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Risk factors for mortality and effectiveness of treatment protocol in severely malnourished children admitted into a tertiary hospital in Nigeria

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ABSTRACT

Background: Mortality in children with Severe Acute Malnutrition (SAM) remains high despite the adoption of available standard operative procedures for treatment. **Aim**: To determine the risk factors for mortality and assess the effectiveness of treatment protocol in severely malnourished children. **Materials and Methods**: This was a retrospective study based on data extracted from the case files of children aged six months to 5-years who were admitted and managed for Severe Acute Malnutrition in the Emergency Paediatrics Unit (EPU) and Paediatrics Medical Ward (PMW) of the Usmanu Danfodiyo University Teaching Hospital (UDUTH) Sokoto, Nigeria, over five years (from January 1 2015 to December 31 2019). Data were analyzed using the IBM SPSS version 25 computer statistical software package. **Results**: Whereas the presence of pneumonia, coma, gastrointestinal loses ≥ 5 times/day, small pulse volume, use of Rehydration Solution for the Malnourished (ReSoMal), and hypoglycaemia were associated with mortality in SAM ($p < 0.05$), in logistic regression analysis, none of them was a significant risk factor for mortality. ReSoMal was effective in correcting dehydration among the discharge group but ineffective among the mortality group due to severe dehydration and intolerance. **Conclusions**: ReSoMal was effective for correcting dehydration in children who could tolerate it orally and were not severely dehydrated. Healthcare providers should triage children with SAM into those who can tolerate the oral route for ReSoMal administration, while those who cannot and those who are severely dehydrated should be considered for initial resuscitation with intravenous fluid to optimize survival.

Keywords: Severe acute malnutrition, ReSoMal, treatment effectiveness, mortality, risk factors

INTRODUCTION

Severe acute malnutrition (SAM) is a worse form of undernutrition and a risk factor for mortality, requiring urgent survival treatment. It is also an underlying cause of childhood illnesses, including diarrhoea and pneumonia (which are among the leading causes of mortality in children under 5).[1] About 16 million children below five years are affected by SAM worldwide; of these, two million are in Nigeria.[2] Treatment of SAM is the last opportunity to save a child's life when all other efforts to prevent SAM fail. World Health Organization (WHO), in collaboration with United Nations Children Funds (UNICEF), formulated F-75 and F-100 for nutritional rehabilitation and a Rehydration Solution for the Malnourished (ReSoMal) for rehydration of severely malnourished children. These formulations are components of the treatment protocols for inpatient management of Severe Acute Malnutrition (SAM) established by the World Health Organization (WHO) and Medecins San Frontiere.[3] According to WHO, this treatment protocol can bring the case fatality rate to <10% among SAM patients, even in cases of complicated SAM.[3] However, health facilities in sub-Saharan Africa still record case fatality rates as high as 40% among hospitalized patients with SAM despite adopting this treatment protocol.[1, 2, 4] Ugege *et al.* in UDUTH Sokoto, Nigeria, reported SAM as the leading cause of death among hospitalized children under the age of five years.[5] Despite this high mortality record, there are no publications from the study area to identify risk factors for the high mortality recorded.

In a case-controlled retrospective study, Roy et al. in Bangladesh identified small-volume pulses, pneumonia, severe anaemia, hypothermia, leucocytosis and septicaemia as risk factors for mortality.[6] Similarly, Kumar *et al.* reported shock, severe dehydration, oliguria, and

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hyponatraemia as independent risk factors for mortality.[7] Desyibelew *et al.* and Kebede *et al.* in Northwest Ethiopia reported congestive heart failure, shock, vomiting, diarrhoea, nasogastric therapy and respiratory tract infections as significant predictors for mortality among children admitted for SAM.[8, 9] Nigeria is among the African countries most hit by SAM and its mortality.[10] Yet, there is a lack of information on why mortality during inpatient management of SAM remains high.[11] Chamla *et al.,* in a conflict setting in Borno, Nigeria, reported co-morbidity with pneumonia and diarrhoea as significant risk factors among children admitted for SAM.[12]

The few reports cited only identified risk factors for mortality in SAM patients. There were no further evaluations to assess the effectiveness of the treatment protocol and to know why the mortality rate during inpatient treatment of SAM remains high despite the adoption of the treatment protocol. This study set out to identify the risk factors for mortality in SAM patients in the study area, assess the effectiveness of ReSoMal in the correction of dehydration in SAM patients, and identify the possible reason(s) for the high mortality recorded despite the adoption of ReSoMal for rehydration. It is envisaged that the findings will add to existing knowledge and improve clinical practice to ensure the survival of children with SAM in the study area.

