Prevalence and outcome of hypernatraemic dehydration among under-5 children with diarrhoea at the University Teaching Hospital, Lusaka, Zambia

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ABSTRACT

Diarrhoea is the second commonest cause of under-five mortality globally (second to Pneumonia) and kills one (10 percent) out of every ten children who die before their fifth birthday. In Zambia dehydration due to diarrhoea is a leading cause of morbidity and mortality among under-five children. Hypernatraemic dehydration is the most dangerous and fatal form of dehydration. Despite the availability of well known effective treatment modalities for dehydration in diarrhoea, mortality remains high in many developing countries. The situation is not any different in Zambia and at The University Teaching Hospital (UTH) Department of Paediatrics. Therefore, this study sought to determine the prevalence and outcome of hypernatraemic dehydration as a possible contributing factor to the high mortality rate among children with diarrhoea. It was a cross-sectional study conducted at the UTH Department of Paediatrics. The study population was under-five children presenting with acute diarrhoea with dehydration. Independent variables were age, sex, feeding modality, prior ORS therapy, rotavirus vaccine status and serum sodium. The dependent or outcome variables were discharge/mortality and duration of hospital stay. Data analysis was done with the help of SPSS version 20. There were a total of 148 participants with an almost 1:1 male/female ratio (73/75), the mean age of 14.7 months ranging 1-60 months. The prevalence of hypernatraemic dehydration was approximately 19 percent (29/148) among children presenting with diarrhoea and dehydration. Hypernatraemia was associated with a high risk of mortality (7/29) with an OR 5.8 (adjusted OR 3.6, 95% CI 2.9-8.0, p 0.002), compared to (7/74) OR 1.8 (adjusted OR 1.1, 95% CI 0.8-2.2, p 0.06), and (5/33) OR 3.1 (adjusted OR 2.3, 95% CI 1.7-4.4, p 0.03) for normal and low initial sodium level respectively. Hypernatraemia was also associated with longer hospital stay with a mean duration of 3.09 days (74.2hrs) compared to 2.01 days (48.2 hours) and 2.13 days (51.1 hours) for normal and low sodium respectively. Hypernatraemia is prevalent among under-five children presenting with diarrhoea at UTH department of paediatrics and a major contributing factor to high diarrhoeal associated mortality. Recognition of its occurrence through diligent laboratory services is therefore critical for appropriate patient care.

INTRODUCTION

Hypernatraemic dehydration is the most dangerous and fatal form of dehydration that occurs in children with diarrhoea and contributes greatly to mortality.1,2,3,4,5Diarrhoea is the commonest cause of dehydration and a major cause of mortality among under-5 children.6 As many as 10-20% of children with diarrhoea present with hypernatraemic dehydration.3,6 Dehydration may be due to many causes that result in a relative or absolute body water deficit in relation to solutes. Gastroenteritis, however, accounts for over 90% of cases of dehydration among children in developing countries.6,7 Despite well known cost-effective and straightforward control and treatment measures, dehydration due to diarrhoea continues to kill many children.6Diarrhoea is the second commonest cause of under-five mortality globally (second to Pneumonia) and kills one (10%) out of every ten children who die before their fifth birthday.6 The World Health Organisation (WHO) has thus established the integrated Global Action

Plan for the Prevention and Control of Pneumonia and Diarrhoea (GAPPD) whose goal is to end preventable childhood deaths due to diarrhoea and Pneumonia by 2025.6

In Zambia dehydration due diarrhoea is a leading cause of morbidity and mortality among under-five children.7 In 2013, over 2000 children are estimated to have died from the disease.7 This figure is underestimated as many more children die at home before even accessing care.7 Many more deaths still occur in health facilities depicting gaps in case management of children with diarrhoea. At The University Teaching Hospital (UTH) department of paediatrics, diarrhoea is among the leading causes of morbidity and mortality accounting for 6% of all admissions and 5% of all deaths in 2015.9 Oral rehydration solution (ORS) has shown to be effective in treating diarrhoea and associated physiological derangements especially correcting dehydration and electrolytes.10 With the widespread availability and use of ORS, most children with diarrhoea can be treated at home. However, some children still require health facility care for intravenous fluid administration even to the extent of requiring tertiary hospital care.10

