncontrollable muscular contractions that make the body shake rapidly.

Z-score – Weight in kg/ length in meters.

Traditional medicine – Alternative or complementary medicines used in maintenance of health or treatment of illness based on the theories and beliefs indigenous to different cultures.

No dehydration – Diarrhoea/ Gastroenteritis with fewer than 2 signs of dehydration namely: sunken eyes, return of skin pinch 1-2 seconds, restlessness/ irritability.

Some dehydration – Ability to drink adequately but with **2 or more** of: sunken eyes, return of skin pinch 1-2 seconds, restlessness/ irritability.

Severe dehydration – Inability to drink **or** AVPU <A **plus**: sunken eyes and return of skin pinch ≥ 2 seconds.

Shock – Cold hands **plus** weak/ absent pulse and **either**: capillary refill> 3 seconds or AVPU< A.

Sick – physically or mentally ill, not well or healthy.

ABSTRACT

Introduction

Hypoglycemia is a common metabolic derangement in childhood that if not treated promptly, has a high risk of causing brain damage and is an independent risk factor for death.

Hypoglycemia also complicates common childhood illnesses. Children are most susceptible because of their developing brain and its dependence on glucose as its primary fuel.

Study design

This is a descriptive hospital-based cross- sectional study aimed at determining the prevalence of hypoglycemia in sick children admitted at Kenyatta National Hospital.

Study Objectives

The primary objective was to determine the prevalence of hypoglycemia in sick children requiring admission aged between 2 months and 5 years. The secondary objectives were to determine the risk factors associated with hypoglycemia and the outcome at 24 hours of admission.

Methodology

Consecutive enrolment of patients who satisfied the study criteria had blood samples taken by heel prick following aseptic measures and analyzed using the Hemocue® glucose analyzer. A questionnaire was issued to the parent or guardian after performing resuscitation measures on the child where necessary and a physical examination done thereafter. The outcome of the child at 24 hours after admission was then documented.

Results

Four out of the 111 children enrolled into the study were found to have hypoglycemia with a prevalence of 3.6%. However, five children (4.5%) were found to be hyperglycemic.

Hypoglycemia was found to complicate various childhood illnesses. None of the factors assessed such as fasting more than 12 hours, childhood diseases such as Malaria, Pneumonia, Meningitis, Gastroenteritis and Malnutrition was found to be statistically significantly associated with hypoglycemia.

Similarly, the presence of hypoglycemia was not significantly associated with the outcome at 24 hours of admission.

1.0 BACKGROUND AND LITERATURE REVIEW

1.1 INTRODUCTION

Hypoglycemia in childhood is one of the most common metabolic abnormalities that needs to be treated promptly or prevented because it is a frequent cause of neurological damage or death (1, 2).

WHO defines hypoglycemia as blood glucose levels <1.1, <2.5, and <3.0 mmol/ltr depending on different clinical categories as defined below (3, 4).

Clinical category	**BGC (Blood glucose conc.)**
Newborn/Infant/Child with 'signs of illness'	<2.5mmol/ltr or 45mg/dl
Healthy term/preterm newborn- 'feeding well'	<1.1mmol/ltr or 19.8mg/dl
Infant/Child with severe malnutrition	<3.0mmol/ltr or 54mg/dl

The child's developing brain is more susceptible to hypoglycemia than the adult brain (1, 2, 5). Although it can use lactate, ketone bodies and amino acids, its primary fuel is glucose, thus making it highly vulnerable to low plasma glucose levels during fasting (6). Recurrent hypoglycemia may result in permanent neurological damage (2, 5, 7). The major long-term sequela of severe prolonged hypoglycemia is neurological damage resulting in mental retardation, transient cognitive impairment, neurological deficit and recurrent seizures.

Young age, fasting, and severe infectious diseases are considered important risk factors for the development of hypoglycemia (8).

In the fasting state, the plasma glucose level is maintained within the lower normal range by a delicate balance between endogenous glucose production (EGP) through gluconeogenesis and glycogenolysis on one hand and glucose utilization on the other hand.

Children have a limited tolerance to fasting because they have less glycogen stores. They are able to maintain a normal plasma glucose level during a fasting period of only 12 hours (9,10).

Healthy adults are able to maintain normal plasma glucose levels for up to 86 hours of fasting (11). Many infectious diseases are characterized by starvation due to disease- induced anorexia as well as cultural customs and traditional restriction of feeding in disease (12).

Several studies suggest that fasting is a major factor in the occurrence of hypoglycemia in children because of an association between the occurrence of hypoglycemia and the time since the last meal (13-17). Children presenting after 12 hours of their last meal are more likely to be hypoglycemic compared to those presenting within 12 hours of their last meal.

Studies have been done to determine the prevalence of hypoglycemia in paediatric emergency admissions. Elusiyan et al (17) found a prevalence of 6.4% in a Nigerian paediatric emergency ward while Solomon et al (15) obtained a prevalence of 7.1% among paediatric admissions in an urban hospital in Mozambique. Osier et al (13) found a prevalence of 7.3% among pediatric admissions in a rural district Kenyan hospital, whereas Pershad et al (18) obtained a prevalence of 6.54% of 100000 visits in an urban emergency department in the U.S.A.

The above studies show that hypoglycemia is a common childhood problem with an almost similar prevalence worldwide.

In all these studies, hypoglycemia was found to be associated with an increase in mortality and was also shown to complicate many childhood illnesses.

Elusiyan et al (17) found that of the total number of deaths, 28.6% had hypoglycemia against 4.2% of the normoglycemic children who died. In the study by Osier et al (13), mortality in hypoglycemic children was found to be 20.2% compared to 3.8% found in normoglycemic children. Solomon et al (15) found that of the children who died, 16.3% had hypoglycemia compared to 3.2% of the normoglycemic children.

1.2 HYPOGLYCEMIA AND MALARIA

Hypoglycemia has been found to complicate many childhood illnesses such as malaria, pneumonia, protein energy malnutrition (PEM) as well as diarrhoeal diseases (13, 15-17, 19-21).

In a Nigerian study (17), 44% of the hypoglycemic cases were suffering from severe malaria, compared to 5.2% reported by Solomon et al (15) in Mozambican children and 16% in Kenyan

children as reported by English et al (16). A frequency of 11.6% of hypoglycemia in malaria cases was found in Togo children (22) and 11.4% in Ugandan children (23) with malaria.

The highest prevalence rates of hypoglycemia among children with malaria are the 31% reported in Gambian children (24) and 20% in Malawian children (25).

In African children with malaria, impairment in hepatic gluconeogenesis in the prescence of adequate precursors has been considered to be the most likely mechanism in the causation of hypoglycemia.

English et al (16) found that hypoglycemia tends to occur in children who are more acidic and who have greater evidence of renal impairment. Acidosis is known to inhibit hepatic uptake of lactate at high concentrations (>2mmol/ltr) and to impair gluconeogenesis. The normal kidneys on the other hand, partly compensate for this reduction in hepatic metabolism of lactate under conditions of acidosis with an increase in fractional lactate uptake. Such a compensatory mechanism may be lost if renal function is impaired.

Increased glucose consumption by malaria parasites is considered to be a contributing factor. Parasitized erythrocytes consume up to 30-75 times the quantity of glucose consumed by non-infected cells. Another well known contributing factor is the stimulation of insulin release in vivo by quinine and quinidine administration in malaria treatment with resultant hyperinsulinemic hypoglycemia (26).

Cerebral malaria is also a leading contributor to hypoglycemia. The sequestration of parasitized red cells in the venules and capillaries of deep tissues has been implicated in the pathogenesis of both cerebral malaria and hypoglycemia (27). Hypoglycemia is an important feature in children with malaria because it predicts an increased mortality (28, 29). The mortality rate increases 4-6 fold in children with malaria complicated with hypoglycemia (13, 28, 29). 20-30%of the children admitted with malaria who had hypoglycemia did not survive compared with a mortality rate of 3.8% in normoglycemic children (13). Thus, hypoglycemia is considered to be one of the major predictors of adverse outcome in children with severe malaria.