MATERIALS AND METHODS

Study Design, Population and Area

It was a retrospective study based on data extracted from the case files of children aged six months to 5-years who were admitted and managed for Severe Acute Malnutrition in the Emergency Paediatrics Unit (EPU) and Paediatrics Medical Ward (PMW) of the Usmanu Danfodiyo University Teaching Hospital (UDUTH) Sokoto, Nigeria, over five years (from January 1 2015 to December 31 2019). The hospital is a tertiary health facility located in Sokoto, Northwestern Nigeria. It is a referral centre for people from Sokoto, Zamfara, Niger, Kebbi, Katsina States, and the neighbouring Niger and Benin Republics in the West African sub-region. The children's wards have a bed capacity of at least 50 patients and admit about 5 -15 SAM patients monthly. All admitted cases of SAM who stayed at least 24 hours on admission, giving enough time for the commencement of treatment, were considered eligible and included in the study. Cases of SAM whose admission outcomes (death or discharge) were unknown and those with background chronic diseases like cardiac, kidney or HIV infection that could increase the risk for mortality were excluded.

Data Collection

A designed proforma was used to extract information on the research variables from the patients' case files. These include the patients' sociodemographic characteristics (age and sex, and socioeconomic status of the parents or caregivers), clinical parameters of patients including being identified as a SAM case, frequency of diarrhoea and vomiting, systemic examination findings including pulse volume, features of shock (absent or weak pulse, cold extremities, etc.), presence of crepitation and Blantyre coma score, as well as laboratory results (random blood sugar), and the treatments given while on admission (Resomal, IVF, ORS, F-75, F-100, Plumpy nuts, Kwash pap, anti-malarial and antibiotics).

Data Analysis

Data were analyzed using IBM SPSS version 23 computer statistical software package. Data clearing was done to remove data of patients with incomplete records concerning some of the clinical parameters of interest. Diagnosis of severe acute malnutrition was according to WHO criteria using one or more of the following parameters: Mid-upper arm circumference <11.5cm, weight for height (Z-score) <-3SD, and bilateral pitting pedal oedema.[13] The SAM patients who died during treatment were classified as cases, while those who survived and were discharged were classified as controls. The socioeconomic class of the parents was determined using the revised Oyedeji's classification system.[14] The chi-square test was employed to ascertain the association of sociodemographic and clinical parameters with mortality in SAM patients, while binary logistic regression analysis was used to explore the risk factors for mortality in SAM. Pulse volumes at admission and after treatment with ReSoMal were compared to assess for improvement (as a measure of its effectiveness) using the paired sample t-test. All levels of statistical significance were set at $p \leq 0.05$.

Ethical Consideration

Ethical approval for the study was obtained from the Health Research and Ethics Committee of the Usmanu Danfodiyo University Teaching Hospital (UDUTH), Sokoto, Nigeria (with approval number NHREC/30/012/2019). Permission to conduct the study was obtained from the management of the hospital.

RESULTS

Out of the 118 children given ReSoMal for hydration, only 45 (38.1%) had the original WHO ReSoMal, while the remaining 73 (61.9%) had constituted ReSoMal. The use of constituted ReSoMal was because WHO ReSoMal was out of stock in 2018 and 2019.

