

# Relationship between Hypoglycemia and Home Remedies among Critically Ill Children in a Developing Country: An Undisclosed Danger

Uleanya Nwachinemere Davidson<sup>1</sup>, Aniwada Elias Chikee<sup>2</sup> and Nduagubam Obinna Chukwuebuka<sup>1</sup>

<sup>1</sup>Department of Pediatrics, Enugu State University Teaching Hospital, Parklane, Enugu, Nigeria, <sup>2</sup>Department of Community Medicine, University of Nigeria Teaching Hospital, Ituku-Ozalla, Nigeria

## Corresponding author:

Uleanya Nwachinemere Davidson,  
Department of Pediatrics,  
Enugu State University Teaching  
Hospital, Parklane, Enugu, Nigeria,  
Tel: 234(0)7061286817;  
E-mail: nulesa2001@yahoo.com

## Abstract

**Background:** Critically ill children are those in need of immediate attention on presentation. Hypoglycemia is known to complicate many critical illnesses and lead to higher morbidity and mortality for affected children in sub-Saharan Africa. Its effect is lethal as it has been shown to be an independent risk factor for increased mortality and worsening organ function. Many are of the opinion that herbal (home remedies) medications contribute to hypoglycemia among critically ill children. **Aim:** The study aims to determine the association between herbal medications and hypoglycemia. **Subjects and methods:** Analytical cross sectional method was used to study critically ill children aged  $\geq 1$  month to  $\leq 10$  years admitted into the Children Emergency Room of Enugu State University Teaching Hospital. Their admission blood glucose was done at presentation. Interviewer administered questionnaire was used to collect information needed. Both bivariate and multivariate logistic regressions were done. **Results:** A total of 300 patients were recruited. Seventeen children received home remedies while 283 did not. Among those that received home remedies 47.1% (8/17) had hypoglycaemia while 16.7% (47/283) of those that did not receive home remedies had hypoglycaemia ( $p < 0.01$ ). Those that received home remedies were about 4.4 times ( $p < 0.01$ , AOR=0.23, 95% CI: 0.08 - 0.67) adjusting and unadjusting ( $p < 0.01$ , UOR=0.23, 95% CI: 0.08 - 0.62) for other factors respectively more likely to have hypoglycemia than those who did not receive home remedies. **Conclusion:** Herbal medications are sinister cause of hypoglycemia especially in the critically ill nondiabetic children and needs to be discouraged.

**Keywords:** Herbal medications, Hypoglycemia, Children, Home remedies

## Introduction

Critical illness is a common finding in children emergency rooms in developing countries. These children present with such symptoms as fast or difficulty in breathing, cyanosis, convulsion, irritability or lethargy, dehydration, refusal of feeds, hypothermia, hyperpyrexia and floppiness [1,2]. They have varied clinical conditions that are life threatening. Such conditions include severe malaria, diarrheal diseases, lower respiratory tract infections, sepsis, burns etc [3]. Many of these conditions are characterized by hypermetabolism and increased tissue catabolism, higher nutritional needs, and a decreased capacity for utilization of parenteral substrate [3-5]. Hypermetabolism in these patients is associated with increased lipolysis and catabolism despite increased caloric intake. The energy requirement of children with critical illness is thought to be increased by more than 30% above normal [3,4]. The effect is such complications as hypoglycemia.

Hypoglycemia is a well-recognized complication among critically ill children and it is associated with increased mortality and neurological sequelae, particularly among under-fives [5-9]. The cause is not well understood but various pathogenic mechanisms have been postulated to explain the occurrence of hypoglycemia in critically ill children and these include increased glucose consumption due to fever, parasites

and infections, increased peripheral utilization of glucose as a result of increased anaerobic glycolysis, starvation and hepatic glycogen depletion and/or impaired gluconeogenesis [7,10,11]. Despite the controversies, it is agreed that cytokine-induced impairment of gluconeogenesis, impaired counter-regulatory hormone response and depletion of glucose stores in starvation contribute significantly to hypoglycemia in critically ill children [12-14]. Hypoglycemia therefore is a marker of disease severity [9,15]. Currently hypoglycemia has been recognized as an independent risk factor for increased mortality rates and worsening organ function. This risk being greater the more severe and longer the hypoglycemia [15]. Clinical hypoglycemia is a risk factor for mortality in critical illness, even if only detected as a single episode, increasing the associated mortality from 39.5% to 55.9% [16].

