PREVALENCE AND OUTCOME OF HYPERNATRAEMIC DEHYDRATION AMONG UNDER-5 CHILDREN WITH DIARRHOEA AT THE UNIVERSITY TEACHING HOSPITAL, LUSAKA, ZAMBIA

BY

JOMBO NAMUSHI

COMP NO. 511600748

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The University of Zambia
School of Medicine
Department of Paediatrics & Child Health

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DECLARATION

The dissertation prevalence and outcome of hypernatraemic dehydration among children seen at The University Teaching Hospital is my own work. Where other people's work has been used (either from a print source, internet or any other source) this has been carefully acknowledged and referenced in accordance with departmental requirements.

Signature: …….

Candidate

Signature:……

Name: Dr E. Mpabalwani (Consultant Paediatrician, Honorary Lecturer, UNZA School of Medicine)

Supervisor

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APPROVAL

This dissertation of Jombo Namushi is approved as partial fulfillment of the requirements for the award of Master of Medicine in Paediatrics and Child Health by The University of Zambia.

Signed:…….

Date:…….

Dr S.S. Sinyangwe

Head of Department

Paediatrics and Child Health

The University of Zambia

School of Medicine

Examiners

1. Name:……

   Signature:……..

   Date:……

2. Name:…….

   Signature:……

   Date:……

3. Name:…….

   Signature:……

   Date:…….

ABSTRACT

Introduction: Diarrhoea is the second commonest cause of under-five mortality globally (second to Pneumonia) and kills one (10 percent) out of every 10 children who die before their fifth birthday. In Zambia dehydration due to diarrhoea is a leading cause of morbidity and mortality among under-five children. Hypernatraemic dehydration is the most dangerous and fatal form of dehydration. Despite the availability of well known effective treatment modalities for dehydration in diarrhoea, mortality remains high in many developing countries. The situation is not any different in Zambia and at The University Teaching Hospital (UTH) Department of Paediatrics. In view of the high mortality of children due to diarrhoea, it is not known whether hypernatraemic dehydration could be a significant contributing factor. This study therefore sought to determine the prevalence and outcome of hypernatraemic dehydration as a possible contributing factor to the high mortality rate among children with diarrhoea.

Objective

To determine the prevalence and outcome of hypernatraemic dehydration among under-five children presenting with diarrhoea associated dehydration to UTH Department of Paediatrics.

Method: The study was a prospective cohort study conducted at the UTH Department of Paediatrics. The study population was under-five children presenting with acute diarrhoea with dehydration. Independent variables were age, sex, feeding modality, prior ORS therapy, rotavirus vaccine status and serum sodium. The dependent or outcome variables were discharge/mortality and duration of hospital stay. Data analysis was done with the help of SPSS version 20.

Results: There were a total of 148 participants with an almost 1:1 male/female ratio (73/75), mean age of 14.7 months ranging 1-60 months. The prevalence of hypernatraemic dehydration was approximately 19 percent (29/148) among children presenting with diarrhoea and dehydration. The prevalence is within the range of 10-20 percent cited in many previous studies, however relatively higher than most previous studies done in other countries. Hypernatraemia was associated with a high risk of mortality (7/29) with an OR 5.8 (adjusted OR 3.6, 95% CI 2.9-8.0, *p* 0.002), compared to (7/74) OR 1.8 (adjusted OR 1.1, 95% CI 0.8-2.2, *p* 0.06), and (5/33) OR 3.1 (adjusted OR 2.3, 95% CI 1.7-4.4, *p* 0.03) for normal and low initial sodium level respectively. Hypernatraemia was also associated with longer hospital stay with a mean duration of 3.09 days (74.2hrs) compared to 2.01 days (48.2 hours) and 2.13 days (51.1 hours) for normal and low sodium respectively.

Conclusion: Hypernatraemia is prevalent among under-five children presenting with diarrhoea at UTH department of peadiatrics and probably a major contributing factor to high diarrhoeal associated mortality. Recognition of its occurrence through diligent laboratory services is therefore critical for appropriate patient care.

Key words: Under-five years, diarrhoea, dehydration, and hypernatraemia.

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List of abbreviations

ADD	Acute Diarrhoeal Disease
AGE	Acute Gastroenteritis
GAPPD	Integrated Global Action Plan for the Prevention and control of Pneumonia and Diarrhoea
HMIS	Health Management Information System
MOH	Ministry of Health
mEq/L	Miliequivalents per Litre
ORS	Oral Rehydration Solution
UNICEF	United Nations Children Emergency Fund
UTH	University Teaching Hospital

CHAPTER ONE

1.1. Introduction

Hypernatraemic dehydration is the most dangerous and fatal form of dehydration that occurs in children with diarrhoea and contributes greatly to mortality (Adrogué and Madias, 2000; Chisti *et al,* 2011; Haycock, 2006; Kliegman *et al,* 2008; Neena, 2007). Diarrhoea is the commonest cause of dehydration and a major cause of mortality among under-5 children (WHO/UNICEF, 2013). As many as 10-20% of children with diarrhoea present with hypernatraemic dehydration (Heycock, 2006, Reynolds *et al,* 2006). Dehydration due to diarrhoea is among the leading causes of child morbidity and mortality globally (WHO/UNICEF, 2013). Dehydration may be due to many causes that result in a relative or absolute body water deficit in relation to solutes. Gastroenteritis however, accounts for over 90% of cases of dehydration among children in developing countries (Kotlof *et al,* 2013; WHO/UNICEF, 2013). Dehydration is the hallmark of all diarrhoeal diseases and remains a major cause of childhood mortality (World Health Organisation, 2006). Despite well known simple and cost effective control and treatment measures, dehydration due to diarrhoea continues to kill many children (WHO/UNICEF, 2013). Diarrhoea is the second commonest cause of under-five mortality globally (second to Pneumonia) and kills one (10%) out of every 10 children who die before their fifth birthday (WHO/UNICEF, 2013). The World Health Organisation (WHO) has thus established the integrated Global Action Plan for the Prevention and control of Pneumonia and Diarrhoea (GAPPD) whose goal is to end preventable childhood deaths due to diarrhoea and pneumonia by 2025 (WHO/UNICEF, 2013).

In Zambia dehydration due diarrhoea is a leading cause of morbidity and mortality among under-five children (Ministry of Health, 2013). In 2013 over 2000 children are estimated to have died

from the disease (Ministry of Health, 2013). This figure is by far an underestimate as many more children die at home before even accessing care (Ministry of Health, 2013). Many more deaths still occur in health facilities depicting gaps in case management of children with diarrhoea. At The University Teaching Hospital (UTH) department of paediatrics, diarrhoea is among the leading causes of morbidity and mortality accounting for 6% of all admissions and 5% of all deaths in 2015 (UTH HIMS, 2015 unpublished). Oral rehydration solution (ORS) has shown to be effective in treating diarrhoea and associated physiological derangements especially correcting dehydration and electrolytes (World Health Organisation, 2005). With the wide spread availability and use of ORS most children with diarrhoea can be treated at home, however some children still require health facility care for intravenous fluid administration even to the extent of requiring tertiary hospital care (World Health Organisation, 2005).

Dehydration due to fluid loss being the hallmark of any diarrhoeal disease is commonly associated with electrolyte imbalances mainly hyponatreamia, hypernatreamia and hypokaleamia (Friedman *et al,* 2004; World Health Organisation, 2013, 2005). Among the electrolytes imbalances associated with dehydration, hypernatraemia is associated with more severe dehydration and may not be easily amenable with the standard WHO treatment for dehydration (Adrogué and Madias, 2000; Chouchan *et al*, 2003). In view of the high mortality among children due to diarrhoea in Zambia and at UTH, it is not known whether hypernatraemic dehydration could be a significant contributing factor.

1.2. Problem Statement

Dehydration due diarrhoea is one of the top five causes of under-five morbidity and mortality in Zambia, causing thousands of admission and killing over 2000 children per year (MOH, 2013). At the University Teaching hospital, Lusaka, Zambia, Department of Paediatrics and Child

Health, diarrhoea remains among the top five causes of morbidity and mortality (UTH HMIS, 2012-2015; appendix 2). In 2015 diarrhoea was the fifth commonest cause of morbidity and mortality contributing 6% of all admissions and 5% of all mortalities at UTH, Department of Paediatrics and Child Health (UTH HMIS, 2015). Diarrhoea case fatality rate was 8.9% (89/1000 cases) and 8.2% (82/1000 cases) in 2014 and 2015 respectively, being among the top five case fatality rates in the department of paediatrics (UTH HMIS, 2012-2015). However, there has been a generally downward trend in diarrhoea morbidity and mortality from 2012-2015 as shown below.

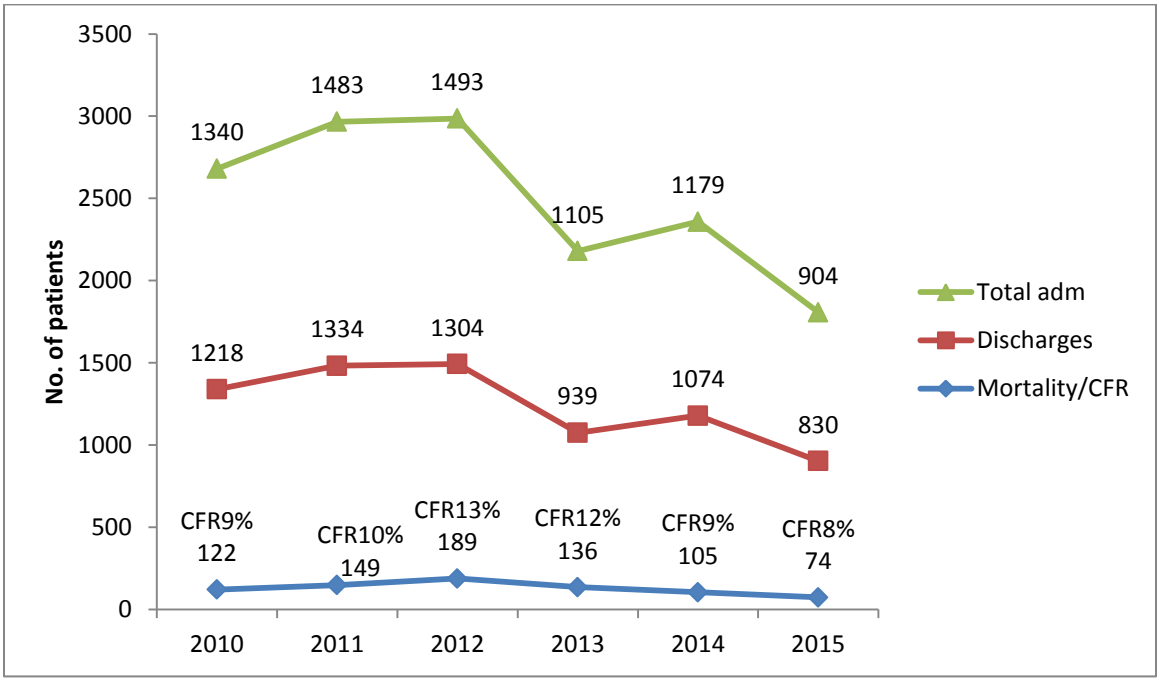

Figure1. Diarrhoea morbidity and mortality trend from 2012 to 2015 (UTH HMIS 2012;2015)

Most diarrhoeal deaths occur within 24 hours of admission despite initiation of what is deemed appropriate fluid replacement therapy (WHO, 2013, personal observation). Severe dehydration remains the leading cause of mortality in children with diarrhoea (WHO, 2012, 2005). However,

co-morbidities and electrolyte derangements especially hypernatraemia may increase risk of mortality (WHO, 2012, 2005).

Despite the variable electrolyte derangements that may be associated with dehydration, the standard of care for dehydration implemented at UTH does not take into account the specific electrolyte derangements. Management of dehydration at UTH is based on WHO guideline of managing dehydration which focuses on fluid replacement and not the specific electrolyte derangements like hypernatraemia which may require a different management approach. The incidence of hypernatraemic dehydration remains unknown in our patients presenting with dehydration. It is therefore not known whether hypernatraemic dehydration is being missed and managed like any other dehydration hence the high mortality rates from diarrhoeal diseases. Most deaths occur within 24 hours of admission before results come back from the laboratory or before patients are investigated adequately. The erratic availability of electrolyte reagents in the laboratory results in tests not being carried out consistently. Electrolytes may therefore not be used to influence patient care in the current clinical practice in the management of dehydration. With regards to hypernatraemic dehydration, being the most fatal form of dehydration, failure to diagnose it may lead to fatalities of children.

