ORIGINAL ARTICLE

Insight into potassium's role in childhood mortality due to severe acute malnutrition

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ABSTRACT

Hypokalaemia is associated with an increase in mortality in children with severe acute malnutrition (SAM) and diarrhoea. This is a descriptive cross-sectional retrospective study conducted in the Nutritional Ward at Mohamed Alamin Hamid Pediatrics Hospital in Omdurman, Sudan. It aimed to assess the frequency of hypokalaemia among children with SAM to understand the influence of hypokalaemia and potassium supplementations contributed on the children survival rates (January–December 2015). It included 215 patients with SAM and acute diarrhoea. The potassium levels of all the patients were assessed upon hospital admission and this correlated with the mortality according to the degree of hypokalaemia and treatment initiated. Hypokalaemia was evident in 70.2% of the patients. Mortality was 3.1% in normokalaemic and 13.9% in hypokalaemic patients. The patients' survival was significantly associated with their serum potassium levels and the treatment received. The survival rates have been assessed via the Multinomial Logistic Model, which reveals that normokalaemic children had a chance of 157.349 (95% confidence interval 18.479–1,339.811) times higher than that compared to the baseline children with advanced hypokalaemia with serum levels <2 mEq/l (p-value < 0.001). Children with mild hypokalaemia within the serum levels of 3.0–3.4 mEq/ml showed an increased survival chance of 549.970 (95% CI 19.293–3,238.716) times compared to the baseline children (p-value = 0.000). In patients with SAM, who presented with acute diarrhoea, there was an increase in mortality in patients with hypokalaemia compared with patients who presented with normal potassium levels. Corresponding mortality rates increased significantly with the severity of hypokalaemia. In severe hypokalaemia, there is a significant difference in mortality between patients treated with oral rehydration solutions for malnutrition in relation to patients treated with oral potassium supplements or with intravenous potassium.

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INTRODUCTION

Living cells store almost 98% of body's potassium, so potassium is mainly found intracellular; whereas, serum (extracellular) potassium represents only 2% of the body potassium. Hypokalaemia is common among hospitalised children [1–3]. It is defined as serum potassium level falling below 3.5 mEq/l and further classified into mild hypokalaemia (3–3.5 mEq/l), moderate hypokalaemia (2.5–3 mEq/l) and severe hypokalaemia (<2.5 mEq/l).

Children with severe acute malnutrition (SAM) and diarrhoea in the developing countries frequently present with hypokalaemia. Mortality rates increase if potassium levels are below 2.5 mEq/l (severe hypokalaemia) [4]. Poor intake and poor muscle bulk in malnourished children results in the fall of total serum potassium levels (by as much as 25%). Patients with SAM complicated by diarrhoea show hypokalaemia as the commonest presenting electrolyte disturbance [5]. Hypokalaemia in children with (SAM) may be asymptomatic, but during the diarrhoeal illness, these children become at higher risk to develop serious manifestations, such as muscle weakness and cardiac arrhythmias—which may be life-threatening if not immediately diagnosed and urgently treated [6–9].

The cornerstone of treatment of hypokalaemia is a potassium replacement. Potassium supplementation may be through enteral route; oral or through feeding tubes in case of asymptomatic or mild hypokalaemia patients, which in some cases may resolve spontaneously. But, in symptomatic or severe hypokalaemia, potassium replacement should be through parenteral route using intravenous (IV) potassium preparations [10]. According to World Health Organization (WHO) protocol for inpatient management of patients with SAM, the management of hypokalaemia is by using just oral potassium supplements either Rehydration solution of Malnutrition (ReSoMal), which contains higher potassium concentrations than the standard WHO oral rehydration solution (ORS) or extra added potassium to feeds or to (ReSoMal) [11,12]. Both malnutrition and electrolyte disturbances are considered to be risk factors for death among children with diarrhoea [13–15]. Sudan is one of the Sub-Saharan African countries, the area with the highest under-five mortality rates in the world up till the date of this publication [16]. With the under-five mortality rate in 2015 in Sudan being 70.1 per 1,000 lives [16]. That means approximately 1 in every 12 children dies before their fifth birthday—compared with only 1 in 147 in the developed countries. About 45% of deaths in children less than 5 years of age are contributed to by malnutrition. Yet, the mortality due to common childhood illnesses, such as diarrhoea is higher among those with (SAM) [16,17]. These disorders when observed together could exacerbate each other with deleterious consequences. Therefore, this survey was conducted to assess the prevalence of hypokalaemia among children with (SAM) admitted to our hospital, and to understand the influence of hypokalaemia and the potassium supplementation on the survival of (SAM) children.