Several herbal medicines have been reported to have hepatotoxic

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effects and cause hypoglycemia [17]. The mechanisms of these herbs include increasing insulin secretion, enhancing glucose uptake by adipose and muscle tissues, inhibiting glucose absorption from intestine and inhibiting glucose production from hepatocytes [18]. It has been documented that in resource poor countries, hypoglycemia among critically ill children maybe caused or aggravated by the local idiosyncrasies, including use of potentially toxic herbal preparations at home, an altered nutritional status, delay in arrival and admission to hospital [19,20]. We hypothesized that hypoglycemia would be observed in critically ill children who received herbal medications at home (Home remedies) before presenting to Pediatric Emergency Room. The aim of this study was then to document the relationship between home remedies and hypoglycemia among critically ill children admitted into the Children Emergency Room.

## Methods

### Study site

The study was conducted in the pediatric emergency ward of Enugu State University teaching Hospital, situated in Enugu metropolis. It currently serves as the only not-for-profit government owned emergency room in Enugu metropolis. The hospital serves mainly people of Igbo ethnic group reflecting the population distribution of Enugu. This study period was from February 2014 to October 2015.

### Patients and consent

Ethical clearance was obtained from the Enugu State University Teaching Hospital Health Research and Ethics committee. Both written and oral informed consent was obtained from each parent(s)/caregiver and confidentiality maintained in the entire study. A total study was done involving 300 critically ill children 1 month to 10 years of age who met the inclusion criteria (symptomatology mentioned above) and had at least one blood glucose measurement on admission before commencement of intravenous fluid were recruited. All children in the study were studied from day of admission and followed up till discharge or death. Exclusion criteria include those children whose parent(s)/caregiver did not consent, all diabetics, all children who have received prior vasopressors or steroids and all those who did not present with the features mentioned above. A structured interviewer questionnaire was administered to Parent(s)/caregiver of each child. Some of the information sought by the questionnaire included: sociodemographics, presence of recurrent vomiting, hepatomegaly and use of herbal medication/home remedies. One microliter (1  $\mu$ L) of whole blood was collected at each measurement and tested for blood glucose level using the Accu-chek test strip and glucometer (Roche Diagnostics GmbH, Mannheim, Germany) on admission. Quality assurance followed standard hospital laboratory procedures. The calibration was based on the Hexokinase method and the measuring interval is 10-600 mg/dl. Hence blood glucose level of  $\leq 9$  mg/dl read low and High if  $> 600$  mg/dl. The Accu-chek active blood glucose measurement has been validated in Nigeria and correlates positively with laboratory blood glucose measurement by spectrophotometry,  $r=0.84, p=0.05$ . Its sensitivity is 75% with a specificity of 99.8% relative to the gold standard. It also has a positive predictive

value of 94.7% and a negative predictive value of 98.7% [21]. For the purposes of this study, we chose to define hypoglycaemia as blood glucose level of  $\leq 40$  mg/dl [22]. Socioeconomic class of a child was obtained by calculating the socioeconomic class of the parents using the method proposed by Oyedeji [23].

All data were analysed using IBM SPSS software version 20 (Chicago, USA). Tables were presented accordingly. Associations between socio-demographics, hepatomegaly, recurrent vomiting, and home remedies with glycaemic levels were determined using Chi-square test. Multivariate logistic regression was equally done to ascertain predictors of hypoglycemia. *P* value at level of  $\leq 0.05$  was accepted as significant.