1.3. Justification

Despite the availability of well known effective treatment modalities for dehydration in diarrhoea, mortality remains high in many developing countries (WHO, 2013). The situation is not any different in Zambia and at UTH department of paediatrics as highlighted earlier (UTH HMIS, 2012-2015; appendix 2). This study therefore sought to determine the prevalence and outcome of hypernatraemic dehydration among children presenting with diarrhoea. Information is currently not available as no such study has been conducted at UTH and no data was found

elsewhere in Zambia. The study adds to the pool of knowledge aimed at targeted individualized therapy to improve management of diarrhoea associated dehydration and possibly outcomes at a tertiary level hospital. The results of the study may also be a platform to advocate and lobby for diligence in provision of laboratory services at a tertiary level hospital especially electrolytes which currently are erratic.

1.4. Objectives

1.4.1. General objective

To determine the prevalence and outcome of hypernatraemic dehydration among under-five children presenting with diarrhoea to UTH department of paediatrics.

1.4.2. Specific objectives

1. Determine prevalence of hypernatraemic dehydration among under-five children presenting with diarrhoea.

2. Study the outcome of hypernatraemic dehydration among under-five children with diarrhoea.

3. Describe the demographic patterns (age, sex) of children and other associated risk factors of mortality among children with diarrhoea associated dehydration.

CHAPTER TWO

2. LITERATURE REVIEW

2.1. Diarrhoea

2.1. 1. Definition

Diarrhoea is the passage of at least 3 unusually loose or waterly stools within 24 hours (WHO, 2005; 2009). Loose or waterly stool is stool the takes up the shape of a container (WHO/UNICEF, 2005). Clinically diarrhoea is divided in four clinical sub-types; i) acute waterly diarrhoea which lasts several hours or days but less than 14 days, ii) acute bloody diarrhoea or dysentery usually infective, characterized by mucosal damage, iii) persistent diarrhoea lasting more than 14 days and iv) diarrhoea with severe malnutrition (WHO/UNICEF, 2005). All forms of diarrhoea can lead to dehydration; bloody diarrhoea and persistent diarrhoea also have an increased risk for malnutrition, while diarrhoea with malnutrition is often a serious condition (WHO/UNICEF, 2005).

2.1.2. Epidemiology

Over 700 million of diarrhoea episodes are estimated to occur per year in developing countries in children below 15 years with an incidence of 3.2 per child years (Kliegman *et al*, 2007; Steiner *et al*, 2004). About 2 million children under the age of 5 years die from diarrhoea each year and 80% of deaths occur in the first 2 years of life (WHO/UNICEF, 2005). Sub-saharan Africa and south-east Asia contribute 90% of all diarrhoeal deaths globally. In Zambia, diarrhea kills close to 2000 children below five years per year and remains a major cause of under five morbidity and mortality (MoH, 2012).

2.1.3. Aetiology

Almost all acute diarrhoeal diseases are caused by infectious agents (Kotloff *et al*, 2013; WHO, 2005). Infectious acute diarrhoea is a food/water borne (feaco-oral) disease hence mainly ensues from ingestion of food/water contaminated with organisms or toxins/poison that results in gastrointestinal irritation and dysfunction (Kliegman *et al*, 2009). In view of the high burden of diarrhoeal diseases in developing countries the Global Enteric Multicentre Study (GEMS) was conducted whose aim was to highlight the aetiology and burden of diarrhoeal diseases in sub-Saharan Africa and south-east Asia, which account for over 90% of the global diarrhoea burden (Kotloff *et al*, 2013). The GEMS study indicates that most of diarrheal episodes in children are infective, 83% of children had pathogens isolated of which 45% had multiple pathogens (Kotloff *et al*, 2013). The top four causative agents/organisms of diarrhoea identified were; rotavirus (affecting especially infants and toddlers), cryptosporidium (also more common in infants but also older children especially in Africa), shigella (especially in older children) and enterotoxigenic E coli (ST-ETEC) (affecting all age groups of under-fives) (Kotloff *et al*, 2013). Other pathogens includes, adenovirus 40/41, aeromonas, *V. cholera O1, C. jejuni*, other *E. coli* species, norovirus, sapovirus, salmonella, and *E. histolytica* (Kotloff *et al*, 2013; Kliegman *et al*, 2008; WHO, 2005). There are many more organisms that may cause acute diarrhoeal disease in children, but the above pathogens account for the majority of cases (Kotloff *et al*, 2013).

2.1.4. Pathophysiology

Infective diarrhoea may be inflammatory or noninflammatory depending on the pathogen. Noninflammatory diarrhoea results mainly from pathogens that produce enterotoxins which alter fluid transport systems and/or villus destruction. The toxins work in various ways by binding to specific transport channels leading to secretory diarrhoea resulting in copious watery diarrhoea

causing severe dehydration, classical example being the cholera toxin. Inflammatory diarrhoea is the result of direct invasion of the enterocytes by the pathogen causing destruction and dysfunction such as shigella. Destruction leads to villus loss and shortening reducing the absorptive surface. Enterocyte destruction also results in bloody diarrhoea. Some pathogens which invade enterocytes causing inflammatory diarrhoea may also produce toxins which alter fluid transport systems and damage enterocytes such as Rotavirus (Kliegman *et,* 2008; Peters *et al,* 2009).

2.1.5. Electrolytes in Diarrhoea

Fluid loss through loose stool is the hallmark of Diarrhoea. The fluid contains water and various electrolytes mainly sodium, potassium, chloride, glucose and bicarbonate (Kliegman *et al,* 2008; WHO, 2005). The main electrolyte disturbances associated with diarrhoea however are; hypernatraemia, hyponatraemia and hypokalaemia (Cheng, 2011; WHO, 2005).

i) Hypernatraemia

Hypernatraemia is defined as serum sodium above 150mmol/l. It may occur in some children with diarrhoea, termed as hypernatraemic dehydration (WHO, 2005). It ensues from a more water deficit in relation to the body sodium content (Adroque and Madias, 2000). The main causes are prior therapies especially administration of concentrated drinks with high sugar content such as commercial soft/fruit drinks, concentrated formular and salt intake such as home made ORS or iatrogenic through saline administration in hospitalised patients (Adroque and Madias, 2000; WHO, 2005). Hypernatraemia is further discussed in detail below in section 2.2 being the focus of the study.

ii) Hyponatraemia

Hyponatraemia is defined as serum sodium less than 130mmol/l. It may occur in diarrhoea as a result of loss of more sodium in relation to water or a result of fluid replacement therapies consisting mainly of water or hypotonic fluids. It is also commonly associated with diarrhoea in malnutrition and shigellosis (WHO, 2005). In a study by Hanna and Saberi in 2010 on the incidence of hyponatraemia in children with diarrhoea, found that 12% had hyponatraemia. In another study by Freedman and Geary in 2013 on bolus fluid therapy and sodium homeostasis in paediatric diarrhoea, found that 38% of the children had hyponatraemia at baseline. Cerebral oedema is the hallmark of the clinical features seen in hyponatraemia. The associated neurological signs include anorexia, nausea, vomiting, malaise, lethargy, confusion agitation, headache, decreased reflexes, seizures and coma. It can also result in respiratory failure due to muscle cramps and weakness (Kliegman *et al*, 2008; WHO, 2006). Hyponatraemia is easily amenable with any sodium containing solutions. Milder forms may correct easily with oral rehydration solutions while severe hyponatraemia requires rapid hypertonic saline infusion to prevent or correct cerebral oedema (WHO, 2009; NIHCE, 2009)

iii) Hypokalaemia

Hypokalaemia is defined as serum potassium less than 3mmol/l (WHO, 2005). It often results in loss of potassium in diarrhoea coupled with inadequate replacement. It is commonly associated with diarrhoea occurring in children with malnutrition (Alam, 2009). Clinical signs of hypokalaemia include muscle weakness, paralytic ileus, arrhythmias and impaired renal function. Caution should be taken when correcting acidosis which is a common feature in severe dehydration as base administration may worsen the hypokalaemia. Hypokaleamia is easily corrected with any potassium containing intravenous fluids such as darrows, and ringers lactate

solutions. Milder forms are easily amenable with ORS while severe hypokalaemia my require administration of potassium chloride (WHO, 2005; 2009). Hyperkalaemia is rare in gastroenteritis. It usually results from severe renal compromise due to severe dehydration or shock. Hyperkalaemia may correct spontaneously with improved hydration and renal perfusion. Severe form may require insulin therapy or dialysis (Kliegman *et al*, 2008; Nagar *et al*, 2010)

There are other electrolytes/metabolic disorders that may be associated with the above electrolyte imbalances such as hyperglycemia and secondary hypocalcaemia associated with hypernatraemia which correct once the hypernatraemia is corrected.

2.1.6. Clinical features/assessment of dehydration

Table.1. WHO clinical assessment of degree of dehydration and management

	A	B	C
LOOK AT: CONDITION	Well, alert	Restless, irritable	Lethargic or unconscious
EYES	Normal	Sunken	Sunken
THIRST	Drinks normally, not thirsty	Thirsty, drinks eagerly	Drinks poorly, or not able to drink
FEEL: SKIN PINCH	Goes back quickly	Goes back slowly	Goes back very slowly
DECIDE	The patient has **no signs of dehydration**	If the patient has two or more signs in B, there is **some dehydration**	If the patients has two or more signs in C, there is **severe dehydration**
FLUID DEFICIT	<5% BW (<50mls/kg)	5-10% BW (50-100mls/kg)	>10% BW (>100mls/kg)
TREAT	Plan A: ORS <2yrs 50-100mls per loose stool >2yrs 100-200mls per loose stool	Plan B: ORS 75mls/kg BW in 4 hours	Plan C: IVF 100mls/kg BW < 1yr 30% in 1hr, 70% 5hrs >1yr 30% in 30mins, 70% in 2.5hrs

(Source: WHO, 2005)

2.1. 7. Management of diarrhoea

The principles of managing diarrhoea focus on prevention of dehydration, treating dehydration, shorten duration of illness at the same time prevent future episodes and preserve nutritional status (WHO, 2009; 2005). WHO recommends a comprehensive 7 point treatment and prevention strategy which stipulates; treatment by 1) fluid replacement to treat and prevent dehydration and 2) Zinc treatment/supplementation. The prevention package focuses on preventing future episodes of diarrhea 3) Rotavirus and measles vaccinations 4) Promotion of early and exclusive breastfeeding and vitamin A supplementation 5) Promotion of handwashing with soap 6) Improving water safety and quantity 7) improving Community sanitation (WHO, 2009; 2005). Zinc treatment has shown to reduce the duration of diarrhoea by 25% and a reduction in treatment failure and mortality by 40% (WHO, 2009).

The introduction of low osmolarity ORS in 2004 was another milestone in the fight to reduce diarrhoeal deaths. Low osmolarity ORS reduces treatment failure of oral rehydration therapy (ORT) and the need for intravenous fluids by 60% compared to initial standard ORS (WHO, 2009). Another landmark in the fight against diarrhoea was the introduction of rotavirus vaccine (Peter *et al,* 2009; WHO, 2009; 2005). Rotavirus accounts for 40% of all under-five diarrhoea admissions and is responsible for 20% of all diarrhoea deaths, 90% of which occur in poor countries like Zambia (Peter *et al,* 2009). Rotavirus vaccine has shown to reduce severe rotavirus diarrhoea and disease of any severity by 90-100% and 74-85% respectively (Peter *et al,* 2009). With all these advances in diarrhoea treatment and prevention (low osmolarity ORS, Zinc, and rotavirus vaccine) diarrhoea deaths are expected to reduce significantly (WHO, 2005; 2009).

Intravenous fluid therapy is recommended for severe dehydration and shock (Bailey, 2010; Goldman *et al,* 2008; Freedman *et al,* 2011; Sunoto, 1990; WHO, 2005). The recommended fluid

management in severe dehydration is 100mls/kg body weight in two aliquots. The initial 30mls/kg given in 30 minutes and the remaining 70mls/kg in two and half hours for children above 1 year and the first aliquot given in 1 hour and the remaining in 5 hours for infants (Friedman, 2005; Nager & Wang, 2010; WHO, 2005; 2009). The type of fluid used can be any polyelectrolyte fluid mainly darrows of varying strengths preferably half strength in children or ringers lactate (Guarino *et al,* 2008; Levy & Bachur, 2007; Williams *et al,* 1999; WHO, 2005). Children in shock require a bolus of saline at 20mls/kg repeated up to 3 times maximum depending on response to restore intravascular volume then followed by appropriate therapy as above for severe dehydration (Juca *et al,* Maitland *et al,* 2011; 2005; WHO, 2009). The approach however is different in the presence of hypernatraemic dehydration as the rapid fluid therapy may be deleterious (Holliday *et al,* 1999; Moineau & Newman, 1990; Reid & Bonadio, 1996; WHO, 2009).