Hypoglycemia does not only occur in children with malaria but is also seen in children with other infectious diseases such as pneumonia and diarrhoea, both in tropical (13-15,17,19-21) and

in Western countries (30,31). In a Kenyan rural district hospital, Osier et al (13) found hypoglycemia in 8.2% of all children seen in the hospital, with the highest prevalence occurring in neonates and children between 2 and 4 years.

The proportion of children with hypoglycemia varied significantly with the primary diagnosis, with the highest proportion being observed in children with meningitis at 36%. The proportion in children with malaria was 8.4%. Multiple logistic regression analysis identified prostration, deep breathing, severe malnutrition, fasting of more than 12 hours and a positive malaria slide as independent indicators of hypoglycemia in the same study.

1.3 HYPOGLYCEMIA AND PNEUMONIA

Elusiyan et al (17) found septicemia to be the second most frequent diagnosis associated with hypoglycemia at 24%, after malaria at 44%. Most of the diagnoses of septicemia in the same study were based on clinical assessment with only a few bacteriological confirmations. Solomon et al (15) found pneumonia as the leading diagnosis associated with hypoglycemia at 21% while a Nigerian study found pneumonia associated with hypoglycemia to be at 8.6% (17).

1.4 HYPOGLYCEMIA AND GASTROENTERITIS

Diarrhoeal diseases represent a major health problem in developing countries and also a high risk to travellers visiting these countries. It is estimated that the global death toll from diarrhoeal disease is about 2 million deaths per year (1.7-2.5 million deaths), ranking third among all causes of infectious disease deaths worldwide.

Huq et al (21) performed a prospective study in under-five children who presented with diarrhoeal illnesses and found that 11% of those children had hypoglycemia. Among hypoglycemic children, 11% had bacteremia while among the non-hypoglycemic children, only 5% had bacteremia. In this study, the case fatality rate was proportionately higher in children who had both bacteremia and hypoglycemia (43%) compared to those who had bacteremia, but not hypoglycemia (30%).

Decreased stores of glycogen, impaired gluconeogenesis, increased peripheral utilization of glucose and intestinal malabsorption have all been associated with hypoglycemia. In children, hypoglycemia is associated with deaths from infectious diarrhoea regardless of their nutritional

status (32). Bacteremic children with clinical sepsis were found to be 4 times more likely to develop hypoglycemia. This study concluded that a rapid bedside blood glucose test should be considered as an inexpensive alternative in the management decisions of diagnosing bacteremia and initiating empiric antibiotic treatment in children with diarrhoeal disease. In the Kenyan study (13), 5.5% of children with hypoglycemia had gastroenteritis and in another study by Nyikuri et al (33) in Kenyatta National Hospital, 4.2% of children with acute diarrhoea had hypoglycemia.

1.5 HYPOGLYCEMIA AND MALNUTRITION

Severe malnutrition is a known cause of hypoglycemia. WHO defines hypoglycemia in severe malnutrition as a blood glucose concentration below 3mmol/ltr (54mg/dl).Nzioki et al (34) performed an audit of care for children aged 6-59 months admitted with severe malnutrition at Kenyatta National Hospital, and found that diagnosis, treatment and prevention of hypoglycemia were inadequately done both at the pediatric filter clinic (PFC) and the wards.

Malnourished children have diminished glycogen stores and may not be able to mobilize hepatic gluconeogenic substrates.

Indeed Step 1 of the WHO guidelines on care of severely malnourished children is the treatment of hypoglycemia (35). Nzioki et al (34) found that out of the 100 children in the study, only 29.9% had a rapid blood glucose test done in either PFC or the wards despite the tools needed being largely available.

There was also a long delay in initiating feeds in the wards with a median waiting time of 14.7 hours. 34% of patients overall received their initial feed after 19 hours of admission to the ward.

In the Nigerian study (17), one (50%) of the two cases of Kwashiorkor had hypoglycemia but the two patients that died from PEM in this study both had hypoglycemia. In the Kenyan study (13), mortality was high at 31.8% in hypoglycemic children who had signs of severe illness (prostration or deep breathing) on admission or severe malnutrition while in normoglycemic children the mortality was found to be 9%.Hypoglycemia is, thus, associated with childhood illnesses and increased mortality. Currently, the only local sources of data on prevalence of hypoglycemia are that of a study by Nyikuri et al on the prevalence of hypoglycemia in childhood diarrhoeal cases. This study will determine the prevalence of hypoglycemia in an

urban referral centre as well as describe the risk factors associated with hypoglycemia. It will also determine the outcome of the patients at 24 hours of admission.

1.6 STUDY JUSTIFICATION AND UTILITY

Hypoglycemia is a common and serious condition associated with brain damage and an increase in mortality, yet it is amenable to inexpensive and widely available treatment. It is a frequent but poorly explored feature of severe infectious diseases and malnutrition in children.

Children have a limited tolerance to low blood sugar because they have less glycogen stores and are therefore unable to maintain normal plasma glucose after a prolonged fasting period.

A study by Nzioki et al (13) at KNH showed that only 29.9% of children seen either in PFC or in the wards had a rapid blood glucose test done despite the tools needed being largely available. Out of these, 13.3% were found to have hypoglycemia. The locally available data on the prevalence of hypoglycemia is restricted to childhood diarrhoea cases in a study done by Nyikuri et al in 1994 (33).

It is hoped that this study will provide data on the prevalence of hypoglycemia among sick children aged 2 months to 5 years. Such data will be useful for developing a policy on evaluation of all sick children for hypoglycemia and its prompt management with the aim of reducing morbidity and mortality.

2.0 STUDY OBJECTIVES

2.1 Primary objective:

To determine the prevalence of hypoglycemia in sick children requiring admission into Kenyatta National Hospital.

2.2 Secondary objectives:

1. To determine some of the factors that may be associated with hypoglycemia. (Potential risk factors include fasting more than 12 hours, drugs such as Quinine, childhood illnesses such as Malaria, Pneumonia, Meningitis, Gastroenteritis and Malnutrition).

2. To determine the effect of hypoglycemia on the outcome at 24 hours of admission (Dead or Alive).

3.0 RESEARCH METHODOLOGY

3.1 STUDY DESIGN

This was a hospital based descriptive Cross-Sectional study.

3.2 STUDY AREA

Kenyatta National Hospital (KNH) serves as the national referral hospital. It is an urban tertiary teaching hospital that serves a population of mainly medium to low socio-economic status. The study was conducted at the Paediatric Filter Clinic (PFC) where all children requiring admissions are seen before transfer to the wards. Subsequent follow up was done in the wards to determine the outcome at 24 hours of admission.

3.3 STUDY PERIOD

The study was conducted over a period of 3 months (September- November 2012).

3.4 STUDY POPULATION

All sick children aged 2-60 months requiring admission whose parent/guardian gave informed consent were recruited into the study.

3.5 INCLUSION CRITERIA

Sick children aged 2-60 months requiring admission.

Children whose parent/guardian gave informed consent to participate in the study.

3.6 EXCLUSION CRITERIA

Children known to have Type 1 Diabetes Mellitus.

Children referred from other hospitals having received initial treatment for hypoglycemia elsewhere within 12 hours of arrival.

Children whose parent/guardian did not give consent.

3.7 SAMPLE SIZE CALCULATION

The sample size was calculated using the Fisher's formula for Prevalence studies.

$n= Z^2PQ/D^2$

Where:

n=desired sample size.

Z= standard deviation which corresponds to the 95% confidence level (1.96).

P= the estimated prevalence as reported by Osier et al in Kenya was 7.3 %. (13)

Q= (1-P) =1-0.05 =0.95

D= the degree of accuracy desired, set at 0.05.

Hence:

n=1.96*1.96*0.073*0.95/ 0.05*0.05

=106

3.8 SAMPLING TECHNIQUE

The children who satisfied the inclusion criteria were consecutively recruited into the study after obtaining informed consent.