## Results

A total of 300 patients were studied. Of these 50.3% (151/300) were aged  $\leq 1$  year while 49.7% (149/300) were aged  $> 1$ -10 years (median age: 12.4 months). As much as 62.3% (187/300) were boys and 37.7% (113/300) were girls and of these, 95.0% (285/300) were Igbos. Seven percent (21/300) of the patients belonged to the upper class, 41.7% (125/300) belonged to the middle class while 51.3% (154/300) belonged to the lower class [Table 1].

Of the 300 critically ill patients studied, 18.3% (55/300) had hypoglycemia while 5.7% (17/300) received home remedies (herbal medications). Among the 17 children who received home remedies, 8 belonged to the middle class while 9 belonged to the lower class with 4 children in each class having hypoglycemia.

On bivariate analysis, among those that received home remedies 47.1% (8/17) had hypoglycemia while 16.7% (47/283) of those that did not receive home remedies had hypoglycemia. There

**Table 1: Socio-demographic characteristics of respondents**

Frequency n = 300	Percent (%)	
<b>Age categories (years)</b>		
$\leq 1$	151	50.3
$\geq 1 \leq 10$	149	49.7
<b>Sex</b>		
Male	187	62.3
Female	113	37.7
<b>Tribe</b>		
Igbo	285	95.0
Others	15	5.0
<b>Social Class</b>		
Upper	21	7.0
Middle	125	41.7
Lower	154	51.3

was strong significant association between hypoglycemia and home remedies ( $p < 0.01$ ,  $\chi^2 = 9.932$ ). However, there was no significant association between socio-demographics, recurrent vomiting, hepatomegaly and hypoglycemia [Tables 2 and 3]. About 53% (9/17) of the children who received home remedies had hepatomegaly while 47% (8/17) did not have hepatomegaly. None had jaundice.

On multivariate analysis, unadjusted, those children who received home remedies were about 4.4 times more likely to have hypoglycemia than those who did not have home remedies ( $p < 0.01$ , UOR=0.23; 95% CI: 0.08-0.62). Adjusting for socio-demographic characteristics, hepatomegaly and recurrent vomiting, the children who received home remedies were about 4.4 times more likely to have hypoglycemia than those who did not receive home remedies ( $p < 0.01$ , AOR=0.23; 95% CI: 0.08-0.64) [Table 3].

## Discussion

The population characteristics in this study are typical in sub-Saharan African emergency rooms<sup>[9,19,24]</sup>. The under-fives, of which the greatest bulk are the infants are the most commonly admitted with critical illnesses. And usually, the government hospitals which are most times busy are mostly attended by the middle and lower socioeconomic class.

Hypoglycemia is a common finding among critically ill children. This study has demonstrated a hypoglycemia prevalence rate of 18.3% among critically ill children. This is higher than that

recorded by Osier, et al.<sup>[19]</sup> in Kenya, Sambany et al.<sup>[20]</sup> in Madagascar and Ameyaw et al.<sup>[24]</sup> in Ghana. This may be as a result of the fact that these studies did not study specifically critically ill children. It may also be due to the high rate of hypoglycemia induced by the herbal medications in this study. However, it compares well with that recorded by Onyiriuka et al.<sup>[9]</sup> in Benin though the study used higher values to define hypoglycemia.

A significant proportion (5.7%) of this study population received herbal medications at home before presentation to the emergency room. This was given with the good intention to heal or ameliorate fever and whatever condition that the child may have. These herbal medications are locally obtained and freely advertised as being potent in treating different ailments. However, undisclosed are the side effects of such herbs.

