THE ELECTROLYTE PROFILE OF SEVERELY MALNOURISHED CHILDREN AGED 6-59 MONTHS, PRESENTING TO THE UNIVERSITY TEACHING HOSPITAL, LUSAKA.

BY

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DECLARATION

I, Dr Natasha Noria Ngwenya, hereby declare that this study is my own work and that it has not been previously submitted for a degree at any university and that it is not being used for another degree.

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ABSTRACT

Objective: To determine the electrolyte profile of severely malnourished children aged 6-59 months, presenting to UTH, Lusaka.

Methods: This was a cross sectional study conducted at UTH, malnutrition ward, where patients with SAM with complications are admitted.

On admission, patients presenting to the malnutrition ward were assessed by taking history and performing physical examination. The patients` anthropometric measurements like weight and height were done. Weight for height Z scores (WHZ) were determined using the WHO growth charts. Patients with Weight for Height Z scores < -3 SD or with nutritional bipedal pitting oedema and aged 6-59 months were enrolled in the study. Convenience sampling method was used and consent was obtained from the caregivers. Children in the study were managed and received feeds and fluids as per WHO protocol for SAM.

 Electrolytes were done on admission, on day 3 and on day 8, and children were either classified as hypo /hyper natremic or hypo/hyper kalemic depending on their electrolyte levels and comparisons were done using appropriate statistical analysis.

Results: In this study, **245** participants were enrolled. 60.41% (148/245) were male and 39.59% (97/245) were female. 75.10% (184/245) of the participants were in the 12-35 months age group. 57.55% (141/245) had diarrhoea and 42.45% (104/245) had no diarrhoea. 69.80% (171/245) had severe wasting while 30.20% (74/245) had bilateral pitting pedal oedema. Of those tested for HIV, 79.06 % (185/234) were HIV negative and 20.94% (49/234) were HIV positive.

Sodium

On day 1 (n=243), 54.73% (133/243) had hyponatremia, 4.94% (12/243) had hypernatremia, and 40.33% (98/243) had normal sodium serum levels. Mean sodium was 133.23± 8.40 (range 100-154).

On day 3 (n=41), 60.98% (25/41) had hyponatremia, 5.00% (2/41) had hypernatremia and 34.15% (14/41) had normal serum sodium. Mean sodium was 131.75 ± 8.17 (range 110-158).

On day 8 (n=18), 50% (9/18) had hyponatremia, 5.56% (1/18) had hypernatremia, and 44.44% (8/18) had normal serum sodium. Mean sodium was 135 ± 9.9 (range 126-173).

Potassium

Day 1 (n=235), 36.60% (86/235) had hypokalemia, 34.47% (81/235) had hyperkalemia,and 28.94% (68/235) had normal serum potassium levels. Mean potassium was 4.08 ± 1.57 (range 1.5-8.7).

Day 3 (n=41), 85.37% (35/41) had hyperkalemia, 2.44% (1/41) had hypokalemia and 12.20% (5/41) had normal serum potassium. Mean potassium was 5.46 ± 1.02 (range 2.9-7.7).

Day 8 (n=17), 5.88% (1/17) had hypokalemia, 72.22% (13/17) had hyperkalemia and 17.65% (3/17) had normal serum potassium. Mean potassium was 5.5 ± 1.34 (3.3-9.2)

Statistical analysis showed that patients who presented with diarrhoea were more likely to have hypokalemia as a potassium derangement; 62.79% of patients with hypokalemia had diarrhoea as compared to 37.21% of patients without diarrhoea (P=0.015<0.05).

In those with hyponatremia (n=133), 51.8% (72/133) had diarrhoea while, 58.7% (61/133) had no diarrhoea. 75% (9/12) of those with hypernatremia (n=12) had diarrhoea while 25% (3/12) had no diarrhoea. 59.18% (58/98) of those with normal sodium values had diarrhoea and 40.82% (40/98) had no diarrhoea. However, there was no significant hyponatremia or hypernatremia in those with diarrhoea, (P=0.329>0.05)

There was no significant serum electrolyte changes among those with oedema and those with severe wasting, those with HIV and those with no HIV, those who died and those who were alive.

Conclusion: Most of the children with SAM and electrolyte derangements also had diarrhoea. Therefore determination of the electrolyte profile of all patients with SAM immediately on admission and proceeding days after admission is vital as it helps the clinician to decide on the most appropriate fluids to give to help reduce on the morbidity and mortality associated with life threatening electrolyte derangements.

Keywords: serum sodium, potassium, severe acute malnutrition, diarrhoea.

DEDICATION

To my family – My dear husband Frederick Kapondo and precious daughters, Lubuto and Tamika, for all the time spent away from them in order to complete this dissertation.

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ABBREVIATIONS/ ACRONYMS

SAM – Severe acute malnutrition

WHO – World Health Organisation

K^+ - Potassium

Na^+ - Sodium

sNa – Serum sodium

Ca^{2+} - Calcium

Mg^{3+} - Magnesium

UNICEF – United Nations Children`s Fund

SiADH – Syndrome of inappropriate anti-diuretic hormone

ADH – Anti-diuretic hormone

HIV/ AIDS – Human immune-deficiency virus/ Acquired immunodeficiency syndrome

ADD – Acute diarrhoeal disease

PDD – Persistent diarrhoeal disease

ReSoMal – Rehydration solution for severely malnourished children

ORS – Oral rehydration solution

IgA – Immunoglobulin A

UTH – University Teaching Hospital

TB – Tuberculosis

ECF – Extracellular fluid

ICF – Intracellular fluid

ECG – Electrocardiogram

PTH – Parathyroid hormone

WHZ – Weight for height Z scores

OR – Odds ratio

CI – Confidence interval

DNA -PCR – Deoxyribonucleic acid polymerase chain reaction

STATA V 11– General purpose Statistical Software Package -version 11

CHAPTER ONE

1.0 INTRODUCTION

Globally, severe acute malnutrition (SAM) contributes to 1 million deaths among children annually (**1**). It is estimated that nearly 20 million children under the age of five years suffer from SAM at any one point in time (**2**). This suggests that there are potentially 40 million children suffering from SAM every year (**3**).

In developing countries, including   Zambia, severe acute malnutrition has long been recognised as a serious public health problem, with case fatality rates of up to 40%.

Diarrhoea, defined as 3 or more watery stools per day, often complicates SAM (**4**), or may cause SAM and it is a leading cause of malnutrition in children under five years old. Diarrhoea can be acute or persistent. Acute diarrhoea is an episode that has an acute onset and. lasts no longer than 14 days and persistent diarrhoea is an episode that lasts longer than 14 days. It results in loss of fluids leading to dehydration and loss of electrolytes like sodium and potassium. Most children who die from diarrhoea actually die from severe dehydration and electrolyte derangements (**5**). Management of diarrhoea and dehydration continues to be a challenge in the treatment of severe acute malnutrition (**6**). In some studies, diarrhoea has been considered to be a predictor of poor outcome in patients with SAM especially when accompanied with other features of severity (**7**).

In a well-nourished child, most potassium is intracellular, and the plasma concentration does not always reflect the total body potassium content. A variety of conditions can alter the distribution of potassium between the intracellular and extracellular compartments. The Na+, K+-ATPase pump, which is protein in nature, maintains the high intracellular potassium concentration by pumping sodium out of the cell and potassium into the cell. This balances the normal leak of potassium out of cells via potassium channels that is driven by the favourable chemical gradient. Insulin increases potassium movement into cells by activating the Na+, K+-ATPase pump (**8**).

When a child develops SAM, however, physiological changes do occur due to a phenomenon called reductive adaptation. In reductive adaptation, the Na+, K+-ATPase systems of the body begin to 'shut down'. This means that the body is unable to pump sodium out of the cells and potassium into the cells. As a result, the level of sodium in the cells rises, and potassium leaks out of the cells and is lost (for example, in urine or stools), leading to high intracellular sodium and low serum potassium. As the child is treated, the Na+K+ATPase is regenerated and the body's systems gradually adapt to function fully again. Rapid changes (such as rapid feeding or fluids) would overwhelm the systems, so feeding must be done slowly and increased cautiously (**9**).

Patients with SAM, therefore, do present with electrolyte imbalances which may not be evident initially but may become evident in the presence of diarrhoea that also causes loss of electrolytes in the stool. Therefore, an even greater electrolyte derangement may occur when diarrhoea is superimposed on SAM.

In view of the reductive adaptation, feeds with high potassium (K+) and low sodium (Na +) have been recommended by the World Health Organisation (WHO). Magnesium (Mg3+) supplementation, which is essential for potassium to enter the cells and be retained, is also recommended for children with SAM. (3-4 mmol/kg/day K+ and 0.4-0.6 mmol/kg, Mg) (**9**).

When patients with SAM have diarrhoea, it is also recommended that they receive a Rehydration Solution for Severely Malnourished children called ReSoMal, which has less sodium and more potassium than regular or low-osmolarity, ORS (**9**).

Children with severe acute malnutrition suffer in greater proportion from bacterial gastrointestinal and respiratory infections (**10**). This is because SAM significantly compromises mucosal epithelial barriers in the gastrointestinal, respiratory and urogenital tracts. This loss of the protective mucus blanket increases susceptibility to infection by pathogens that would ordinarily be trapped in the mucus and swept away by the cleansing flow of mucus out of the body, and this is critical in the pathogenesis of respiratory and gastrointestinal tract infections (**11**), like pneumonia and diarrhoea

respectively. This is why pneumonia and diarrhoea in patients with SAM tends to have a long course and may ultimately cause mortality.

With appropriate case management for SAM in Inpatient Care and additional treatment in Outpatient Care, the lives of many children can be saved, and mortality associated with SAM can be drastically reduced to less than 10%((12).

Although many studies have been done worldwide, no studies have been done so far in Zambia to study the electrolyte profile of children with SAM presenting with different co-morbidities and the resultant electrolyte profile after the feeds are commenced.

This study was thus intended to determine the electrolyte profile of children with severe acute malnutrition between 6 and 59 months, presenting to the Paediatrics Department, UTH.

2.0 LITERATURE REVIEW

There are several causes of severe acute malnutrition. The causes are essentially poverty, social exclusion, poor public health and loss of entitlement, and most cases can be prevented by economic development and public-health measures to increase dietary quantity and quality alone, with no need for clinical input (13).

In order to summarise the causes of malnutrition, UNICEF came up with a conceptual framework as shown below;

UNICEF Conceptual Framework of malnutrition

(**http://www.unicef.org/sowc98/silent4.htm**)
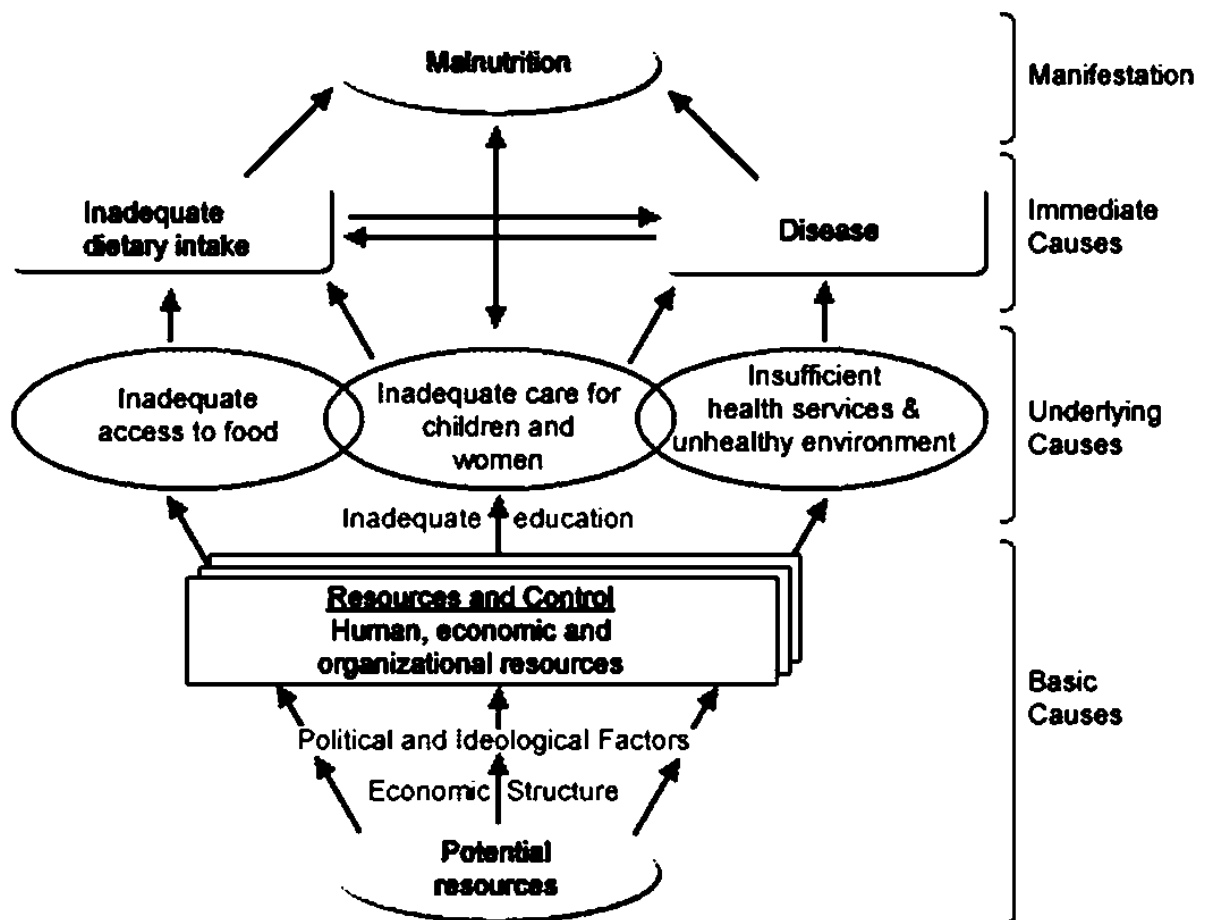
The economic structure of a nation forms the basis upon which the UNICEF framework lies. A poor economic structure results in inadequate facilities for education, and with poor education, individuals are not empowered economically and thus have poor access to food, and inadequate care for children and women. The nation also has insufficient health services and an unhealthy unsanitary environment that poses a threat for diseases like diarrhoea.

