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Research Article

Clinical Presentation and Immediate Outcome of Critically Ill Children with Hypoglycemia Presenting to the Acute Care Unit of Mulago Hospital, Kampala Uganda

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Abstract

Background: Hypoglycemia is a common complication among critically ill children presenting to emergency paediatric units and it is associated with prolonged hospital stay and increased risk of mortality.

Objective: To determine the prevalence, clinical presentation and immediate outcome of critically ill children with hypoglycemia presenting to the Acute Care Unit (ACU) of Mulago Hospital.

Methods: Four hundred and fifty seven critically ill children aged 2 months -12 years presenting to the ACU were enrolled. A random blood sugar, history and physical examination, blood slide for malaria parasites and a complete blood count were done. All participants were followed for seven days.

Results: Of the 457 enrolled participants, the median age was 15 months (Range 2-144) and the male to female ratio was 1.2:1. Hypoglycemia was present in 27 of 457 participants 5.9% (95% CI 3.7-8.1). Clinical features significantly associated with hypoglycemia were inability to breastfeed or drink, difficulty in breathing, last meal ≥ 12 hours before presentation, prostration, prolonged capillary refill > 3 seconds and leukocytosis (≥ 11000 cells /µl). Of 27 hypoglycemic participants 9 (33.3%) died, while only 16 of 423 (3.8%) participants without hypoglycemia died, hypoglycemic and non-hypoglycemic participants who survived had comparable durations of hospital stay.

Conclusions/Recommendations: Hypoglycemia in critically ill children is associated with high mortality and morbidity. Critically ill children should be screened for hypoglycemia and corrective measures taken.

Keywords: Children; Hypoglycemia; Glucose

Introduction

Hypoglycemia (defined as blood glucose below 60mg/dl(3.3mmol/dl) in children beyond the neonatal period) is a common complication among children presenting to emergency paediatric units with severe illness and it contributes significantly to increased risk of mortality [1-4] and prolonged hospital stay [3]. Children with severe malaria, septicemia, pneumonia, and protein energy malnutrition have been found to be most affected [4]. Hypoglycemia is usually associated with prolonged fasting and loss of consciousness [4].

Uganda has a relatively high infant (35.4per 1000 live birth) and under age five years (49 per 1000 live birth) mortality rates [6]. A previous study at the Mulago Hospital paediatric emergency unit showed that hypoglycemia was present in 28.4% of the 130 critically ill children [7], but a later study at the same unit showed a much lower prevalence of hypoglycemia of 7.8% [8]. The two studies were done at different times of the year, with different age groups, and in the first study; not all study participants were tested for blood sugar.

In the present study we set out to establish the prevalence and clinical consequences of hypoglycemia among critically ill children aged 2 months to 12 years presenting to the Acute Care Unit of Mulago Hospital.

Methods

The study was conducted in the ACU and the paediatric wards of Mulago Hospital, Uganda's national referral hospital and the teaching Hospital for Makerere College of Health Sciences. Prevalence and clinical presentation were studied by cross sectional design, while for the evaluation of immediate outcome a longitudinal observational study design was used.

Inclusion criteria included, age 2 months -12 years, not previously enrolled in this study, one or more features of critical illness according to the WHO definition (obstructed breathing, central cyanosis, rapid and weak pulse, cold and blue hands, capillary refill time > 3 seconds, lethargy or unconsciousness, sunken eyes, very slow skin pinch, active convulsions) [9], written informed consent from care takers, including assent for children aged 8-12 years. Critically ill children who had been treated with intravenous dextrose in the previous 24 hours were excluded from the study.

Children presenting to the ACU were triaged by a study clinician or nurse for features of critical illness. The principal investigator or research assistant asked for a verbal consent to do a Random blood sugar test. Those with a blood sugar level < 60mg/dl (3.3mmol/dl) were treated with 10% dextrose 5mls/kg and a repeat blood glucose test was done after 30 minutes. Written informed consent and assent were deferred until participants were stable. Investigations such as blood glucose concentration, malaria blood smear for malaria parasites and a complete blood count were done on all enrolled participants. Blood glucose concentration was measured from one drop of blood collected by a finger prick with an Optium Xceed glucometer (Abbot Diabetes care Ltd). The performance of the glucometer used in this study was quality-controlled in the Mulago Hospital Clinical Chemistry Laboratory before the beginning of the study and after each series of 50 measurements.