Non severe dehydration can safely be managed with ORS (WHO, 2005; 2009). Even severe dehydration in the absence of facilities for intravenous fluids may be managed with ORS preferably via a nasogastric tube (Nagar &Wang 2002; Spandorfer *et al,* 2005; WHO, 2005; 2009)

2.1.8. Prognosis

There are many factors that influence prognosis of children with diarrhoea. Critical is the age, most deaths (80%) occurring in the first 2 years of life with infants being the most at risk group (Kotloff, 2013; Peter *et al,* 2009; WHO, 2009; 2005). Causative organism is also a prognostic factor, in the GEMS study *E. coli* (especially in infancy) and cryptosporidium (in order children) was associated with high risk for mortality (Kotloff *et al,* 2013). Nutritional status was noted to be a risk factor in the GEMS study, height for age Z score was inversely proportion to risk of

mortality. Co-morbidities such as Malaria and HIV are also associated with an increased risk of mortality (Kotloff *et al,* 2013). Type of electrolyete disturbance may also influence prognosis. Hypernatraemia if not corrected timely and appropriately is the most fatal electrolyte imbalance associated with diarrhoea (Adrogue and Madias, 200). In a study by Chouchane *et al* in 2003 documented 11% higher fatality rate among children with hypernatraemic dehydration compared to other electrolyte derrangements. Rotavirus vaccination status is another well recognised prognostic factor. It prevents and reduces the severity of rotavirus diarrhoea which is the commonest cause of diarrhoea in infancy where the risk of mortality is highest (Peter *et al,* 2009)

2.2. Hypernatraemic dehydration

2.2.1. Sodium metabolism

The human body is about 70% water, which occurs as extracellular and intracellular fluid compartments. Intracellular contains about 40% and the extracellular about 25% of the total body water. (Kliegman *et al,* 2008; Adrogué and Madias, 2000). The main solutes, in terms of cations and anions vary between the two spaces. Sodium is the main extracellular cation coupled with chloride as the corresponding anion (Reynolds *et al,* 2006). On the other hand, potassium is the predominant intracellular cation with phosphate and proteins as the corresponding anions (Kliegman *et al,* 2008; Reynolds, *et al,* 2006). The maintenance of the differences in the concentration of sodium and potassium in the two compartments is an active process by activity of the N+, K+-ATPase pump (Shaw, *et al,* 2010). About 40% of total sodium is in the bones, with only less than 3% in the intracellular space, while the remainder is in the extracellular space. Being mostly extracellular, sodium is responsible for maintenance of extracellular osmolality and intravascular volume (Kliegman *et al,* 2008; Shaw *et al,* 2010). In view its central

role in the body fluid balance mechanisms, derangements of sodium concentration may have devastating physiological consequences.

Body sodium content is mainly determined by diet being the major source. Breast milk provides about 7mEq/l of sodium which is the major source in exclusively breast fed infants. Sodium deficiency due to gastrointestinal pathology is uncommon as it is readily absorbed throughout the gastrointestinal tract. This also entails sodium poisoning is easy as most it is absorbed. Sodium absorption from the gastrointestinal tract is by the sodium-glucose co-transport system. The co-transport system is the basis for ORS formulation content. Sodium excretion is through stool, sweat and urine. Urine is the major excretory pathway, the kidneys being the major regulator of sodium balance and excretion. Stool sodium excretion may be variable in diarrhoeal diseases (Kliegman, *et al,* 2008).

2.2.2. Definition and aetiology

Hypernatraemic dehydration is a body fluid deficit associated with a high sodium concentration above 150mEq/l (Kliegman *et al,* 2008; Adrogué and Madias, 2000, WHO/UNICEF, 2005). It may result from a sodium excess, water deficit or both sodium and water deficit in which the water loss is in excess of the sodium loss which may occur amidst increased, normal or low total body sodium content (Gorelick, 2002; King *et al,* 2003; Neena, 2007). There are many conditions that may lead to hypernatraemic dehydration such as diabetes insipidus, hyperaldosteronism, ineffective breast feeding especially in neonates, improperly mixed formula and diarrhoea. However, diarrhoea remains a leading cause of dehydration and hence hypernatraemic dehydration among children in developing countries (Chouchane *et al,* 2003; Chilton, 1995; Kotlof *et al,* 2013).

Diarrhoea associated hypernatraemic dehydration ensues from a water deficit in relation to the body sodium content (Adroque and Madias, 2000; WHO, 2005). The main causes are prior therapies especially administration of concentrated drinks with high sugar content such as commercial soft/fruit drinks and concentrated formular resulting in osmotic diarrhoea (Chilton, 1995; Kocaoglu et al, 2014; Thullen 1988). Also excessive salt intake such as home made ORS or iatrogenic through saline administration in hospitalized patients (Adroque and Madias, 2000; WHO, 2005). Hypernatraemic dehydration in diarrhoea is most likely to occur in younger children who depend on adults for access to water or those with inadequate intake due to severe dehydration in which the child is comatose or lethargic, anorexia or excessive vomiting (Eke and Nte, 1996). Inadequate breast feeding has also been noted to be a major cause of hypernatraemic dehydration among infants especially during exclusive breast feeding (Cooper *et al* 1995; Kaplan *et al*, 1989; Peters, 1998)

2.2.3. Incidence

The incidence of hypernatraemic dehydration varies depending on the associated aetiological condition. In diarrhoea, 10-20% cases may have associated hypernatraemia (Eke and Nte, 1996, WHO, 2005). In a study by Chouchane *et al*, in 2003, hypernatraemic dehydration accounted for 11.5% of all dehydration and was associated with more severe dehydration (87%) and neurological signs (77%) with a mortality rate of 11%. Dommelen *et al* (2007) indicates that the incidence of hypernatraemic dehydration among breast fed infants may be about 7.1 per 10,000 breast fed infants, being highest in the early neonatal period due to ineffective breast feeding during that period as a result of poorly established lactation (Sofer *et al*, 1993). In a study by Eke and Nte, (1996) among children with diarrhoea in Nigeria showed that 13.7% of all cases had

hypernatraemia. In other conditions such as diabetes insipidus, diabetes mellitus and hyperaldosteronism the incidence of hypernatreamia may even be higher (Kliegman *et al,* 2008)

2.2.4. Clincal features

Signs of dehydration tend to occur late in hypernatraemic dehydration as the increased vascular osmolality draws water from the intracellular space and tend to preserve the intravascular volume till late in the disease process (Chouchane *et al,* 2003). Hypernatraemia is thus often associated with more severe dehydration at presentation (Chouchane *et al,* 2003). The clinical picture of hypernatraemic dehydration is a combination of features of dehydration and hypernatraemia. Hypernatraemic dehydration when severe usually at sodium levels exceeding 165mEq/l may present with overt clinical signs such as convulsions (Adroque and Madias, 2000; Parkin *et al,* 2010). Other clinical signs include hyperpnea, muscle weakness, restlessness, a characteristic high-pitched cry, insomnia, lethargy, and even coma sometimes which may be associated with permanent brain damage (Adroque and Madias, 2000, Peruzzo *et al,* 2010; WHO, 2005). Unlike other forms of dehydration, hypernatraemic dehydration may be associated with significant neurodevelopment sequelae (Escobar *et al,* 2007). It may cause cerebral haemorrhage, wide spread thromboses including cerebral thrombosis, subdural effusions and cerebral oedema resulting from inappropriate fluid management, all of which may be associated with permanent neurological deficit (Chisti *et al,* 2012). Other complications/clinical features of include peripheral gangrene, stroke and renal vein thrombosis resulting from the hypercoagulable state associated with hypernatraemic dehydration (Kliegman *et al,* 2008; Smith, 1998).

2.2.5. Management of hypernatraemic dehydration

Management of hypernatraemic dehydration must be undertaken with caution as mortality often results from complications of treatment such as cerebral oedema and fluid overload (Peruzzo *et*

al, 2010; Shawn, 2010). In any form of dehydration especially when severe, correction of hypovolemia takes precedence to correction of any associated electrolyte derangements (Reynolds *et al*, 2006; Gorelick, 2002). As opposed to the WHO plan C of treating severe dehydration of 100ml/kg body weight in 6 hours for infants and 3 hours for older children, hydration in hypernatraemia is done over a longer period of time. Treatment is aimed at decreasing the serum sodium by less than 12mEq/L in 24 hours to prevent cerebral oedema, taking into account the current sodium level in relation to the expected sodium level to guide the fluid deficit required to correct the mismatch (Heycock, 2006; Kanaan *et al*, 2003; WHO, 2005; 2009). Thus in a study by Kocaoglu *et al, (*2013) the mean duration required to ameliorate dysnatraemia was longer in hypernatraemia than hyponatraemia using appropriate fluid management for age. Initial hydration to restore intravascular volume must be with a sodium containing fluid, saline being preferred to reduce the risk of cerebral oedema (Kliegman *et al*, 2008; King *et al*, 2003; Molteni, 1994). In view of the risk associated with rehydration, identifying hypernatraemia is critical for appropriate management (Neville, 2006; Parkin *et al*, 2010).

CHAPTER THREE

3. METHODOLOGY

3.1. Study site

The study was conducted at the University Teaching Hospital Department of Paediatrics and Child Heath.

3.2. Study design

It was a cross sectional study. The study involved recruitment of children meeting the inclusion criteria and documenting clinical events as at discharge. Children identified with hypernatraemia from the initial specimen required a repeat sodium determination 24hrs from admission. Twenty-four hours being the minimum time required to hydrate patients to ameliorate hypernatreamia but still 48 hours is recommended.

3.3. Target/study population

The target population was children presenting to the department, while the study population was under-five children with diarrhoea associated dehydration meeting the inclusion criteria.

3.4. Inclusion Criteria

Children under-five years with diarrhoea associated dehydration as per WHO criteria of dehydration as indicated in table 1 above whose parent/guardian consented to participate in the study.

3.5. Exclusion criteria

Children above five years of age were excluded, acute diarrhoea mainly being an under-five disease. Children whose parents/guardian did not consent to participate in the study were also excluded.

3.6. Sampling

Sampling was convenient, recruiting all children meeting the inclusion criteria. The sample size was calculated using the sample size formula as below. Assuming 95% significance, and a 10% proportion of hypernatraemic dehydration among all diarrhoea cases, the sample size required to demonstrate statistical significance was 148 participants.

$N = z2\ [p(1-p)/D2]$

Where;

N = required sample size

Z = Z statistic at 95% CI (1.96)

P = estimated incidence of hypernatraemic dehydration of 10% (0.1)

D = acceptable standard deviation or precision of 0.05

3.7. Recruitment

Participants were recruited on first contact in the emergency room upon assessing eligibility and consent obtained. The participant was coded or numbered and a data entry form was filled to capture the demographic data and assessment for dehydration. A 2ml blood sample was collected in a heparin green top bottle bearing the code or name of patient plus other investigations required for the patient. Care was taken to ensure appropriate treatment was initiated as per

current standard of care with possible alteration of treatment upon receipt and communication of results to the attending doctors. Recruitment was done only during week days and during day time bearing in mind that the laboratory does not function fully at night and weekends and that long stay of samples may affect electrolytes. The main data collection days coincided with the times the principal investigator was working from the emergency room. However the help of a research assistant (nurse working in emergency room) was sought to enhance recruitment and data collection on other days.

3.8. Data collection

A questionnaire form was used to collect data. The data captured independent variables which included; age, sex, prior therapy and feeding mode- breast milk or formula (for infants and toddlers) and sodium level. The dependent variables captured were outcome in terms of discharges or mortality and duration of hospital stay.

3.9. Data analysis

Data was analysed using Statistical Package for Social Sciences (SPSS) version 20. Continuous numerical variables were analysed using means and medians, while categorical variables were analysed using simple proportions. Odd ratios were used to determine any possible associations between the demographic features (independent variable) and the dependent variables (sodium level, mortality/discharge). Multivariate analysis was used for adjusted odd ratios bearing in mind the many factors that may influence the outcomes (age, sex, prior therapy).

