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Research Article

The Prevalence of Refeeding Syndrome Among Children with Severe Acute Malnutrition: An Observational Study in Kenyatta National Hospital, Kenya

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Abstract

Background: Background: Refeeding syndrome is a complication of severe Acute Malnutrition occurring during initial feeding because of electrolyte changes; mostly potassium, phosphorus and magnesium. The highest mortality in SAM is observed between 48-72 hours of initiating feeds, the same time that Refeeding Syndrome occurs.

Objectives: To establish prevalence of Refeeding Syndrome among children with SAM in Kenyatta National Hospital, find out its associated factors and outcomes.

Design: Observational study

Setting: Kenyatta National Hospital Paediatric wards

Study Participants: Children 6-59 months diagnosed with Severe Acute Malnutrition Interventions: Potassium, phosphorus and magnesium levels were measured at admission and repeated 48 hours after feed initiation. Anthropometric measurements, oedema, dehydration, HIV status, type of feed were evaluated and patients followed for outcomes.

Main Outcome measures: Recovery, persistence, undetermined, death.

Results: Total of 160 children with SAM recruited. Prevalence of Refeeding Syndrome was 21% (95% CI 15.2 to 28.4). Refeeding Syndrome was significantly associated with HIV (P=0.032). Odds of Refeeding Syndrome increased six-fold with HIV infection (OR=5.99, 95% CI 1.23 to 29.1) after age and sex adjustment.

Of the 34 children who developed refeeding syndrome, 65% recovered with treatment, 3% died, 12% had persistently low electrolytes despite treatment while 20% were lost to follow up.

Conclusion: Prevalence of refeeding syndrome in Kenyatta National Hospital among children admitted with SAM was 21% with HIV being significantly associated with its development (P=0.032). The outcomes of those who developed refeeding syndrome were recovery (65%), mortality (3%), lost to follow up (20%) and persistence (12%).

Key words: *Hepatorenal Syndrome, Terlipressin.*

Introduction

Refeeding Syndrome is a complication of Severe Acute Malnutrition caused by electrolyte changes that occur once feeding is initiated. Severe Acute Malnutrition is defined as a weight for height Z score of -3SD and contributes to 35% mortality of children under 5 [1]. In Kenya 1% of children are severely malnourished [2]. Prior to introduction of therapeutic milk feeds in the treatment of SAM children were fed on special milk and mortality was much higher, 56% [3]. Special milk delivers 100 Kcals/100mls and may predispose to refeeding syndrome. F75 delivers 75 Kcals/100 mls which is approximately 50% of the caloric need and may be protective as far as refeeding syndrome is concerned. Dr Kimutai found the prevalence of hypophosphatemia which is a marker refeeding syndrome to be 93% [4].

Despite change in feeding regimen, Dr Nzioki still found mortality from SAM to be 38%. These deaths would mostly occur between 48-72 hours, the same time frame as refeeding syndrome [5]. Refeeding syndrome is a well described but often forgotten condition. In 2006, a guideline was published by the National Institute for Health and Clinical Excellence (NICE) in England and Wales. A starving person has low levels of glucose in blood. Thus, he also has low levels of insulin. When he is fed, glucose levels increase in the blood thus stimulating insulin levels to rise too. The movement of glucose into the cells requires potassium. Phosphorus and magnesium move into the cell also as they are required for various cellular processes [6]. Doctors Pulcini and Zettle published an article in AAP noting several risk factors associated with developing RS. Among them were dehydration, HIV and SAM [7].