METHODOLOGY

Setting and design

This is a retrospective descriptive cross-sectional study conducted at the Nutritional Ward at Mohamed El Amin Hamid Pediatric Hospital in Omdurman, from January to December 2015.

Patients and sampling technique

A total of 215 patients were admitted to the ward during this period who fulfilled the inclusion criteria for the study—being (SAM) patient; between 6 and 59 months of age; with mid upper arm circumference <115 mm; weight-for-height/length < −3 *Z*-score of WHO growth standards; ±bilateral oedema, according to WHO diagnostic criteria [18], and presented with acute diarrhoea. Children with secondary malnutrition due to systemic illnesses were excluded. The data

were collected by trained house officers either from hospital medical records after discharge or death of each patient. The information covers a number of relevant variables, such as patient's age, weight-for-height/length *Z*-score, mid upper arm circumference and the presence or absence of oedema. Additional data were obtained about the potassium levels, on admission and treatment for hypokalaemia—if present. Hypokalaemia was defined as potassium levels of less than 3.5 mEq/l, (<3.5–3 mEq/l) is mild hypokalaemia, (<3–2.5 mEq/l) is moderate hypokalaemia, (<2.5 mEq/l) is severe hypokalaemia. Children with severe hypokalaemia were subdivided into two groups, group 1 with potassium level (<2.5–2 mEq/l) and group 2 with potassium level <2 mEq/l.

Statistical analysis

Then, the data were analysed using the Statistical Package for Social Sciences version 23 for Windows. The data presented as frequencies, percentage, mean and standard deviation. *p*-value of less than 0.05 was considered as statistically significant.

RESULTS

The study covered 215 children diagnosed with SAM in Mohamed Elamin Pediatric Hospital in Omdurman, Khartoum—Sudan. The age distribution was mainly between 6 and 48 months. The majority aged between 6 and 24 months (94% of the subjects) (Table 1).

In our study, the potassium levels for all the patients was obtained and the result was that 64 patients had normal potassium levels at presentation (29.8%), and 151 patients presented with hypokalaemia (70.2%) (Table 2). The patients who had severe hypokalaemia (59.1%), had potassium levels less than 2 mEq/ml. They represented (18.1%) of the total patients (Table 2).

Table 1. Characteristics of study subjects (n = 215).

Age (months)	Frequency	Percent
6–12	93	43.3
13–24	109	50.7
25–36	12	5.6
37–48	1	0.5
Total	215	100

The majority of the study subjects survived (89.3%), while the rest died (10.7% of the subjects) (Table 3).

Patients presented with mild hypokalaemia were 47 patients, just one patient died (2.1%). Patients with moderate hypokalaemia equalled 38 patients, four of whom died (10.5%). Sixteen patients out of 66 patients with severe hypokalaemia died (24.2%). Patients with severe hypokalaemia were further classified into two groups. The first group was patients with potassium levels between 2 and 2.4 mEq/l, while the second group had potassium levels <2 mEq/l. The first group consisted of 27 patients, two of who died (7.4%). The second group consisting of patients with severe potassium deficiency totalled 39 patients, 14 of who died (35.9%) (see Table 4).

The mortality was compared in patients with hypokalaemia in relation to treatment given and found that, all the patients presented with mild hypokalaemia (47 patients) were treated with (ReSoMal). Only one patient died (2.1%). Patients presenting with moderate hypokalaemia and treated with (ReSoMal) were 31 patients, three of who died (9.4%). In addition to (RoSoMal) supplementation these patients, three of who received oral potassium and three of whom were treated with IV potassium outside the protocol guidelines, fortunately with zero mortality [12]. The odds of mortality prevalence were supported with the logistic model. Patients with severe hypokalaemia were classified in two groups, the 27 patients in first group, 18 patients of them treated with (ReSoMal), two of whom died (11.1%). Seven patients and two patients were treated with oral potassium or IV potassium, respectively, with no deaths. For the patients with potassium levels <2 mEq/l, 12 patients treated with (ReSoMal), 10 of whom died (83, 3%). Sixteen patients managed with oral potassium and five of whom died (31.3%). There were no deaths among patients treated with IV potassium outside the (SAM) protocol (Tables 5 and 6).