Blood smears for malaria were stained with Giemsa and read by an experienced laboratory technologist.

Complete blood counts were done by an automated Beckman coulter ACT 5 DIFF CP (Beckman Coulter Inc) in the Haematology Laboratory of Mulago Hospital.

Enrolled participants were followed for seven days. A study specific sticker was put on the patients' charts for easy identification.

Data were recorded on structured pre-coded pre-tested case record forms and then entered into a computer using EPI-DATA version 3.1 and exported to STATA Version 10 for analysis.

The proportions of hypoglycemic critically ill children, who were discharged, died or were still on the ward by day seven of follow up were compared.

Permission to conduct this study was obtained from the Department of Pediatrics and Child Health Makerere College of Health Sciences, School of Medicine Research and Ethics Committee of Makerere College of Health Sciences. The nature of the study and its potential risks and benefits to the child were explained to the parents or caretaker in their native language.

Results

The socio-demographic characteristics of the 457 participants: 55% were males, 48% were aged 12 to 59 months (Table 1). Seven (1.5%) study participants were lost to follow-up, all participants without hypoglycemia.

Characteristic	Frequency (n = 457)	Percentage
Gender		
Male	251	55.
Female	205	45
Age (months)		
< 12	164	35.9
12 – 59	221	48.6
≥ 60	72	15.8
Care taker		
Mother	359	78.7
Father	58	12.7
Others	39	8.6
Care taker's education		
None	27	5.9
Primary	219	48.0
Secondary	189	41.5
Tertiary	21	4.6
Estimated family income		
< 150000 Uganda Shillings	235	51.4
≥ 150000 Uganda Shillings	222	48.6

Table 1: Study participant's socio-demographic characteristics.

Prevalence and clinical presentation of hypoglycemia

Of the 457 enrolled children, 27 (5.9%) (95% CI 3.3-8.1) had hypoglycemia on presentation.

As shown on Bivariate analysis (Tables 2 and 3) and then logistic regression (Table 4) the clinical features significantly and independently associated with hypoglycemia were inability to breastfeed or drink, difficulty in breathing, last meal ≥ 12 hours before presentation, prostration, prolonged capillary refill > 3 seconds and leucocytosis(≥ 11000 cells /µl).

Feature	Hypoglycemia		Odds Ratio (95% CI)	p-value
	Yes n=27	No n=430		
Age < 12 months	13	151	1.72 (0.78, 3.74)	0.1713
>= 12 months	14(4.8)	279(95.2)		
Fever				
Yes	23(6.5)	332(93.5)	1.70 (0.57, 5.03)	0.3348
No	4(3.9)	98(96.1)		
History Convulsions				
Yes	8(10)	72(90)	2.09 (0.88, 4.97)	0.0878
No	19(5.0)	358(95)		
Loss of consciousness				
Yes	7(14.8)	40(85.2)	3.41 (1.36, 8.56)	0.0059
No	20(4.8)	390(95.2)		
Inability to drink				
Yes	18(12.2	129(87.8)	4.67 (2.04, 10.66)	<.0001
No	9(2.9)	201(97.1)		
Cough				
Yes	21(6.1)	321(93.9)	1.19 (0.47, 3.02)	0.7168
No	6(5.2)	109(94.8)		
Difficulty in breathing				
Yes	16(8.7)	168(91.3)	2.25 (1.02, 4.97)	0.0402
No	11(4.0)	262(96.0)		
Vomiting				
Yes	17(7.7)	202(92,3)	1.92 (0.86, 4.29)	0.1071
No	10(4.2)	228(95.8)		
Diarrhea				
Yes	11(5.6)	185(94.4)	0.91 (0.41, 2.01)	0.8164
No	16(6.1)	245(93.9)		
≥ 12hrs since last feed				
Yes	12(22.6)	41(77.4)	7.59 (3.33, 17.31)	<.0001
No	15(3.7)	389(93.3)		
<3 feeds in 24 hrs				
Yes	11(12.1)	81(87.9)	2.96 (1.32, 6.62)	0.0060
No	16(4.4)	349(95.6)		