Sociodemographic characteristics of patients

Seventy-five SAM mortality cases and seventy-five SAM discharges who met the inclusion criteria were included in the study as cases and controls, respectively. The mean age of the SAM discharges group was 18.8±5.9 months, while the mean age of the SAM mortality group was 20.5±9.6 months, but there was no statistically significant difference ($p > 0.05$) in the mean ages of the two groups. The majority of the patients in both groups were in the >1-2 years age group (SAM discharges, 72.0%; SAM mortality, 73.3%) and were males (SAM discharges, 58.7%; SAM mortality, 56.0%). There was no significant difference ($p > 0.05$) between the two groups in the distribution of patients by age and gender. Although the parents of most of the patients in both groups were in the low socioeconomic class, the proportion of patients whose parents were of the low socioeconomic class was significantly higher among the SAM mortality group (97.3%) than the SAM discharges group (73.3%); $\chi^2 = 17.259$, $p = 0.001$ (Table 1).

Table 1: Sociodemographic characteristics of patients

Variables	SAM TREATMENT OUTCOME		Test of significance
	DISCHARGE (n = 75) Frequency (%)	DEATH (n = 75) Frequency (%)	
Age (months)			
Mean	18.8 ± 5.9	20.5 ± 9.6	t = 1.603, p = 0.207
Age group (years)			
≤1	17 (22.7)	11 (14.7)	$LR\chi^2$= 5.867, p = 0.320
1.1-2.0	54 (72.0)	55 (73.3)	
2.1-3.0	4 (5.3)	6 (8.0)	
3.1-4.0	0 (0.0)	1 (1.3)	
4.1-5.0	0 (0.0)	2 (2.7)	
Sex			
Male	44 (58.7)	42 (56.0)	χ^2= 0.109, p = 0.741
Female	31 (41.3)	33 (44.0)	
Socioeconomic class			
Middle	20 (26.7)	2 (2.7)	χ^2= 17.259, p < 0.001*
Low	55 (73.3)	73 (97.3)	

t = Independent t-test; $LR\chi^2$: Likelihood Ratio chi-square test; *Statistically significant ($p<0.05$)

Factors associated with mortality in patients with severe acute malnutrition

The factors that were associated with mortality in children with SAM were bronchopneumonia, loss of consciousness, GIT loses, especially diarrhoea and vomiting, profuse GIT loses >5 times/day, use of ReSoMal only in contrast to use of IVF and then ReSoMal, small pulse volume after rehydration, and hypoglycemia. Compared to the SAM discharges group, a significantly higher proportion ($p < 0.05$) of the SAM mortality group had bronchopneumonia (SAM discharges, 0%; SAM mortality, 28.0%), loss of consciousness (SAM discharges, 5.3%; SAM mortality, 37.3%), diarrhoea and vomiting (SAM discharges, 16.1%; SAM mortality, 36.5%), use of ReSoMal only for rehydration (SAM discharges, 83.9%; SAM mortality, 96.8%), small pulse volume (SAM discharges, 3.6%; SAM mortality, 63.5%), and hypoglycemia (SAM discharges, 0%; SAM mortality, 14.3%) [Table 2].

Risk factors for mortality in SAM patients

In logistic regression analysis, none of the factors significantly associated with mortality predicted mortality in SAM patients (Table 3).

Table 2: Factors associated with mortality in SAM patients

Variables	SAM TREATMENT OUTCOME		Test of significance
	DISCHARGE (n = 75) Frequency (%)	DEATH (n = 75) Frequency (%)	
Bronchopneumonia			
No	75 (100)	54 (72.0)	χ^2= 24.419, p < 0.001*
Yes	0 (0)	21 (28.0)	
Loss of consciousness			
No	71 (94.7)	47 (62.7)	χ^2= 22.881, p < 0.001*
Yes	4 (5.3)	28 (37.3)	
Heart failure			
No	54 (96.4)	57 (90.5)	χ^2= 1.675, p = 0.196
Yes	2 (3.6)	6 (9.5)	
Forms of GIT loses			
None	13 (23.2)	0 (0)	LRχ^2= 24.862, p < 0.001*
Diarrhoea	32 (57.1)	36 (57.1)	
Vomiting	2 (3.6)	4 (6.3)	
Diarrhoea and vomiting	9 (16.1)	23 (36.5)	
Severity of GIT loses			
None	13 (23.3)	0 (0)	LRχ^2= 38.237, p < 0.001*
<5times/day	34 (60.7)	25 (39.7)	
≥5times/day	9 (16.1)	38 (60.3)	
Pulse volume at admission			
Full volume	0 (0)	2 (3.2)	LRχ^2= 6.035, p = 0.110
Moderate volume	30 (53.6)	24 (38.1)	
Small volume	26 (46.4)	36 (57.1)	
Not checked	0 (0)	1 (1.6)	
Fluid for rehydration			
ReSoMal	47 (83.9)	61 (96.8)	LRχ^2= 10.156, p = 0.006*
IVF then ReSoMal	9 (16.1)	1 (1.6)	
None	0 (0)	1 (1.6)	
Pulse volume after rehydration			
Full volume	30 (53.6)	3 (4.8)	χ^2= 56.620, p < 0.001*
Moderate volume	24 (42.9)	20 (31.7)	
Small volume	2 (3.6)	40 (63.5)	
Random blood sugar			
Normal	7 (12.5)	16 (25.2)	LRχ^2= 17.077, p < 0.001*
Hypoglycemia	0 (0)	9 (14.3)	
Not documented	49 (87.5)	38 (60.3)	