3.10. Quality assurance

For quality assurance purposes standardized dehydration clinical assessment forms were devised based on the WHO clinical assessment for use during patient assessment and were part of the data entry form. Protocols on management of hypernatraemic dehydration were provided in the

clinical areas where patients were managed. Sodium determination was conducted at the same laboratory throughout the study period for consistency. Entries by the research assistant were counter checked by the principal investigator to ensure completeness and consistence.

3.11. Ethical consideration

The research was approved by ERES and permission was granted by UTH for commencement of recruitment and data collection. Written consent was obtained from parent/guardian after explaining the condition of the child and the purpose of the study. Parents/guardian were explained to that participating in the study was at their own free will and that declining would not have affected care rendered to the child in any way as per routine treatment standards and that the study had no financial gains.

3.12. Benefits/risks of the study

Patients enrolled benefitted from the extra investigations such as sodium determination/electrolytes which are not routinely done. The study may also influence the outlook and approach to dehydration which may benefit future patients. The only identifiable risk was needled prick pain during blood sample collection. Needle pricks however comprised part of the standard care children received, as both participants and non participants had intravenous access for administration of fluids as part of treatment and sample collection for investigations.

CHAPTER FOUR

4. RESULTS

4.1. Demographic characteristics of the study population

There were a total of 148 participants with an almost 1:1 male/female ratio (73/75). The mean age was 14.7 months while the age range was 1-60 months. The majority were infants (1-12 months) comprising 57.4% of all participants. Of the infants 56.5% were 6 months or below, while 84.5% of all participants were 24 months of age or less while only 15.6% were aged between 25 and 60 months (Also refer appendix 1).

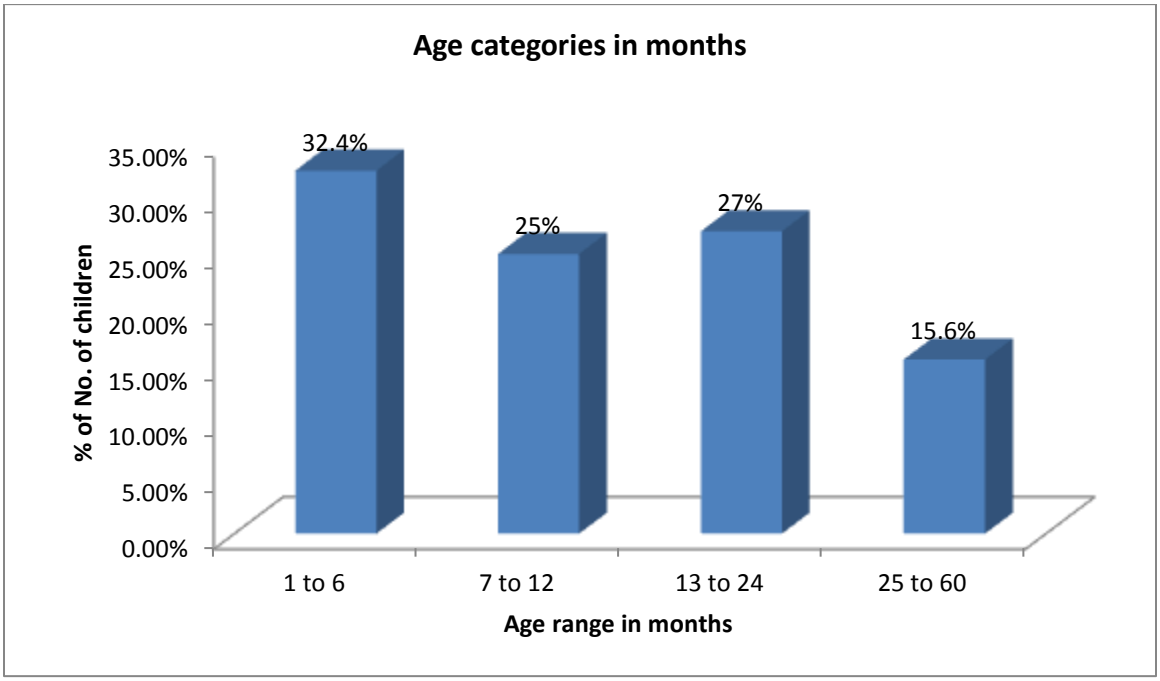

Figure 4.1: Age category distribution of participants in months.

4.2. Breast feeding trends

The recommended duration of breast feeding is 24 months (ZDHS, 2007), of those children still in the recommended period of breast feeding only 68.8% were still breast feeding. It is recommended to exclusively breast feed for the first 6 months (WHO, 2005; 2006), of the children aged 6 months or less 22.9% were not breast feeding. The proportion of children breast feeding diminished with age towards 24 months. There were 22 participants ranging between 18 and 24 months of whom only 2 were still breast feeding by 18 months and 1 was still on formula by 19 months. There was none breast feeding by 20 months and above, the oldest breast feeding participants were two 18 months old children, and 1 participant was on formula by 19 months being the oldest participant on milk based feeds. Among HIV exposed infants only 40% were still breast feeding by 1 year of age.

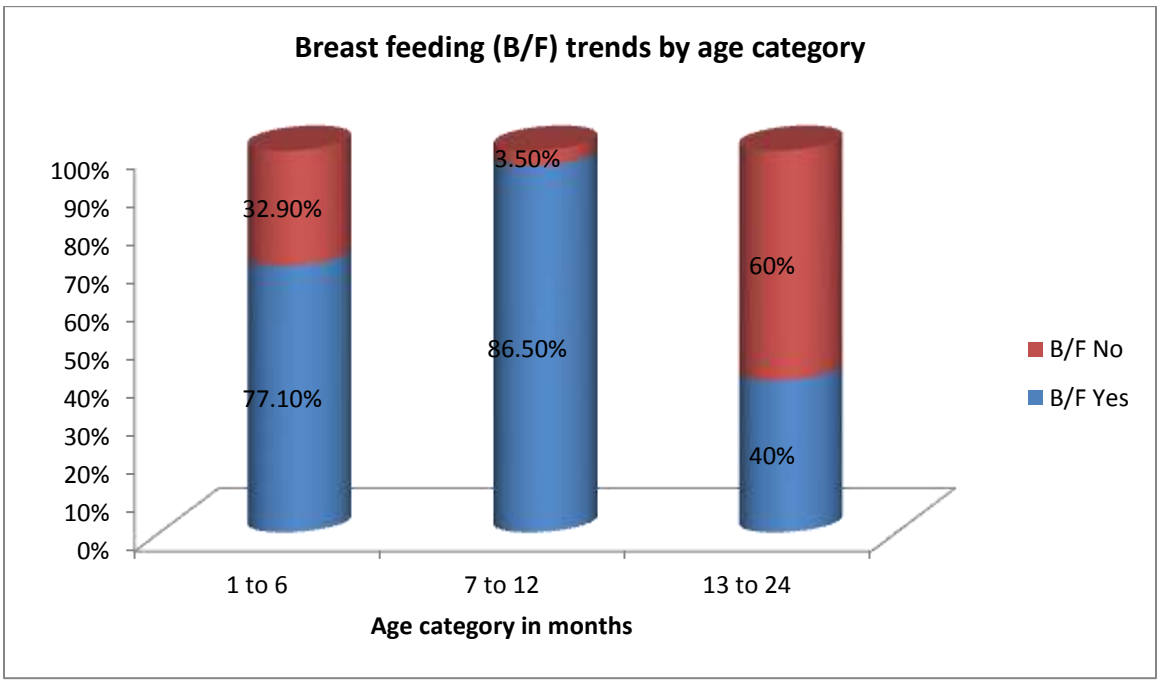

Figure 4.2: Breast feeding trends by age category

4.3. Duration of symptoms at time of hospital presentation

Most participants (48%) presented within 24-48 hours (by the third day) of illness, the mean duration of illness at presentation being 62.9 hours (2.62 days), ranging from the earliest presentation of within 24 hours (with a day) and the latest being 144 hours (6 days) of symptoms. About 15% (14.9%) of participants presented after 72 hours of illness.

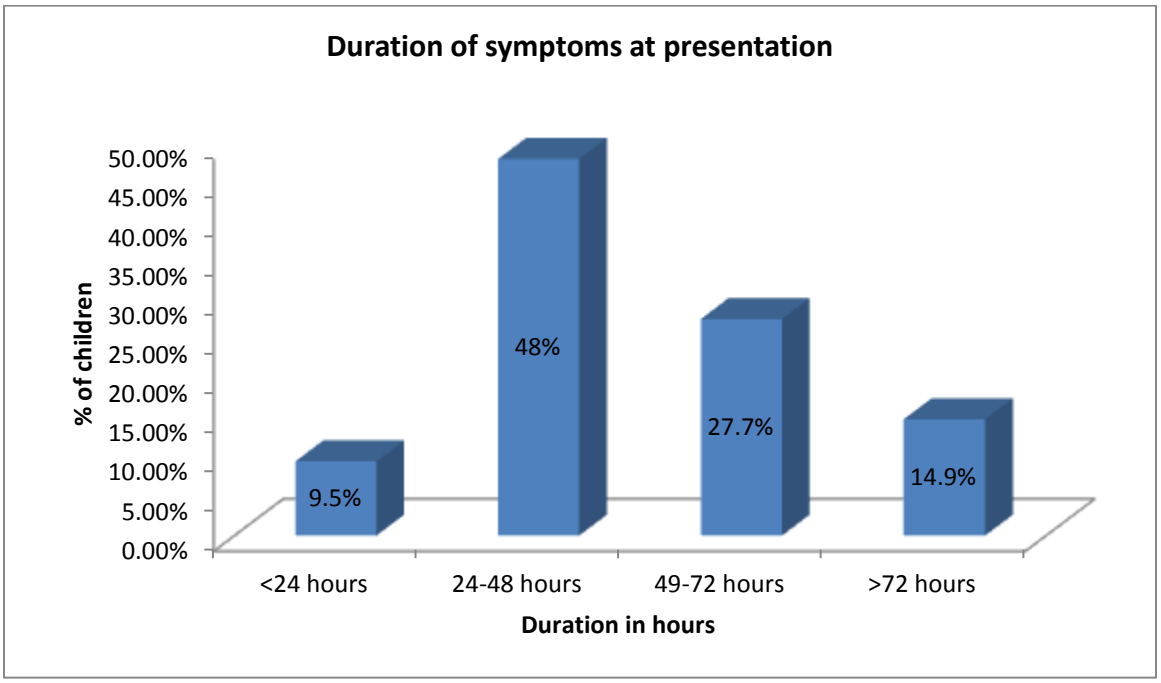

Figure 4.3: Duration of Symptoms at presentation

4.4. Other associated symptoms at presentation

All participants presented with diarrhoea and other symptoms. The commonest associated symptom was vomiting which was noted in 42.6% of the participants. The second commonest associated symptom was fever noted in 23.6% of the participants. Other associated symptoms in smaller proportions included coughing and convulsions. Thirty-three percent of all participants had 2 or more other symptoms which included, fever and cough in any combination. Among other co-morbidities included in the analysis was HIV. Only 2 % (3) of the participants were

confirmed HIV positive and ART naïve, 25 % were exposed in the 18 months and below age category, while 72.8% were negative.