Dehydration due to the fluid loss is the hallmark of any diarrhoeal disease is commonly associated with electrolyte imbalances, mainly hyponatreamia, hypernatreamia and hypokalaemia.10,11 Among the electrolytes imbalances associated with dehydration, hypernatraemia is associated with more severe dehydration and may not be readily amenable with the standard WHO treatment for dehydration.1,12Hypernatraemia is defined as serum sodium above 150mmol/l. It may occur in some children with diarrhoea, termed as hypernatraemic dehydration (WHO, 2005). It ensues from a more water deficit in relation to the body sodium content (Adroque and Madias, 2000). The main causes are prior therapies, especially concentrated drinks with high sugar content such as commercial soft/fruit drinks, concentrated formula and salt intake such as homemade ORS or iatrogenic through saline administration in hospitalised patients (Adroque and Madias, 2000; WHO, 2005). Given the high mortality among children due to diarrhoea in Zambia and at UTH, the prevalence of hypernatraemic dehydration was not known and a possible contributing factor.

MATERIALS AND METHODS

The study was conducted at the University Teaching Hospital Department of Paediatrics and Child Health. It was a cross-sectional study. The study involved the recruitment of children meeting the inclusion criteria and documenting clinical events as at discharge. The study population was under-five children with diarrhoea and dehydration meeting whose guardians consented to participate. Sampling was convenient, recruiting all children whose guardians consented. The sample size was 148 participants.

A questionnaire was used to collect data. The data captured independent variables which included; age, sex, prior therapy, rotavirus vaccination status, level of dehydration on admission and sodium level. The dependent variables captured were discharges or mortality and duration of hospital stay. Data was analysed using Statistical Package for Social Sciences (SPSS) version 20. Continuous numerical variables were analysed using means and medians, while categorical variables were analysed using simple proportions. Odds ratios were used to determine associations between the demographic features (independent variable) and the dependent variables (mortality/discharge). Multivariate analysis was used for adjusted odds ratios bearing in mind the many factors that may influence the outcomes.

Ethical consideration

The research was approved by the research ethics committee (ERES), and UTH granted permission to conduct the study in the institution. Written consent was obtained from parents/guardians.

RESULTS

Demographic characteristics of the study population

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

Rotavirus vaccination status and prior ORS therapy

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

Level of dehydration on admission and initial sodium level

Most participants presented severe dehydration (66.9%) and 8.8% (13/148) presented in shock. Of those presenting in shock, 46.2% (6/13) had hypernatraemia, 38.5% (5/13) had hyponatraemia, and only 15.4% (2/13) had normal sodium level. Among patients presenting in shock with hypernatraemia, 33.3% died. The overall mortality among patients in shock was 30.8%. The dehydration level may be related to the severity of diarrhoea which may correlate to some extent with the numbers of stools per day. However, the volume of stools is a factor to consider but often difficult to measure or estimate; hence, the crude proxy frequency is often used.

Duration of hospital stay

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

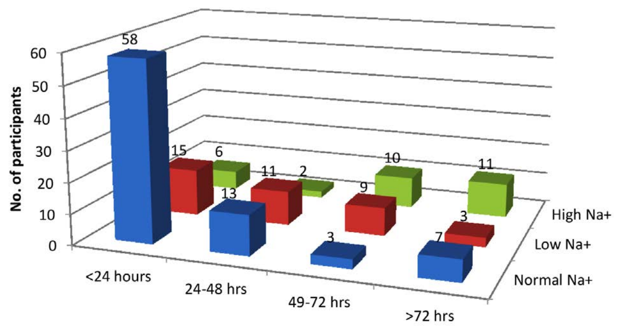

Figure 1: Duration of hospital stay in relation to mortality/discharge/sodium level

Initial sodium level evaluation in relation to discharge/mortality

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

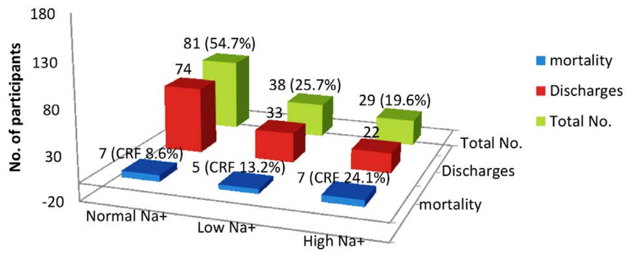

Figure 2: Number of participants in relation to Sodium level/discharges/mortality