Multinomial logistic model was developed to assess the contribution of the level of potassium on

Table 2. The patient's potassium levels (mEq/ml) on admission (n = 215).

Potassium level	Total
Normal potassium	64 (29.8%)
Hypokalaemia	151 (70.2%)
Classification of Hypokalaemia	
Mild Hypokalaemia	47 (31.1%)
Moderate Hypokalaemia	38 (25.2%)
Sever Hypokalaemia	66 (43.7%)
Extent of hypokalaemia severity	
Sever hypokalaemia (group1: 2.4–2 mEq/L)	27 (40.9%)
Sever hypokalaemia(group2: <2 mEq/L)	39 (59.1%)

Table 3. Treatment outcome among the study subjects (n = 215).

Outcome	Frequency	Percent
Survival	192	89.3
Death	23	10.7
Total	215	100.0

Table 4. Effects of potassium level on mortality (n = 215).

Potassium level	Total	Deaths
Normal potassium	64	2 (3.1%)
Hypokalaemia	151	21 (13.9%)
Classification of Hypokalaemia		
Mild Hypokalaemia	47	1 (2.1%)
Moderate Hypokalaemia	38	4 (10.5%)
Severe Hypokalaemia	66	16 (24.2%)
Extent of hypokalaemia severity		
Severe hypokalaemia (group1: 2.4–2 mEq/l)	27	2 (7.4%)
Severe hypokalaemia (group2: <2 mEq/l)	39	14 (35.9%)

Table 5. Medical treatment prescribed for the study subjects (n = 215).

Treatment	Frequency	Percent
ReSoMal*	171	79.5
Extra added oral potassium	26	12.2
I.V Potassium	18	8.4
Total	215	100.0

*ReSoMal, Rehydration Solution for Malnutrition.

the treatment outcome (either death or survival). The impact of age on the survival probability was not clear when analysing age groups. This finding would necessitate the development of further studies to stress on its role. The model revealed significant contribution of the child's serum potassium levels on the survival probability. The normokalaemic children had a survival rate of

Table 6. Effects of treatment of hypokalaemia on patient's mortality (n = 215).

Potassium (mmol/l)	Outcome	ReSoMal	Oral potassium	IV Potassium	*p*-value
3.5–5	Survival	62	-	-	NA
	Death	2	-	-	
	Total	64	-	-	
3–3.4	Survival	45	-	1	0.882
	Death	1	-	0	
	Total	46	-	1	
2.5–2.9	Survival	28	3	3	0.658
	Death	4	0	0	
	Total	32	3	3	
2.4–2	Survival	16	7	2	0.583
	Death	2	0	0	
	Total	18	7	2	
<2	Survival	2	11	12	<0.001
	Death	9	5	0	
	Total	11	16	12	

Table 7. Multinomial logistic model for the survival predictors among the study subjects.

	p-value	Odd ratio	95% CI	
			Lower bound	Upper bound
Intercept	<0.001	-	-	-
Age	0.762	0.865	0.34	2.204
Normo-kalemia	<0.001	157.349	18.479	1,339.811
Potassium 3.0–3.40	<0.001	549.97	19.293	3,238.716
Potassium 2.5–2.9	<0.001	35.613	5.503	230.475
Potassium 2.4–2.0	0.001	39.888	4.83	329.386
Potassium <2	-	-	-	-

157.349 [95% confidence interval (CI) 18.479–1,339.811] times of survival compared to the baseline of children having serum potassium of less than 2 mEq/ml (*p*-value = 0.000). Moreover, the children with mild hypokalaemia within the serum levels of 3.0–3.4 mEq/ml showed an increased survival chance of 549.970 (95% CI 19.293–3,238.716) times compared to the baseline children (*p*-value = 0.000).

Finally, the children with potassium serum levels of 2.0–2.4 mEq/ml showed also improved survival probability of 39 (4.830–329.386) compared to the baseline children (*p*-value = 0.000).

The baseline group for potassium levels was children whose serum levels fell below 2 mEq/ml, which is the most severe level of hypokalaemia. The adjustment for comorbidities and other medical intervention remains a priority for further studies. However, the inflated odds of mortality prevalence remain questionable and prioritise the role of potassium in the treatment outcome and children survival (Tables 7).