This study has also revealed a 47.1% prevalence of hypoglycemia among children who received herbal medications at home compared with 16.7% among those who did not receive herbal medications before presenting at the emergency room indicating that hypoglycemia is more common among critically ill non-diabetic children who received herbal medications at home before presentation. It was observed that the difference was strongly statistically significant, revealing the potent effect of these herbs in inducing hypoglycemia. It has been postulated that the effects of hypoglycemia among critically ill patients are manifold including increased mortality, organ dysfunction and

**Table 2: Association between socio-demographics, hepatomegaly, recurrent vomiting, home remedies and glycemic level**

	n = 300		$\chi^2$	p-value
	Hypoglycemia n (%)	No Hypoglycemia n (%)		
<b>Age categories (years)</b>				
≤ 1	26 (17.2)	125 (82.8)	0.252	0.615
≥ 1 ≤ 10	29 (19.5)	120 (80.5)		
<b>Sex</b>				
Male	37 (19.8)	150 (80.2)	0.700	0.403
Female	18 (15.9)	95 (84.1)		
<b>Tribe</b>				
Igbo	53 (18.6)	232 (81.4)	0.264	0.608
Others	2 (13.3)	13 (86.7)		
<b>Social class</b>				
Upper	3 (14.3)	18 (85.7)	2.388	0.303
Middle	28 (22.4)	97 (77.6)		
Lower	24 (15.6)	130 (84.4)		
<b>Hepatomegaly</b>				
No	26 (17.8)	120 (82.2)	0.052	0.819
Yes	29 (18.8)	125 (81.2)		
<b>Recurrent Vomiting</b>				
No	29 (17.9)	133 (82.1)	0.044	0.834
Yes	26 (18.8)	112 (81.2)		
<b>Home remedies</b>				
No	47 (16.7)	236 (83.3)	9.932	0.002*
Yes	8 (47.1)	9 (52.9)		

Table 3: Regression of socio-demographics and Home remedies on Hypoglycemia

	OR	Sign	95% CI	
			Lower	Upper
<b>Home remedies</b>				
UOR	0.226	0.004	0.083	0.616
AOR	0.230	0.005	0.083	0.638
<b>Ages in categories</b>				
	0.848	0.607	0.451	1.592
<b>Sex</b>				
	1.243	0.504	0.657	2.354
<b>Upper</b>				
		0.315		
<b>Middle</b>				
	0.690	0.582	0.184	2.583
<b>Lower</b>				
	1.121	0.867	0.294	4.280
<b>Tribe</b>				
	1.539	0.594	0.315	7.522
<b>Recurrent vomiting</b>				
	0.986	0.965	0.535	1.818
<b>Hepatomegaly</b>				
	0.945	0.858	0.507	1.759

promotion of oxidative stress and neuronal cell death, primarily as a consequence of neuronal NADPH oxidase activation and extracellular zinc release during glucose reperfusion. Thus, heightened glucose concentrations during reperfusion can lead to cell death [25-28]. The damage caused by the hypoglycemia cannot be overemphasized as the long-term consequences of hypoglycemia among the surviving children include decreased head size, lowered IQ, and specific regional brain abnormalities observed using magnetic resonance imaging (MRI) [15,29].

On multivariate analysis, unadjusting and adjusting for sociodemographics and other factors, herbal medication was found to be a predictor of hypoglycaemia. Those children who received herbal medications at home before presentation were more than 4 times more likely to be hypoglycemic compared with those who did not. Studies have shown that the odds of death were highest at hypoglycemic levels of  $\leq 40$  mg/dl (severe hypoglycemia) [15]. This may mean more deaths among those receiving home remedies before presentation.

### Conclusion

Herbal medications are sinister causes of hypoglycemia especially in the critically ill nondiabetic children and needs to be discouraged.

### Author's contributions

UND: Conceived and designed the study, designed the questionnaire, data collection, directed analysis, literature review, manuscript writing, and read the final draft. AEC: Participated in questionnaire design, analyzed data, and literature review, manuscript writing and read the final draft. NOC: Data collection, literature review, manuscript writing and read final draft. All authors approved final draft and acknowledge that the manuscript is an honest and original work.

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### Conflict of interest

Authors declare no conflict of interest among them.

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