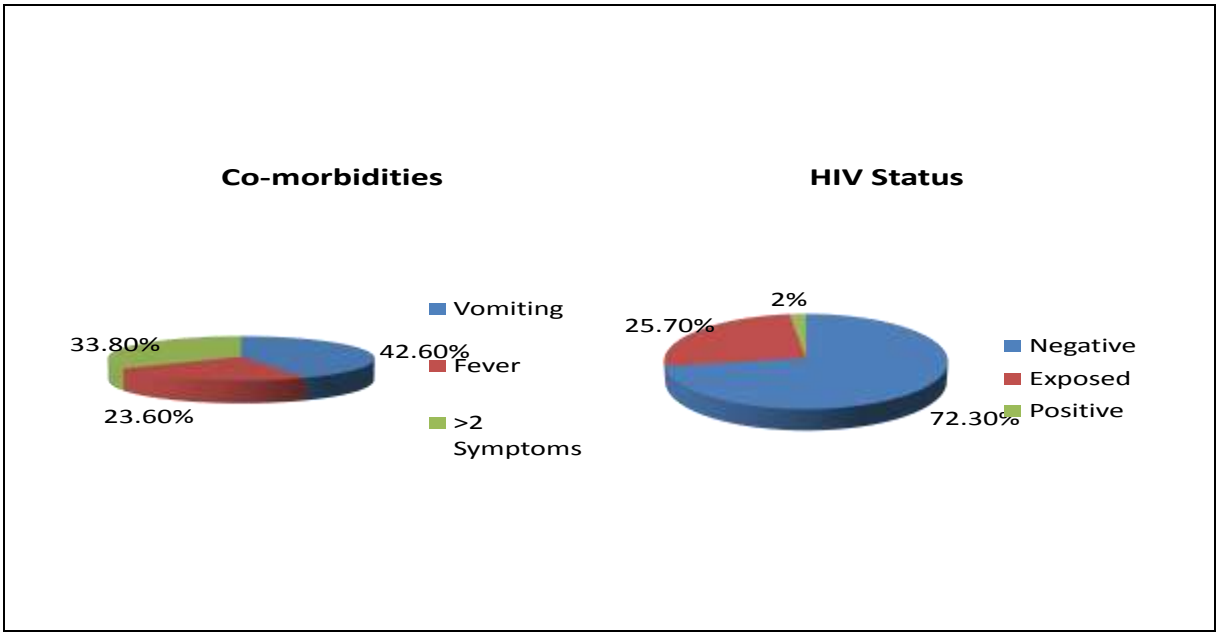

Figure 4.4: co morbidities and HIV status of participants

4.5. Level of dehydration and number of stools per day at presentation

Most participants presented with severe dehydration (66.9%) and 8.8% (13/148) presented in shock. Of those presenting in shock 46.2% (6/13) had hypernatraemia, 38.5% (5/13) had hyponatraemia and only 15.4% (2/13) had normal sodium level. Among patients presenting in shock with hypernatraemia 33.3% died (table 2 below). The overall mortality among patients in shock was 30.8%. The level of dehydration may be related to the severity of diarrhoea which may correlate to some extent with the numbers of stools per day, however volume of stools is a factor to consider but often difficult to measure or estimate hence frequency of stools is the crude proxy often used. Hence evaluating the number of stools per day was conducted. The mean number of stools per day at presentation was 3.74, ranging 2-12 stools/day. Majority of participants (48%) presented with 2-3 stools/day, 34.5% had 4-5 stools/day and 17.5% has more than 5 stools per day. This shows that 52% presented with 4 or more stools per day.

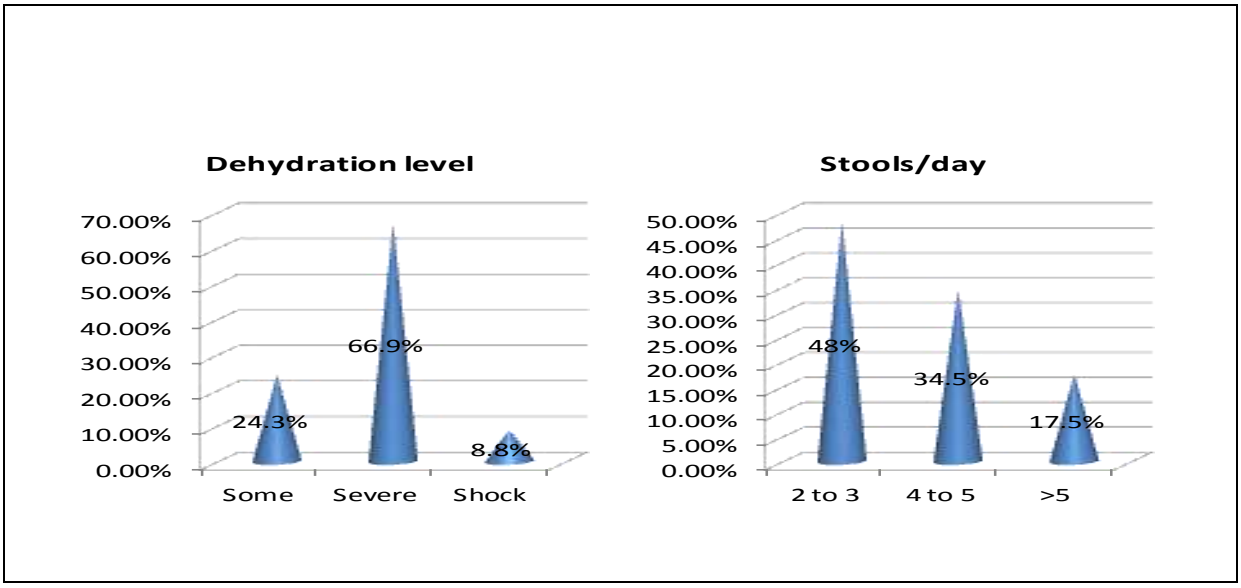

Figure 4.5a: Level of dehydration and number of stools per day at presentation

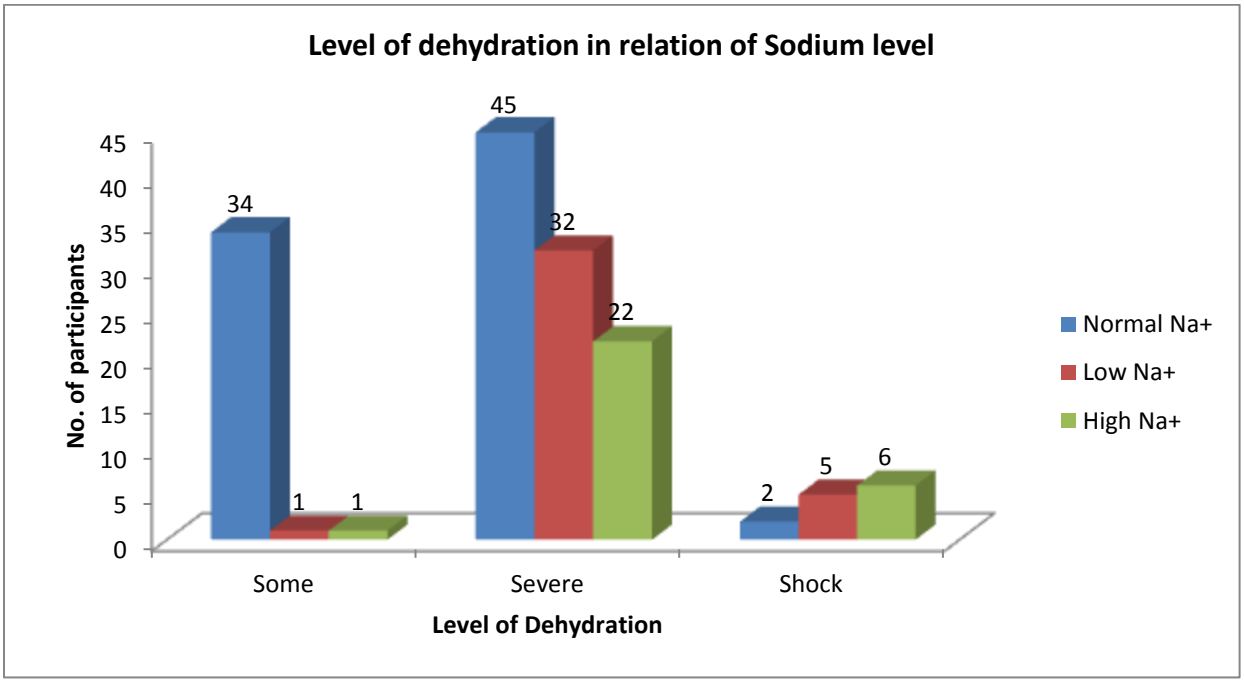

Figure 4.5b: Level of dehydration in relation to sodium level

4.6. Rotavirus vaccination status and prior ORS therapy

Most of the participants were rotavirus vaccinated; only 10% were not vaccinated most them being the very young ones 6 months of age or below. Sixty-eight percent (68%) of participants had prior ORS therapy at presentation while 31.8% did not. The very young especially 6 months of age and below were less likely to have prior ORS therapy at presentation.

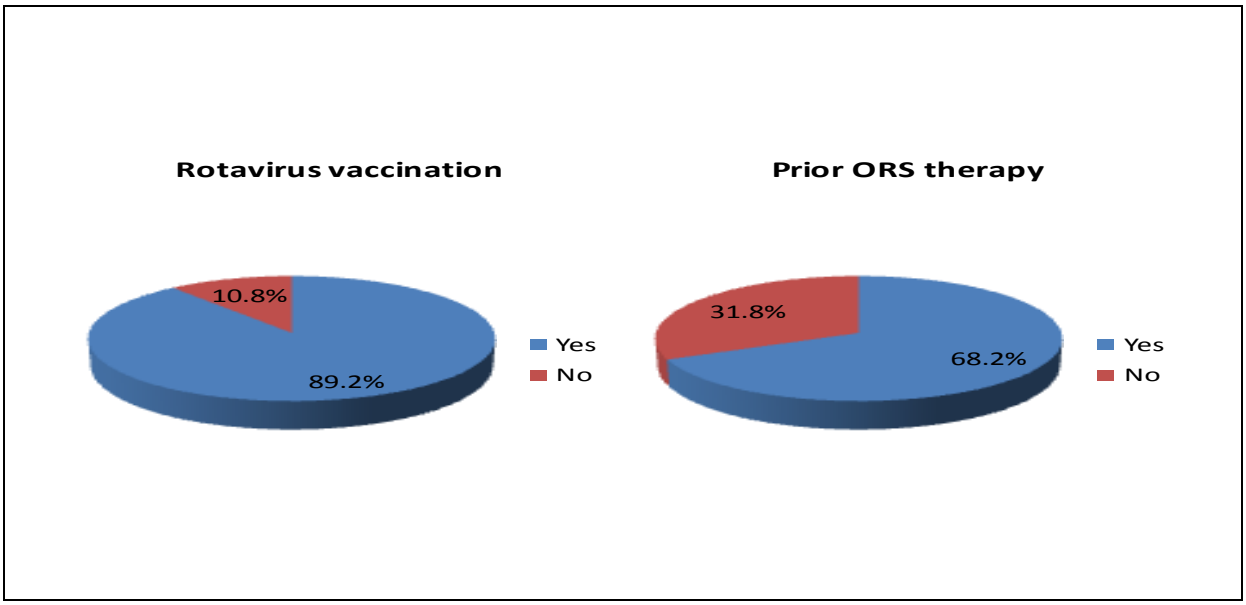

Figure 4.6: Rotavirus vaccination status and priors ORS therapy at presentation

4.7. Initial sodium level evaluation in relation to discharge/mortality

The initial sodium determination showed that 19.6% of the participants had hypernatraemia at presentation with sodium levels above 150mmol/L, 25.7% were hyponatraemic with sodium levels below 130mmol/L, while 54.7% had normal sodium levels between 130mmol/L and 150mmol/L (Appendix 1). Of those with hypernatraemia only 10.3% (3/29) had a 24 hour repeat sodium determination. The case fatality rate among children with hypernatraemia was 24.1% (7/29), while it was 13.2% (5/33) and 8.6% (7/74) for patients with hyponatraemia and normal sodium respectively. The overall mortality was 12.8% (19/148). Figure 4.7 shows number of participants in relation to their sodium level, discharge and mortality.