Factors associated with mortality in a multivariate model

Table 1 shows the association of mortality with other variables in a cross-tabulation multivariate model. The variables entered in the model were age in months, level of dehydration, rotavirus vaccination status, prior ORS therapy, initial sodium level and mortality/discharge as the outcome variable. Young age below the age of 6 months was associated with high mortality with an odds ratio (OR) of 2.2 (adjusted OR 1.8, 95% CI 1.3-3.5, p 0.01) compared to the older age groups above six months. The level of dehydration was an obvious prognostic factor. A total of 5 children died of shock in the emergency room upon arrival or while being resuscitated during the study period; four others were brought in dead with a history of diarrhoeal disease. These groups were excluded from any further analysis. The risk of mortality was highest among children presenting in shock with an OR of 3.6 (adjusted OR 2.4, 95% CI 2.1-5.6, p 0.001) compared with an OR of 1.6 and 2.3 for patients with some dehydration severe dehydration respectively. Children who were rotavirus vaccinated had a relatively lower risk of mortality with an OR of 0.2 (adjusted OR 0.7, 95% CI 0.1-1.0, p 0.05), compared to OR 1.7 (adjusted OR 1.3, 95% CI 1.1-2.2, p 0.03) for unvaccinated children. Children with prior ORS use before presentation had a relatively low risk of mortality with an OR 0.4 (adjusted OR 0.8, 95% CI 0.2-1.0, p 0.009) compared with an OR of 2.9 (adjusted OR 1.7 95% CI 1.2-4.0, p 0.009) for children not treated.

Hypernatraemia was associated with a high risk of mortality with an OR 5.8 (adjusted OR 3.6, 95%

CI 2.9-8.0, p 0.002). Normal sodium level had an OR for mortality of 1.8 (adjusted OR 1.1, 95% CI 0.8-2.2, p 0.06) while low sodium had an OR of 3.1 (adjusted OR 2.3, 95% CI 1.7-4.4, p 0.03).

Table 1: **Association of mortality with other variables in a multivariate analysis**

Variable	*Number (N)*	*Unadjusted OR*	*Adjusted OR*	*95% CI*	*P-value*
Age (months)					
0-6	48	2.2	1.8	1.3-3.5	0.01
7-12	37	1.9	1.5	1.1-2.6	0.04
>12	63	1.4	1.1	0.8-1.8	0.08
Dehydration					
Some	36	1.6	1.0	0.8-2.1	0.1
Severe	99	2.3	1.6	1.4-4.1	0.02
Shock	13	3.6	2.4	2.1-5.6	0.001
Rota vaccine					
Yes	132	0.2	0.7	0.1-1.0	0.05
No	16	1.7	1.3	1.1-2.2	0.03
Prior ORS					
Yes	101	0.4	0.8	0.2-1.0	0.009
No	47	2.9	1.7	1.2-4.0	0.004
Initial Na+ result (mmol/l)					
130-150 (N)	81	1.8	1.1	0.8-2.2	0.06
<130 (Low)	38	3.1	2.3	1.7-4.4	0.03
>150 (High)	29	5.8	3.6	2.9-8.0	0.002

DISCUSSION

This study highlights that hypernatraemic dehydration is quite prevalent among under-five children presenting with diarrhoea at UTH Department of Paediatrics and Child Health with a prevalence of 19.6%. This figure is higher than recorded in most previous studies.10,12,14 However, the prevalence remains within the documented range of 10%-20% prevalence of hypernatraemicdyhydration among children with acute diarrhoea.10 Like other previous studies, diarrhoea is mainly an under-five disease most prevalent in the first two years of life as 84.5% of participants were under-2 years, most of which is rotavirus associated.7,10,15

The incidence of rotavirus diarrhoea reduces with age following the acquisition of immunity from earlier infections.15 With the introduction of the rotavirus vaccine in the Zambian routine immunisation programme in 2012, it is hoped that the incidence of rotavirus associated diarrhoea among under-five children will reduce. Rotavirus being the major cause, this will see to the overall reduction in the incidence of diarrhoeal diseases and hence mortality, including from hypernatraemic dehydration. The 2015 preliminary report presented to the department of paediatrics at UTH on the national monitoring of the efficacy of rotavirus vaccine, has shown promising results on the reduction of diarrhoea associated morbidity and mortality.9 However, from the study, some children were not covered in the immunisation programme as 10% of the participants were not rotavirus vaccinated, and it was a significant prognostic factor as unvaccinated children had a higher risk of mortality than vaccinated children (adjusted OR 1.3 and 0.7 respectively). Rotavirus vaccine has shown to prevent severe rotavirus diarrhoea by 90-100% and diarrhoea of any severity by 74-85%.15