Diarrhoea is the leading cause of malnutrition in children under five years old (**9**), and if it persists, it may cause SAM. The relationship between diarrhoea and malnutrition is bidirectional: diarrhoea leads to malnutrition while malnutrition aggravates the course of diarrhoea. Many factors contribute to the detrimental effect of diarrhoea on nutrition. These include reduced intake (due to anorexia, vomiting, and withholding of feeds), maldigestion, malabsorption, increased nutrient losses, and the effects of the inflammatory response are some of the factors involved.

High volume stool losses (greater than 30 ml/kg/day) are associated with a negative balance for protein, fat, and sugar absorption. Enteric infections often cause increased loss of endogenous proteins, particularly after invasive bacterial infections (**14**).

 The most severe threat posed by diarrhoea is dehydration. During a diarrhoeal episode, water and electrolytes (sodium, chloride, potassium and bicarbonate) are lost through liquid stools, vomit, sweat, urine and breathing. When these losses are not replaced, dehydration and electrolyte derangements occur.

Electrolytes

Electrolytes are ionized molecules found throughout the blood, tissues and cells of the body. Their mole is either positive or negative and they conduct an electric current and help to balance pH and acid base level in the body. They also facilitate the passage of fluid between and within cells through process of osmosis and play a part in regulating the function of neuromuscular, endocrine and excretory systems. The main serum electrolytes are:

1. Sodium- It helps to balance fluid level in the body and facilitate neuron functioning. It is the main cation in the extracellular compartment (ECF).

2. Potassium- It is the main component of intracellular fluid (ICF) and helps to regulate neuromuscular function and osmotic pressure.

3. Bicarbonate- It carries negative charge and assists in regulation of blood pH. Increase or decrease in bicarbonate cause acid base disorder (15).

4. Chloride- It is a negatively charged ion located in all body fluids responsible for maintaining acid/base balance, transmitting nerve impulses and regulating fluid in and out of cells (16).

Sodium

Sodium is the dominant cation of the extracellular fluid (ECF) with a concentration of 135-145mmol/l and it is the principal determinant of extra cellular osmolality. It is therefore necessary for the maintenance of intravascular volume.

 < 3% of Na is intracellular and >40% of total body sodium is in bone. The remainder is in the interstitial and intravascular spaces. The low intracellular Na concentration, approximately 10mmol/L, is maintained by Na+, K+ ATPase, which exchanges intracellular sodium for extracellular potassium (17). The sodium content of erythrocytes and muscle of patients with SAM has been reported to be higher than normal. Muscle analysis also indicated an increase in intracellular sodium concentration (18).
 Low sodium level however, is a bad prognostic sign (19).

In severe acute malnutrition, the Na+K+ATPase pump malfunctions, due to reductive adaptation and this results in a disruption of the electrolytes in the ECF and ICF, leading to electrolyte derangements (7).

Children with SAM are thus most at risk of life-threatening diarrhoea (20). This is attributed to the fact that malnourished children physiologically have electrolyte derangements which become more marked when accompanied by diarrhoea.

In order to support the bidirectional relationship of diarrhoea and SAM, some studies done indicate that severe acute malnutrition , is often preceded by an episode of infection, with diarrhoea and respiratory infection being the most common precipitating factors. Community studies carried out in South India showed that a peak incidence of kwashiorkor was preceded by a peak incidence of diarrhoea. Repeated attacks of diarrhoea were shown to be responsible for poor growth of Guatemalan children and was found to be the most significant infection contributing to malnutrition in Gambian children. Weight faltering was most dramatic during the weaning period, when the diarrhoea incidence was at its maximum (21).

Immunity in severe acute malnutrition and causes of electrolyte derangements

The relationship between nutritional status and the immune system has been a topic of study for decades. Several studies have demonstrated that SAM impairs host immune responses, including cell-mediated immunity (22) and secretory IgA production (23, 24). SAM is a major cause of secondary immune deficiency in the world.

Lung infections such as pneumonia, tuberculosis, abscesses (pocket of infection), or aspergillosis (fungus) may cause syndrome of inappropriate ADH secretion (SiADH). Other lung problems such as asthma may also cause SIADH. It is a condition where the body makes too much antidiuretic hormone (ADH). ADH is a chemical that helps keep the right balance of fluids in the body. Increased ADH may cause too much water to remain inside the body. SiADH leads to hyponatremia (25).

Malnourished children suffer in greater proportion from bacterial gastrointestinal and respiratory infections (26). The first line of defence against these types of infection is the innate immune response, particularly epithelial barriers and the mucosal immune response (27). SAM significantly compromises mucosal epithelial barriers in the gastrointestinal, respiratory and urogenital tracts. For example, vitamin A deficiencies induce the loss of mucus-producing cells. This loss of the protective mucus blanket increases susceptibility to infection by pathogens that would ordinarily be trapped in the mucus and swept away by the cleansing flow of mucus out of the body. Barrier

defects of mucous membranes are critical in the pathogenesis of respiratory and gastrointestinal tract infections (28).

In particular, mucosal barrier immunity is impaired in the malnourished host in the gastrointestinal tract due to the altered architecture and composition of the intestinal mucosal tissues which includes flattened hypotrophic microvilli, reduced lymphocyte counts in Peyer's patches or reduced IgA secretion (29). Secretory IgA is an important component of the mucosal immune response that protects the upper respiratory and gastrointestinal tracts against infection with pathogenic organisms.

This is why patients with SAM are so prone to gastrointestinal infection that culminates into diarrhoea and consequential electrolyte derangement.

The following is an illustration of the link between infection and malnutrition;
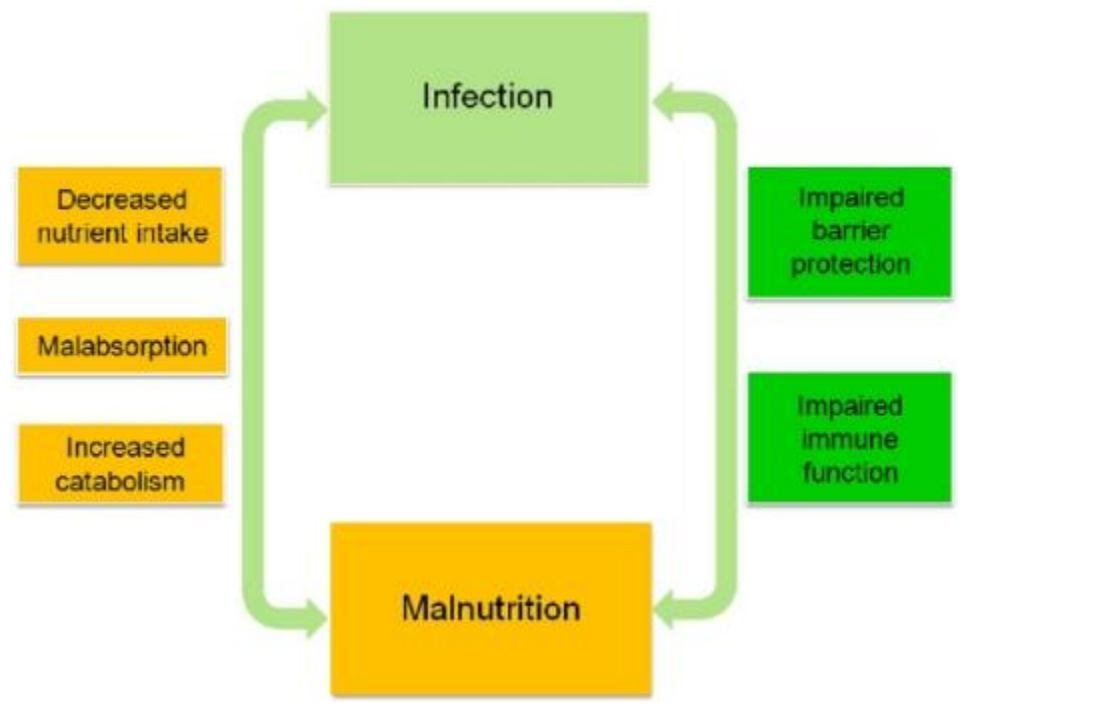
In order to appreciate the magnitude of diarrhoea in patients with SAM, a study by Irena A.H (2009), on acute diarrhoeal disease in severely malnourished children was

done in Lusaka – UTH, and it indicated that the majority of severely malnourished children presenting to UTH had diarrhoea- 67.3% and these children had two and a half increased odds of mortality compared to those who did not have diarrhoea.

It was concluded from the study results that diarrhoea is a major cause of death in children with severe acute malnutrition and under the current standard management approach, diarrhoea in children with SAM was found to increase their odds of death substantially (**30**).

SAM and HIV

Severe acute malnutrition is also associated with the depletion of the lymphocyte subsets of immunity, and this depletion is exacerbated by the presence of HIV-1 infection (**31**). The resulting severe depletion of lymphocytes predisposes the patients to different kinds of infections.

In sub-Saharan African countries with the highest case fatality of malnutrition, HIV/AIDS and tuberculosis (TB) have led to an epidemic of secondary severe malnutrition related to these co-morbidities. Severely sick malnourished children with AIDS and TB appear to differ in their pathophysiological and clinical response to the accepted WHO therapeutic guidelines, compared with children with primary severe malnutrition due to food shortage and non-HIV/TB related infection (**32**).

A study done by Amadi B et al (2001), at the University Teaching Hospital, Lusaka, on Intestinal and systemic infection, HIV, and mortality in Zambian children with persistent diarrhoea and malnutrition, showed that out of 200 children followed up, 108 of the children (54%) were HIV positive.

HIV-seropositive children were more likely to have severe wasting (z- score <-3 SD) whereas HIV-seronegative children were more likely to have bi-pedal oedema.

The common intestinal infections were caused by Cryptosporidium parvum (26%), nontyphoid Salmonella species [18%]), and septicaemia (17%).

Of the 200 children, 39 (19.5%) died within 28 days and cryptosporidiosis and severe wasting were the only independent predictors of death.

It was concluded from the study that although intestinal and systemic infections did not differ for HIV-seropositive and HIV-seronegative children, HIV influenced

nutritional status of all children. Cryptosporidiosis and severe wasting were associated with higher mortality (33).

Severely sick malnourished children with AIDS and TB appear to differ in their pathophysiological and clinical response to the accepted WHO therapeutic guidelines, compared with children with primary severe malnutrition due to food shortage and non-HIV/TB related infection (34).

A study by Heikens et al (2008), on the case management of HIV infected severely malnourished children, revealed that the HIV pandemic in sub-Saharan Africa has substantially altered the epidemiology, clinical presentation, pathophysiology, case management, and survival of severely malnourished children. Case-fatality rates ranged from 20% to 50%, despite the use of WHO guidelines.

Infants with HIV present with multiple co-morbid conditions such as persistent diarrhoea, pneumonia, Pneumocystis jirovecii pneumonia (PJP), extensive skin infections, and oral thrush. Children presenting with profuse diarrhoea, have a high case fatality rate and their response to management as set out in current guidelines is poor (34).

It was inferred from the above study that patients with SAM with HIV present with electrolyte derangements due to electrolyte losses from diarrhoea and from the syndrome of inappropriate antidiuretic hormone (SiADH) resulting from pneumonia. As mentioned earlier, SiADH causes hyponatremia.
More research has been recommended for management of patients with SAM with HIV.

Electrolyte disturbances with HIV infection
Hyponatremia and hyperkalemia are the two major electrolyte disorders that may be associated with HIV infection. They are more likely to occur in sicker patients, with the highest rates in those who are hospitalized. In addition, lactic acidosis, hypophosphatemia have been described.
Hyponatremia occurs in as many as 35 to 55 percent of hospitalized HIV-infected patients, but can also be seen in ambulatory patients. The hyponatremia is usually due

to one or more of three disorders, each of which is associated with an impaired ability to excrete water due to increased release of antidiuretic hormone (ADH): syndrome of inappropriate ADH secretion, volume depletion, and adrenal insufficiency.

Hyponatremia

The Syndrome of inappropriate ADH secretion — (SIADH) is usually due to pneumonia (with Pneumocystis carinii or other organisms), malignancy, or occult or symptomatic infection of the central nervous system. Among patients treated with intravenous trimethroprim-sulfamethoxazole, the fluid required to dilute the drug may contribute to the development of hyponatremia.

Volume depletion — Volume depletion in HIV-infected patients is most often caused by gastrointestinal fluid losses, primarily from diarrhoea. Hypovolemia can be distinguished from the SIADH by a low urine sodium concentration (usually below 15 mmol/L) and correction of the hyponatremia with volume repletion (35).

Effects of hyponatremia

Hyponatremia causes a decrease in the osmolality of the extracellular space. Because the intracellular space then has a higher osmolality, water inevitably moves from the extracellular space to the intracellular space to maintain osmotic equilibrium. The increase in intracellular water causes cells to swell. Although cell swelling is not problematic in most tissues, it is potentially dangerous in the brain because it is contained in a fixed shell, the skull. As brain cells swell, there is an increase in intracranial pressure. Acute, severe hyponatremia can cause brainstem herniation and apnea; respiratory support is often necessary. Brain cell swelling is responsible for most of the symptoms of hyponatremia. Neurologic symptoms of hyponatremia include anorexia, nausea, emesis, malaise, lethargy, confusion, agitation, headache, seizures, coma, and decreased reflexes. Patients may have hypothermia and Cheyne-Stokes respirations. Hyponatremia can cause muscle cramps and weakness (36).

Several studies have been done worldwide to demonstrate the electrolyte derangements seen in patients with SAM with or without diarrhoea. They are highlighted below;

A study by Khine Z.T el al in Burma, showed that malnourished children lost more sodium in their stools and urine during diarrhoea, so that they had significantly diminished gut net sodium balance and significantly diminished total body sodium balance causing hyponatremia (37).

Another study by Kathryn.M (2012), at Kilifi Hospital in Kenya, looked at risk factors and outcome of patients with SAM with diarrhoea. On admission 592 children (49%) had diarrhoea of which 122 (21%) died compared to 72/614 (12%) deaths in those without diarrhoea at admission. A further 187 (16%) children developed diarrhoea after 48 hours of admission and 33 died (18%). Any diarrhoea during admission resulted in a significantly higher mortality 161/852 (19%) than those uncomplicated by diarrhoea 33/351 (9%).

Features associated with a fatal outcome in children presenting with diarrhoea included bacteraemia, hyponatremia, low mid-upper arm circumference <10 cm, hypoxia, hypokalemia and oedema. Bacteraemia had the highest risk of death; and complicated 24 (20%) of fatalities. Positive HIV antibody status was more frequent in cases with diarrhoea at admission (23%) than those without (15 %,) but did not increase the risk of death in diarrhoea cases.