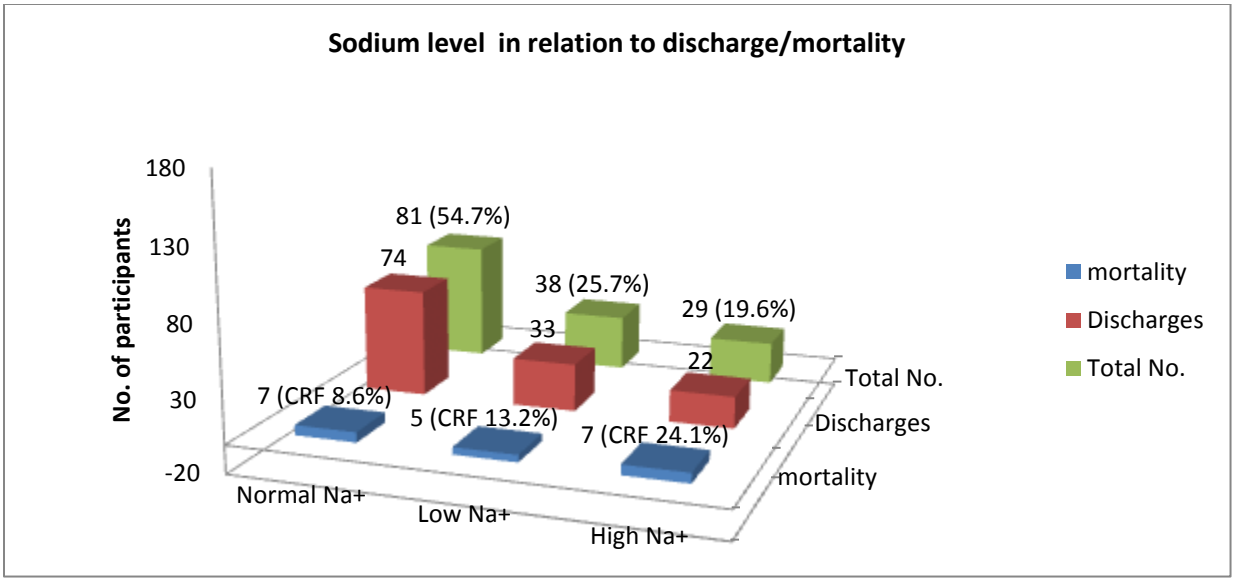

Figure 4.7: Number of participants in relation to Sodium level/discharges/mortality

4.8. Duration of hospital stay

The overall mean hospital stay was 49 hours (2.04 days, range 1-7 days). The mean hospital stay among discharges was 50 hours (2.08 days, range 1-6 days). Among mortalities the mean hospital stay was 41.8 hours (1.74 days, range 1-3 days). When stratified by sodium level, the mean hospital stay among patients with normal sodium was 48.2 hours (2.01 days, range 1-4 days), 51.1 hours (2.13 days, range 1-5 days) for patients with hyponatraemia and a mean hospital stay of 74.2 hours (3.09 days, range 1-7 days) for patients with hypernatraemia (table 2; figure 4.8; appendix 1).

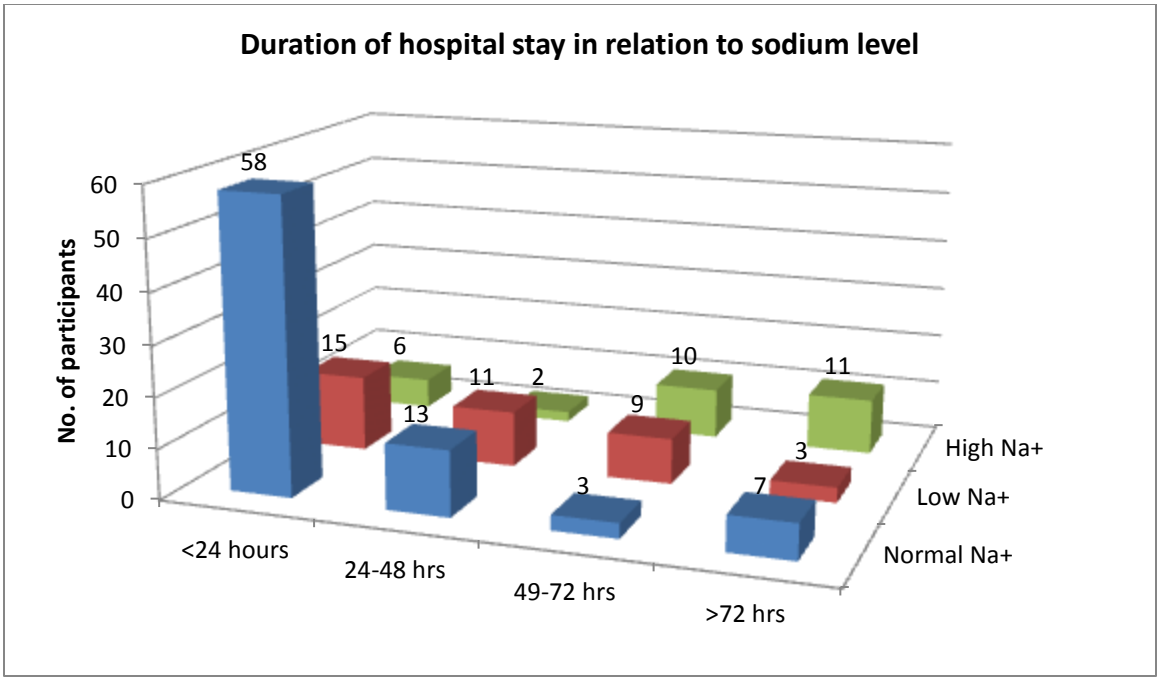

Figure 4.8. Duration of hospital stay in relation to mortality/discharge/sodium level

4.9. Factors associated with mortality in a logistic regression model

Table 3 below shows the association of mortality with other variables in a cross tabulation logistic regression/multivariate model. The variables entered in the model were age in months, breast feeding or not, days of symptoms before presentation, co-mobidities, level of dehydration, rotavirus vaccination status, prior ORS therapy, and initial sodium level. Young age below the age of 6 months was associated with high mortality with an odds ratio (OR) of 2.2 (adjusted OR 1.8, 95% CI 1.3-3.5, *p* 0.01) compared to the older age groups above 6 months. For children in the breast feeding period below 2 years, breast feeding was protective with an OR for mortality of 0.4 (adjusted OR 0.7, 95% CI 0.3-1.0, *p* 0.007). The duration of illness before presentation was a prognostic factor with children presenting over 3 days of illness had OR for mortality of 3.5 (adjusted OR 2.9, 95% CI 2.1-4.9, *p* 0.002) compared to OR 1.2 (adjusted OR 1.1, 95% CI 1.0-1.7, *p* 0.05) for children presenting earlier than 3 days. Besides dairrhoea, patients presented

with other symptoms including vomiting, fever, and coughing. It was noted that patients presenting with 2 or more other symptoms were more at risk of mortality with an OR of 3.5 (adjusted OR 2.1, 95% CI 1.7-4.3, *p* 0.004) compared to OR of 1.9 and 1.7 for patients with vomiting and diarrhoea only respectively.

The level of dehydration was an obvious prognostic factor. A total of 5 children died of shock in the emergency room upon arrival or while being resuscitated during the study period, 4 others were brought in dead with a history of diarrhoeal disease. These groups were excluded from any further analysis. The risk of mortality was highest among children presenting in shock with an OR of 3.6 (adjusted OR 2.4, 95% CI 2.1-5.6, *p* 0.001) compared with an OR of 1.6 and 2.3 for patients with some dehydration and severe dehydration respectively. More number of stools where also associated with a high risk of mortality, stools over 5 had an OR of 3.1 (adjusted OR 2.6, 95% CI 1.9-5.0, *p* 0.003) while the risk was less for fewer number of stools. Children who had rotavirus vaccination had a relatively lower risk of mortality with an OR of 0.2 (adjusted OR 0.7, 95% CI 0.1-1.0, *p* 0.05), compared to OR 1.7 (adjusted OR 1.3, 95% CI 1.1-2.2, *p* 0.03) for unvaccinated children. Children with prior ORS use before presentation had a relatively low risk of mortality with an OR 0.4 (adjusted OR 0.8, 95% CI 0.2-1.0, *p* 0.009) compared with an OR of 2.9 (adjusted OR 1.7 95% CI 1.2-4.0, *p* 0.009) for children not treated.

Hypernatraemia was associated with a high risk of mortality with an OR 5.8 (adjusted OR 3.6, 95% CI 2.9-8.0, *p* 0.002). Normal sodium level had an OR for mortality of 1.8 (adjusted OR 1.1, 95% CI 0.8-2.2, *p* 0.06) while low sodium had an OR of 3.1 (adjusted OR 2.3, 95% CI 1.7-4.4, *p* 0.03).

Table 2 Association of mortality with other variables in a multivariate analysis

Variable	Number (*N*)	Unadjusted OR	Adjusted OR	95% CI	*P* value
Age (months)					
0-6	48	2.2	1.8	1.3-3.5	0.01
7-12	37	1.9	1.5	1.1-2.6	0.04
>12	63	1.4	1.1	0.8-1.8	0.08
Breast feeding (<24 months)					
Yes	86	0.4	0.7	0.3-1.0	0.007
No	39	3.1	2.5	2.1-3.8	0.02
Days of symptoms					
1	14	1.2	1.1	1.0-1.7	0.05
2	71	1.3	1.1	1.0-1.9	0.08
3	41	2.2	1.6	1.3-2.9	0.007
>3	22	3.5	2.9	2.1-4.9	0.002
Other associated symptoms					
Vomiting	63	1.9	1.3	1.0-3.1	0.09
Fever	35	1.7	1.2	1.1-3.5	0.01
2 or more	50	3.5	2.1	1.7-4.3	0.004

Dehydration					
Some	36	1.6	1.0	0.8-2.1	0.1
Severe	99	2.3	1.6	1.4-4.1	0.02
Shock	13	3.6	2.4	2.1-5.6	0.001
Stools/day					
2-3	71	1.8	1.1	0.9-2.1	0.09
4-5	51	2.3	1.9	1.5-3.6	0.006
>5	26	3.1	2.6	1.9-5.0	0.003
Rota vaccine					
Yes	132	0.2	0.7	0.1-1.0	0.05
No	16	1.7	1.3	1.1-2.2	0.03
Prior ORS					
Yes	101	0.4	0.8	0.2-1.0	0.009
No	47	2.9	1.7	1.2-4.0	0.004
Initial Na+ result(mmol/l)					
130-150 (N)	81	1.8	1.1	0.8-2.2	0.06
<130 (Low)	38	3.1	2.3	1.7-4.4	0.03
>150 (High)	29	5.8	3.6	2.9-8.0	0.002

CHAPTER FIVE

DISCUSSION

This study highlights that hypernatraemic dehydration is quite prevalent among under-five children presenting with diarrhoea at UTH Department of Paediatrics and Child Health with a prevalence of 19.6%. This figure is higher than recorded in most previous studies (Chouchane *et al,* 2003; Dommelen *et al,* 2007; WHO, 2005). However, the prevalence remains within the documented range of 10%-20% prevalence of hypernatraemic dyhydration among children with acute diarrhoea (WHO, 2005). Like other previous studies, diarrhoea is mainly an under-five disease most prevalent in the first two years of life as 84.5% of participants were under-2 years, most of which is rotavirus associated ((Kotloff *et al,* 2013; Peter *et al,* 2009; WHO/UNICEF, 2005).

The incidence of rotavirus diarrhoea reduces with age following acquisition of immunity from earlier infections (Peter *et al,* 2009). With the introduction of the rotavirus vaccine in the Zambian routine immunization programme in 2012, it is hoped that the incidence of rotavirus associated diarrhoea among under-five children will reduce. Rotavirus being the major cause, this will see to the overall reduction in the incidence of diarrhoeal diseases and hence mortality, including from hypernatraemic dehydration. From figure 1 (trend of diarrhoea morbidity and mortality 2012-2015) and the preliminary report presented to the department of paediatrics at UTH on the national monitoring of the efficacy of rotavirus vaccine, has shown promising results on the reduction of diarrhoea associated morbidity and mortality (Rotavirus surveillance data, 2015; UTH HMIS, 2012-2015). However, some of the children were not covered in the immunization programme as 10% of the participants were not rotavirus vaccinated (figure 4.6) and it was a significant prognostic factor as unvaccinated children had a higher risk of mortality

than vaccinated children (adjusted OR 1.3 and 0.7 respectively). Rotavirus vaccine has shown to prevent severe rotavirus diarrhoea by 90-100% and diarrhoea of any severity by 74-85% (Peter *et al*, 2009).

Breast feeding is well recognized in preventing diarrhoea in children especially in low social economic settings (WHO/UNICEF, 2009; 2013, CSO/MOH, 2007). Exclusive breast feeding is recommended for the first 6 months of life and to continue up to 2 years (WHO/UNICEF, 2009; 2013). From the study it is noted that only 77% of children 6 months and below were exclusively breast fed (Figure 4.2) and that non breast fed children had a higher risk of mortality than breast fed infants for children still in the breast feeding age group i.e $\leq$ 24 months (OR 0.7 and 2.5 respectively). With the current modernization in our society with most mothers becoming career women coupled with a high prevalence HIV/AIDS, breast feeding trends have continued to drop (CSO/MOH, 2007) and its impact on outcomes in relation to diarrhoea associated mortality is evident in this paper. A child's exposure to HIV (i.e being born to an HIV positive mother) was associated with reduced duration of breast feeding as 60% of exposed children were not breast feeding by 1 year of age.