3.9 DATA COLLECTION

- Sick children were triaged and those who were decided for admission by the primary admitting resident paediatrician were recruited into the study if they satisfied the inclusion criteria and consent given by the parent on a predesigned form.
- A structured questionnaire was then issued to the parent to get information such as the bio data, factors associated with hypoglycaemia such as the duration of illness and the patient's last meal. Additional information included the symptoms of the illness and the medication given prior to arrival at the hospital.
- A clinical examination of the child was done by the principal investigator or the research assistant, with the help of a structured clinical bio data form. This included temperature, measurements of weight using a weighing scale, and length or height using a stadiometer so as to determine the Z score (weight for height). A general assessment of the child was also done to assess the factors associated with hypoglycaemia. The primary clinical diagnosis made by the attending doctor was documented in the clinical bio data form.

3.10 COLLECTION OF BLOOD SAMPLES

- Blood samples were taken by heel prick under strict sterile measures. The foot was warmed before sample collection to allow sufficient vasodilatation hence free flow of the required amount of blood without having to compress the foot.
- The heel of the foot was then sterilized with 70% alcohol swabs and pricked using new lancets for each prick. Five micro litres of blood was collected into microcuvettes which were then fed into the Hemo-Cue® glucose analyzer for a reading to be taken. A dry cotton swab was then placed on the affected area of the foot and gentle pressure applied to the area until blood stopped oozing.
- Plasma glucose levels were determined using the Hemo-cue beta glucose analyzer. The Hemo-cue beta glucose analyzer uses a dual wave length photometer to measure glucose in hemolysed whole blood after a modified glucose dehydrogenase reaction using dried

reagents contained in disposable micro-cuvettes. It is portable and very useful as a point of care device (36). The instrument can use whole blood or plasma without additional processing and has been shown to be reliable, accurate and sensitive in the clinical setting and for research purposes (37). It is convenient and technically easy to use requiring very little maintenance (38). The instrument uses only 5 micro litres of blood drawn up by capillary action into a cuvette. This makes it safe to use as sampling of larger amounts of blood (1 or 2ml) for conventional laboratory analysis may contribute to already existing anaemia. Its accuracy and precision is comparable to that of conventional laboratory instrumentation (38). The analyzers are factory calibrated and require minimal maintenance. No calibration is required between cuvette batches (39).

3.11 DATA ANALYSIS

Data was analyzed using SPSS version 17.0 software. It was coded, cleaned and summarized using tables for the different variables. Data was presented using graphs, pie charts and tables. Descriptive statistics of individual variables including means, percentages, standard deviations and standard error was analyzed. Analytical statistics included relative prevalence, Chi-square and student t-test to test for the strength of association between the variables.

3.12 DISSEMINATION OF RESULTS

The findings of the study were distributed to University of Nairobi – Paediatrics department, Kenyatta National Hospital and copies made available in the University of Nairobi library. The results were made available to policy makers and health workers within the hospital and university to facilitate improvement of health services offered to children admitted at KNH.

3.13 ETHICAL CONSIDERATIONS

Approval to carry out the study was sought from Kenyatta National Hospital Medical Review Board and Ethics Committee.

Informed written consent to participate in the study was obtained from the parent or primary caregiver accompanying the child after explanation of the study and voluntary nature of participation. Caregivers were informed that refusal to participate in the study would not affect the treatment of their child.

Extreme care was taken while undertaking the procedure of sample collection, which was done under sterile conditions.

Any information pertinent to the management of the child discovered during the interview or blood glucose determination was communicated to the primary attending doctor.

Any child found to be hypoglycaemic was given a bolus of 5mls/kg of 10% dextrose intravenously followed by feeds if able to take orally or by dextrose saline solution as a maintenance fluid. Hyperglycaemic children had their blood sugars monitored in the wards. No intervention was undertaken at the filter clinic.

Confidentiality was maintained.

3.14 CONTROL OF ERRORS AND BIAS

The questionnaire was pretested on a sample population to ensure validity before commencement of the study.

The research assistant was trained and provided with standard definitions of terminologies used in the questionnaire to ensure uniform interpretation.

Data collected was entered daily into a pre-programmed computer. The data entered was crosschecked to ensure validity and completeness.

4.0 RESULTS

One hundred and eleven children admitted to KNH were recruited into the study.

4.1 Characteristics of the study population

The study subjects recruited were aged between 2 and 60 months, 56 (50.4%) were males while 55 (49.5%) were females. The median age was 12 months with an interquatile range of (7.0-24.0) months. **Table 1** below shows the nutritional status and temperature recordings of the children recruited into the study as part of the assessment of factors associated with hypoglycemia. 21 (18.9%) children were found to have severe malnutrition with a Z-score of -3SD and below. 49(44.1%) children had Z-scores of -2SD and below while 28 (25.2%) children had a Z-score of between-2SD and -3SD. 2 (1.8%) children, however, had missing data. 35(31.5%) children were febrile with temperatures above 38.6°C while 75(67.5%) children had temperatures below 37.5°C. 1 child had missing data. The clinical examination findings of all the 111 children as they were examined are also represented in the table below. 22(19.8%) children had an AVPU less than P, while 25(22.5%) children and 8(7.2%) children had severe dehydration and shock respectively.

The characteristics of the study population are as shown in **Table 1** below.

Table 1: Characteristics of the study population

Variable	
Median age (months) Interquartile range (IQR) in months Range (months)	12.0 (7.0 -24.0) 2.0 - 60.0
Sex Male Female	**Frequency (%)** 56 (50.4) 55 (49.5)
Variable	**Frequency (%)**
Mean weight (SD)	8.9 (3.8)
Mean height (SD)	77.1(15.0)
WHZ score <-1SD -1SD to -2SD -2SD to -3SD -3SD to -4SD >-4SD Missing	 35 (31.5) 25 (22.5) 28 (25.2) 14 (12.6) 7 (6.3) 2 (1.8)
Temperature 35.0-36.5 36.6-37.5 38.6-40.0 >040 Missing	 20 (18.0) 55 (49.5) 32 (28.8) 3 (2.7) 1 (0.9)
Duration of illness before admission(days) <01 01-7 07-30 >30	 13 (11.7) 56 (50.5) 30 (27.0) 12 (10.8)
Time from the last meal at admission(hours) <012 >012	 85 (76.6) 26 (23.4)
Presence of:	
Fever	91 (82.0)
Cough	81 (73.0)
Difficulty in breathing	59 (53.2)
Vomiting	37 (33.3)
Convulsions	58 (52.3)
Diarrhoea	45 (40.5)

Level of consciousness	
A	83 (74.8)
V	6 (5.4)
P	19 (17.1)
U	3 (2.7)
Dehydration	
No dehydration	64 (57.7)
Some dehydration	14 (12.6)
Severe dehydration	25 (22.5)
Shock	8 (7.2)
Able to drink/ breastfeed	80 (72.1)
Deep breathing	41 (36.9)
Lower chest wall indrawing	64 (57.7)
Respiratory rate	
02-11months>50	53 (47.7)
>012months>40	52 (46.8)
No pneumonia	6 (5.4)
Stiff neck	9 (8.1)
Oedema	6 (5.4)
Pallor	31 (27.9)

4.2 Blood glucose levels

Four (4) out of the 111 children who took part in the study were found to be hypoglycemic giving a prevalence of **3.6%.** 102 (91.9%) children had normal blood glucose levels while 5(4.5%) children were hyperglycaemic. The mean blood glucose was 6.7mmol/ltr. The results are shown in **Table 2** and **3** as well as **Figure 1** below.