Low utilisation of ORS at home despite its widespread availability is worrying realising the great benefits of low osmolality ORS. The study shows that children who had no prior ORS therapy had a higher risk of mortality than those who had (adjusted OR 1.7 and 0.8, respectively). Early and appropriate ORS use has shown to be effective in treating dehydration and preventing hospitalisation. The introduction of low osmolarity ORS, which has shown to be superior compared to the initial standard ORS in treating dehydration and correcting electrolyte and other metabolic derangements has further improved outcomes in treating diarrhoea.6,13 ORS remains one of the major cost-effective interventions to foster the elimination of preventable deaths from diarrhoea by 2025.6 Low ORS utilisation is worrying especially that UTH is a third level referral hospital receiving patients who are first seen at local clinics where ORS therapy should have been initiated.

Most children (66.9%) presented with severe dehydration while 8.8% presented in shock, this may be expected, UTH being a third level referral hospital only children with severe dehydration are likely to be referred from the local clinics. Poor home ORS utilisation may be a contributing factor to most children presenting with severe dehydration. It is obvious that the severity of dehydration is directly proportional to the risk of mortality, as even noted in this study. Level of dehydration may be influenced by several factors such as number of stools per day, the volume of stools and co-morbidities/symptoms such as vomiting which contribute to losses. Hence children with more of these factors may have a higher risk of mortality.

Despite not having been analysed, these factors have a bearing on the level of dehydration and probable electrolyte derangement, which may be the ultimate pathways for mortality. These factors, however, may be significant possible confounders.

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

Dysnatraemias are among the commonest electrolyte derangements in acute diarrhoea. Of all the participants, 54.7% had normal sodium level while the remaining 45.3% either had low sodium (hyponatraemia 25.7%) or high sodium (hypernatraemia 19.6%). Of the dysnatraemias, hypernatraemia despite being the less common one was associated with more deaths and therefore with a higher case fatality rate of 24.1% compared to 13.2% and 8.6% for low and normal sodium respectively. Hypernatremia dehydration is the most dangerous and fatal form of dehydration.1 Shock was associated with a high risk of mortality. Despite hypernatreamia being associated with more severe dehydration,4,17 shock was less common among participants with hypernatremic dehydration. Among patients presenting in shock, 46.2% had hypernatreamia, while the remaining 53.8% had either normal or low sodium. Sodium being the major extracellular cation has a central role in maintaining plasma osmolality and hence fluid balance, especially in maintaining the plasma volume.1,4,17Hypernatraemia, therefore, enables preservation of the plasma volume until the dehydration is profound, hence for the same amount of fluid deficit a patient with hyponatraemia may be in shock while one with hypernatraemia may not. On the contrary, a patient with hypernatraemia will have a larger fluid deficit for the same dehydration level assessed clinically. This may lead to delayed presentation and initiation of appropriate fluid replacement therapy in patients with hypernataremic dehydration.

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

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

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

CONCLUSION

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

LIMITATIONS / CHALLENGES

The study's major challenge was long turnaround time of results as the study depended on routine laboratory services. Hence most results could not be used to inform patient care as they could not depict the patient's current status. Definitive HIV status determination was not possible during the short period of admission to be factored as a prognostic factor which may have a bearing on the outcome. Lack of standardisation of treatment implementation may have influenced outcomes in some patients. The initial laboratory planned to conduct electrolytes for the study ran out of reagents, and at some point, the entire hospital had run out of reagents and recruitment was put on hold which may have created bias. These challenges highlight the reality faced in managing such patients in a resource-limited setting. Finally, the study does not demonstrate causality between hypernatraemic dehydration and mortality but merely demonstrates association.

RECOMMENDATIONS

1. Hypernatraemia is prevalent among under-five children presenting with diarrhoea at UTH Department of Paediatrics and Child Health; it is therefore recommended that all such children have an electrolyte determination on admission for appropriate management.
2. There is a need for investment in laboratory equipment and reagents to improve capacity for timely results to inform patient care.
3. The department of paediatrics should have a stand-alone chemistry laboratory for an emergency test like electrolytes when needed.
4. There is a need for standardised care in the management of diarrhoea, and this is only possible if patients are managed in the same place by the same group of caregivers (nurses). Therefore re-establishment of a diarrhoea ward may be a solution as was the situation in the past.
5. There is a need for continued community sensitisation on timely ORS home use whenever a child has diarrhoea and the importance of immunisation, especially rotavirus vaccination in this regard.

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