χ^2: Pearson's chi-square test ; LRχ^2: Likelihood Ratio chi-square test; *Statistically significant (p<0.05)

Effectiveness of ReSoMal for rehydration in SAM

In the category of SAM children that were successfully managed and discharged, ReSoMal was effective in correcting small pulse volumes. The proportion of patients with small pulse volume significantly reduced ($p < 0.05$) from 46.4% before rehydration to 3.6% after rehydration. However, in the category of SAM mortality, the use of ReSoMal did not result in any improvement of small-volume pulses; rather, the dehydration worsened, and the number of children with small pulse volume increased from 57.1% before rehydration to 63.5% after rehydration, but the increase was not statistically significant ($p > 0.05$) [Table 4].

DISCUSSION

This study assessed the risk factors for severe acute malnutrition in UDUTH, Sokoto state and the effectiveness of ReSoMal for rehydration in SAM patients. Infection (bronchopneumonia), hypoglycaemia, coma, use of ReSoMal, frequent diarrhoea and vomiting and resultant dehydration marked by small-volume pulses were associated with mortality.

Table 3: Risk factors for mortality in SAM patients

Variables	aOR	95% CI		p-value
		Lower	upper	
Bronchopneumonia (No vs Yes*)	0.000	0.000	----	0.998
Loss of consciousness (No vs Yes*)	0.000	0.000	----	0.997
Forms of GIT loses (Diarrhoea and vomiting vs Others)	0.000	0.000	----	0.997
Severity of diarrhoea and vomiting (≥5times/day vs others*)	6.597	0.039	0.646	0.010
Fluid for rehydration (ReSoMal vs IVF then ReSoMal*)	6.426	0.004	0.494	0.011
Pulse volume after rehydration with ReSoMal (Small volume vs Others*)	4.590	0.011	0.818	0.032
Random blood sugar (Hypoglycemia vs Others*)	0.000	0.000	----	0.999

aOR: Adjusted Odds Ratio; CI: Confidence Interval; *Statistically significant (p<0.05)

Table 4: Effectiveness of ReSoMal for rehydration in SAM patients

Pulse volume	SAM DISCHARGE		SAM DEATH	
	Before ReSoMal	After ReSoMal	Before ReSoMal	After ReSoMal
Full volume	0 (0)	30 (53.6)	2 (3.2)	3 (4.8)
Moderate volume	30 (53.6)	24 (42.9)	24 (38.1)	20 (31.7)
Small volume	26 (46.4)	2 (3.6)	36 (57.1)	40 (63.5)
Not checked	0 (0)	0 (0)	1 (1.6)	0 (0)
	$LR\chi^2$= 66.663, p < 0.001*		$LR\chi^2$= 2.167, p = 0.539	

$LR\chi^2$: Likelihood Ratio chi-square test; *Statistically significant (p<0.05)