Table 2: Prevalence of hypoglycemia

Variable	Point estimate	95% CI
Mean blood glucose	6.7	6.3, 7.1
Hypoglycemia, n (%)	4 (3.6)	0.9, 7.2

Table 3: Blood glucose levels

Variable	Frequency (%)
Hypoglycemia	4 (3.6)
Normoglycemia	102 (91.9)
Hyperglycemia	5 (4.5)

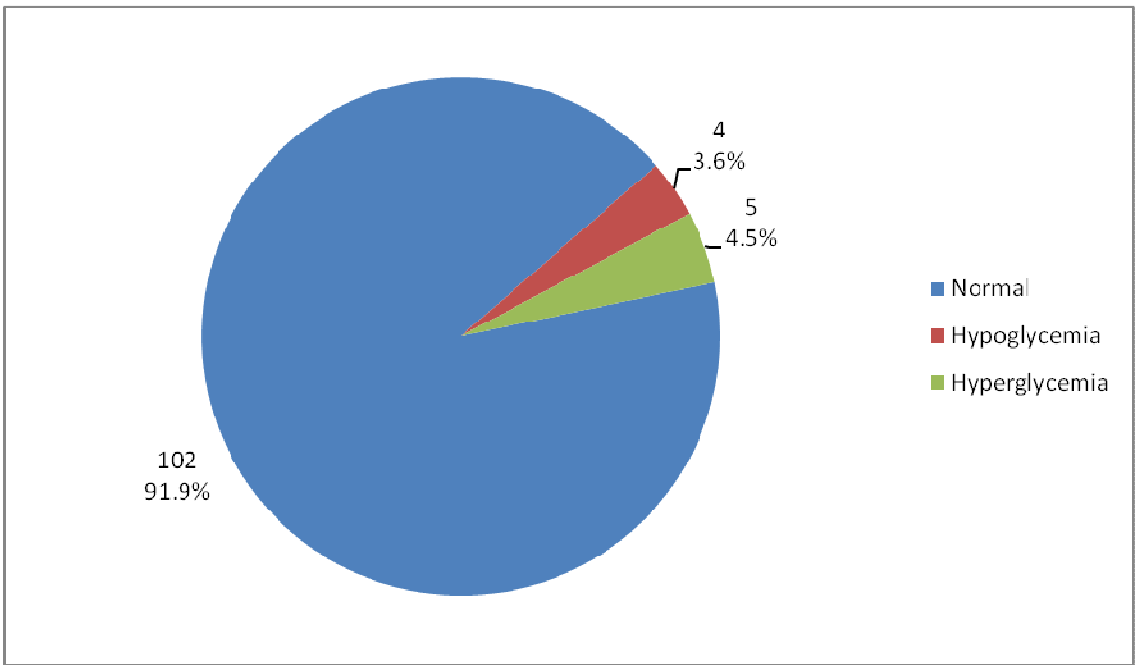

Figure 1: Blood glucose levels

4.3 Assessment of associated factors

Sixty nine children (62.2%) out of the 111 children recruited into the study had been unwell for less than a week prior to arrival at the hospital while the remaining 42 (37.8%) were found to have been unwell for more than a week. The majority of the children (76.6%) had their last meal within 12 hours prior to admission. This is illustrated in **Figures 2** and **3** below.

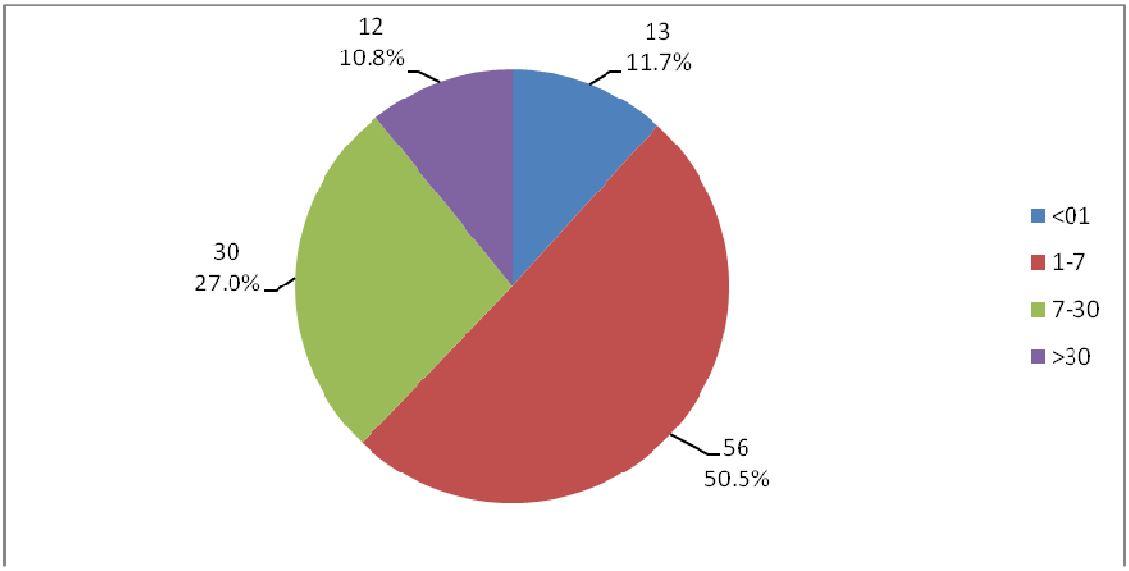

Figure 2: Duration of illness before admission in days

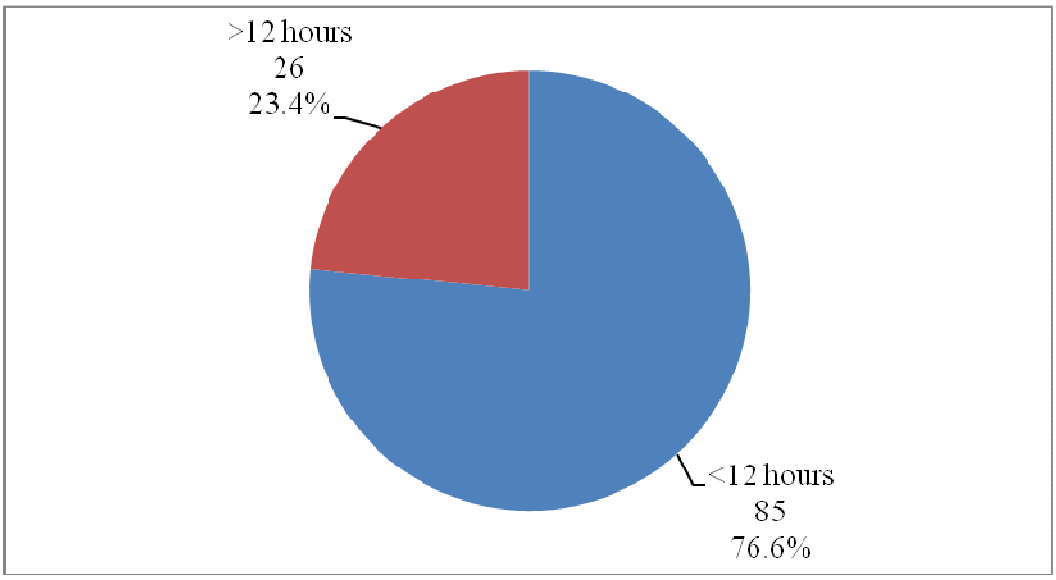

Figure 3: Last meal

Table 4 below shows the medications that were administered prior to arrival at the hospital. 59.5% and 60.4% of the children were on antibiotics and analgesics respectively before arrival at the hospital. 8 children (7.2%) had been given antimalarials while 12 (10.8%) children and 6(5.4%) children were on antihistamines and cough syrups respectively on arrival at the hospital. 2 (1.8%) children received traditional medicines prior to admission.

Table 4: Medications given before admission

Variable	**Frequency (%)**
Antibiotics	66 (59.5)
Antimalarials	8 (7.2)
Analgesics	67 (60.4)
Antihistamines	12 (10.8)
Cough syrups	6 (5.4)
Traditional medicine	2 (1.8)

4.4 Primary clinical diagnosis

The primary clinical diagnoses made by the attending doctor after history taking and physical examination are shown in **Table 5** and **Figure 4** below. Out of the 8 (7.2%) suspected cases of malaria, 5 children (4.5%) had a positive malaria slide. 44 (39.6%) were diagnosed to have pneumonia, 18 (16.2%) had severe malnutrition, 20 (18%) were diagnosed with meningitis and 30 (27%) with gastroenteritis.