DISCUSSION

All of the 215 patients were diagnosed as (SAM) and presented with acute diarrhoea [18]. A proportion of 13.9% of children with hypokalaemia were died, compared to only 3.1% mortality among patients presented with normal potassium. From the descriptive data and the survival rates among the treatment group, there was a clear gradient pattern of causality as the more hypokalaemic the child was, resulted in higher the incidences of death. When superimposed upon malnutrition, diarrhoea may cause death and it will always continue to be one of the most serious issues facing our children. Electrolyte disturbances in children with (SAM) are becoming more obvious during the diarrhoeal illness, and needs immediate therapy to avoid serious to life threatening situations. So, measurement for serum electrolytes is essential at presentation [19].

The sample included in this study when stratified, the power for chi-square test lost, however, for the children with severe hypokalaemia (serum levels < 2 mEq/ml), the number of children helped elucidating the statistical association between treatment used and the survival rates. The IV potassium showed significant association to survival as, out of 12 children received the treatment zero of whom died (100% survival) (Chi-square = 16.95, *p*-value 0.000). This is compared to 11 children who received (ReSoMal) with survival rate of 18.18% only. The extra oral supplementation of potassium alongside the (ReSoMal) showed a little improvement with no statistical significance (Chi-square =1.08, *p*-value 0.583). Previously published data about potassium implications in mortality support our findings. Serious cardiovascular complications rapidly develop when potassium levels are severely disturbed. Ventricular tachycardia and fibrillation can result from even moderate hypokalaemia by causing the inhibition of the sodium-potassium pump of the heart muscle cells [20]. Muscle weakness, depression of the deep-tendon reflexes, and even flaccid paralysis can complicate hypokalaemia, and the respiratory muscles are the most seriously affected. Hypokalaemia is associated with increased mortality among hospitalised patients, especially due to cardiac arrhythmias and sudden cardiac death [20]. In the International Centre for Diarrhoeal Disease Research, Bangladesh, case fatality was 17%, but after the introduction of a standardised protocol, based on the WHO guidelines, case fatality rate decreased to 9% and then to 3.9%. Also, in South Africa, the mortality rate decreased from 30%–40% to less than 15% [12].

The new WHO guidelines modify treatment of (SAM) patients taking in consideration the physiological and metabolic changes occurring in severe malnutrition. The machinery of the cells in malnourished patients is impaired; tissue function and abnormal body composition cannot be restored unless this machinery is repaired. So, the use of intravenous fluids for rehydration and rapid manipulation of abnormal blood chemistry can increase mortality [12].

Concerning the management guidelines 2014 of correction of electrolyte imbalance in inpatients with SAM, the guidance sets that correction of hypokalaemia may take at least 2 weeks, and hypokalaemia should be corrected during rehydration with ReSoMal, which contains higher potassium than the standard WHO ORS, or by using extra potassium supplements added to the feed or to the (ReSoMal) which slowly corrects hypokalaemia based on the theory of that the rapid manipulation of blood chemistry in severely malnourished child may be fatal [12]. Within the SAM guideline, nothing mentioned about the degree of hypokalaemia, what is the minimal potassium level that can be tolerated by the malnourished child to be corrected slowly over days? Is there any potassium level beyond which I should interfere and correct rapidly by IV potassium replacement? Our study revealed that there are questions about the management of hypokalaemia in patients with SAM, questions that needs further studies to be answered, aiming to improve the survival among (SAM) children in our country.

The Limitations of this study is that of being an observational retrospective study with limited collected data. The current data about co-morbidities is lacking, besides the medical treatment used other than nutritional support

and potassium supplementation. However, the currently observed odds of mortality prevalence are high enough to reveal the role of potassium.

CONCLUSION

In patients with SAM, who present with acute diarrhoea, there is an increased mortality in patients with hypokalaemia in comparison to patients who present with normal potassium levels and mortality rates increased significantly with the severity of hypokalaemia. There was significant differences in mortality between patients who were treated with (ReSoMal) in relation to patients treated with oral potassium supplements or with IV potassium in severe hypokalaemia. This revealed the impact of intravenous potassium supplementation as the best treatment option for severe hypokalaemia with the least mortality followed by the oral supplementation of extra potassium along with the (ReSoMal) solution.

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COMPETING INTERESTS

The authors declare no conflict of interest.

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ETHICS

Ethical approval was obtained from the Ethics and Research Committees at Mohamed Alamin Hamid Pediatrics Hospital. Confidentiality was maintained at all levels.

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