However, none of these factors was a significant risk for mortality in children with SAM. While using ReSoMal, small volume pulse and recurring GIT losses were risk factors for SAM. ReSoMal was effective for rehydration among control but was not effective in the cases. Bronchopneumonia causes pulmonary congestion, resulting in ventilation-perfusion mismatch with resultant hypoxaemia and respiratory failure. Pneumonia and respiratory failure are associated with congestive heart failure even in healthy children without heart risk.[15] Added to the already structurally defective heart of malnourished children could worsen congestive heart failure, a recognized cause of death in malnourished children.[16] Also, because of their suppressed immunity, malnourished children may not curtail pneumonia, resulting in septicaemia, multiple organ failure, and death. The hypoglycaemia in this study is a direct consequence of reduced energy intake seen in severe acute malnutrition.[17] Hypoglycaemia could have also resulted from the vomiting and diarrhoea because of their interference with feeding. The vomiting and diarrhoea can also explain the dehydration (small pulse volume)

reported among the mortality.[17] Small volume pulse is a pointer to severe dehydration in SAM patients.

The World Health Organization recommends treatment for severe dehydration to start with intravenous fluid (Ringers lactate or Half strength Darrow's or even Normal saline) for immediate resuscitation before continuing the oral route (ReSoMal).[3, 18] These fluids have higher sodium concentration for rapid resuscitation than ReSoMal. Intravenous fluid can also bypass GIT losses and their interference with the oral route of rehydration. However, in this study, though the SAM mortalities largely had small volume pulses at admission, they did not receive intravenous fluid for resuscitation, and this may have accounted for the persistence of small volume pulses despite rehydration with ReSoMal. On the other hand, intravenous resuscitation was used in some of the SAM controls (discharges), and this may have accounted for the sharp drop in the number of patients with small-volume pulses and the increase in the number of patients with full-volume pulses, signifying improved hydration and hence the better outcome (discharge).

Also, despite using ReSoMal (an SOP) for rehydration in the mortality group, the number of patients with small-volume pulses (severe dehydration) increased. This was because the GIT losses, especially vomiting, could have interfered with the oral route of rehydration among the mortality group, causing a worsening of pulse volume from moderate to small volume pulse and an overall increase in the number of patients with small volume pulse and eventual high mortality. Compared with the SAM discharge group, where vomiting was less prominent, there was not much interference with the oral route of rehydration (ReSoMal).

Alam *et al.* in Bangladesh reported worsening hyponatraemia with ReSoMal therapy in SAM children with persistent GIT loss (Diarrhoea).[19, 20] This resulting hyponatraemia may be because ReSoMal, which is known to be low in sodium may not have been adequate to replace the sodium lost in Diarrhoea.[21] As such, the mortality group of SAM in the index study who also had profuse GIT losses may have developed worsening hyponatraemia, which may have been responsible for the persistent small volume pulse despite ReSoMal for rehydration. Similar to the findings in this study, Kebede *et al.* in Ethiopia reported shock, GIT losses (vomiting and diarrhoea) and oral therapy (NG route) as significant causes of death in children with SAM.[9] In Bangladesh, Roy *et al.,* in a case-control study, reported small-volume pulses and pneumonia as risk factors for mortality, while Kumar found that mortality was higher in SAM children with shock (p=<0.001), severe dehydration (p=<0.001) and hyponatraemia (p=<0.001).[6,7]Chamla *et al.* in Borno state, Nigeria reported that co-morbidity with pneumonia and diarrhoea increased the likelihood for mortality in children with SAM.[12]

CONCLUSION

Although infection (bronchopneumonia), hypoglycaemia, coma, use of ReSoMal, frequent diarrhoea and vomiting and resultant dehydration marked by small-volume pulses were associated with mortality, none of them was a significant risk for mortality in children with SAM. Whereas ReSoMal was effective for rehydration among SAM children who were neither severely dehydrated nor in shock and among those who could tolerate the oral route of administration, it was not effective for rehydration in those with severe dehydration and profuse GIT losses. Healthcare providers should triage children with SAM into those who can tolerate the oral route (defined by the absence of persistent vomiting or profuse diarrhoea) for ReSoMal administration, while those who cannot and those who are severely dehydrated should be considered for initial resuscitation with intravenous fluid to optimize survival.

Study Limitation

The study's main limitation was the unavailability of WHO ReSoMal for all the SAM patients, as some of them had constituted ReSoMal.

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Nil.

Conflict of interest

None declared.

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