It was concluded from the study that children with SAM complicated by diarrhoea had a higher risk of death than those who did not have diarrhoea during their hospital stay (38).

Hyponatremia and mortality

When electrolyte derangements are not corrected, they may cause morbidity and mortality. A study by Chawla et al (2011) in New York, showed that severe hyponatremia (<120 mmol/L) in hospitalized patients had a high mortality rate. Mortality rates tended to increase as the sNa fell from 134 to 120 mmol/L, rising above 10% for patients with sNa of 120 to 124 mmol/L. More than two thirds of patients who died after sNa <120 mmol/L had at least two additional acute severe progressive illnesses, most commonly sepsis and multiorgan failure. Three deaths (5.6%) were plausibly related to the adverse consequences of hyponatremia, and one (1.8% of the fatal cases and 0.15% of all patients with serum sodium <120 mmol/L) were from cerebral oedema (39).

Patients with SAM with diarrhoea are given a rehydration solution for severely malnourished children, ReSoMal, which has a higher potassium content and lower sodium content compared to the standard oral rehydration solution, ORS. In view of its low sodium content, some patients with severe hyponatremia (Na+ <120mmol/l) persist to have hyponatremia despite adequate supervised rehydration with ReSoMal. On the contrary, patients with hypokalemia benefit more from the high potassium containing rehydrating solution and the hypokalemia is reversed.

Efficacy and safety of ReSoMal

A study in Bangladesh by N.Alam et al (2003) looked at the Efficacy and safety of a modified oral rehydration solution (ReSoMaL) in the treatment of severely malnourished children with watery diarrhoea. The results showed that ReSoMaL had a large beneficial effect on potassium status compared with standard ORS. However, ReSoMaL therapy may have resulted in symptomatic hyponatremia and seizures in patients with severe diarrhoea (40), because adequate sodium was not replaced by the Resomal.

Hypernatremia is a sodium concentration >145 mmol/L, although it is sometimes defined as >150 mmol/L. Mild hypernatremia is fairly common in children, especially among infants with gastroenteritis. Hypernatremia in hospitalized patients may be iatrogenic, caused by inadequate water administration or, less often, by excessive sodium administration. Moderate or severe hypernatremia has significant morbidity, including the result of underlying disease, the effects of hypernatremia on the brain, and the risks of overly rapid correction. Hypernatremia may be caused by excess salt intake e.g. improperly constituted formula or salt poisoning, water deficit e.g. diarrhoea with poor intake of rehydration solution or from renal losses of water e.g. central diabetes insipidus or nephrogenic diabetes insipidus (41).

Effects of hypernatremia

Hypernatremia, even without dehydration, causes central nervous system symptoms that tend to parallel the degree of sodium elevation and the acuity of the increase. Patients are irritable, restless, weak, and lethargic. Some infants have a high-pitched cry and hyperpnoea. Alert patients are very thirsty, even though nausea may be present. Hypernatremia may cause fever, although many patients have an underlying

process that contributes to the fever. Hypernatremia is associated with hyperglycemia and mild hypocalcemia; the mechanisms are unknown. Beyond the sequelae of dehydration, there is no clear direct effect of hypernatremia on other organs or tissues, except the brain (41). Brain haemorrhage is the most devastating consequence of hypernatremia. As the extracellular osmolality increases, water moves out of brain cells, resulting in a decrease in brain volume. This can result in tearing of intracerebral veins and bridging blood vessels as the brain moves away from the skull and the meninges. Patients may have subarachnoid, subdural, and parenchymal haemorrhage. Seizures and coma are possible sequelae of the haemorrhage, although seizures are more common during correction of hypernatremia (41).

Potassium and Magnesium

The intracellular concentration of potassium, approximately 150 mmol/L, is much higher than the plasma concentration. The majority of body potassium is contained in muscle. As muscle mass increases, there is an increase in body potassium. The majority of extracellular potassium is in bone; <1% of total body potassium is in plasma.

Because most potassium is intracellular, the plasma concentration does not always reflect the total body potassium content. A variety of conditions alter the distribution of potassium between the intracellular and extracellular compartments. The Na+, K+-ATPase maintains the high intracellular potassium concentration by pumping sodium out of the cell and potassium into the cell. This balances the normal leak of potassium out of cells via potassium channels that is driven by the favourable chemical gradient (42).

However, metabolic balance studies and analysis of muscle biopsy specimens have indicated potassium deficiency in severely malnourished children which rises to normal levels after therapy. Serum magnesium is usually normal but may fall in the presence of severe gastroenteritis. The evidence for magnesium depletion comes from balance studies and muscle biopsies of patients with SAM. During recovery from malnutrition, retention of magnesium is greater than would be predicted from the nitrogen balance. Muscle magnesium is low in severely malnourished children though the reduction is not as great as that of potassium, perhaps because of the large store in bone (43).

Effects of Hypokalemia

The heart and skeletal muscle are especially vulnerable to hypokalemia. ECG changes include a flattened T wave, a depressed ST segment, and the appearance of a U wave, which is located between the T wave (if still visible) and the P wave. Ventricular fibrillation and torsades de pointes may occur, although usually only in the context of underlying heart disease. Hypokalemia makes the heart especially susceptible to digitalis-induced arrhythmias, such as supraventricular tachycardia, ventricular tachycardia, and heart block. The clinical consequences in skeletal muscle include muscle weakness and cramps. Paralysis is a possible complication, generally only at levels <2.5 mmol/L. This usually starts with the legs, followed by the arms. Respiratory paralysis may require mechanical ventilation. Some patients have rhabdomyolysis; the risk increases with exercise. Hypokalemia slows gastrointestinal motility. This manifests as constipation or, with levels <2.5 mmol/L, an ileus may occur. Hypokalemia impairs bladder function, potentially leading to urinary retention (42).

In a study by Odey F.A et al (1998), in Nigeria, Hypokalemia was seen in 45 (23.4%) patients with severe acute malnutrition. This was second to acidosis. Metabolic acidosis was the commonest abnormality in this study and was seen in 108(56.3%) of the patients included in the study. There was hyponatraemia in 25(13%).Hypochloraemia in 8(4.2%) and hypernatremia in 6(3.1%) of the patients respectively (44).

Another study in Pakistan by Memon Y et al(2004) showed that electrolyte disturbance were mostly seen in patients with severe acute malnutrition and the electrolyte disturbance mostly affected the serum potassium seen in 48(48%) and bicarbonate seen in 56(56%) cases while sodium imbalance is seen in 25(25%) cases. The study also showed that hypokalemia, acidosis and hyponatremia were seen more frequently in those who had diarrhoea as compared to those who had no diarrhoea (45).

Hyperkalemia, in patients with severe acute malnutrition, would occur if potassium supplements were given in addition to the enteral formula, particularly in high risk

patients such as those with renal failure. Even standard formula may contain more potassium than some patients can tolerate (46).

ECG changes of hyperkalemia include peaked T wave, increased P-R interval, flattening of the P wave and widening of QRS complex, Ventricular fibrillation and Asystole. Parasthesias, weakness and tingling can also occur (42).

Magnesium

Magnesium (Mg^{3+}) is one of the most abundant ions in human cells, and its serum concentration is remarkably constant in healthy subjects. Although the measurement of serum Mg does not always reflect the overall status of Mg^{3+} metabolism, serum Mg^{3+} correlates well with intracellular-free Mg, the physiological active form of the elements.

The causes of magnesium depletion and hypomagnesemia are decreased gastrointestinal absorption and increased renal loss. Decreased Gastrointestinal absorption is frequently due to diarrhoea, malabsorption, and inadequate dietary intake. Common causes of excessive urinary loss are diuresis due to alcohol, glycosuria, and loop diuretics.

Medical conditions putting persons at high risk for hypomagnesemia are alcoholism, congestive heart failure, diabetes, chronic diarrhoea, hypokalemia, hypocalcemia, and malnutrition. Evidence suggests that magnesium deficiency is both more common and more clinically significant than generally appreciated (47).

Magnesium (Mg^{3+}) modulates vasomotor tone, blood pressure, and peripheral blood flow. Mg^{3+} deficiency has been shown to trigger vasoconstriction and enhance vascular endothelial injury (48)

A critical serum magnesium level is less than 0.5 mmol/L and is associated with seizures and life-threatening arrhythmias (49).

A study by Cahit K. et al, in 2011, investigated the effects of hypomagnesemia in malnutrition. It included 25 children with SAM. During the follow-up period, four (16%) patients died within four days after admission. Serum Mg^{3+} levels were lower than normal value in three (75.0%) of the four deceased and in six (28.6%) of the 21 surviving patients with SAM. The odds ratio (odds ratio= (3/1)/ (6/15) =7.5) for

mortality was 7.5 times higher in the malnourished children with hypomagnesaemia (n=9) than in the malnourished children without hypomagnesaemia (n=16).

The findings of this study called for giving attention to hypomagnesaemia as a mortality risk factor in SAM (**50**).

Calcium

Calcium has received very little attention in studies of patients with severe acute malnutrition (**51**). Ninety-eight percent of the calcium in the body is stored in bone, so that from the point of view of maintaining the concentration in other tissues, there is a huge reserve. In spite of the large differences in dietary intake, the concentration of ionised calcium in plasma and extracellular fluid is regulated within narrow limits by the combined effects of three hormones, parathyroid hormone, calcitonin and the vitamin D metabolite 1,25- dihydroxy-cholecalciferol (**52**).

The constancy of cytoplasmic ca2+ concentration is of great importance, since it plays a fundamental role in the integrated control of membrane permeability, the cellular response to stimulation and intracellular signalling (**53**).

A small but significant fall in ionised calcium was reported in marasmus (**54**).

Rickets is not a typical feature of severe acute malnutrition, because the classical changes in the long bones do not occur in the absence of growth. Bhattacharyya and Dutta in Calcutta described atrophic rickets in children with severe acute malnutrition, with gross decalcification and thinning of the bone cortex, but without the classical cupping and spreading of the metaphyses.

Hypocalcemia is a frequent feature of hypomagnesemia in man and several other species. To elucidate the cause of this hypocalcemia, a study by Se Mo Suh et al was done on a child, with primary hypomagnesemia and secondary hypocalcemia during magnesium supplementation when he was normomagnesemic and normocalcemic and after magnesium restriction for 16 days when he quickly became hypomagnesemic (0.5 mmol/liter) and hypocalcemic (3.4 mmol/liter) and had positive Chvostek's and Trousseau's signs.

The concentrations of serum parathyroid hormone (PTH) were measured and were normal in the normomagnesemic state ranging from 0.15 ng/ml to 0.40 ng/ml. Serum PTH did not increase in the hypomagnesemic state in spite of hypocalcemia. Indeed,

PTH became unmeasurable in four consecutive samples at the end of the period of magnesium restriction.

The concentrations of serum calcitonin remained unmeasurable (< 0.10 ng/ml) throughout the study, implying that excess calcitonin was not the cause of hypocalcemia in magnesium depletion.

The findings in this study supported their thesis that magnesium depletion causes impaired synthesis or secretion of parathyroid hormone. This impairment would account for the hypocalcemia observed in the hypomagnesemic state (55).

Majority of studies done in the past have demonstrated that the main electrolyte derangements seen in patients with SAM are derangements with **sodium** and **potassium**. The laboratory at the University of Zambia where the samples for this study were analysed, was only capable of analysing sodium and potassium. It is for these two reasons that in this study, the electrolytes analysed were **sodium** and **potassium.**

CHAPTER THREE

3.0 OBJECTIVES

3.1 MAIN OBJECTIVE;

To describe the electrolyte profile of severely malnourished children aged 6 – 59 months, presenting to the University Teaching hospital , Lusaka.

3.2 SPECIFIC OBJECTIVES

i.   To describe the electrolyte profile in severely malnourished children on day1, day 3 and day 8 of admission to the malnutrition ward.

ii. To describe the electrolyte profile of severely malnourished children with diarrhoea and those without diarrhoea.

iii. To describe the electrolyte derangements of patients with the different forms of malnutrition- oedematous type and severe wasting.

iv. To describe electrolyte derangements between HIV positive and HIV negative children with SAM.

v.   To describe the outcome of children with electrolyte derangements.

CHAPTER FOUR

4.0 STUDY METHODOLOGY

4.1 Study design and period

This was a cross sectional study involving children, aged 6-59 months admitted to the Malnutrition ward at UTH. The study was conducted from1st August 2014 to 31st March 2015. Part of the study period fell within the peak season of malnutrition: December and January being the peak months for SAM in Lusaka.

4.2 Study location

The study was conducted in the malnutrition ward, at UTH, which is the main in-patient malnutrition unit with a bed capacity of 60 that provides treatment to patients with SAM with complications. The most common complications include anorexia, diarrhoea, pneumonia and severe anaemia. The ward provides in-patient care to children with SAM with complication coming from several parts of Lusaka. This means that during the peak seasons of SAM, the ward receives more patients, exceeding the bed capacity of the ward. And inevitably, patients share bed spaces. The ward is divided into bay 1, 2 3 and 4. On admission, patients are admitted to bay 1 for stabilisation and treatment of complications.

4.3 Sampling method

Convenience sampling method was used. On admission, every consecutive child with SAM presenting to the malnutrition ward, UTH was assessed by the clinician on call, taking detailed history and performing physical examination. Anthropometric measurements such as weight, and height were also done before admission. Weight for height Z scores (WHZ) were determined using the WHO growth charts. Children with

WHZ < -3 were recruited for the study after obtaining consent from the caregiver.

4.4 Target population

All children aged 6-59 months with SAM admitted to malnutrition ward.

4.5 Study population

Children with SAM aged between 6 – 59 months meeting criteria for selection.

4.6 Eligibility criteria

Inclusion criteria

    i.   All patients with SAM between 6 and 59 months whose guardians consented to be part of the study

Exclusion criteria

    i   Patients less than 6 months and those above 5 years

    ii   No consent from the caregiver

4.7 Sample size

The sample size was calculated using the following formula;

$$N = \frac{Z^2 \times P (1-P)}{D^2}$$

Z=1.96

D=0.05 precision of 3-5%

P= Prevalence of the most common electrolyte derangement in a study by Odey F.A et al in Nigeria, in 1998 who found hypokalemia in 23.4%, approximated to 20% in this Study. Using prevalence of 20%, with an estimated power of 80%, and confidence Interval of 95%, the sample size was calculated to be **245.**

Data collection

4.8 Clinical data

On admission, permission and consent was sought from the care givers to participate in the study and social and demographic data were collected using structured questionnaires, (see appendix).All children were examined by the attending physician. Height was measured using a Stadiometer and weight was measured using a UNISCALE (Nearest 100g).