Study Population and Sampling

Figure 1

Clinical Procedures

After identifying the study subjects, blood samples for electrolytes

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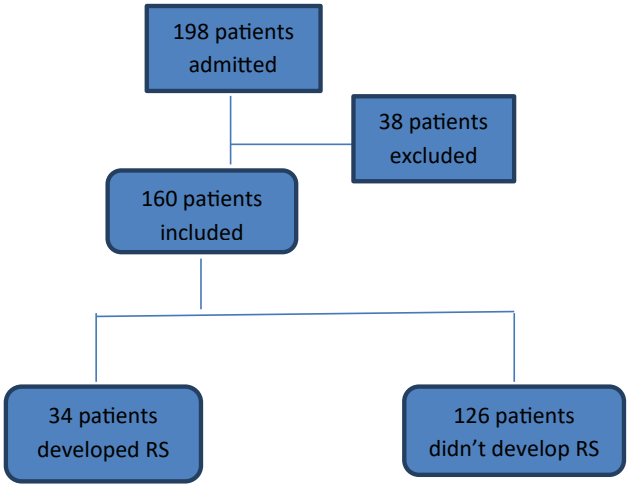

Reasons for exclusion: age less than 6 months or above 5 years, chronic illnesses and refusal to have a HIV test.

Figure 1: Patient flow chart.

(phosphorus, potassium and magnesium) feeding was observed. Patients were fed according to the standard of care. Type of feed and various clinical characteristics were noted down. Electrolytes were repeated after 48 hours of feeding. Patients with a drop of > 0.3 mmols/lt from baseline of either potassium or phosphorus were diagnosed as having refeeding syndrome. Those with RS were treated by electrolyte supplementation and observed again on day 7 to evaluate for outcome.

Data Analysis

Univariable analysis was done on continuous and categorical data. In the initial descriptive analysis, continuous variables such as age were summarized using a measure of central tendency (median) and an appropriate measure of dispersion (range). Categorical variables such as sex and HIV status were analysed using frequency tables of counts and percentages.

Bivariable analysis during which cross tabulations were conducted between the binary variable for Refeeding Syndrome and potential risk factors including demographics, type of feed, HIV infection and Chi square statistics calculated for each cross tabulation. Statistical significance was based on alpha level of 0.05 with p values of <0.05 indicating significant associations.

A multivariable logistic regression analysis was then conducted with Refeeding syndrome as the dependent variable and the factors significantly associated with the syndrome in the bivariable analysis were included as independent variables. In this analysis, the dependent variable (Refeeding Syndrome) was determined while controlling for factors such as age and sex.

Results

Demographic and Clinical Characteristics

The study recruited a total of 160 severely malnourished in KNH. The characteristics of the sample are summarized in Table 1. The median age was 12.5 months and mode was 12 months. Male to Female ratio was 1:1 with 83(51%) males. There 7 (4%) HIV Severely Malnourished patients. Out of 160 children 90% presented with fever and 74% with a cough (Table 1).

Prevalence of refeeding syndrome

Out of 160 children with SAM, 34 developed Refeeding Syndrome representing a proportion of 21%.

(Figure 2)

Table 1: Characteristics of the Sample.

Parameter	Specific	Frequency (n=160)
Sex	Male	83 (51%)
	Female	77 (49%)
HIV Infection	Positive	7 (4%)
	Negative	153(96%)
Presenting complaint	Diarrhea	70(44%)
	Cough	118(74%)
	Vomiting	58(36%)
	Fever	144(90%)
	Convulsions	38(24%)
Type of feed	F75	44(28%)
	F100	42(26%)
	RUTF	3(2%)
	Hospital diet	71(44%)
Chart adherence	Adherence	142(89%)
	Non- adherent	18(11%)
Mother's Education	Primary	127 (79%)
	Secondary	31 (20%)
	Tertiary	2 (1%)
Income	<10000kshs	108 (68%)
	10000-50000kshs	52 (32%)
WHZ Score	<-3Z score	145(90%)
	<-4Z score	15 (10%)
MUAC	<11.5 cm	148 (93%)
	>11.5 cm	12 (7%)
Feed frequency	3 hourly	139 (87%)
	2 hourly	15 (9%)
	other	6 (4%)
Electrolytes on day 1	Hypokalemia <3.5 mmols/lt	17 (11%)
	Hypophosphatemia <0.8 mmols/lt	1 ((0.6%)
	Both hypokalemia & hypophosphatemia	9 (6%)
	Normal electrolytes	133 (83%)
Electrolytes on day 2	Drop to hypokalemia <3.5 mmols/lt	14 (9%)
	Drop to hypophosphatemia <0.8 mmols/lt	18 (11%)
	Drop to both hypokalemia and hypophosphatemia	2 (0.01%)
	Total of those with drops	34
	Normal Electrolytes	126 (79%)
Electrolytes on day 7 (Only for those who developed Refeeding Syndrome) N=34	Return of potassium to normal	11 (32%)
	Return of phosphorus to normal	10 (29%)
	Return of both to normal	2 (6%)
	Persistence of hypokalemia	3 (8%)
	Persistence of hypophosphatemia	1 (3%)
	Participant couldn't be found	7 (22%)