Table 5: Primary clinical diagnosis

Variable	Frequency (%)
Malaria parasite	
Positive	5 (4.5)
Negative	106 (95.5)
Malaria	8 (7.2)
Pneumonia	44 (39.6)
Severe Malnutrition	18 (16.2)
Meningitis	20 (18.0)
Gastroenteritis	30 (27.0)

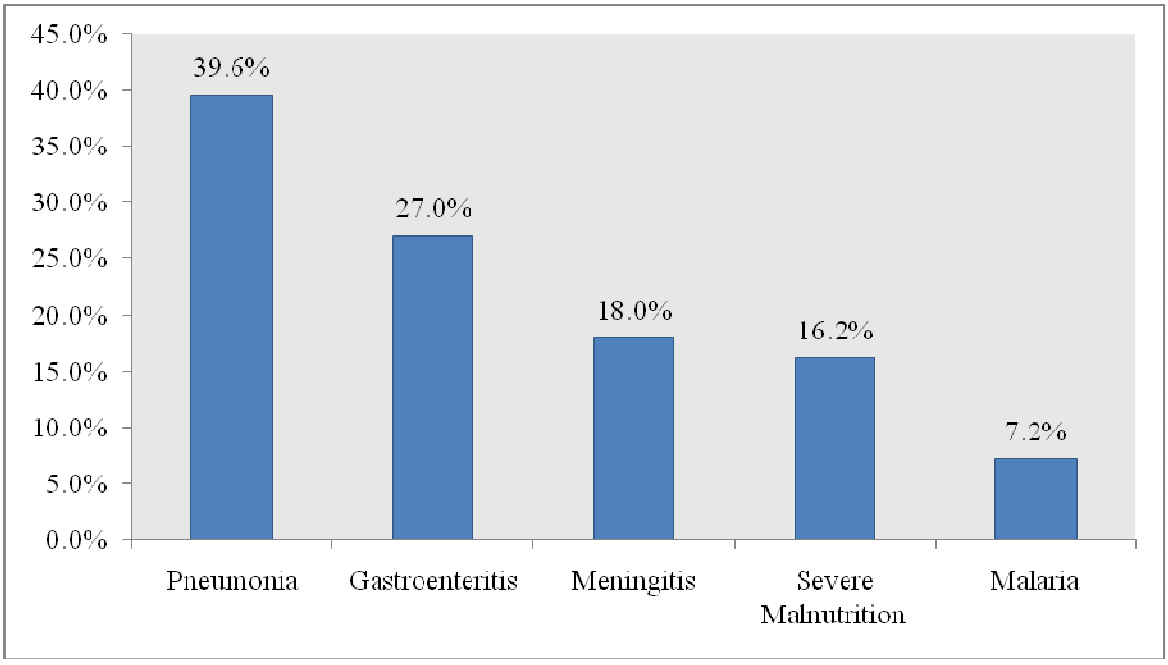

Figure 4: Primary clinical diagnosis

4.5 Outcome at 24 hours of admission

As shown in **Table 6** below, of all the children recruited into the study and subsequently admitted, only one child (0.9%) succumbed within 24 hours of admission. All the other children (99.1%) were alive 24 hours after admission.

Table 6: Outcome at 24 hours of admission

Variable	Frequency (%)
Outcome	
Alive	110 (99.1)
Dead	1 (0.9)

4.6 Factors associated with hypoglycemia

In this study, none of the factors assessed was significantly associated with the occurrence of hypoglycaemia as can be seen in **Table 7** below.

Table 7: Lack of association between hypoglycemia and potential associated factors

Variable	Hypoglycemia n (%)	Normal n (%)	P value
Last meal			
<012	3 (75.0%)	77 (75.5%)	1.000
>012	1 (25.0%)	25 (24.5%)	
WHZ score			
Appropriate	2 (50.0%)	32 (32.0%)	0.341
-1SD	0 (0.0%)	24 (24.0%)	
-2SD	1 (25.0%)	26 (26.0%)	
-3SD	0 (0.0%)	13 (13.0%)	
-4SD	1 (25.0%)	5 (5.0%)	
Temperature			
035-36.5	0 (0.0%)	19 (18.8%)	0.166
36.6-37.5	2 (50.0%)	51 (50.5%)	
38.6-40	1 (25.0%)	29 (28.7%)	
>040	1 (25.0%)	2 (2.0%)	
Level of consciousness			
A	3 (75.0%)	76 (74.5%)	1.000
V	0 (0.0%)	5 (4.9%)	
P	1 (25.0%)	18 (17.6%)	
U	0 (0.0%)	3 (2.9%)	
Dehydration			
No dehydration	2 (50.0%)	60 (58.8%)	0.483

Some dehydration Severe dehydration Shock	0 (0.0%) 2 (50.0%) 0 (0.0%)	14 (13.7%) 21 (20.6%) 7 (6.9%)	
Unable to drink or breastfeed Yes No	 3 (75.0%) 1 (25.0%)	 72 (70.6%) 30 (29.4%)	 1.000
Difficulty in breathing Yes No	 2 (50.0%) 2 (50.0%)	 38 (37.3%) 64 (62.7%)	 0.632
Lower chest wall indrawing Yes No	 3 (75.0%) 1 (25.0%)	 57 (55.9%) 45 (44.1%)	 0.631
Respiratory rate 02-11months>50 >012months>40	 3 (75.0%) 1 (25.0%)	 46 (47.9%) 50 (52.1%)	 0.357
Neck stiffness Yes No	 0 (0.0%) 4 (100.0%)	 9 (8.8%) 93 (91.2%)	 1.000
Oedema Yes No	 0 (0.0%) 4 (100.0%)	 6 (5.9%) 96 (94.1%)	 1.000
Pallor Yes No	 0 (0.0%) 4 (100.0%)	 29 (28.4%) 73 (71.6%)	 1.000
Antimalarials Yes No	 0 (0.0%) 4 (100.0%)	 7 (6.9%) 95 (93.1%)	 1.000
Malaria parasite Positive Negative	 1 (25.0%) 3 (75.0%)	 3 (2.9%) 99 (97.1%)	 0.145
Malaria Yes No	 0 (0.0%) 4 (100.0%)	 8 (7.5%) 99 (92.5%)	 1.000
Pneumonia Yes No	 2 (50.0%) 2 (50.0%)	 42 (39.3%) 65 (60.7%)	 0.648
Malnutrition Yes No	 1 (25.0%) 3 (75.0%)	 18 (17.6%) 84 (82.4%)	 0.552
Meningitis Yes No	 0 (0.0%) 4 (100.0%)	 20 (18.7%) 87 (81.3%)	 1.000
Gastroenteritis Yes No	 1 (25.0%) 3 (75.0%)	 29 (27.1%) 78 (72.9%)	 1.000

4.7 Hypoglycemia and its effect on the outcome at 24 hours of admission

The presence of hypoglycaemia was not significantly associated with the outcome at 24 hours of admission as shown in **Table 8** below.

Table 8: Effect of hypoglycemia on the outcome at 24 hours of admission

Variable	**Hypoglycemia n (%)**	**Normoglycemic n (%)**	**P value**
Outcome			
Alive	4 (100.0%)	106 (99.1%)	1.000
Dead	0 (0.0%)	1 (0.9%)	

5.0 DISCUSSION

Hypoglycemia is not a disease-specific symptom but may be regarded as a serious metabolic complication in acute severe infections in young children. It is an independent risk factor for death in severe childhood infections in the tropics.

In this study, the prevalence of hypoglycemia was found to be 3.6%; with a 95% C.I (0.9, 7.2). The cut off plasma glucose level used in this study was 2.5mmol/litre in sick children and 3/0mmol/litre in severely malnourished children. Studies from other developing countries such as a study by Elusiyan et al (17) in Nigeria found a prevalence of 6.4% while Solomon and colleagues (15) reported a prevalence of hypoglycemia of 7.1% among Mozambican children. Osier (13) reported a prevalence of 7.3% among paediatric emergency admissions at a Kenyan rural district hospital. A study in the United States by Pershad et al (18) reported a prevalence of 6.54% of 100000 visits among patients seeking care in their emergency department. Our prevalence of hypoglycemia of 3.6% among sick children at KNH is much lower than the prevalences reported from other studies (13, 15, 17, 18) probably because of our smaller sample size and excluding infants below two months of age.