Immunization status, including Rota virus vaccination was collected from the children`s under five cards. Diarrhoea was defined as presence of > 3 stools per day. Information of Diarrhoea occurring after admission was collected from stool charts for patients (see appendix).

Two HIV Serology tests-Determine HIV test kit and Unigold (for children >18 months) were done by HIV counsellors after obtaining consent from caregivers.

DNA PCR tests were done on all severely malnourished children less than 18 Months, with a positive serology test.

4.9 Laboratory data

After obtaining consent from caregivers to participate in the study, 3mls of blood (as recommended by the laboratory) was collected from the patients in the screening room before feeds were commenced, on day 1, and the blood was stored in heparinized bottles.

The blood sample was then taken to the laboratory (low cost laboratory within the premises of UTH), where it was screened for **sodium** and **potassium** using the ABX pentra 400 chemistry analyser with ABX pentra 400 reagents.

Some results would be ready after a minimum of 2 hours following submission of specimens.

Results showing life threatening electrolyte derangements were communicated to the care givers and the patients were treated promptly, as guided by the malnutrition unit.

Another sample was collected on day 3 and day 8 after feeds were commenced. Other tests were also conducted such as Full Blood Count, Malaria Parasite Slide, stool and blood cultures to assess co-morbidities.

4.10 Clinical and nutritional care

During the study, patients were managed by a team of Doctors; two Paediatric Consultants, one acting senior registrar, three registrars, one senior house officer and two junior resident medical officers. In addition, patients were attended to by five to seven nurses; one to two per shift and five ward attendants; one per shift. Patients were managed according to the WHO guidelines. All children received 10% dextrose, intravenous antibiotics, antimalarial, antihelminthics and folic acid ,on admission, as per protocol, children with diarrhoea were given ReSoMal and the rehydration was monitored by the ward attendants and nurses, using the stool charts (appendix).

Patients admitted with diarrhoea with hypovolemic shock were given intravenous fluid- ½ strength Darrows in 10% dextrose, as per ward protocol.

A starter feed called F75 with 75Kcal/100mls, was initiated at 130kcal/kg and was given every 3 hours, using F75 charts. Stabilisation of children with SAM usually takes 2-7 days. With improvement of appetite, reduction of oedema, resolution of diarrhoea and improvement in the general condition, patients were transferred to bay 2 and transitioned to a higher caloric feed RUTF (500Kcal/sachet). If the patient had feeding difficulties with RUTF, they were transitioned to F100 instead which has 100Kcal/100mls, given via mouth if appetite was good or via naso- gastric tube, if appetite was poor. The transition was done over 3 days. RUTF sachets were given to the patients, according to the patients` weight, using the RUTF chart. For F100, on day 1and 2 of the transition phase, patients were given the same amount of F100 as the initial amount of F75. On day 3, 10mls extra of the F100 was added to each feed until the maximum feed for that patient was reached, according to the patients 'weight, using the F100 chart. Thereafter, F100 was given at 150-220kcal/kg, every 4 hours. When patients were able to complete 80% of the feed, they were transferred to bay 3 for rehabilitation where feeds with RUTF or F100 are continued and a high energy protein supplement (HEPS) porridge is added to the feed. With resolution of complications, further reduction in oedema (to at least 1+ oedema), when patient is alert and smiling, patients were prepared for discharge and the care givers were given nutritional counselling.

After discharge, the patients were reviewed in the outpatient clinic, at UTH after 2 weeks, then again, after a month .With progressive increment in weight, patients were finally discharged from our care and referred to a community clinic offering outpatient therapeutic program for follow-up and complete recovery.

4.11 Measurements / Definitions

Severe acute malnutrition was defined as a child with bipedal pitting
Oedema or severe wasting with a weight for height / length Z score of less than -3
SD

Diarrhoea was defined as ≥ 3 loose stools per day

Stabilisation phase was defined as the first 2- 7 days after initiation of treatment

Normal Potassium –K$^+$= 3.5-4.5mmol/L

Hypokalemia – K$^+$ <3.5mmol/L

Hyperkalemia –K$^+$ > 5.5mmol/L

Hyponatremia – Na$^+$ <135mmol/L,   Na$^+$ <120mmol/L- Severe

Hypernatremia – Na+ > 145mmol/L

Normal sodium –Na$^+$ =135-145mmol/l

Electrolyte derangements were defined as either sodium or potassium
derangement

Note: Treatment of the different electrolyte derangements were guided by the heads
of the malnutrition unit

4.12 Data analysis

Dependant variables: Electrolyte derangements.

Outcomes

  i. Total number (percentage) of electrolyte derangements on day 1, 3 and 8

 ii. Proportion of children with electrolyte derangements with diarrhoea and
      without diarrhoea

iii. Proportion of children with electrolyte derangements with nutritional oedema
      and / severe wasting

 iv. Proportion of children with electrolyte derangements in   HIV+ and HIV−

4.13 Data analysis plan

Baseline characteristics were presented in frequency tables

Description of electrolyte profiles and electrolyte derangements were done by

Calculating percentages.

 Effect size was measured using Odds ratios (OR) and results were significant at 95%

Confidence Intervals (CI). Comparisons were between electrolyte

Derangements in patients with diarrhoea vs. no diarrhoea, oedema vs severe wasting,
and

HIV positive vs. HIV negative.

Bi-variate and multivariate analysis (logistic regression) were used to

identify factors associated with electrolyte derangements.

Collected data was Stored in Epi Data version 3.1 and analysed using STATA 11 Significant statistics were declared at P < 0.05.

4.14 Data management
Double entry of results were done to reduce any entry errors
A copy of the results will be sent to ERES Converge IRB

4.15 Ethical issues
Permission was sought from ERES CONVERGE IRB. Any amendments made to the study was communicated to ERES CONVERGE and permission sought again.

Permission was sought from the Department of Paediatrics and Child health
Consent was requested for from the care givers of the children eligible to be enrolled in the study.
Confidentiality was to be upheld by coding all entries .Patients with life threatening electrolyte derangements immediately received treatment as guided by the malnutrition unit.
Other Standard investigations were also done, such as Random Blood Sugar, Malaria Parasite Slide, and Full Blood Count.

CHAPTER FIVE

5.0 RESULTS
Between August 2014 and March 2015, 280 eligible participants were screened. Consent was obtained and 245 were enrolled and were followed up on day 1. However, 2 samples were not analysed for sodium, thus only 243 we analysed on day 1.

Out of the 245 participants, 60.41% (148/245) were male and 39.59% (97/245) were female. Majority of patients were in the 12-35 months age group. Mean age was 17 months (IQR 13-23 months). The youngest patient enrolled was 6 months and the oldest was 53 months.

Of the 245 participants, 57.55% (141/245) had diarrhoea and 42.45% (104/245) had no diarrhoea.

69.80% (171/245) had severe wasting while 30.20% (74/245) had bilateral pitting pedal oedema.

20.94% (49/234) were HIV positive, while 79.06% (185/234) were HIV negative

In terms of deaths, 118 of the participants died.

Table 1 below shows the summary of the participants;

Table 1: **SUMMARY OF PARTICIPANTS**

	DAY1	DAY3	DAY8
Screened 286			
Consented 280			
Analysed 243			
Number of participants	245	41	18
Male	148 (60.41%)		
Female	97 (39.59%)		
6-11 months	53 (21.63%		
12-35 months	184 (75.10%)		
36-59 months	8 (3.27%)		
Mean age	17months (IQR 13-23 months		
Oedematous	74 (30.20%)		
Severe wasting	171 (69.80%)		
With diarrhoea	141 (57.55%)		
No diarrhoea	104 (42.45%)		
HIV positive	49 (20.94%)		
HIV negative	185 (79.06%)		
Died	118 (48.2%)		

SUMMARY OF RESULTS

5.1 Sodium profile on day 1, 3 and 8

On day 1 n=243 (2 samples not analysed)

We obtained serum samples for sodium from 245 participants. 2 samples were not analysed due to unavailability of reagents, thus 243 were analysed .The mean sodium on day 1 was 133.23±8.40 (range 100-154).

The majority of participants, 54.73% (133/243) had hyponatraemia, 4.94% (12/243) had hypernatremia and 40.33% (98/243) had normal serum sodium.

On day 3 (n=41)

By day 3, 108 had died, 44 withdrew from the study,17 absconded from the ward, 22 left against medical advice and 11 were transferred out of the malnutrition ward to the isolation ward because they were diagnosed with an infectious condition - tuberculosis, leaving 41 participants. Withdrawal from the study was determined by the caregivers` refusal to have blood collected from the patients on day 3 and this was documented on the consent forms.

We obtained serum samples for sodium from 41 participants. 60.98% (25/41) had hyponatraemia. Out of theses 25 participants, 16 were hyponatremic even on day 1 while 9 developed hyponatremia after admission. Coincidentally, all of these 9 patients who developed hyponatremia had also developed diarrhoea after feeds were initiated. 5.00% (2/41) had hypernatremia and 34.15% (14/41) had normal serum sodium.

On day 8 (n= 18)

By day 8, 10 more participants had died, 6 withdrew from the study, and 7 absconded from the ward, leaving 18 participants.

We obtained serum samples for sodium from 18 participants. 50% (9/18) had hyponatraemia, (7 of whom were hyponatremic from day 1, 2 developed hyponatremia on day 8) . 5.56% (1/18) had hypernatremia, and 44.44% (8/18) had normal serum sodium. The summary of the sodium profile are shown in table 2 and graph 1 below;

Table 2: Sodium profile on day 1, 3 and 8

	Day 1	Day 3	Day 8
Sodium	N=**243**	N=**41**	N=**18**
Hyponatraemia (Na<135mmol/l)	133 (54.73%)	25 (62.5%)	9 (50%)
Hypernatremia(Na>145mmol/l)	12 (4.94%)	2 (5.00%)	1 (5.56%)
Normal sodium	98 (40.33%)	14 (34.15%)	8 (44.44%)
Mean sodium ± SD	133.23±8.40(range 100-154)	131.75±8.17(range110-158	135.8±9.9(range 126-173)

Graph 1: Mean sodium levels on day 1, 3 and 8

The graph 1 below shows the mean sodium levels on days 1, 3 and 8.

Graph 1
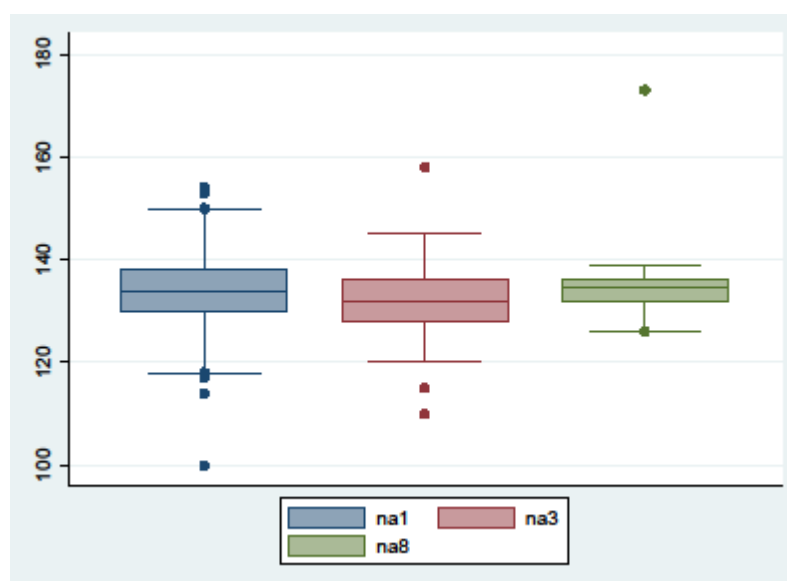
Day 1 133.23±8.40 (sodium range 100-154mmol/l)

Day3 131.75±8.17 (sodium range 110-158mmol/l)

Day 8 135.8±9.9 (sodium range 126-173mmol/l)

Graph 1 above also shows that the proportion of patients with serum sodium derangements tended to reduce from day 1 to day 8.

5.2 Potassium profile on day 1, 3 and 8

Day 1(n=235) (10 samples not analysed)

We obtained serum samples for potassium from 245 participants. 10 samples were not analysed due to unavailability of reagents, thus only 235 were analysed.

36.60% (86/235) had hypokalemia, 34.47% (81/235) had hyperkalemia and 28.94% (68/235) had normal serum potassium.

Day 3 (n=41)

We obtained serum samples for potassium from 41 participants. 85.37% (35/41) had hyperkalemia, (15 of whom were hyperkalemic even on day 1, 20 developed hyperkalemia after admission), 2.44% (1/41) had hypokalemia and 12.20% (5/41) had normal serum potassium.

Day 8 n=17 (I sample not analysed)

5.88% (1/17) had hypokalemia, 72.22% (13/17) had hyperkalemia and 17.65% (3/17) had normal serum potassium.

It was noted with serious concern that a significant number of participants had hyperkalemia on day 1, 34.47% that is incompatible with life, and did not tally with the patient's clinical picture, as these patients were relatively stable. Further scrutiny revealed that collected samples would get to the laboratory within an hour but not processed immediately due to shortage of staff in laboratory or lack of reagents at that moment. This could have resulted in haemolysis of most of the samples, hence the hyperkalemia.