For many years the mission statement for The Ministry of Health has been fostering the provision of quality, equitable, cost effective health services as close to the family as possible (MOH, 2013). However from the mean duration of illness of 63 hours (2.62 days) taken before seeking health care, this goal seem not to be achieved, especially seeing that duration of illness at home before seeking care was noted to be proportional to the risk of mortality. Children who presented early had a better outcome. It is true for all illnesses that seeking treatment early is critical for good outcomes. There are many factors which may lead to delayed health seeking which are beyond the scope of this study. Late presentation is further compounded by the low

utilization of ORS at home despite its wide spread availability. The study shows that children who had no prior ORS therapy had higher risk of mortality than those who had (adjusted OR 1.7 and 0.8 respectively). Early and appropriate ORS use has shown to be effective in treating dehydration and preventing hospitalization. The introduction of low osmolarity ORS which has shown to be superior compared to the initial standard ORS in treating dehydration and correcting electrolyte and other metabolic derangements has further improved outcomes in treating diarrhoea (WHO, 2006; 2013). ORS remains one of the major cost effective interventions to foster elimination of preventable deaths from diarrhoea by 2025 (WHO/UNICEF, 2013). Low ORS utilization is worrying especially that UTH is a third level referral hospital receiving patients who are first seen at the local clinics where ORS therapy should have been initiated.

Most children (66.9%) presented with severe dehydration while 8.8% presented in shock (figure 4.5), this may be expected, UTH being a third level referral hospital only children with severe dehydration are likely to be referred from the local clinics. The long duration taken before seeking care and the poor home ORS utilisation may be contributing factors to most children presenting with severe dehydration. It is obvious that the severity of dehydration is directly proportional to risk of mortality as even noted in this study. Level of dehydration may be influenced by several factors such as number of stools per day, volume of stools and co-morbidities/symptoms such as vomiting which contribute to losses. Hence children with more of these factors had a higher risk of mortality. Despite having been analysed separately, these factors have a bearing on the level of dehydration and probable electrolyte derangement which may be the ultimate pathways for mortality. These factors however remained individually significant as noted from the adjusted odds ratios that remained statistically significant even after adjusting for possible confounders.

HIV/AIDS status was not statistically significant due to the small number of patients that were confirmed HIV positive (only 3/148 patients being confirmed positive). HIV exposure also was not evaluated further as a prognostic factor because of its indeterminate status as some may indeed be positive and some negative. It is however obvious that it may have an influence on outcome of HIV infected children who may suffer more opportunistic infections that may be associated with more severe diarrhoea and other co-morbidities that may increase the risk of mortality.

Dysnatraemias are noted to be among the commonest electrolyte derangements in acute diarrhoea. Of all the participants 54.7% had normal sodium level while the remaining 45.3% either had low sodium (hyponatraemia 25.7%) or high sodium (hypernatraemia 19.6%). Of the dysnatraemias, hypernatraemia despite being the less common one, was associated with more deaths and therefore with a higher case fatality rate of 24.1% compared to 13.2% and 8.6% for low and normal sodium respectively. Hypernatreamic dehydration remains the most dangerous and fatal form of dehydration (Adroque and Madias, 2000). Shock was associated with a high risk of mortality; however despite hypernatreamia being associated with more severe dehydration (Kliegman *et al,* 2008; Shaw *et al,* 2010), shock was less common among participants with hypernatreamic dehydration. Among patients presenting in shock 46.2% had hypernatreamia, while the remaining 53.8% had either normal or low sodium (table 2). Sodium being the major extracellular cation has a central role in maintaining plasma osmolarity and hence fluid balance especially in maintenance of the plasma volume (Adroque and Madias, 2000; Kliegman *et al,* 2008; Shaw *et al,* 2010). Hypernatraemia therefore enables preservation of the plasma volume until the dehydration is profound, hence for the same amount of fluid deficit a patient with hyponatraemia may be in shock while one with hypernatraemia may not. On the

contrary, a patient with hypernatraemia will have a larger fluid deficit for the same level of dehydration assessed clinically. This may lead to delayed presentation and initiation of appropriate fluid replacement therapy.

There are several prognostic factors that have been evaluated and to what extent they may contribute to mortality as seen from the associated odds ratios. One factor that may contribute to mortality and could have been a potential confounder in this case was the quality of treatment rendered. For participants with some dehydration the treatment depended on the mother to be able to give the ORS per loose stool as per instruction. It is not uncommon that a mother may not give the ORS appropriately and the child may end up being severely dehydrated or even in shock. However the number of participants with such changes was too small for further statistical evaluation and factoring such changes was difficult hence only the initial hydration status was considered. Participants were monitored all through admission by the attending doctors and management adjusted accordingly if need be.

Patients were put on standard treatment based on their level of dehydration and adjusted according to sodium level for the few patients who had a timely result and the few who had repeat sodium determination. The challenge however was that all patients had an initial sodium determination, but due to long results turnaround time, it was difficult to collect a repeat specimen exactly 24 hours of admission as that depended on the initial result hence only 10% (3/29)) of patients needing a repeat sodium did get a repeat. Management was altered as soon as it was established by results that the patient had hypernatraemic dehydration for the few patients who had a timely sodium determination. However, most results could not be used to influence management as results took too long (over 24 hours) and could not accurately correlate with the patient's current electrolyte status or the patient had already died.

Standardisation of the actual treatment received was also a challenge; due to shortage of nurses to monitor all patients and ensure that a 3 hour or 6 hour fluid replacement plan is give in the stipulated time. Most often fluid replacement duration was longer than expected, while few were shorter than expected. Also the fact that patients were subsequently being managed by various groups of nurses in the various wards makes standardization difficult in as much as doctor's orders may be standard. However, those in shock and those with severe dehydration got the initial resuscitation fluids and the initial part of plan C (table 1) respectively as expected, as these were given in the emergency room following establishing the need upon arrival. The subsequent variations may have influenced outcomes (discharge/mortality) and duration of hospital stay. Treatment in this case may have been a non differential error or confounder in that it was not confined to a single group of patients. In as much as treatment definitely affected the outcome, the effect may have been across all patient groups.

CHAPTER SIX

6.1. Conclusion

Hyperntraemic dehydration is prevalent among children presenting with diarrhoea and dehydration. The prevalence is almost similar to many cited previous studies, although higher than most previous studies done in other countries. Despite what is deemed appropriate therapy, mortality from diarrhoea remains relatively high. Identification and appropriate management of hypernatraemic dehydration and other electrolyte derangements, may be the missing link to curb high mortality from diarrhoeal associated deaths at a tertiary level hospital. It is evident from the study that electrolyte evaluation is still a challenge as only a very small proportion of patients had a repeat sodium evaluation at the stipulated time. From the findings of this study, investment in improved laboratory capacity for timely determination of electrolytes especially sodium for appropriate targeted therapy for better outcomes in children with diarrhoea associated dehydration is critical.

6.2. Limitations / challenges

The study was not without challenges. The major challenge of the study was long turnaround time of results as the study depended on routine laboratory functions. Hence most results could not be used to inform patient care as they could not depict the patient's current status. Definitive HIV status determination was not possible during the short period of follow up to be factored as a prognostic factor which may have a bearing on the outcome. Lack of standardization of treatment implementation may have influenced outcomes in some patients. The initial laboratory planned to conduct electrolytes for the study ran out of reagents and at some point the entire hospital had run out of reagents and recruitment was put on hold which may have created bias. These challenges highlight the reality faced in managing such patients. Finally, the study does

not demonstrate causality between sodium level and outcome in terms of mortality but merely demonstrates association.

6.3. Recommendations

1. Hypernatraemia is prevalent among under-five children presenting with diarrhoea at UTH Department of Peadiatrics and and Child health, it is therefore recommended that all such children have an electrolyte determination on admission for appropriate management.

2. There is need for investment in laboratory equipment and reagents to improve capacity for timely results to inform patient care.

3. The department of paediatrics should have a stand-alone chemistry laboratory for emergency test like electrolytes when needed.

4. There is need for standardized care in management of diarrhoea and this is only possible if patients are management in the same place by the same group of caregivers (nurses), therefore re-establishment of a diarrhoea ward may be a solution as was the situation in the past.

5. There is need for continued community sensitization on timely ORS home use whenever a child has diarrhoea, timely health seeking behavior and the importance of immunization especially rotavirus vaccination in this regard.

6. Further research to established causal relationship of hypernatraemia and mortality in children with hypernatraemic dehydration.

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APPENDICES

1. Data table of results

Demographic characteristic	**Number (*N*)**	**Proportion (%)**
Sex	**148**	
Male	73	49%
Female	75	51%
Age (months)		
Mean	14.72 (SEM 0.100)	
Range	1-60	
1-6	48	32.4%
7-12	37	25%
13-24	40	27%
25-60	23	15.6%
<25	125	84.5%
Breast feeding (<24 months)	**125**	
Yes	86	68.8%
Formula	10	8%
No	29	23.2%
1-6 :Yes No	37 11	29.6% 9%
7-12:Yes No	32 5	25.6% 4%
13-24:Yes No	16 24	13% 19%

Duration of symptoms (days)	**148**	
Mean	2.62 (SEM 0.112)	
Range	1-6	
< 24 hours (1day)	14	9.5%
24-48 hours (1-2 days)	71	48%
49-72 hours (2-3 days)	41	27.7%
>72 hours (>3 days)	22	14.9%
>48 hours (>2 days)	63	42.6%
Children with Co morbidities (other symptoms)	**148**	
Vomiting	63	42.6%
Fever	35	23.6%
2 or more symptoms	50	33.8%
HIV status	**148**	
Negative	107	72.3%
Exposed	38	25.7%
Positive	3	2%
Level of Dehydration	**148**	
Some	36	24.3%
Severe	99	66.9%
Shock	13	8.8%

Variable	Number (*N*)	Proportion (%)
Stools/day	**148**	
Mean	3.74 (SEM 0.132)	
Range	2-12	
2-3	71	48%
4-5	51	34.5%
>5	26	17.5%
Rota vaccination status	**148**	
Yes	132	89.2%
No	16	10.8%
Prior ORS therapy	**148**	
Yes	101	68.2%
No	47	31.8%
Initial Na+ result	**148**	
Normal (130-150mmol/l)	81	54.7%
Low (<130mmol/l)	38	25.7%
High (>150mmol)	29	19.6%

Outcome (Discharge/Mortality)	**148**	(As proportion of total Discharges/Mortality)
Discharges:	**129**	87.2%
Normal Na+ (130-150mmol/l)	74	57.4%
Low Na+ (<130mmol/l)	33	25.6%
High Na+ (>150mmol/l)	22	17%
Mortality:	**19**	12.8%
Normal Na+ (130-150mmol/l)	7	CRF 8.6%
Low Na+ (<130mmol/l)	5	CRF 13.2%
High Na+ (>150mmol/l)	7	CRF 24.1%
Hospital stay (days)		
Mean	2.04 (SEM 0.119)	
Range	1-7	
Discharges: Mean	2.08 (SEM 0.110)	
Range	1-6	
Mortalities: Mean	1.74 (SEM 0.110)	
Range	1-3	
Normal Na+: Mean	2.01 (SEM 0.120)	
Range	1-4	
Low Na+: Mean	2.13 (SEM 0.113)	
Range	1-5	
High Na+: Mean	3.09 (SEM 0.117)	

Range	1-7	

Table 2: Duration of hospital stay in relation to mortality/discharge and sodium level

Duration of stay		**Variable and number of participants**				
	Total	Discharges	Mortality	Normal Na+	Low Na+	High Na+
<24 hours (<1day)	79	69	8	58	15	6
24-48 hours (2days)	26	20	6	13	11	2
48-72 hours (3days)	22	19	3	3	9	10
>72 hours (>3days)	21	21	2	7	3	11

3. Top five causes of morbidity and mortality at UTH Dept of paediatrics in 2012 to 2015

2012 **Morbidity**		**2013** **Morbidity**	
1.Other bacterial diseases	2,157	1.Other bacterial diseases	2,356
2. Other pneumonia	1,924	2. Other pneumonia	2,168
3. Diarrhoeal diseases	**1,493 (9%)**	3. Malnutrition	1,273
4. Malnutrition	1,265	4. Sickle cell disease	1,178
5. Typhoid fever	904	**5. Diarrhoeal diseases**	**1,105 (7%)**
Sub-total	7,743	Sub-total	8,080
Other causes	8,821	Other causes	8,111
Grand Total	16,564	Grand Total	16,191