Children have a limited tolerance to fasting because they have less glycogen stores. In this study, only one child (25%) had their last meal over 12 hours prior to admission but this was not found to have a statistically significant association with the presence or absence of hypoglycemia. This was not in keeping with the findings of other workers (13, 15, 17) who reported significant associations between the interval of the last meal and presence or absence of hypoglycemia. Elusiyan et al (17) found that patients presenting more than 12 hours of their last meal were more likely to be hypoglycemic ($p<0.001$) while Osier and others (13) reported a prevalence of 20.8% with a strong association to hypoglycemia (O.R =2.1; 95%CI=1.4-3.1, $p<0.001$).

There was no observed statistically significant association between age, sex and duration of illness and hypoglycemia in the present study. This was in agreement with the findings of other workers (13, 17). The Nigerian study (17), however, found an increasing prevalence of hypoglycemia in children who had a longer duration of illness before admission. Osier et al (13) found the highest prevalence of hypoglycemia among neonates (23%) and children aged between two and four years.

Nutritional status was not found to have a statistically significant association with hypoglycemia in this study as well as among Nigerian children (17) but was significantly associated with hypoglycemia in Kenyan children (13) with a WAZ<3 ($p=0.023$). One would generally expect a significant relationship between nutritional status and hypoglycemia. The reason why this is so is not clear but it is thought that the hormonal compensatory interplay prevents the occurrence of hypoglycemia.

There was a statistically significant association between the coma score of patients and the presence of hypoglycemia in work done by Elusiyan et al (17),($p<0.01$) and Osier et al (13), ($p<0.001$) who reported a mortality rate of 31.8%. The present study found a prevalence of hypoglycemia of 25% in children with a reduced level of consciousness but this was not found to be statistically significant.

This study has shown that hypoglycemia can complicate many childhood diseases. This is in agreement with the findings of other workers (13, 15-17, 22-25). Out of the four hypoglycemic cases, one child (25%) was diagnosed with malaria and had a positive blood slide for malaria parasites. Elusiyan et al (17) reported malaria as the leading cause of hypoglycemia in Nigerian children at 44%, followed by 31% in Gambian children (24) and 20% in Malawian children (25). This was high compared to 8.4% reported by Osier et al (13), 16% reported by English et al (16) and 5.2% reported in Mozambican children (15). A frequency of hypoglycemia of 11.6% was found in Togo children (22) and 11.4% in Ugandan children (23) with severe malaria. The impairment in hepatic gluconeogenesis has been considered to be the most likely mechanism in the causation of hypoglycemia especially if there is acidosis and renal impairment (16). The Kenyan study (13) also found a strong association between hypoglycemia and a positive malaria slide ($p=0.006$).

Hypoglycemia has also been associated with severe malnutrition. 25% of the hypoglycemic cases in the present study had severe malnutrition but this was not statistically significant. Osier et al (13), on the other hand, found a strong association between severe malnutrition and hypoglycemia ($p=0.023$) with a prevalence of 6.6%. However, there was no evidence of association of hypoglycemia with mortality in children with malnutrition. This was in contrast to the Nigerian study (17) where there was 100% mortality of the patients who had protein energy malnutrition, specifically Kwashiokor, as well as hypoglycemia. Huq et al (21) did not find any

significance between hypoglycemia and malnutrition. One of the reasons could be hormonal compensatory interplay preventing hypoglycemia.

Diarrhoeal illness has been associated with hypoglycemia. In this study, 25% of the hypoglycemic cases had diarrhoeal disease. This prevalence was high when compared to other studies, possibly due to the lower sample size. Huq et al (21) enrolled 782 under-5 children with diarrhoea to determine the prevalence of hypoglycemia which he found to be 11%. In his study, hypoglycemia was strongly associated with bacteremia (p=0.026). Among the hypoglycemic children, 11% were found to have bacteremia compared to 5% of the non-hypoglycemic children. Logistic regression in his study found that bacteremic children with clinical sepsis were four times more likely to develop hypoglycemia (OR=4.2, 95% CI=1.4-12.9, p=0.012). Osier et al (13) found a prevalence of 5.5% while Solomon et al (15) found a prevalence of 7.1% among Mozambican children with diarrhoeal disease. Nyikuri et al (33) found a prevalence of hypoglycemia of 4.2% in children admitted with diarrhoeal disease at Kenyatta National Hospital. Contrary to the studies mentioned above where hypoglycemia was found to be associated with diarrhoeal diseases, hypoglycemia was not found in any of the patients admitted for gastroenteritis in the Nigerian study (17).

Pneumonia has been found to be the leading cause of hypoglycemia in this study with a prevalence of 50% although there was no statistically significant association between the two. The only child who succumbed in this study within 24 hours of admission had pneumonia and was normoglycemic. A prevalence of 21% was reported among Mozambican children (15) and pneumonia was the leading diagnosis associated with hypoglycemia in that study while Elusiyan et al (17) reported a prevalence of 8.6%. Elusiyan attributed the low prevalence in his study to be due to the high usage of antibiotics for upper respiratory tract infections thereby preventing its spread or progression to the lower respiratory tract.

Hypoglycemia is a serious complication of malaria and other infectious diseases and markedly increases mortality rates. Contrary to the findings in previous studies (13, 15-17, 21, 29), none of the children found to be hypoglycemic in this study succumbed to their illness. This may be attributed to the small sample size. This study also looked at mortality within the first 24 hours of admission unlike other mortality audits in KNH which are conducted over a longer period of time with recruitment of a wider age group. Most deaths occur after 48 hours and even more 7

days after admission. The presence of hypoglycemia at admission has been found to be significantly associated with death and dying within 24 hours of admission (17). It is also possible that due to the ETAT training that almost all residents undergo before being posted to clinical areas has led to stabilization of the sick children especially within the first 24 hours hence the lower mortality rate during this period. There is need, however, for larger studies on hypoglycemia as a cause of death in children admitted to KNH.

Elusiyan et al (17) in 2006 reported the highest mortality in hypoglycemic children at 28.6% compared to other studies, against 4.2% mortality in normoglycemic children ($p<0.01$). This was followed by Huq et al (21) who reported a mortality rate of 28% in hypoglycemia compared to 14% in normoglycemia (OR 2.4), English et al (16) reported a mortality rate of 28% compared to 7% in normoglycemic children ($p=0.003$), while Osier et al (13) reported a mortality rate of 20.2% compared to 3.8% mortality in normoglycemic children ($p<0.001$). Solomon et al (15) reported a mortality rate of 16.3% in hypoglycemic cases compared to 3.2% in normoglycemic children (RR-5.8) while Schellenberg et al (29) reported a mortality rate of 12.4% compared to 3% in normoglycemic children (OR 6.7).

In conclusion, hypoglycemia is a serious complication of infectious diseases and is not itself a disease-specific symptom. All emergency admissions should be screened for hypoglycemia and aggressively managed if present. Presumptive treatment is recommended for severely ill children where diagnostic facilities are lacking.

6.0 CONCLUSIONS

The prevalence of hypoglycaemia among sick children aged 2-60 months admitted to KNH was found to be 3.6%.

None of the factors studied were found to be significantly associated with hypoglycaemia.

Hypoglycaemia did not have an effect on the outcome at 24 hours of admission in this study.

7.0 STUDY LIMITATIONS

Some children had more than one co-morbidity at admission therefore relating hypoglycemia with the primary diagnosis proved to be a challenge.

The number of patients found to have hypoglycemia was small therefore analysis was limited.

8.0 RECOMMENDATIONS

There is need for further, larger studies on the prevalence of hypoglycaemia and the long term outcomes of hypoglycaemia in children.