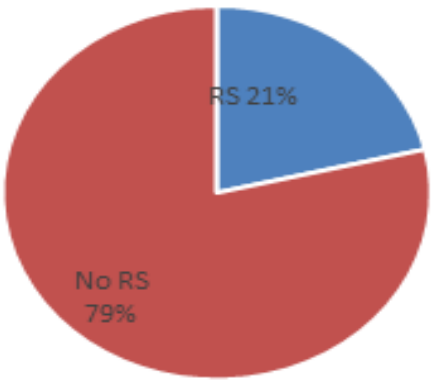

Figure 2: Prevalence of Refeeding Syndrome.

Factors associated with refeeding syndrome

The prevalence of Refeeding Syndrome was significantly associated with HIV infection (P=0.032) but not with dehydration status (p=0.418), top up feeding (p=0.915), caloric dense feeding (p=0.503), oedema or type of diet (F75 p=0.952; F100 p=0.18; hospital diet p=0.418 (table 2). Specifically, the prevalence of Refeeding Syndrome was five-fold higher in the HIV positive (57%) compared to the HIV negative (19.6%) children. (OR=5.47% 95% CI 1.16 to 25.74). This information is summarized in table 2.

Table 3 shows the effect of HIV infection on prevalence of Refeeding Syndrome after adjusting for the effect of age and sex. The odds of Refeeding Syndrome increased six-fold with HIV infection (OR=5.99 95% CI 1.23 to 29.1) after adjusting for the effect of patients' age and sex.

Outcomes of Refeeding Syndrome

(Figure 3)

Of the 34 children who developed Refeeding Syndrome, 22 (65%) recovered, 4(12%) had persistent hypokalemia and hypophosphatemia despite adequate electrolyte replacement, 1 (3%) died and 7 (20%) were lost to follow up (indeterminate), giving an atresion rate of 7%.

Table 3: Multivariable analysis of the effect of HIV on RS.

	Odds Ratio	Std.	Err.	Z Statistic	95% CI	P Value
HIV Status						
Negative	1					
Positive	5.99	4.82	2.22	1.23	29.1	0.026
Age						
Age in months	0.99	0.02	-0.46	0.96	1.03	0.644
Gender						
Male	1					
Female	1.28	0.51	0.61	0.58	2.8	0.543

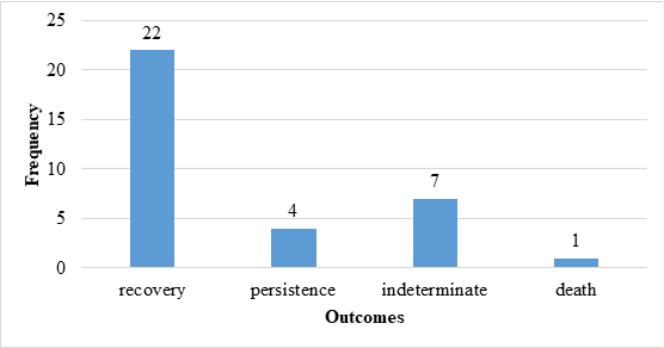

Figure 3: Outcomes of Refeeding Syndrome.