Table 2: Bivariate analysis for presenting features of participants with hypoglycemia compared to those with no hypoglycemia.

Feature	Hypoglycemia		Odds Ratio (95% CI)	p-value
	Yes	No		
Very slow skin Pinch				
Yes	7(8.9)	71(91.1)	1.77 (0.72, 4.34)	0.2077
No	20(5.3)	359(94.7)		
Sunken eyes				
Yes	12(7.8)	142(92.2)	1.62 (0.74, 3.56)	0.2238
No	15(4.9)	288(95.1)		
Severe pallor				
Yes	5(15.1)	28(84.9)	3.26 (1.15, 9.27)	0.0195
No	22(5.2)	402(94.8)		
Cyanosis				
Yes	3(21.4)	11(78.6)	4.76 (1.25, 18.21)	0.0125
No	24(5.4)	419(94.6)		
Prostrated				
Yes	24(16.8)	119(83.2)	20.91 (6.18, 70.72)	<.0001
No	3(0.9)	311(99.1)		
Hypothermia (≤ 35.4 ˚C)				
Yes	3(27.3)	10(72.7)	5.25 (1.36, 20.34)	0.0078
No	24(5.4)	420(94.6)		
Reduced Consciousness				
Yes	14(22.2)	49(77.8)	8.37 (3.72, 18.85)	<.0001
No	13(3.3)	381(96.7)		
Lethargic				
Yes	25(7.3)	319(92.7)	4.35 (1.01, 18.66)	0.0317
No	2(1.8)	111(98.2)		
Actively convulsing				
Yes	5(14.3)	30(85.7)	3.03 (1.07, 8.57)	0.0289
No	22(5.2)	400(94.8)		
Pulse rate ≥ 170 b/m				
Yes	11(21.6)	40(78.4)	6.70 (2.91, 15.43)	<.0001
No	16(3.9)	390(96.1)		
Thin pulse volume				
Yes	14(11.2)	111(88.8)	3.04 (1.38, 6.66)	0.0034
No	13(3.9)	319(96.1)		
Capillary refill time >3 S				
Yes	10(25)	30(75)	15.22 (6.02, 38.46)	<.0001
No	17(4.1)	400(95.9)		
Cold peripheries				
Yes	11(17.2)	53(82.8)	4.89 (2.15, 11.10)	<.0001
No	16(4.1)	377(95.9)		

Total WBCs ≥ 11000				
Yes	18(8.6)	192(91.4)	2.48 (1.09, 5.64)	0.0261
No	9(3.6))	238(96.4)		
Neutrophil % ≥ 75 %				
Yes	2(22.2)	7(77.8)	4.83 (0.95, 24.48)	0.0362
No	25(5.6)	423(94.4)		
Severe Pneumonia				
Yes	9(5.4)	157 (94.6)	0.87 (0.38, 1.98)	0.7393
No	18(6.2)	273(93.8)		
Severe Malaria				
Yes	4(8.0)	46(92.0)	1.45 (0.48, 4.38)	0.5066
No	23(5.7)	384(94.3)		
Severe acute malnutrition				
Yes	3(4.8)	60(95.2)	0.77 (0.23, 2.64)	0.6781
No	24(6.1)	370(93.9)		
Hemoglobin < 5:				
Yes	3(10.4)	26(89.6)	0.77 (0.26, 2.30)	0.6422
No	24(5.9)	404(94.1)		

Table 3: Bivariate analysis for clinical signs and laboratory findings of participants with hypoglycemia compared to those with no hypoglycemia.