The summary of the potassium profile are tabulated in table 3 below;

Table 3: potassium profile on day 1, 3 and 8

	Day 1	Day 3	Day 8
Potassium	N =**235**	N=**41**	N=**17**
Hypokalemia(K<3.5mmol/l)	86 (36.60%)	1 (2.44%)	1 (5.88%)
hyperkalemia K>5.5mmol/l	81 (34.47%)	35 (85.37%)	13(76.47%)
Normal potassium	68(28.94%)	5 (12.20%)	3 (17.65%)
Mean potassium ± SD	4.08±1.57 (range 1.5-8.7)	5.46±1.02 (range2.9-7.7)	5.5±1.34 (range3.3-9.2)

5.3 Effect of diarrhoea on serum electrolytes

Out of the 243 patients analysed, 83.95% (204/243) had abnormal electrolytes while 16.05% (39/243) had normal electrolytes. Of those with abnormal electrolytes

(n=204), 56.4% (115/204) had diarrhoea while 43.60% (89/204) had no diarrhoea. Of those with normal electrolytes (n= 39), 61.5% (24/39) had diarrhoea while 38.50% (15/39) had no diarrhoea,(P value = 0.550 >0.05). Analysis showed that there was no significant relationship between diarrhoea and serum electrolytes. This is shown in table 4 below;

Table 4: Effect of diarrhoea on serum electrolytes

	Abnormal electrolytes N=204	**Normal electrolytes N=39**
Diarrhoea n=139	115 (56.4%)	24 (61.5%)
No diarrhoea n=104	89 (43.60%)	15 (38.50%)

P = 0.550

Graph 2; Effect of diarrhoea on serum sodium

Of the 133 participants that had hyponatraemia (Na <135mmol/l), 54.14% (72/133) had diarrhoea and 45.86% (61/133) had no diarrhoea. Of the 12 participants who had hypernatremia, 75% (9/12) had diarrhoea and 25% (3/12) had no diarrhoea. Of the 98 who had normal sodium values, 59.18% (58/98) had diarrhoea and 40.82% (40/98) had no diarrhoea. This gave a P value of 0.329 (P > 0.05) Therefore, there was no significant relationship between serum sodium levels and diarrhoea. This is illustrated in table 5 and graph 2 below;

Table 5 : Effect of diarrhoea on serum sodium

Serum electrolytes	**Hyponatremia**	**Normal sodium**	**Hypernatremia**	Total
Diarrhoea	72 (54.14%)	58 (59.18%)	9 (75%)	139
No diarrhoea	61 (45.86%)	40 (40.82%	3 (25%)	104
Total	133	98	12	243

P value 0.329

Graph 2: Effect of diarrhoea on serum sodium
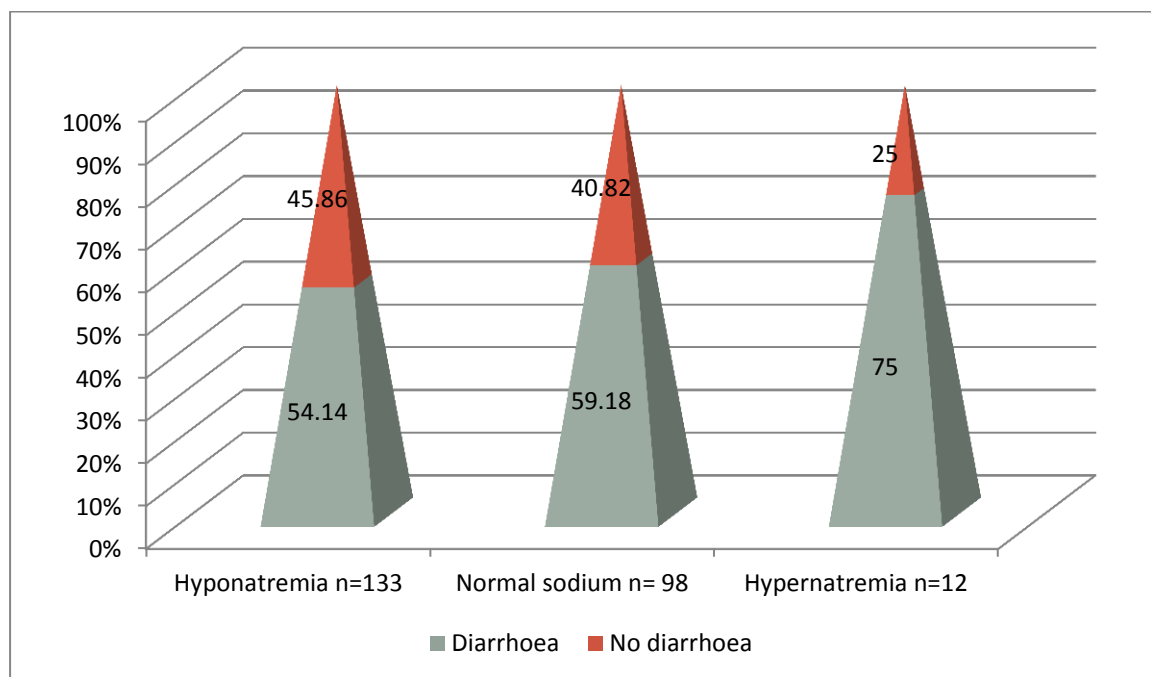
P=0.329

Effect of diarrhoea on serum potassium

In terms of potassium , 36.60% (86/235) had hypokalemia. Of these, 62.79% (54/86) had diarrhoea while 37.21% (32/86) had no diarrhoea. 28.94% (68/235) had normal serum potassium, 67.65% (46/68) of whom had diarrhoea and 32.35% (22/68) of whom did not have diarrhoea. 34.47% (81/235) had hyperkalemia, 45.68% (37/81)) of whom had diarrhoea and 54.32% (44/81) had no diarrhoea. Statistical analysis gave a P value of 0.015 (P<0.05) which was statistically significant. This meant that those presenting with diarrhoea were more likely to have hypokalemia as a potassium derangement.This is illustrated in table 6 and graph 3 below;

Table 6: Effect of diarrhoea on serum potassium

Serum electrolytes	Hypokalemia	Normal potassium	Hyperkalemia	Total
Diarrhoea	54 (62.79%)	46 (67.65%)	37 (45.68%)	137
No diarrhoea	32 (37.21%)	22 (32.35%)	44 (54.32%)	98
Total	86	68	81	235

P value 0.015

31

Graph 3: Effect of diarrhoea on serum potassium
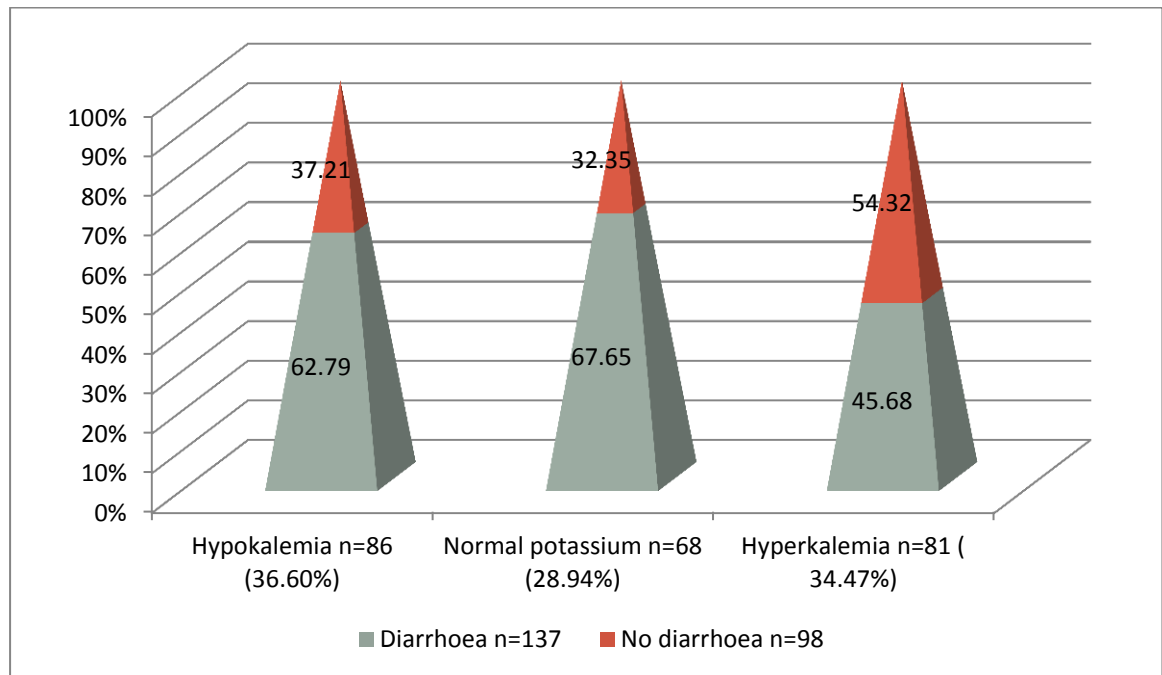
P =0.015

5.4 Comparison of electrolyte derangements between patients with oedema and those with severe wasting

0n admission, 69.55% (169/243) had severe wasting (weight for height <-3SD) while 30.45% (74/243) had bilateral oedema.

Comparison of the serum electrolytes in these two groups showed that most of the electrolyte derangements were seen in those with severe wasting- 141 (69%). However, when subjected to analysis, there was no significant statistical difference between the two groups meaning that presence or absence of oedema was not related to the development of electrolyte derangements. (p =0.739>0.05). This is illustrated in graph 4 below;

Graph 4: Comparison of electrolyte derangements between patients with oedema and those with severe wasting
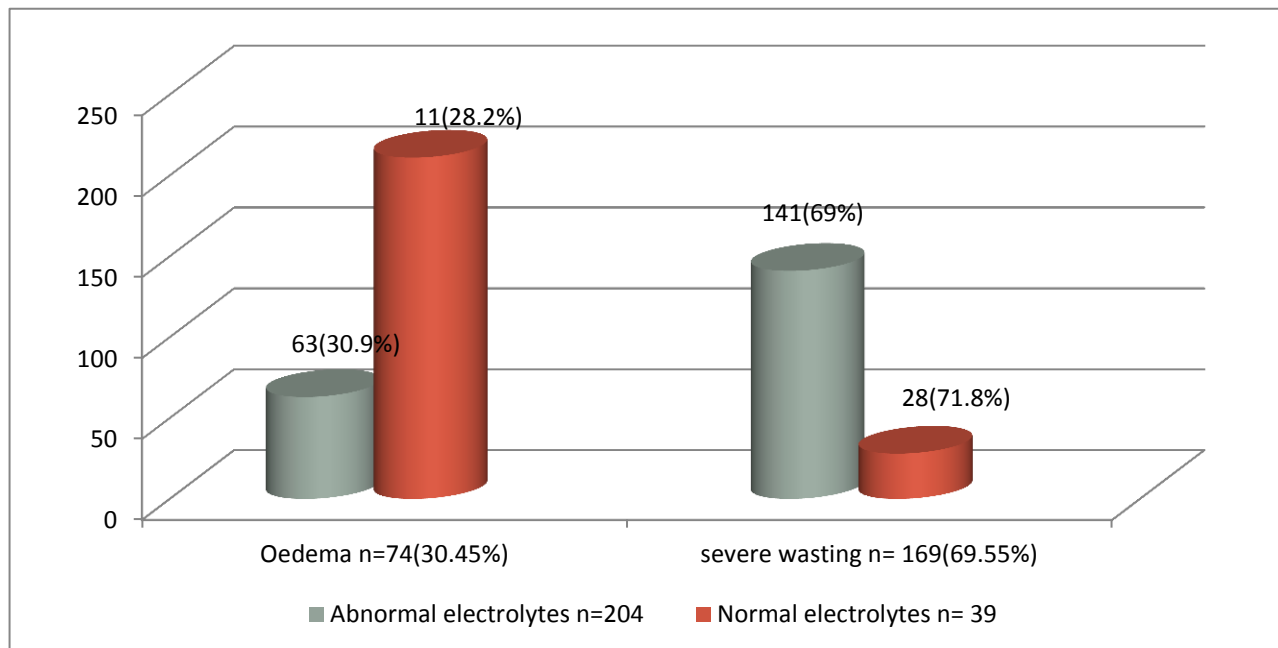
P= 0.739

5.5 Effect of HIV status on serum electrolytes

Out of 245 enrolled study participants, 234 were tested. Majority were HIV negative -79.06% (185/234) and 20.94% (49/234) were HIV positive. It was evident that the majority of participants with electrolyte derangements were HIV negative.

Comparison of the serum electrolytes between those who were HIV positive and those who were HIV negative showed no significant statistical difference, (P=0.441 >0.05) thus there was no significant association between electrolyte derangements and HIV status. Graph 5, table 7 and table 8 below illustrate this comparison;

Graph 5: **Effect of HIV status on serum electrolytes**
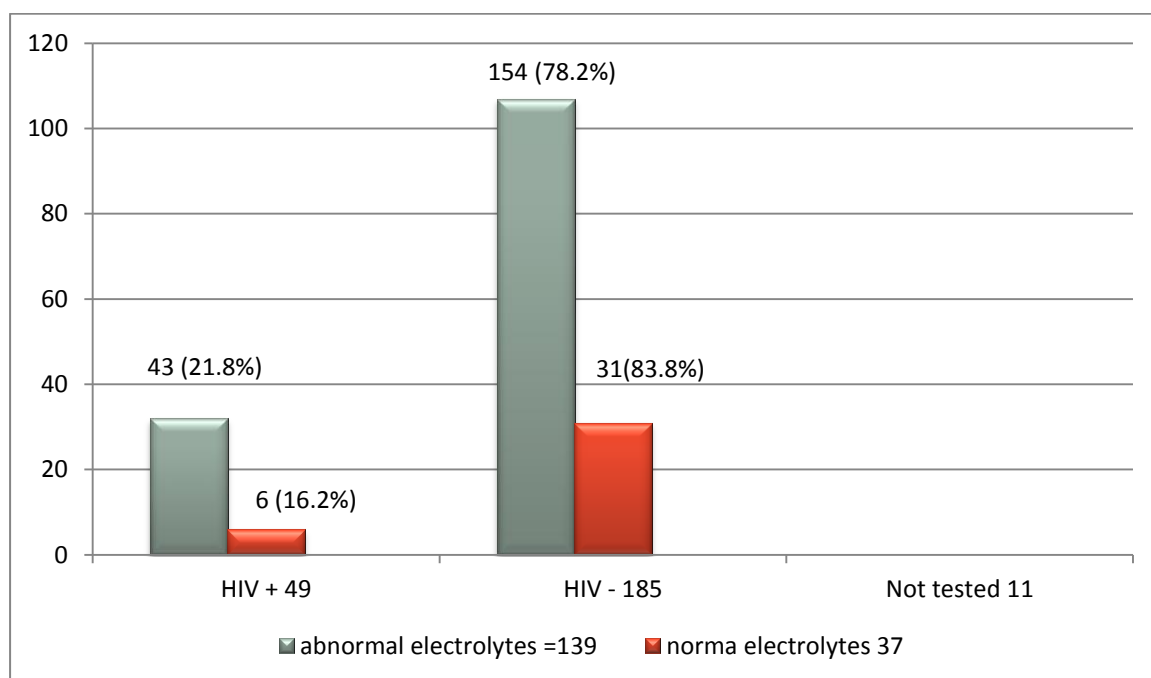
P=0.441