APPENDIX I: QUESTIONNAIRE

Study Identification Number_____ Date of Interview_____

Biodata

1. Age of the patient

   Years _____ Months_____

   Date of Birth_____

2. Sex

   a) Male _____ b) Female _____

Assessment of risk factors

3. Duration of illness before admission (days).

   a) <1 _____

   b) 1-7_____

   c) 7-30_____

   d) >30_____

4. Last meal

   a) <12 hours_____

   b) >12 hours_____

5. **Symptoms** **i) Present** **ii) Absent**

a) Fever _____ _____

b) Cough _____ _____

c) Difficulty in breathing _____ _____

d) Convulsions _____ _____

e) Vomiting _____ _____

f) Diarrhoea _____ _____

g) Others (specify) _____

6. Medication given before admission:

a) Antibiotics_____

b) Antimalarials _____

c) Analgesics_____

d) Antihistamines _____

e) Cough syrups _____

f) Traditional medicine _____

g) Others (specify) _____

APPENDIX II: CLINICAL BIODATA FORM

Study Number_____ Date of admission_____ Time of admission_____

I.P number_____ Ward_____

Biodata

1. Sex

   a) Male _____ b) Female _____

2. Age

   Years _____ Months _____

Assessment of Risk Factors

3. Nutritional status.

   Weight (kg) _____ Height (cm) _____

   Z- Score (weight for length/height) a) appropriate _____

   b)-1SD_____

   c)-2SD_____

   d)-3SD_____

   e)-4SD_____

4. **Observations**

   a) Temperature at admission (°C)

   i) 35.0-36.5_____

   ii) 36.6-37.5_____

iii) 37.6-38.5_____

iv) 38.6-40_____

v) >40_____

b) Blood glucose level (mmol/L) _____

c) Blood slide for malaria parasites i) positive _____ ii) negative_____

5. Examination

a) Level of consciousness: i) A ii) V iii) P iv) U

b) Dehydration:

i) No dehydration _____

ii) Some dehydration _____

iii) Severe dehydration _____

iv) Shock _____

c) Able to drink/breastfeed i) Yes_____ ii) No_____

d) Deep breathing _____ _____

e) Lower chest wall indrawing _____ _____

f) Respiratory rate:

i) 2-11 months ≥50_____ ii) >12 months ≥40_____

g) Stiff neck i)Yes_____ ii)No_____

h) Oedema _____ _____

i) Pallor _____ _____

Assessment of the outcome at 24 hours of admission

Outcome of admission

a) Alive _____
b) Dead _____

Primary clinical diagnosis (by the attending doctor)

a) Malaria _____
b) Pneumonia _____
c) Gastroenteritis _____
d) Malnutrition _____
e) Meningitis _____
f) Others (specify)_____
g) Missing _____

APPENDIX III: CONSENT FORM FOR PARTICIPATION IN THE STUDY

Study Identification Number:_____ Date:_____

Study title:

Prevalence of hypoglycemia among children admitted at Kenyatta National Hospital (KNH).

Investigator: Dr Joan Ong'are (MBChB)

Paediatric Registrar, University of Nairobi

Tel: 0722237083

Supervisors: Dr Daniel Njai

Senior Lecturer, Department of Paediatrics and Child health

University of Nairobi, Tel 0722682929

Dr Ahmed Laving

Lecturer, Gastroenterologist

Department of Paediatrics and Child health, University of Nairobi

Tel: 0724644122

Investigator's statement

My name is Dr Joan Ong'are; I am a postgraduate student in the Department of Paediatrics and Child Health at the University of Nairobi undertaking a study to determine the number of children admitted who have low blood sugar. We request permission for you and your child to participate in this study. The consent form provided is to allow you to make an informed decision on whether or not to participate in the study. Please read this form carefully, asking any questions or seeking any clarifications from the information provided.

Brief description of the Study

Hypoglycemia or low blood sugar is a common metabolic abnormality in childhood that can be treated immediately once diagnosed. If left untreated, it can cause brain damage and even death. Hypoglycemia is also associated with childhood diseases and malnutrition. It worsens these conditions and puts the affected children at a higher risk of death. All sick children should therefore have their blood sugar taken and if low, treated accordingly. This study will help us know how often this condition occurs in sick children admitted to KNH.

Benefits

The results of the study will be discussed with you and the baby's doctor. If your baby is found to have any abnormality in the blood glucose levels, the doctor caring for the baby will immediately be informed and treatment given. The results will help us know the burden of the condition and help health workers in this facility and beyond to improve care given to all sick children. The results will also inform caregivers of the risk factors that can lead to low blood sugars and the dangers of a child having low blood sugar levels.

Risks

The study will involve pricking the foot of the child to obtain a very small amount of blood (5 micro litres equal to a very small drop of blood) in order to measure blood glucose level. The quantity of blood required is not great enough to lower the child's haemoglobin levels. Extreme care will be taken while sampling to ensure the highest possible standards of cleanliness are followed.

Voluntariness

Participation in this study is completely voluntary. Your baby will not be included in the study without your informed and written consent. There will be no financial rewards for participation in the study and no added expenses will be incurred for participating in the study. The care of your baby will not be compromised in any way as a result of refusal to participate.

Confidentiality

Information obtained about you and your child will be kept strictly confidential. In the event that your child is found to have abnormal blood glucose levels, it will be communicated to the child's doctor and nursing staff for immediate intervention to be undertaken. Overall findings of this study will be discussed in the Department of Paediatrics and Child Health, University of Nairobi, however, we will not reveal the identity of you and your child during the discussion.

Study Procedure

The study will be conducted as follows: on receiving informed written consent, blood will be obtained from a prick on the underside of the child's foot. The amount of blood required is very minimal (five micro litres) and all measures will be taken to ensure complete safety of the baby. Abnormal blood glucose if found will communicated to the attending doctor for immediate correction. You will then be assisted to fill in a questionnaire after which your child will be examined.

Problems or Questions

If you have any questions about the study or the use of the results, you can contact the principal investigator: **Dr Joan Ong'are** by calling **0722 237-083.**

If you have any questions regarding your rights as a research participant, you can contact the **Kenyatta National Hospital Ethics and Research Committee (KNH-ERSC)** by calling **2726300 Ext 44355.**

Consent Form: Participant's Statement:

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

Parent's Signature: _____ Date _____

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

Interviewer's Signature _____ Date _____

APPENDIX IV: KIBALI CHA KUSHIRIKI KWA MTOTO

Mimi nikiwa mzazi wa motto…….(jina la mtoto) nimeelezewa utafiti unaofanyika. Nimeelewa yote yale itakayofanyika na maswali yangu imejibiwa. Ninaelewa kwamba ninaweza kukataa kushiriki na hakuna madhara itakayonipata kwa kutoshiriki. Nimeelezwa kuwa hakuna manufaa kwangu kibinafsi nitakayopata lakini manufaa itakuwa kwa binadamu wote kwa ujumla.

Ninapeana ruhusa kwa mtoto wangu kushiriki kwa utafiti huu.

Jina ……...Sahihi……

Tarehe ……...Saa……

Nimeeleza mshiriki kuhusu utafiti huu vile ipasavyo.

Mtafiti……Sahihi……

Tarehe……Saa……

APPENDIX V: TIME FRAME

Number	Activity	Estimated Time
1	Proposal Development and Presentation	Dec 2011 to Jan 2012
2	Submission of proposal for ethical approval	Feb 2012
3	Pretesting and seeking permission	May to June 2012
4	Data Collection	July to September 2012
5	Data Analysis	October to November 2012
6	Thesis writing	December 2012
7	Thesis submission	January 2013

APPENDIX VI: STUDY REQUIREMENTS AND BUDGETARY ESTIMATES

Category	Remarks	Units	Unit Cost (KShs)	Total (KShs)
Proposal Development	Printing drafts	1000 pages	5	5,000
	Proposal Copies	10 copies	300	3,000
Data Collection	Pens	10	10	100
	Training research assistants	1 day	500 * 2	1, 000
	Blood glucose tests	106	200*106	21,200
Data Analysis	Statistician	1		20,000
Thesis Write Up	Computer Services			5,000
	Printing drafts	1000 pages	5	5,000
	Printing Thesis	10 copies	500	5,000
Contingency funds				40,000
Total				105,300

REFERENCES

1. Aynsley-Green A. Glucose, The brain and the paediatric endocrinologist. Horm Res 1996; 46:8-25.

2. Vannucci RC, Vannucci SJ. Hypoglycemic brain injury. Semin Neonatol 2001; 6:147-155.

3. World Health Organization. Severe and Complicated malaria. Trans R Soc Trop Med Hyg 2000; 94:1-190.

4. Achoki R, Opiyo N, English M, et al. Mini-Review: Management of hypoglycemia in children aged 0-59 months. J Trop Pediatr 2010; 56(4):227-234.