Variable	Adjusted OR (95% CI)	P-value
Inability to breast feed or drink	3.17 (1.17 – 8.58)	0.0229
Difficulty in breathing	2.92 (1.08 – 7.87)	0.0344
≥ 12 hours since last feed	4.87 (1.63 – 14.57)	0.0046
Prostration	10.76 (2.90 – 39.84)	0.0004
Capillary refill time >3 seconds	6.46 (1.88 – 22.22)	0.0031
Leucocytosis ≥ 11000	3.07 (1.05 – 8.99)	0.0404
Severe pallor	1.27 (0.27 – 6.09)	0.7616
Loss of consciousness	1.79 (0.32 – 10.11)	0.5097
< 3 feeds in last 24 hours	1.32 (0.39 – 4.44.)	0.6512
Cyanosis	1.00 (0.10 – 10.03)	0.9982
Pulse rate ≥ 170 b/m	1.59 (0.39 – 6.51)	0.5199
Actively convulsing	1.35 (0.23 – 7.98)	0.7372
Cold peripheries	2.18 (0.36 – 13.41)	0.3985
Thin pulse volume	1.35 (0.37 – 4.90)	0.6468

Table 4: Logistic regression for features associated with hypoglycaemia.

Mortality among participants with hypoglycemia

Of the 27 critically ill children with hypoglycemia 9 (33.3%) died within the seven days of follow up compared to mortality of 16/423 (3.8%) among critically ill children without hypoglycemia (OR 12.72, 95% CI 4.95 - 32.67, P value < .0001) (Table 5). All the 27 hypoglycemic participants received 10% dextrose 5mls/kg, and a repeat blood glucose test showed a rise of blood glucose level above 60mg/dl in 26 of them.

Most deaths among participants occurred in the first 2 days of admission (Figure 1).

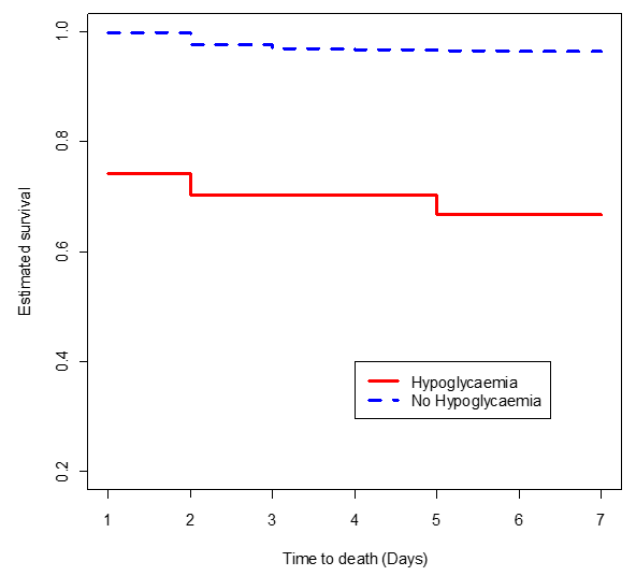

Figure 1: Kaplan-Meier estimate for survival curve (time to death) among children with hypoglycaemia and those with no hypoglycaemia within 7days of follow-up.
Log rank, P value = < 0.0001

Length of hospital stay among participants with hypoglycemia

Of the 18 study participants with hypoglycemia who survived, 10 (55.6%) were discharged before day seven of admission (Table 5). The likelihood of discharge was the same in those with or without hypoglycemia.

	Hypoglycemia		OR (95% CI)	P Value
	Yes	No		
Died within 7 days				
Yes	9	16	12.7 (4.9-32.6)	<.0001
No	18	407		
Discharged before day 7				
Yes	10	228		
No	8	179	0.98 (0.4, 2.5)	0.9691
On ward on day 7				
Yes	8	179	1.01 (0.22, 1.68)	0.3407
No	10	228		

Table 5: Association between outcomes of critically ill children and presence of hypoglycemia.