Effect of HIV status on serum electrolytes

Table 7: Effect of HIV on serum sodium

Day1	Serum electrolytes	Hyponatremia	Normal sodium	Hypernatremia	Total
	HIV positive	29 (22.83%)	17 (17.90%)	3 (25%)	49
	HIV negative	98 (77.17%)	78 (82.10%)	9 (75%)	185
	Total	127 (100%)	95 (100%)	12 (100%)	234

P = 0.629

Table 8: Effect of HIV on serum potassium

Day 1	Serum electrolytes	**Hypokalemia**	**Normal potassium**	**Hyperkalemia**	Total
	HIV positive	16(19.3%)	15 (23.44%)	18 (22.78%)	49
	HIV Negative	67(80.7%)	49 (76.56%)	61 (77.22%)	177
	Total	83 (100%)	64 (100%)	79 (100%)	226

P value 0.796

5.6 Outcome of patients with electrolyte derangements

196 out of 245 participants had a known outcome by the end of the study. 84.18% (165/196) of them had abnormal electrolytes while 15.82% (31/196) had normal electrolytes. 40% (66/165) of those with abnormal electrolytes were alive while 60% (99/165) of them died. This is illustrated in table 9 and graph 6 below;

Table 9: Outcome of patients with electrolyte derangements

Serum electrolytes	**Alive**	**Died**	**Total**
Abnormal electrolytes	66 (40%)	99 (60%)	165
Normal electrolytes	12 (38.7%)	19 (61.3%)	31
Total	78	118	196

Graph 6: Outcome of patients with electrolyte derangements
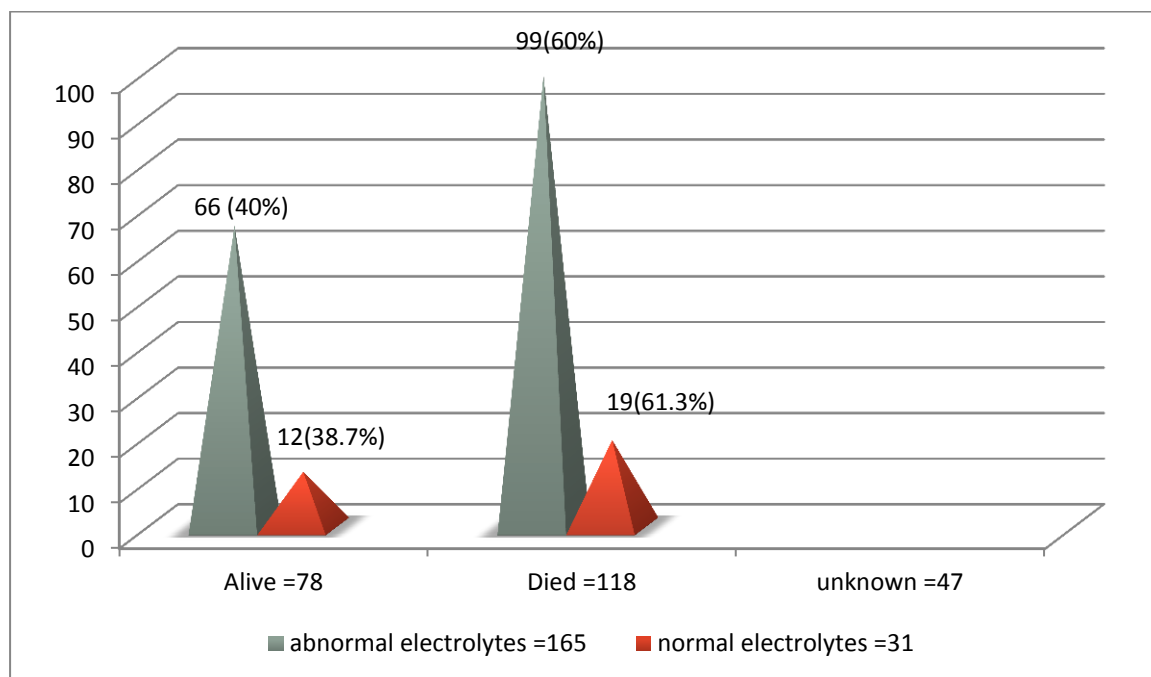
P = 0.893

Statistical analysis of those who died and those who were alive gave a P value of 0.893, (P >0.05), implying that electrolyte derangements were not a predictor of death. Tables 10 and 11 below show the different electrolyte derangements that were seen in those who were alive and those who died.

Table 10: Outcome of patients with sodium derangements

Serum electrolytes	**Alive**	**Died**	Total
Hyponatremia	38 (48.7%)	65(55.1%	103
Normal sodium	35(44.9%)	48 (40.7%)	83
Hypernatremia	5 (6.4%)	5 (4.2%)	10
Total	78	118	

P value 0.609

Table 11: Outcome of patients with potassium derangements

Serum electrolytes	Alive	Died	Total
Hypokalemia	26 (33.8%)	48 (42.1%)	74
Normal potassium	19 (24.7%)	35 (30.7%)	54
Hyperkalemia	32 (41.6%)	31(27.2%)	63
Total	77	114	

P = 0.117

5.7 Outcome of those with diarrhoea and those with no diarrhoea

Further analysis showed that most of those who died had diarrhoea 61.02% (72/118). However, there was no significant statistical difference between outcome of patients with diarrhoea and those without diarrhoea (P=0.429 >0.05), as seen in table 12 below;

Table 12: Outcome for those with diarrhoea and those with no diarrhoea

	Patient Alive	**Died**	**Total**
Diarrhoea	43 (55.13%)	72 (61.02%)	115
No diarrhoea	35 (44.30%)	46 (38.66%)	81
Total	78	118	196

P value =0.429

CHAPTER SIX

6.0 DISCUSSION

This study was carried out to describe the electrolyte profile of children with severe acute malnutrition (SAM) aged 6 -59 months, presenting to the University Teaching Hospital, Lusaka.

This study targeted children between 6- 59 months, as it is this critical age group that coincides with the weaning period and these children are at risk of developing SAM. During the weaning period, many mothers either introduce the wrong food, with poor nutritional value or introduce the right food in insufficient amounts, which is given infrequently. These poor feeding practises are attributed to their poor social economic status which renders them incapable of providing the required type of food for optimal growth.

Other mothers, who are HIV positive, stop breastfeeding altogether as part of Prevention of Mother to Child Transmission strategy, or due to their ill health. The mothers then introduce formula feeds, which may be constituted wrongly. In view of their economic limitations, some mothers constitute the formula feeds very dilutely as a way to conserve the formula feed and this contributes significantly to the poor growth of the children, with eventual development of SAM. Good hygiene practices are also not followed during the preparation of feeds, and this contributes to the onset of diarrhoeal diseases that contribute to electrolyte derangements.

In this study it was observed that the majority of participants , 75.1% (184/245)) were in the 12-35 months age group , followed by those in the 6-11months age group amounting to 21.6%(53/245).

This finding is similar to results found in a study done by Gangaraj S. et al, (in 2008-2009), in Kamla Raja Hospital in India, with majority of severely malnourished children being 6-12 months (30.26%) and 13-24months (32.8%) (**58**).

On admission, day 1 (n=243), 54.73% (133/243) had hyponatremia (Na+<135mmol/l), 4.94% (12/243) had hypernatremia (Na>145mmol/l), and 40.33% (98/243) had normal serum sodium levels.

By day 3, 108 out of the 243 participants had died, 44 withdrew from the study,17 absconded,-were absent from the ward for 48hours, 22 left against medical advice and 11 were transferred to the isolation ward because they were diagnosed with tuberculosis, leaving only 41 participants . 60.98% (25/41) had hyponatraemia. Out of the 25 participants, 16 were hyponatremic even on day 1 while 9 developed hyponatremia after admission and coincidentally also developed diarrhoea. The 16 patients who were still hyponatremic on day 3 all had diarrhoea of variable duration. 10 had persistent diarrhoeal disease (PDD) while 6 were admitted with acute diarrhoeal disease (ADD). Stools were collected for microscopy and culture for all the patients admitted with persistent diarrhoeal disease and 8 of them had cryptosporidium isolated in their stool. These patients were treated with the standard low osmolarity ORS that had more sodium compared to ReSoMal.

With the shortage of staff experienced often in the malnutrition ward, the hydration of some of these patients were not monitored adequately as was evident on the stool charts of the patients and thus some patients were not receiving the prescribed amounts of resomal on time. The stool charts indicated how much weight patients had lost during the episodes of diarrhoea and the interventions that were instituted for the fluid deficits. With only one ward attendant per shift, and one or two nurses per shift to monitor the hydration of a large number of patients with diarrhoea, the management of the children was a challenge. The presence of caregivers and other sibling on the ward made the already congested ward even more congested and this impacted negatively on the quality of service. This could explain why some patients still had electrolyte derangements by day 3 and explain why so many caregivers absconded from the ward or left against medical advice.

4.88% (2/41) participants had hypernatremia and 34.15% (14/41) had normal serum sodium.

By day 8, 10 more participants had died, 6 withdrew and 7 absconded leaving 18 participants. 50% (9/18) had hyponatraemia, (7 of whom were hyponatremic from

day 1, 2 developed hyponatremia after admission on day 8), 5.56% (1/18) had hypernatremia, and 44.44% (8/18) had normal serum sodium.

Majority of the participants -57.55% (141/245) had diarrhoea of variable duration while 42.45% (104/245) had no diarrhoea. This is similar to the results in a study by Irena A.H.et al (2009) on Acute diarrhoeal disease in severely malnourished children done in Lusaka – UTH, which indicated that the majority of severely malnourished children presenting to UTH had diarrhoea- 67.3% and these children had two and a half increased odds of mortality compared to those who did not have diarrhoea (**30**).

Of the 133 (54.73%) participants with hyponatremia, 54.14% (72/133) had diarrhoea, while 45.86% (61/133) had no diarrhoea. Of the 12 (4.94%) patients with hypernatremia, 75% (9/12) had diarrhoea and 25% (3/12) had no diarrhoea. Of the 98 participants with normal serum sodium , 59.18% (58/98) had diarrhoea while 40.82% (40/98) had no diarrhoea. Statistical analysis gave a p value of 0.329, indicating that there was no significant association between serum sodium levels and diarrhoea.

These findings are contrary to what Gangaraj et al (2013) found in their study where 31.57% had hyponatremia and 15.7% had hypernatremia. 40.8% of patients with diarrhoea and 14.8% of patients with no diarrhoea had hyponatremia (p=0.019 < 0.05) and 4.25% of patients with diarrhoea and 18.5% of patients with no diarrhoea had hypernatremia (p=0.62). There was significant hyponatremia in malnourished children who had diarrhoea or vomiting (**58).**

The findings in this study were also contrary to a study done in Pakistan by Y.Memon et al (2004), that showed that electrolyte disturbance were mostly seen in patients with severe acute malnutrition and the electrolyte disturbance mostly affected the serum potassium seen in 48(48%) and bicarbonate seen in 56(56%) cases while sodium imbalance is seen in 25(25%) cases. However the study also showed that acidosis and hyponatremia were seen more frequently in those who had diarrhoea as compared to those who had no diarrhoea (**45**) which was similar in this study.

These findings were also similar to the findings in a study by Z.T-Khine el al in Burma that showed that malnourished children lost more sodium in their stools and

urine during diarrhoea, so that they had significantly diminished gut net sodium balance and significantly diminished total body sodium balance causing hyponatremia **(37).** Theoretically, this is expected because sodium tends to be lost in the stool during episodes of diarrhoea, resulting in hyponatremia.

On day 1, of the 133 participants with hyponatremia, 25 of them had severe hyponatremia (Na+<120mmol/l), 18(72%) of whom had diarrhoea and 7(46.7%) of whom had no diarrhoea.

Severe hyponatremia can have deleterious effects on the patients. Severe hyponatremia can cause anorexia, nausea, emesis, malaise, lethargy, confusion, agitation, headache, seizures, coma, and decreased reflexes (36), which some of our patients with hyponatremia manifested.

In view of the sodium losses in stool during episodes of diarrhoea, patients with persistent diarrhoeal disease (PDD) with SAM are therefore more prone to develop hyponatremia and thus would benefit more when hydrated with the standard ORS because it has a higher sodium content than from ReSoMal. A few patients with PDD in this study had their stool cultured and cryptosporidium was isolated. These patients were rehydrated with the standard ORS and their serum electrolytes normalized after a few days.

By day 8, the 9 patients who still had hyponatremia were the same patients we were treating for Persistent diarrhoeal disease (n=10) and the stool culture results indicated that the patients had cryptosporidiosis., which causes a very watery diarrheal and PDD. 2 out of the 9 patients had convulsions, thought to have been due to electrolyte derangements, particularly hyponatremia as their sodium levels were < 120mmol/l, and other causes of convulsions were excluded in the patients, i.e. they had normal CSF and no growth on blood culture. These results were discussed with the malnutrition ward team and it was advised that these patients would benefit more from the low osmolarity oral rehydration solution (ORS) which has more sodium content than the resomal to help correct the hyponatremia. Convulsions were controlled and the patients` sodium levels were corrected eventually with the ORS.

A study in Bangladesh by N.Alam et al, looked at the Efficacy and safety of a modified oral rehydration solution (ReSoMaL) in the treatment of severely

malnourished children with watery diarrhoea. The results showed that ReSoMaL has a large beneficial effect on potassium status compared with standard ORS. However, ReSoMaL therapy may result in symptomatic hyponatremia and seizures in patients with severe diarrhoea (40).

In terms of potassium, on day 1, majority had hypokalemia; 36.6% (86/235) had hypokalemia, 34.47% (81/235) had hyperkalemia , and 28.94% (68/235) had normal serum potassium levels. 62.79% (54/86) of those with hypokalemia had diarrhoea and 32.7% (32/86) did not have diarrhoea. Of the patients with hyperkalemia (n=81), 45.68% (37/81) had diarrhoea while 54.32% (44/81) had no diarrhoea. 67.65% (46/68) of patients with normal serum potassium had diarrhoea while 32.35% (22/68) had no diarrhoea.

Statistical analysis indicated that patients with diarrhoea were more likely to have hypokalemia as a potassium derangement, (P=0.015<0.05). This is similar to the study by Gangaraj et al (2013) where there was significant hypokalemia 61.22% in patients with diarrhoea compared to 33% with no diarrhoea, p=0.018 (**58**). This is so because in addition to sodium, potassium is also lost in stool during episodes of diarrhoea.