5. Flykanaka-Gantenbein C. Hypoglycemia in childhood: long-term effects. Pediatr Endocrinol Rev 2004; 1:530-536.

6. Robinson PJ, Rapoport SI. Glucose transport and metabolism in the brain. Am J Physiol 1986; 250:127-136.

7. Bober E,Buyukgebiz A. Hypoglycemia and its effects on the brain in children with type 1 diabetes mellitus. Pediatr Endocrinol Rev 2005; 2:378-382.

8. Wahren J, Ekberg K, Nair S, et al. Brain substrate utilization during acute hypoglycemia. Diabetologia 1999; 42:812-818.

9. Chaussain JL, Georges P, Calzada L, et al. Glycemic response to 24-hour fast in normal children :III. Influence of age. J Pediatr 1977; 91:711-714.

10. Jahoor F, Peters EJ, Wolfe R, et al. The relationship between gluconeogenic substrate supply and glucose production in humans. Am J Physiol 1990; 258:288-296.

11. Corssmit EP. J.A. Rojimin, Sauerwein H, et al. Regulation of glucose production with special attention to nonclassical regulatory mechanisms: a review. Metabolism 2001; 50:742-755.

12. Ali NS, Azam SI, Noor R. Women's beliefs regarding food restrictions during common childhood illnesses: a hospital based study. J Ayub Med Coll Abbottabad 2003; 15:26-32.

13. Osier FH, Berkley JA, Ross A, et al. Abnormal blood glucose concentrations on admission to a rural Kenya district hospital: Prevalence and outcome. Arch Dis Child 2003; 88:621-625.

14. Kawo NG, Msengi A, Swai A, et al. Specificity of hypoglycemia for cerebral malaria in children. Lancet 1990; 336:454-457.

15. Solomon T, Felix JM, Samuel M, et al. Hypoglycemia in pediatric admissions in Mozambique. Lancet; 343:149-150.

16. English M, Wale S, Binns G, et al. Hypoglycemia on and after admission in Kenyan children with severe malaria. QJMed 1998; 91:191-197.

17. Elusiyan JB, E.A, Adejuyigbe, Adeodu O, et al. Hypoglycemia in a Nigerian paediatric emergency ward. J Trop Pediatr 2006; 52:96-102.

18. Pershad J, Monroe K, Atchison J, et al. Childhood hypoglycemia in an urban emergency department: Epidemiology and a diagnostic approach to the problem. Pediatr Emerg Care 1998; 14:268-271.

19. Planche T, Agbeyenga T, Bedu-Addo G, et al. A prospective comparison of malaria with other severe disease in African children: prognosis and optimization of management. Clin Inf Dis 2003; 37:890-897.

20. Bennish ML, Azad AK, Rahman O, et al. Hypoglycemia during diarrhoea in childhood. Prevalence, pathophysiology and outcome. New Engl J Med 1990; 332:1357-1363.

21. Huq S, Hossain MI, Malek MA, et al. Hypoglycemia in under-five children with diarrhoea. J Trop Pediatr 2007; 53:197-201.

22. Assimadi JK, Gbadoe AD, Ata-Kouma DY, et al. Severe malaria in children in Togo. Arch Pediatr 1998; 5:1310-1315.

23. Idro R, Aloyo J. Manifestations, quality of emergency care and outcome of severe malaria in Mulago hospital, Uganda. Afr Health Sci 2004; 4:50-57.

24. White NJ, Marsh K, Turner RC, et al. Hypoglycemia in African children with severe malaria. Lancet 1987; 1:708-711.

25. Taylor TE, Molyneux ME, Wirima J, et al. Blood glucose levels in Malawian children before and during the administration of intravenous quinine for severe falciparum malaria. N Engl J Med 1988; 319:1040-1046.

26. van Hensbroek MB,Kwiatkowski D, Van den Berg, et al. Quinine pharmacokinetics in young children with severe malaria. Am J Trop Med Hyg 1996; 54:237-242.

27. White NJ, Warrell DA, Looareesuwan S, et al. Pathophysiological and prognostic significance of cerebrospinal fluid lactate in cerebral malaria. Lancet 1985; 1:776-778.

28. Marsh K, Foster D, Waruiru C, et al. Indicators of life-threatening malaria in African children. New Engl J Med 1995; 332:1399-1404.

29. Schellenberg D, Menendez C, Kahigwa E, et al. African children with malaria in an area of intense Plasmodium falciparum transmission:features on admission to the hospital and risk factors for death. Am J Trop Med Hyg 1999; 61:431-438.

30. Don M, Valerio G, Korppi M, et al. Hyper- and hypoglycemia in children with community-acquired pneumonia. J Pediatr Endocrinol Metab 2008; 21:657-664.

31. Zurynski YA, Lester-Smith D, Fester MS, et al. Enhanced surveillance for serious complications of influenza in children: role of the Australian Pediatric Surveillance Unit. Commun Dis Intell 2008; 32:71-76.

32. Kliegman RM, Behrman RE, Jenson HB, et al. Nelson textbook of pediatrics 18th edn. WB Saunders, Philadelphia.2007.

33. Nyikuri et al. Hypoglycemia in acute childhood diarrhoea at KNH. MMED UoN dissertation. 1994.

34. Nzioki C, Irimu G, Musoke R et al. Audit of care for children aged 6-59 months admitted with severe malnutrition at KNH, Kenya. Int Health 2009; 1:91-96.

35. Ministry of Health. Basic Paediatric Protocols- Revised (2010). Management of severe malnutrition: page 25-27.

36. Alexander D.M, Stork Hans Kemperman, Willen E, et al. Comparison of the accuracy of the HemoCue glucose analyser with Yellow Springs Instrument glucose oxidase analyser particularly in hypoglycemia. European Journal of Endocrinology vol 153:2: 275-281.

37. Rassam A.G. Use of the HemoCue blood glucose analyser in research studies. Diabetes Care 1998:21:1369-1370.

38. E.Vadasdi, E.Jacobs. HemoCue Beta Glucose Photometer evaluated for use in a NICU. Clinical Chemistry 39:2329-2332.

39. HemoCue World Wide Products.

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

KENYATTA NATIONAL HOSPITAL
APPROVED
18 JUL 2012
ETHICS & RESEARCH COMMITTEE

KNH/UON-ERC
Email: uonknh_erc@uonbi.ac.ke
Website: www.uonbi.ac.ke
Link:www.uonbi.ac.ke/activities/KNHUoN

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

Ref: KNH-ERC/A/206

18th July 2012

Dr. Joan Arwa Ongare
Dept.of Paediatrics & Child Health
School of Medicine
University of Nairobi

Dear Dr. Ongare

Research proposal: "Prevalence of Hypoglycemia among children admitted at Kenyatta National Hospital" (P43/02/2012)

This is to inform you that the KNH/UoN-Ethics & Research Committee(KNH/UoN-ERC) has reviewed and **approved** your above revised research proposal. The approval periods are 18th July 2012 to 17th July 2013.

This approval is subject to compliance with the following requirements:

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

For more details consult the KNH/UoN ERC website **www.uonbi.ac.ke/activities/KNHUoN**

Yours sincerely

PROF. A.N. GUANTAI
SECRETARY, KNH/UON-ERC

c.c.

The Deputy Director CS, KNH
The Principal, College of Health Sciences, UoN
The Dean, School of Medicine, UoN
The Chairman, Dept. of Paediatrics & Child Health, UoN
The HOD, Records, KNH
Supervisors: Dr. Daniel Njai, Dept.of Paediatrics & Child Health, UoN
Dr. Ahmed Laving, Dept.of Paediatrics & Child Health, UoN