Discussion

This study was carried out to determine the prevalence and characterize the clinical consequences of hypoglycemia among critically ill children aged 2 months to 12 years presenting to the ACU of Mulago hospital.

The prevalence of hypoglycemia was 5.9%. This finding calls into question the current practice at the ACU of giving all critically ill children intravenous dextrose, as over 90% may actually not need it.

The prevalence found in this study was lower than what was previously reported by other studies in the same setting. Mbabazi J., *et al.* in 2009 reported a prevalence of hypoglycemia of 28.4% [7]. Possible explanations for this marked difference in the two studies include the fact that participants in the earlier study were younger, aged 2-59 months, and that only half of the study population had a blood glucose test done, with the criteria for testing not indicated. Thus, a bias for sampling children more likely to have hypoglycemia may have been present in the earlier study. Seasonal variations and changes in disease trends might also explain differences in the prevalence of hypoglycemia between the two studies. In a more recent study, Aliku T., *et al.* in 2010 reported a comparable prevalence of hypoglycemia of 7.8% among critically ill children 2-59 months of age presenting to ACU [8].

The prevalence found in this study was also closer to the findings of Osier FH., *et al*, who reported a 7.3% prevalence of hypoglycemia among children being admitted to a rural Kenyan hospital [1], and Elusiyan JB., *et al*, who showed that hypoglycemia was present in 6.4% of children admitted in a Nigerian Pediatric emergency department [4]. These two studies did not describe whether only participants with critical illness were studied.

In this study the clinical features which were independently associated with hypoglycemia included, inability to breast feed or drink, difficulty in breathing, fasting for 12 or more hours, prostration, capillary refill time > 3 seconds, leucocytosis ≥ 11000 cells/µl. Inability to breast feed or drink was present in 66.7% of participants with hypoglycemia, yet only 4.7% of the participants with no hypoglycemia had this feature. This finding has not been described in previous studies, but it would be expected that a child who has inability to breastfeed or drink eventually may develop hypoglycemia due to reduced intake of glucose. Possible causes of inability to breastfeed or drink can include loss of appetite, loss of consciousness or general body weakness. Difficulty in breathing can be a feature of respiratory or cardiac illness, acidosis or even neurological disease [10]. This feature was also reported by Osier FH., *et al.* in 2003 to be associated with hypoglycemia among children admitted in a Kenyan hospital [1]. In severe illnesses leading to difficulty in breathing, metabolic derangements such as impaired gluconeogenesis may occur leading to hypoglycemia [10,11]. During prolonged fasting, the body uses glycogen stores to generate glucose or convert other substrates into glucose by gluconeogenesis [10]. In critically ill children, these metabolic processes also become impaired hence leading to hypoglycemia [10, 11]. Osier FH., *et al.* and Elusiyan JB., *et al.* also reported that lack of feeding for 12 or more hours among admitted children was significantly associated with hypoglycemia [1,4]. Severe weakness with inability to sit unsupported or inability to feed (Prostration) is a sign of hypoglycemia [11] and in this study majority of participants with hypoglycemia had prostration. Prostration was reported by Osier FH., *et al.* to be significantly associated with hypoglycemia [1]. Capillary refill time > 3 seconds is one of the signs of shock, others being cold peripheries, rapid weak pulse, hypotension [9]. Once again critically ill children with shock are likely to have metabolic derangements which can then affect glycogenolysis and gluconeogenesis [10]. This can result into hypoglycemia. There is limited data about a prolonged capillary refill time being found in hypoglycemic patients, previous studies by Osier FH., *et al.* and Elusiyan JB., *et al.* did not report about this feature [1,4]. Leucocytosis has been described as a laboratory finding in patients with bacterial infections [12]. Though this study did not confirm presence of septicaemia among study participants, septicaemia was reported as a common diagnosis among children with hypoglycemia by Elusiyan JB., *et al.* in the Nigerian paediatric emergency department [4].