Mortality			
1.Malnutrition	362	1.Malnutrition	352
2. Other bacterial diseases	263	2. Other pneumonia	275
3. Other Pneumonia	275	3.Other bacterial diseases	260
4. Diarrheal diseases	**189 (11%)**	**4. Diarrheal diseases**	**136 (9%)**
5. Meningitis	83	5. Meningitis	64
Sub-total	1,172	Sub-total	1,087
Other causes	537	Other causes	467
Grand Total	1,709	Grand Total	1,554
2014 **Morbidity**		**2015** **Morbidity**	
1.Other bacterial diseases	2,450	1.Bacterial sepsis newborn	1,458
2. Other pneumonia	1,794	2. Sickle cell anaemia	1,126
3. Typhoid	1,303	3. Other pneumonia	1,333
4. **Diarrhoeal diseases**	**1,179 (7.4%)**	4. Malnutrition	1,139
5. Malnutrition	1,142	**5. Diarrhoeal diseases**	**904 (6.1%)**
Sub-total	7,868	Sub-total	5,960
Other causes	8,182	Other causes	8, 844
Grand Total	16,050	Grand Total	14, 804
Mortality			
1.Malnutrition	313	1.Malnutrition	313
2. Other pneumonia	313	2. Other pneumonia	256
3. Other bacterial diseases	283	3.Bacterial sepsis of newborn	260
4. Diarrheal diseases	**105 (7%)**	4. Meningitis	79
5. Meningitis	43	**5. Diarrhoeal diseases**	**74(5.2%)**
Sub-total	1,058	Sub-total	885

Other causes	442	Other causes	547
Grand Total	1,500	Grand Total	1,432

(Source, UTH HMIS, 2012; 2013; 2014; 2015)

4. Diarrhea morbidity and mortality by age groups at UTH Dept of Paediatrics

	2012			**2013**		
Age	0-11 months (< 1yr)	12-59 months	5-15 yrs	0-11 months	12-59 months	5-15 yrs
Mortalities	82 (43%)	98 (52%)	9 (5%)	64 (47%)	66 (49%)	6 (4%)
Discharges	788	426	90	551	381	37
Totals	870 (58%)	524 (35%)	99 (7%)	615 (56%)	447 (40%)	43 (4%)

(Source, UTH HMIS, 2012; 2013)

5. Information Sheet

5.1. Introduction

How are you madam/sir? I am Jombo Namushi a Master of medicine in Paediatrics (MMED) student at the University Teaching Hospital under the University of Zambia, School of Medicine. I am conducting a research as part of the requirement for my MMED qualification. The study seeks to determine the incidence of high sodium in blood among children who present with diarrhea and dehydration. Sodium is one of the substances contained in the body/blood which helps the body to function properly. During diarrhoea sodium and water are among the things that are lost from the body. Depending on how the loss is occurring the sodium and water content of the body may be low. For a small proportion of children with diarrhoea as much as 10% as observed in other studies, lose relatively more water in diarrhoea compared to other substances like sodium resulting to the concentration of sodium in the body to appear relatively high. High

sodium content in blood is among the dangerous complications of diarrhoea which if not detected and treated early and appropriately can lead to complications and death. My study therefore seeks to test children presenting with diarrhoea who are also dehydrated as a way of detecting the extent of the problem of high sodium among such children and provide the necessary treatment.

5.2. About the study

The study will be performed within the realms of the standard care a child with diarrhoea needs to receive. It will involve the standard history taking of the illness and physical examination of the child, part of which information will be transferred to the data entry form for the study and blood sample collection as part of the standard care and the same result/sample, with your permission will be used for the study. I assure you that the information on the data entry form will be kept confidential like all other patient documents and the information obtained is purely for this study. We wish to also inform you that you have the right to choose not to participate in the study and that you declining do not affect treatment rendered to the child. Even after consenting to participate in the study you are free not to respond to questions you may find uncomfortable during the interview.

5.3. Risks/benefits

The study does pose a risk of pain to the child during sample collection, however sample collection is part of the standard care for a child with diarrhoea and dehydration to determines electrolytes, hence it is not a risk that is limited to this study but to all children undergoing care. Sometimes due to logistical issues in the laboratory, electrolytes may not routinely be done, but for children participating in the study, it shall be ensured that test are done as arrangements have been made with an alternative support laboratory by so doing patients may benefit from an extra

investigation which sometimes may not be available. This also may benefit future patients as we may know how much of the problem of high sodium is among our patients with diarrhoea and hence be on the outlook and inform/impact our patient care as clinicians.

5.4. Results dissemination

As mentioned the study is mainly for academic purposes. The results will however be communicated to you the parents/guardian and the attending doctors to provide information on subsequent management of the child based on findings. Upon completion of the study, data will be analysed and the results will be presented in a final report submitted to the University of Zambia and also shared with the department to inform best practices in our patient care.

5.5. Conclusion

Is there anything you would like to ask me? Or anything you want to say? Is there anything that you think is not clear you would like me to go over? Thank you so much for your time. Are you agreeable for your child to be enrolled to participate in the study?

6. Informed Consent Declaration

I_____ (interviewee/participant) have been explained to and understand the purpose of the study and all other information relating to the study. I hereby agree for my child to participate in the study with full awareness.

Signed_____ Date_____ Place_____

I_____ (Interviewer/researcher) have explained the study and its purpose and confirm that the parent/guardian has consented freely and voluntarily for the child to take part in the study.

Signed_____ Date_____ Place_____

7.1 Translated Information Sheet/Informed Consent

PEPALA YA CHIDZIWITSO / CHIBVOMEREZO

7.1.1 Chiyambi

Mulibwanji Bamboo/ Mai

Ine ndine Jombo Namushi Sing'anga wamakhwala ku chipatala cha ana (paediatrics) ophunzira ku University Teaching Hospital pansi pa ulamuliro wa University Of Zambia sukulu ya mankwala. Ndiri kuchita phunziro yaku fufuza ngati chofunika kwambiri pakupyora pa maphunziro yanga MMED. Phunziro ichitika kupeza bvuto ya kukwela sodiyamu mumagazi pakati pa ana angono amene amaonetsa kuthulula ndi khuta madzi muthupi. Sodiyamu ndi chinthu mwaizo zipezeka muthupi magazi imene ithandizira kugwira nchito bwino. Mukuthulula zina za izo ndi madzi Zimatha muthupi kulingana mwa mwa izo kutha madzi opezeka mthupi angakhale wochepekera.

Paguru ya yingono ya ana angono ali kuthulula mwa 10% kuyanganira mu maphunziro ena, mukuthulula madzi ambiri amatha, kothela kwace sodiyamu ika khala yambiri muthupi yionetsa pamwamba. Ndipo mwaizo sodiyamu ikakhala pamwamba kwambiri mumagazi zimakhala zoopsya muzotulukamo mukuthulula ngati sanapeze njira msanga ndi kuchiritsa mosamala ingalengedze ku imfa. Phunziro yanga ifunika kupima ana ang'ono aonetsa matenda yothulula

ngati njira yopezeka ndi ndi bvuto ya sodiyamu ya pamwamba mu ana angono amabwera ndi matenda yothulula ndi kuchiritsidwa mosamalika.

7.1.2 Za phunziro

Phunziro idzachitika munjira ya ubwino ndi mosamalira ana angono amatenda yothulula afunika kulandira mbiri yopezekamo mumatenda gawo imodzi idzatumidwa kulowetsa mbiri papepala ya phunziro ndi kutengako gawo ya magazi mosamalidwa ndipo chimodzi modzi zotulukamo / magazi. Mwakubvomereza kwanu phunziro iyi idzachitika. Tikhulupirira kuti chidziwitso chakulowetsa mbiri papepala idzasungidwa mwachinsinsi monga mapepala ya odwala ena. Ndipo zidziwitso kutengedwa chabe ku phunziro iri.

Tifuna kukudziwitsaninso. Kuti muli nayo danga kusankha kutengako mbali muphunziro ndipo ngati mwaleka si idzakhuza machiritso yopatsidwa ku mwana wanu.

7.1.3 Zoopsya/ Phindu

Phunziro iri siri yoopsya ndikuwawa pakutenga magazi kuti ikapimidwe, koma ndi gawo imodzi yaku samalira ana ang'ono wothulula ndi kutha madzi siyoopsya imene iri yokhazikika mu phunziro iri koma ku ana onse apita mo kusamalidwa. Nthawi zina kulingana ndi zipangizo ndi zina mu laboratare, mwaizo (electrolytes) sizikha la zochitika nthawi zonse, koma mu ana angono wotengako mbari mu phunziro chidziwike ndithu kuti kupima kuchitike mmene adakonzela kuthandizira laboratare. Pakuchita izi wodwala adzaphindula kuchokera ku zofufuza zina kuti nthawi zina zinga khale kobe. Izi kuti mtsogoro wodwala akhoza kuphindulanso, mmene tadziwira za bvuto yakukwera kwa sodiyamu (sodium) pakati pa wodwala athu ndi

kuthulula ndi khala maso ndi kudziwitsa zotulukamo mu wodwala athu chisamaliro ngati asing'anga.

7.1.4 Zotulukamo muzopima

Mwakufotokozera muphunziro cha chikuru ndi ya ukaswiri yama phunziro. Mayankho yakupima idzapastidwa kwa inu makolo / oyanganira ndi asing'anga woteza kukupatsani chidziwitso chamasamalidwe amwana kulingana ndi zotulukamo.

Mwakusiliza phunziro iyi nkhani idzasamalidwa ndipo zotulukmo zidza patsidwa mulipoti yotsiliza kusukulu ya ikuru ku University Of Zambia ndi ku gawana ndi gawo ya Department ndi kudziwitsa mwa bwina ndithu ku yesesa ku samalira wodwala athu.

7.1.5 Potsiliza

Pali ciri chonse mufuna kufunsa ine ? kapena pali ciri chonse mufuna kukambapo ? kapena pali ciri chonse chimene muganiza si chinamveke bwino ? mufuna kuti ndi bwezere kupitamo ?

zikomo kwambiri Kamba nthawi yanu. Kodi mwabvomereza kuti mwana wanu atengeko mbali mu phunziro iri.

7.2. Cibvomerezo

Ine ……. (Ouzidwa / otengako mbali). Ndauzidwa ndipo ndamvetsa chilingo cha phunziro ndi ziziwitso zonse kulinga kuphunziro. Ine ndavomerekeza mwana wanga kutengako mbali mu phunziro ndi chinenetso chonse.

SAINALA :…… TSIKU :……..

MALO :……..

INE ……..wofufuza / wofunsa mafunso ndafotokozera phunziro ndipo chiringo motsimikizira kumakolo / oyaganira abvomekeza momasuka ndi mwa ufuru kuti atengeko mbali mu phunziro .

SAINALA :…… TSIKU :……..

MALO :……..

8. Data Capturing Form

8.1. Social/demographic data

Name:……

Age:……. Sex:…….

Residential address:……..

Relation with informant:……

8.2. Present illness

Duration of diarrhoea:……

Non blood:…… Bloody…….

Other associated symptoms (e.g. vomiting):……

Estimated motions of diarrhoea per day:……

Treatment received (Home/local clinic:……..

8.3. Past medical/ Immunization/ nutritional history

Illness suffered in the last one month:……

HIV status of child (evidence on under-five card):…….

Immunization status (especially Rotavirus):……...

For the under 2 year: feeding (breast/formula)……

8.4. Assessment for Dehydration: tick appropriate signs

	A	B	C
LOOK AT: CONDITION	Well, alert	Restless, irritable	Lethargic or unconscious
EYES	Normal	Sunken	Sunken
THIRST	Drinks normally, not thirsty	Thirsty, drinks eagerly	Drinks poorly, or not able to drink
FEEL: SKIN PINCH	Goes back quickly	Goes back slowly	Goes back very slowly
	No dehydration	**Some dehydration**	**Severe dehydration**

8.5. Results/Outcome

Initial Na+:……

24 hour Na+:……..

Any clinical events/complications:……

Outcome (Mortality/Discharge):…….

Duration of hospital stay:…….

6. BUDGET

No.	**Activity/Description of expenditure**	**Total cost in ZMK**
1	Stationery (Research tools, reports)	2,000
2	Research assistants	3,000
3	ERES charges	1,000
4	Electrolytes charges	14,500
Total		**20,000**