Patients with diarrhoea were given both feeds (F75) and fluids (ReSoMal) with high potassium content. Resomal is given for 2 hours initially, and then children are reweighed. Thereafter, the Resomal is given every 4 hours according to the stool chart and the patient's weight. Over time, with nutritional rehabilitation, it is expected that the reductive adaptation, which children with SAM suffer from, is reversed and the electrolytes normalise.

On day 3, 85.37% (35/41), had hyperkalemia, 2.44% (1/41) had hypokalemia and 12.20% (5/41) had normal serum potassium levels.
 Out of the 18 participants on day 8, 1 sample was not analysed for potassium due to no reagents, thus 17 participants were analysed. 5.88% (1/17) had hypokalemia, 72.22% (13/17) had hyperkalemia and 17.65% (3/17) had normal serum potassium.

By day 3 and 8, only 1 patient had hypokalemia. This indicates that the rehydration solution helped to correct the hypokalemia. The patient with hypokalaemia on day 3

was the same patient with hypokalemia on day 8. This patient did not have diarrhoea. It was later discovered that the caregiver was not giving feeds to the patient and she opted to give other home feeds. The caregiver was re-counselled on the importance of restricting feeds to those provided for in the malnutrition ward. The feeding of the patient was supervised by the nurses and with improved compliance to feeding, patient improved and was later discharged. This shows that electrolyte derangements in patients with SAM do occur even in patients with no diarrhoea and is attributed to the reductive adaptation that these children undergo. In such cases, electrolytes are eventually corrected with nutritional rehabilitation

If left uncorrected, hypokalemia alters function of several organs and prominently affects the cardiovascular system, neurological system, muscle and kidney. In profound potassium deficiency, muscle paralysis can occur (**42**). Ortuno et al reported hypokalemic induced paralysis secondary to acute diarrhoea in their case series (**57**). Hypokalemia may be sub clinical in malnourished children but during diarrhoeal illness it becomes obvious clinically and may manifests as hypotonia, abdominal distension, paralytic ileus, cardiac arrhythmia and respiratory distress. This would explain why some of the children admitted to the malnutrition ward have abdominal distension with constipation.

The alarming number of patients with hyperkalemia 81, (34.47%) was noted with great concern and discussed with the malnutrition team. However, the levels of hyperkalemia were incompatible with life and did not tally with the patient's clinical picture. The laboratory was notified and an attempt was made to ensure that blood samples got to the laboratory on time after collection. Some patients with hyperkalemia died before we could repeat the electrolytes to confirm the derangement. Some results were available on day 3 when it was time to analyse samples for day 3. 15 participants still had hyperkalemia even on day 3, and 20 participants developed hyperkalemia on day 3. 13 participants out of 17 had hyperkalemia on day 8. This was contrary to studies done by Gangaraj et al (**58**), Memon Y et al (**45**) and Kathryn et al (**38**), who reported no participant with hyperkalemia.

Further scrutiny revealed that collected samples would get to the laboratory within an hour but not processed immediately due to shortage of staff in laboratory or lack of

reagents at that moment. This could have resulted in haemolysis of most of the samples, hence the hyperkalemia and so hyperkalemia in this study was thus attributed largely to laboratory error. This would explain the discrepancy in the proportion of patients with hyperkalemia between those in this study and the studies referred to above.

Out of the 243 participants analysed, 30.45% (74/243) had bilateral pitting pedal oedema and 69.55% (169/243) had severe wasting. Out of the 243 participants, 83.95% (204/243) had electrolyte derangements while 16.05% (39/243) had normal electrolytes. On comparison of the electrolyte derangements between those with severe wasting and those with oedema, it was observed that majority of the electrolyte derangements were seen in the participants with severe wasting i.e. 69% (141/204) and only 30.9% (63/204) of participants with oedema had electrolyte derangements. However, analysis of the electrolyte profile of participants with severe wasting and oedema , demonstrated that there was no statistically significant difference between the two groups ,P > 0.05 and that electrolyte derangements were common in both groups.

This is similar to the study by Gangaraj et al (**58**), who found no significant difference in the electrolyte profile of malnourished children with oedema and those without oedema.

The possible explanation for this lies in the phenomenon called reductive adaptation that occurs in patients with SAM, mentioned earlier. This phenomenon is seen in both those with severe wasting and those with oedema thus the electrolyte derangements seen in both of these two groups are similar. However, Black and Milne et al, in 1952 found that there is good evidence that potassium deficiency promotes retention of water and sodium and therefore may produce oedema, which disappears on administration of potassium (**59**).

234 out of the 245 participants were tested for HIV infection and analysed for serum sodium while 11 were not tested because they were admitted after working hours during the week or over the weekend and died before the test could be done. 79.06% (185/234) were HIV negative and 20.94% (49/234) were HIV positive. This was

contrary to the study done by Amadi B. et al (in 2001) at the University Of Zambia where 54% of patients with severe acute malnutrition were HIV positive (**33**).

It was evident that majority of electrolyte derangements were seen in those who were HIV negative. 54.27% (127/234) had hyponatremia, 98 (77.17%) of whom were HIV negative and 29(22.83%) were HIV positive. 40.60% (95/234) had normal serum sodium levels, 17(17.90%) of whom were HIV positive and 78(82.10%) were HIV negative. 5.13% (12/234) patients had hypernatremia, 9(75%) of whom were HIV negative and 3(25%) were HIV positive. Statistical analysis gave a P value of 0.629 (P > 0.05) which indicated that there was no significant association between serum sodium levels and HIV status.

Of the 234 patients tested for HIV, only 226 patients were analysed for potassium. 36.73% (83/226) had hypokalemia, 67(80.7%) of whom were HIV negative while 16(19.3%) were HIV positive. 28.32% (64/226) had normal potassium levels, 15(23.44%) of whom were HIV positive while 49(76.56%) were HIV negative. 35% (79/226) patients had hyperkalemia,18(22.78%) of whom were HIV positive and 61(77.22%) were HIV negative. Comparison of the serum potassium levels between those who were HIV positive and those who were HIV negative showed no significant statistical difference (P=0.796>0.05) and electrolyte derangements were common in both groups.

196 out of 245 participants had a known outcome by the end of the study, 47 either absconded or left the hospital against medical advice. 118 of the 196 died while 78 were alive within 8 days following admission. 108 (91.53% died within 48 hours following admission while 10 (8.47%) died within 1 week of admission. This is contrary to the study by Irena A.H et al (2009) where 30.6% (53/173) died within 48 hours and 65.3% (113/173) died within 1 week of admission(**4**).

84.18% (165/196), had abnormal electrolytes while 15.82% (31/196) had normal electrolytes. 40% (66/165) of those with abnormal electrolytes were alive while 60% (99/165) of them died. 52.6% (103/196) had hyponatremia, 36.89% (38/103) of whom were alive and 63.11% (65/103) of whom died. 42.35% (83/196) had normal sodium, 42.17% (35/83) of whom were alive and 57.83% (48/83) died. 5.10%

(10/196) had hypernatremia, 50% (5/10) of whom were alive and 50% (5/10) of whom died. Analysis of serum electrolytes to determine an association between electrolytes and outcome was done, and no significant statistical difference was noted between those who died and those who were alive, P>0.05. Therefore, death was not directly associated with electrolyte derangements.

Further analysis showed that among those who died, 61.02% (72/118) had diarrhoea while 38.66% (46/118) had no diarrhoea. 20 of those with diarrhoea were admitted with hypovolemic shock, and despite treating them according to the WHO guidelines, they died eventually.

This high percentage of children dying was contrary to the study done by Amadi et al(2001), at UTH where of the 200 children recruited, 39 (19.5%) died within 28 days and cryptosporidiosis and severe wasting were the only independent predictors of death (**33**). This difference could be attributed to the fact that this study was done during the peak season of malnutrition which coincides with the rainy season. The rainy season is associated with a lot of diarrhoeal disease that predispose the patients to malnutrition and most of the patients, 139 (57.20%) admitted during this study had diarrhoea. However, diarrhoea was not a predictor of death in this study and so other co-morbid conditions may have contributed to the death of the patients.

High mortality rates have been reported from various hospitals worldwide, ranging from 10 – 30 % and the majority of deaths occur in the first few days of admission. Patients admitted to the malnutrition ward have other co- morbid conditions, the most common of which include diarrhoea with dehydration or hypovolemic shock, pneumonia, severe anaemia, sepsis and HIV. Bronchopneumonia and gram negative sepsis are the most fatal infections and may be responsible for the death of the patients in combination with the different life threatening electrolytes derangements. Difficulties in making a diagnosis are encountered in patients with SAM because the usual responses of fever and leucocytosis are absent. This is why in addition to the routine full blood counts done, cultures of urine, stool and blood, and Chest x-rays were also done for proper diagnosis and treatment of patients.

This study was powered to describe the electrolyte derangements with prevalence estimated at 20%, and was not powered to detect any differences in the different comparison groups. This would explain why there were no associations between the electrolyte derangements and the factors that were assessed.

It was observed from this study that majority of patients with SAM had electrolyte derangements 204 (83.95%) and that the number of participants with different electrolyte derangements tended to reduce progressively from day1 to day8 with the interventions available in the malnutrition ward, in terms of fluids and nutritional rehabilitation. This indicates that early detection and intervention for the different life threatening electrolyte derangements may help to reduce on morbidity and mortality.

It should be noted however, that in malnutrition serum electrolytes do not reflect the body content but only the circulating concentration, thus high serum potassium masks intracellular potassium deficiency while low serum sodium mask sodium overload but they have importance in immediate therapy in cases of life threatening derangements. (56).

CHAPTER SEVEN

7.0 CONCLUSION

Majority of patients with SAM had electrolyte derangements 83.95%.

Majority of patients enrolled had diarrhoea 57.55%

Hypokalemia was significantly higher in patients with diarrhoea compared to those with no diarrhoea.

No significant statistical associations were made between the sodium electrolyte profile in those with diarrhoea and those without diarrhoea, between those with the different types of malnutrition, and between those with HIV and those who were HIV negative.

There was no significant statistical difference in the electrolyte derangements seen in participants who died and those who were alive.

Electrolyte derangements may not manifest clinically on admission but may become obvious during episodes of diarrhoea when more electrolytes are lost in the stools or vomitus. Therefore, determination of the electrolyte profile of patients with SAM immediately on admission and also on proceeding days after admission is vital as it helps the clinician to decide on the most appropriate fluids to give to help reduce on the morbidity and mortality associated with life threatening electrolyte derangements.

7.1 RECOMMENDATIONS

- All patients admitted to the malnutrition ward should have electrolytes done on admission and repeated as guided by the results received and by the ongoing losses of the patient.

- The laboratory should be supported with provision of adequate staff so that electrolytes are processed in good time for appropriate emergency interventions to be carried out

- The laboratory should be supported to have adequate reagents at all times so that the processing of electrolytes is sustainable.

- With the high prevalence and observed effect of the diarrhoea on the electrolytes, it calls for a strengthened community level intervention, targeted towards prevention and treatment of diarrhoea.

- Issues on improved sanitation at community level need to be addressed to aid reduction of diarrhoeal diseases.

- A larger study should be done and powered to determine whether statistically significant associations do exists between those with diarrhoea and those without diarrhoea, between the different types of malnutrition and between those with HIV and those without HIV.

7.2 LIMITATIONS

- Patients presenting to UTH at night or over the weekend were missed out. This may have introduced a selection bias
- The laboratory had challenges with availability of reagents at times and so this affected the analysis of samples of some of the participants .
- Shortage of staff in the laboratory to process the electrolytes was also a problem and so some of the samples were not processed on time and may have led to haemolysis of the samples and hyperkalemia.
- Supervision of rehydration is a challenge owing to the serious staff shortages that are present on the malnutrition ward. This means that the hydration of some patients with diarrhoea may not have been supervised adequately and this may have affected their recovery.

7.2 Implications / Benefits

- Determining the most common electrolyte derangements will improve management of patients with SAM and ultimately reduce morbidity and mortality resulting from electrolyte derangement.

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APPENDICES

Appendix I: INFORMATION SHEET

To determine electrolyte profile of severely malnourished children aged 6-59 months, presenting to the University Teaching Hospital, Lusaka.

Why are we giving you this form?

We are giving you this form, so as to give you information about the named study and also to give you a chance to ask questions about this study. Then you can decide if you would like to take part in this study that is trying to find out the electrolyte profile of severely malnourished children presenting to the University Teaching Hospital (UTH).

2. **Who is carrying out this study?**

Dr. Natasha N. Ngwenya as part of specialist training at the University Of Zambia ,School Of Medicine, Department of Paediatrics and Child Health.

3. **Background Information**

You are being asked to take part in the above mentioned study, were we would like to find out the electrolyte profile of children presenting to UTH, on the day of admission as well as on days 3 and 8, after commencement of treatment. By participating in this study, we will be able to get the information that may help in order to make relevant policies and interventions for this problem of electrolyte imbalances in children with Severe acute Malnutrition (SAM). We believe this is very vital information to all of us and you would help by   participating in this study.

4. **What Happens In This Research Study?**

You will be interviewed now and then your child will have a clinical examination. Then anthropometric measurements will be done, to check your child`s weight and height in order to establish the weight for height parameters. **3 mls of blood will** then be taken on day 1 to screen for electrolytes – **Sodium** and **Potassium**.

Blood collection will be repeated on day 3 and day 8 to monitor the changes that may have occurred in the electrolyte profile.

The information collected will be kept confidential.

5. **Possible Problems**

We believe that the processes being used will not be harmful to you and the **child** participating in this study although needle prick would cause pain to your child while collecting blood samples.   However if we notice anything peculiar to you or your child during or after information is collected, we will let you know and facilitate your

(you and your child) seeking appropriate medical help **at the UTH paediatrics emergency room.**

6. Benefits

It is hoped that the study will help determine which of the severely malnourished children are at risk for life-threatening electrolyte derangements so that they are attended to most aggressively. This will help reduce morbidities and mortalities that result from life- threatening electrolyte derangements.

7. Confidentiality

Your name will never be made public by the investigators. The medical record will be treated the same as all medical records at the health centres. A code number that makes it very difficult for anyone to identify you will identify the research information gathered during this study from you. All information will be stored in a secure place. Information from this study may be used for research purposes and may be published; however, your name will not be made public by the investigators**.** It is possible that, after the study is over, we may want to look again at the laboratory and interview record data collected during this study to help us answer another question. If this happens, still your name will not be made public by the investigators.

8. Research Related Injury

In the event that a problem results from a study-related procedure, Dr Ngwenya in LUSAKA should be notified (0n +260 976 433304) or contact ERES Converge IRB (see contact details section), and you or **your** child will be facilitated to seek and receive appropriate medical care at **the** health facility.