As was reported by Elusiyan JB., *et al.* 2006 that hypoglycemia was more common among children with severe malaria, pneumonia, and protein energy malnutrition [4], this study also showed that the commonest clinical diagnosis among participants with hypoglycemia was severe pneumonia, followed by diarrhea, severe malaria, severe acute malnutrition. However in our study no clinical diagnosis was independently associated with hypoglycemia at presentation to the ACU of Mulago hospital.

The mortality rate was significantly higher among participants with hypoglycemia compared to those with no hypoglycemia. The risk of dying was 12 times higher if the participant had hypoglycemia compared to the risk among patients without hypoglycemia. A prior study by Kupper AW., *et al.* also showed that hypoglycemia was significantly associated with higher mortality (16.5%, compared to 2.1% in those without hypoglycemia [3]. Similarly, Rakesh L., *et al.* in 2009 observed that the mortality rate among children admitted with hypoglycemia to the pediatric intensive care unit was significantly higher than mortality rate in normoglycemic children [2]. All these findings suggest that children presenting to hospital with hypoglycemia are at high risk of death compared to non-hypoglycemic ones. This is a cause for concern, as hypoglycemia is preventable if identified and treated appropriately.

In conclusion this study showed that hypoglycemia was present in 5.9% participants. Clinical features significantly associated with hypoglycemia were inability to breastfeed or drink, difficulty in breathing, last meal ≥ 12 hours before presentation, prostration, prolonged capillary refill > 3 seconds and leukocytosis (≥ 11000 cells /µl). There was a high mortality among hypoglycemic participants of 33.3% while only 3.8% participants without hypoglycemia died and hypoglycemic and non-hypoglycemic participants who survived had comparable durations of hospital stay. Thus hypoglycaemia should be suspected among critically ill children, in particular with the risk factors described above.

Glucose testing and 10% dextrose should be available in paediatric emergency units so that hypoglycemic critically ill children can be identified and treated early.

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Bibliography

1. Osier FH., *et al*. "Abnormal blood glucose concentrations on admission to a rural Kenyan district hospital: prevalence and outcome". *Archives of Disease in Childhood* 88.7 (2003): 621-625.
2. Rakesh L., *et al*. "Day 1 Blood Glucose and Outcome in Critically Ill Children". *Indian Pediatrics* 46.9 (2009): 809-810.
3. Kupper AW., *et al*. "Association of Hypoglycemia, Hyperglycemia, and Glucose Variability With Morbidity and Death in the Pediatric Intensive Care Unit". *Pediatrics* 118.1 (2006): 173-179.
4. Elusiyan JB., *et al*. "Hypoglycaemia in a Nigerian paediatric emergency ward". *Journal of Tropical Pediatrics* 52.2 (2006): 96-102.
5. Nicholson J, Pesce M. "Reference ranges for laboratory tests and procedures. In: Behrman R, Kleigman R, Jenson H, eds. Nelson textbook of pediatrics. 17 ed: Philadelphia Saunders (2004): 2396-2427.
6. UNICEF Country Report (2017).
7. Mbabazi J. "Presentation and immediate outcome of critically ill children presenting to acut care unit Mulago hospital. Kampala: Makerere (2009).
8. Aliku T. "Electrolyte abnormalities among critically ill children presenting to Acute Care Unit Mulago Hospital, Types, associated factors and immediate outcome". Kampala: Makerere (2010).
9. WHO. "Pocket book of hospital care for children". (2005): 1-35.
10. Greenbaum L A. "Electrolyte and acid base disorders". In: Behrman R, Kleigman R, Jenson H, eds. Nelson textbook of paediatrics". 17th ed: Saunders (2004): 191-242.
11. Sperling MA. Hypoglycemia. In: Behrman R, Kleigman R, Jenson H, eds. "Nelson textbook of paediatrics". 17th ed: Saunders (2004): 505-518.
12. Powell K R. "Fever of unknown origin". In: Behrman R, Kleigman R, Jenson H, eds. Nelson textbook of pediatrics. 17th ed: Saunders (2004): 843-846.

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