Discussion

Out of the 160 children with SAM 34 developed Refeeding Syndrome giving a prevalence of 21%. This is a marked reduction from the 93% rate of hypophosphatemia noted by Dr. Kimutai in 2006 [4]. the introduction of F75 as the feed of choice in Severe Acute Malnutrition. In 2006 children with Severe Acute Malnutrition were fed on special milk which is calorically dense containing 100 Kilocalories per 100 mls and supplying a child with approximately 130 Kilocalories per kilogram per day of energy. F75 contains 75 Kilocalories per 100 mls and supplies the child with 100Kcalories of energy per kilogram. This is beneficial because it has been shown that starting a malnourished child on a calorically dense feed increases the associated of developing Refeeding Syndrome. Another reason for the reduction of Refeeding Syndrome is that F75 contains minerals, electrolytes and trace elements which go to restore the electrolytes in serum notably potassium, phosphorus, calcium and magnesium. These findings also agree with a previous study in Uganda that showed that F-75, which complies with UN specifications and provides 73 mg phosphorus, seems to prevent refeeding hypophosphatemia in children with [8].

There were 4 patients out of 7 who were HIV positive who developed Refeeding Syndrome (P = 0.032). Further, after controlling for age and sex, the presence of HIV infection increased the risk of developing Refeeding Syndrome by a factor of 6. This is in keeping with a paper published in 2010 by Koethe and Heimburger that suggested that malnourished HIV positive patients on ART would often experience Refeeding Syndrome due to the appetite surge [9]. HIV Causes infiltration of CD4+ laden lymphocytes to the gut mucosa leading to chronic diarrhoea. This leads to loss of electrolytes such as Potassium, Phosphorus and magnesium leading to their low levels in blood. Over time, chronic changes follow with diminution of the protective mucosal barrier. Opportunistic infections may occur as the CD4 T cell count falls below 100–200 cells/mm3 including viral, bacterial, fungal, and parasitic pathogens. Infections usually give the patient diarrhoea leading to more losses of the said electrolytes. HIV enteropathy is characterized histologically with villous atrophy, crypt hyperplasia, epithelial hyperproliferation, and CD4, CD45RA, CD69, CCR5+ depletion within the lamina propria. The associated inflammation, increased permeability, and malabsorption of electrolytes and other trace elements.

Of the children who developed RS, (65%) recovered within 7 days of initiating treatment. Treatment included ensuring the client was on f75 and electrolyte supplementation. Another 20% were lost to follow up despite robust efforts to trace them. This is mostly due to discharge or transfer of the patient before day 7. Of those who developed Refeeding Syndrome, 12% had a persistence of low electrolytes in serum. Differentials for persistent hypophosphatemia include Rickets, Barter's syndrome, Gittellman syndrome, hyperparathyroidism and familial hypophosphatemic rickets [10]. Other differentials for hypokalaemia include GI losses, chronic kidney disease and folic acid deficiency. We experienced one (3%) mortality of those who developed Refeeding Syndrome.

Conclusions

Prevalence of Refeeding Syndrome was high among children with Severe Acute Malnutrition. However, this is a marked reduction from the previous rate which was 93%. The difference is due to the change in type of feed from special milk to F75. There is a positive association between being HIV positive and the development of Refeeding Syndrome (P=0.032). HIV increases the risk of developing Refeeding Syndrome by a factor of 6.

Recommendations

There is need to have all children, especially malnourished tested for HIV. This is because we have seen the significant relationship between HIV and Refeeding Syndrome. Given the high prevalence of Refeeding Syndrome, all patients diagnosed as having Severe Acute Malnutrition require to have their electrolytes monitored at admission and 48-72 hours after feed initiation to assess for its occurrence.

Seeing as therapeutic feeds are vital in prevention of Refeeding Syndrome there needs to be improvement in the supply chain of Kenyatta National Hospital as far as provision of therapeutic milk feeds is concerned. Allow for some overlap of ordering periods so that stock outs are never seen. There is a need for further research on how to feed the malnourished HIV positive child to avoid Refeeding Syndrome.

Disclosures

The author has no potential conflicts of interest to be disclosed. This study had no external funding source. The KNH UON Ethics Committee approved the study protocol. All patients gave written informed consent. This manuscript has not been submitted for publishing elsewhere.

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