9. Contact Details

Should you want further information about this study or your rights as a participant please use the details provided below.

Dr. Ngwenya	ERES CONVERGE IRB
Principle Investigator.	**33 Joseph Mwilwa Road**
University Teaching Hospital,	**Rhodes Park**
Department of Paediatrics and Child Health.	**LUSAKA**
Lamya: 260-976 433304	**Tel: 0955 155633/4**
Email:natnoria@yahoo.co.uk	**E-mail: eresconverge@yahoo.co.uk**

Appendix II: CONSENT FORM

To determine the electrolyte profile of severely malnourished children aged 6-59 months, presenting to the University Teaching Hospital in Lusaka.

Participant

I_____ (participant's parent or guardian's name, signature or thumb-print) have been informed about the study .I volunteer to have my child participate in the study. A copy of this form signed by me and one of the study investigators is being given to me.

Signature/Thumb_____

Date (D/M/Y) _____

Interviewer

I have explained this research study to the subject. I am available to answer any questions now or in the future regarding the study and the subject's rights.

Signature of Investigators & Printed Names   Date of signature

Signature_____

Date (D/M/Y) _____

1. Why are we giving you this form?

We are giving you this form, so as to give you information about the named study and also to give you a chance to ask questions about this study. Then you can decide if you would like to have your child take part in this study that is trying to find out the electrolyte profile of severely malnourished children, aged 6-59 months, presenting to the University Teaching Hospital (UTH).

2. Who is carrying out this study?

Dr. Natasha N Ngwenya who is training to become a children's doctor

3. Background Information

Electrolyte derangements are common in children with severe acute malnutrition because of the changes that take place in the body to try and survive on limited calories. The doctor will talk to you and your guardian then she will examine your child. The doctor will then measure your child's weight and height to establish his/her weight for height parameter. In addition the doctor will collect 3 ml of blood, which

shall be taken to the laboratory to be screened for electrolytes – **sodium** and **potassium.** Results will be ready within 2 hours after collection. This will be a little painful. Another sample will be collected on day 3 and day 8 to monitor any changes that may have occurred after taking the feeds. The importance of you taking part in the study is that you will assist the doctor to try and come up with information that may be useful in helping to decide better ways of treating children with severe acute malnutrition with life-threatening electrolyte derangements.

_____

APPENDIX III: HISTORY DATA SHEET

Identification   :

Name of participant   :

Initials of participant   :

Subject study number:

Part I: Demographics

Age (completed year)

 Sex   1) Male   2) Female

Number of people in the home

Number of rooms in the house

Part II: presenting complaints

2.1 Diarrhoea   1) Yes   2) No

2.2 Vomiting   1) Yes   2) No

2.3 Poor appetite   1) Yes   2) No

2.4 Bi-pedal swelling   1) Yes   2) No

2.5 Weight loss   1) Yes   2) No

2.6 Cough   1) Yes   2) No

2.7 Breathing difficulties   1) Yes   2) No

2.8 Fever   1) Yes   2) No

2.9 Night sweats   1) Yes   2) No

2.10 Fitting   1) Yes   2) No

2.11 Previous admissions to health centre   1) Yes   2) No

Part III: Past medical history

3.1 Tuberculosis   1) Yes   2) No

3.2) Measles   1) Yes   2) No

3.3 HIV   1) Yes   2) No

APPENDIX IV: PHYSICAL EXAMINATION DATA SHEET

Date   :

Subject full name   :

Subject initials   :

Subject study number:

General appearance: 1) Well   2) Ill

 Pale, jaundiced, in respiratory distress, Bi-pedal oedema, dermatosis, severe wasting-prominent ribs, prominent spine, `Baggy pants`, loose axillary skin

Vitals

Pulse:

Respiratory rate:

Temp:

Anthropometry

Weight

Height

Weight for height – (Z- Score) -

Chest

    Abnormal sounds   1) Yes   2) no

 CVS

  Cardiac murmur   1) yes   2) no

   If murmur, characterise . . . .

 Abdomen

    Hepatomegaly   1) yes   2) No

    Splenomegaly   1) Yes   2) No

Musculoskeletal system

 Joint tenderness/swelling   1) Yes   2) No

    If yes, characterise . . . .

Integumentary system

 Skin rash   1) yes   2) No

  If yes, characterise . . . .

Central nervous system

 Abnormality   1) yes   2) No

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Oral cavity

Clear   1) yes   2) no

Oral candidiasis   1) yes   2) no

Treatment given, if any . . . .

Referrals . . . .

Clinician name   signature

APPENDIX V: LABORATORY DATA SHEET

Subject study number

Subject initials

Site

Date specimen collected

1.0 Electrolyte profile, presence of diarrhoea, type of SAM and HIV status

Patient code	Electrolyte	On admission	Day3	Day 8	Diarrhoea	Type of SAM	HIV Infection
	Sodium						
	Potassium						

Signature

APPENDIX VI: CRITICAL CARE PATHWAY

CRITICAL CARE PATHWAY (CCP) — SEVERE MALNUTRITION WARD

NAME _____ M F DATE OF BIRTH OR AGE _____ DATE OF ADMISSION _____ TIME _____ HOSP. ID NUMBER _____

INITIAL MANAGEMENT

Comments on pre-referral and/or emergency treatment already given:

SIGNS OF SEVERE MALNUTRITION

Severe wasting? Yes No

Oedema?	0	+	++
Dermatosis?	0	+	++	+++ (raw skin, fissures)

Weight(kg): _____
Height/length (cm): _____
SD score: _____ or % of median: _____

TEMPERATURE

_____ °C rectal axillary

If rectal <35.5°C (95.9°F), or axillary <35°C (95°F), actively warm child.
Check temperature every 30 minutes.

BLOOD GLUCOSE (mmol/l):

If < 3mmol/l and alert, give 50 ml bolus of 10% glucose or sucrose (oral or NG).
If <3 mmol/l and lethargic, unconscious, or convulsing, give sterile 10%
glucose IV: 5 ml x _____ kg (child's wt). Then give 50 ml bolus NG.
Time glucose given: _____ Oral NG IV

HAEMOGLOBIN (Hb) (g/l):

or Packed cell vol (PCV): _____ Blood type:
If Hb < 40 g/l or PCV<12%, transfuse 10 ml/kg whole fresh blood (or 5-7 ml/kg
packed cells) slowly over 3 hours. Amount: _____ Time started: _____ Ended: _____

EYE SIGNS

None Left Right MEASLES Yes No
Bitot's spots Pus/Inflammation Corneal clouding Corneal ulceration

If ulceration, give vitamin A & atropine immediately. Record on Daily Care page.
Oral doses vitamin A:

< 6 months	50 000 IU
6 - 12 months	100 000 IU
> 12 months	200 000 IU

FEEDING

Begin feeding with F-75 as soon as possible. (If child is rehydrated,
reweigh before determining amount to feed. New weight: _____ kg)
Amount for 2-hourly feedings: _____ ml F-75 * Time first fed: _____
* If hypoglycaemic, feed ¼ of this amount every half hour for first 2 hours; continue
until blood glucose reaches 3 mmol/l.
Record all feeds on 24-hour Food Intake Chart.

ANTIBIOTICS (All receive)

Drug / Route	Dose / Frequency / Duration

SIGNS OF SHOCK

None Lethargic/unconsious Cold hand Slow capillary refill> 3 seconds) Weak/fast pulse

If lethargic or unconscious, plus cold hand, plus either slow capillary refill or weak/fast pulse, give oxygen. Give IV glucose
as described under Blood Glucose (left). Then give IV fluids:

Amount IV fluids per hour: 15 ml x _____ kg (child's wt) = _____ ml

	Start:	Monitor every 10 minutes	*2nd hr:	Monitor every 10 minutes
Time				
Resp. rate				
Pulse rate				

* If respiratory & pulse rates are slower after 1 hour, repeat same amount IV fluids for 2nd hour; then alternate ReSoMal and F-75 for
up to 10 hours as in right part of chart below. If no improvement on IV fluids, transfuse whole fresh blood (or 5-7 ml/kg
packed cells) slowly. (See left, Haemoglobin.)

DIARRHOEA

Watery diarrhoea? Yes No → If diarrhoea, For up to 10 hours, give ReSoMal and F-75 in alternate hours.
Blood in stool? Yes No circle signs Monitor every hour. Amount of ReSoMal to offer:*
Vomiting? Yes No present: 5 to 10 ml x _____ kg (child's wt) = _____ to _____ ml ReSoMal

Skin pinch goes back slowly
Restless/irritable Lethargic Thirsty
Sunken eyes Dry mouth/tongue No tears

If diarrhoea and/or vomiting, give ReSoMal. Every
30 minutes for first 2 hours, monitor and give:*
5 ml x _____ kg (child's wt) = _____ ml ReSoMal

	Start:				
Time					
Resp. rate					
Pulse rate					
Passed urine? Y N					
Number stools					
Number vomits					
Hydration signs					
Amount taken (ml)	F-75	F-75	F-75	F-75	F-75

* Stop ReSoMal if: increase in pulse & resp. rates Jugular veins engorged Increasing oedema, e.g., puffy eyelids

Time of 1st dose

UN logo

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APPENDIX VII; STOOL CHART

STOOL CHART

- WEIGH AND ASSESS ALL PATIENTS WITH DIARRHOEA EVERY 4 HOURS (10hr; 14hrs; 18hrs; 22hrs; 02hrs; 6hrs)
- STOP ReSoMal DRIP DURING FEED & CONTINUE DRIP AFTER FEEDING

Patient's name:………………………………… Sex/Age:………Date of Admission: ……… Wt on adm…..

Date	Time	No. of stools and No. of times vomitted	Weight	Start ReSoMal Drip for all patients with >4 stools
				• Start with 20ml/kg/2hrs initially, THEN weigh after 2 hrs • IF <u>WEIGHT LOSS,</u> Give 10ml/kg/hr for 4 hours • IF <u>WEIGHT STATIC,</u> Give 5ml/kg/hr for 4 hours • IF <u>WEIGHT GAIN,</u> Give ReSoMal 50 – 100/ loose stoo If on initial assessment passed stool <4 stools advice caretaker to: • Give ReSoMal 50-100/loose stool

APPENDIX VIII: APPROVAL BY ERES CONVERGE

30th April, 2014

Ref. No. 2014-Mar-016

The Principal Investigator
Dr. Natasha N. Ngwenya
P.O. Box 36481,
LUSAKA.

Dear Dr. Ngwenya,

**RE: A STUDY TO DETERMINE THE ELECTROLYTE PROFILE OF
SEVERELY MALNOURISHED CHILDREN AGED 6-59 MONTHS
PRESENTING TO THE UNIVERSITY TEACHING HOSPITAL,
LUSAKA.**

Reference is made to your corrections dated 28th April, 2014. The IRB members resolved
to approve this study and your participation as principal investigator for a period of one
year.

Review Type	Ordinary	Approval No. **2013-Mar-016**
Approval and Expiry Date	Approval Date: 30th April, 2014	Expiry Date: 29th April, 2015
Protocol Version and Date	Version-Nil	29th April, 2015
Information Sheet, Consent Forms and Dates	• English	29th April, 2015
Consent form ID and Date	Version-Nil	29th April, 2015
Recruitment Materials	Nil	29th April, 2015
Other Study Documents	Data Sheets – History, Physical Examination and Laboratory. CCP and Stool Chart.	29th April, 2015
Number of participants approved for study	360	29th April, 2015

Specific conditions will apply to this approval. As Principal Investigator it is your responsibility to ensure that the contents of this letter are adhered to. If these are not adhered to, the approval may be suspended. Should the study be suspended, study sponsors and other regulatory authorities will be informed.

Conditions of Approval

- No participant may be involved in any study procedure prior to the study approval or after the expiration date.
- All unanticipated or Serious Adverse Events (SAEs) must be reported to the IRB within 5 days.
- All protocol modifications must be IRB approved prior to implementation unless they are intended to reduce risk (but must still be reported for approval). Modifications will include any change of investigator/s or site address.
- All protocol deviations must be reported to the IRB within 5 working days.
- All recruitment materials must be approved by the IRB prior to being used.
- Principal investigators are responsible for initiating Continuing Review proceedings. Documents must be received by the IRB at least 30 days before the expiry date. This is for the purpose of facilitating the review process. Any documents received less than 30 days before expiry will be labelled "late submissions" and will incur a penalty.
- Every 6 (six) months a progress report form supplied by ERES IRB must be filled in and submitted to us.
- ERES Converge IRB does not "stamp" approval letters, consent forms or study documents unless requested for in writing. This is because the approval letter clearly indicates the documents approved by the IRB as well as other elements and conditions of approval.

Should you have any questions regarding anything indicated in this letter, please do not hesitate to get in touch with us at the above indicated address.

On behalf of ERES Converge IRB, we would like to wish you all the success as you carry out your study.

Yours faithfully,
ERES CONVERGE IRB

Dr. E. Munalula-Nkandu
BSc (Hons), MSc, MA Bioethics, PgD R/Ethics, PhD
CHAIRPERSON

APPENDIX IX: APPROVAL OF AMENDEMENTS OF STUDY

33 Joseph Mwilwa Road
Rhodes Park, Lusaka
Tel: +260 955 155 633
+260 955 155 634
Cell: +260 966 765 503
Email: eresconverge@yahoo.co.uk

I.R.B. No. 00005948
F.W.A. No. 00011697

9th February, 2015

Ref. No. 2014-Mar-016

The Principal Investigator
Dr. Natasha N. Ngwenya
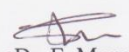P.O. Box 36481,
LUSAKA.

Dear Dr. Ngwenya,

**RE: A STUDY TO DETERMINE THE ELECTROLYTE PROFILE OF
SEVERELY MALNOURISHED CHILDREN AGED 6-59 MONTHS
PRESENTING TO THE UNIVERSITY TEACHING HOSPITAL,
LUSAKA.**

Reference is made to your request to amend the study.

The change of laboratories may create a problem of discrepancy with results. The UTH
laboratory is notorious for unreliability of results and quality control, but considering the
current situation and need for progress permission may be granted, but the author has to
ensure safety and reliability of the laboratory results.

Yours faithfully,
ERES CONVERGE IRB

Dr. E. Munalula-Nkandu
BSc (Hons), MSc, MA Bioethics, PgD R/Ethics, PhD
CHAIRPERSON

Where Research Ethics and Science Converge