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Prevalence and Outcome of Hypoglycaemia Among Children Presenting to the Children Emergency Room of Rivers State University Teaching Hospital

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ABSTRACT

Background: Hypoglycaemia is a common feature seen in children presenting in the paediatric emergency and it contributes to increased morbidity and mortality.
Objective: To determine the prevalence of hypoglycaemia among children admitted into the Children emergency of Rivers State University Teaching Hospital and to assess it's relationship with patient outcome.
Methods: In this cross-sectional study, 94 children whose parents gave informed consent were recruited consecutively. Their socio-demographic characteristics, clinical features, diagnosis, management and outcome were recorded. Random blood sugar was determined using Accu-Chek Active Blood glucose meter, and classified as hypoglycaemia (<3.3mmol/l), normoglycaemia (3.4-8-9mmol/l), hyperglycaemia-prediabetic range(>8.9-11mmol/l), hyperglycaemia-diabetic range(>11mmol/l).
Results: Of the 94 recruited children majority were under five years (75 children,79.8%) with male-female ratio of 1.24:1. Most common diagnosis seen were Malaria, Sepsis, Bronchopneumonia, anaemia and Meningitis; with an overall mortality rate of 5.3%. The prevalence of hypoglycaemia was 11.7%. Of the 11 children with hypoglycaemia, 4(44.4%) had their blood glucose level restored after 1 hour, 3(33.3%) had hypoglycaemia persisting and 2(22.3%) had hyperglycaemia. Out of the 3 children who had hypoglycaemia persisting, 2(66.7%) died while the 3rd (33.3%) was discharged. Mortality rate among those with hypoglycaemia was 27.3%. Hypoglycaemia was found to be significantly associated with a diagnosis of Sepsis and Gastroenteritis, and patient mortality.
Conclusion: Hypoglycaemia is common in children presenting in the emergency room and may be associated with increased mortality. Blood glucose levels should be monitored closely in all sick admitted children and hypoglycaemia corrected appropriately.
Key words: Prevalence Hypoglycaemia Children Emergency Port Harcourt

INTRODUCTION

Glucose is important for energy metabolism in the brain. It is the preferred energy source and its' utilization accounts for nearly all the brain's oxygen consumption. [1] Blood glucose homeostasis involves the liver, extrahepatic tissues (such as the muscles and adipose tissues) as well as several hormones such as

growth hormones, glucagon and insulin. [2] Thus alterations in one or more of these processes could lead to hypoglycaemia. [1]

Hypoglycaemia which refers to blood glucose level below normal, is a common metabolic disorder in children, especially in Emergency Paediatric Units (EPU). [3, 4] It is commoner in the paediatric age groups than in adults. [5] This is not surprising as children have a relatively larger brain to body size thus the rate of glucose utilization in children is higher than in adults, predisposing them more to hypoglycaemia. Also, children have limited glycogen storage reserve, thus, their blood glucose level falls faster during fasting reaching hypoglycaemic levels within a shorter duration of time than adults. [6]

The occurrence of hypoglycaemia usually reflects the presence of an underlying disease condition. This is because glucose is the fundamental energy source of cells thus disorders affecting either its' availability or utilization could result in hypoglycaemia. [1] Severe acute malnutrition, infectious diseases like malaria, diarrhoea, sepsis etc, use of toxic herbal medications and delay in assessing care in hospital are some of the factors that could predispose to hypoglycaemia. [7, 8] Other risk factors include young age, prolonged fasting and disease severity. [9-12] A prospective study carried out over 4 months in the EPU in Gusau, northern Nigeria reported severe acute malnutrition as the commonest morbidity among children with hypoglycaemia followed by acute diarrhoeal disease and severe malaria. [9] A similar study in Nnewi, south east Nigeria, reported malaria as commonest followed by sepsis and gastroenteritis. [10] Similarly, in Abuja, northern Nigeria malaria was also documented as the commonest followed by sepsis and severe acute malnutrition. [12]

Hypoglycaemia could lead to neurological damage especially in the developing brain resulting in severe mental retardation, transient cognitive impairment, speech and language impairment, learning disability, recurrent seizures and even death, if recurrent or prolonged. [1, 13] Thus, hypoglycaemia is a diagnostic emergency requiring urgent treatment in order to reduce childhood morbidity and mortality.

The definition of hypoglycaemia has remained controversial. Affected children can be symptomatic or asymptomatic. The absence of symptoms and signs does not signify a normal blood glucose neither does it mean that blood glucose has normalized. [1] It is also note-worthy that cases of asymptomatic hypoglycaemia could result in neurologic damage. [14] Various values have been attributed to hypoglycaemia in the past but presently, whole blood glucose less than 55mg/dl (3.1mmol/L) and plasma levels less than 60.5 -63.3mg/dl or < 3.4 – 3.5mmol/L now represents hypoglycaemia. [1] This higher cut-off value could be in a bit to prevent complications that could arise from hypoglycaemia which are usually permanent.

Symptoms of hypoglycaemia are generally non-specific. [15] These clinical features could be due to activation of the autonomic system (with release of epinephrine due to rapid decline in the blood glucose) leading to sweating, trembling, anxiety, nervousness, weakness, hunger, nausea and vomiting. [1,16] Other clinical features which could also arise (due to decrease in cerebral glucose utilization resulting from prolonged hypoglycaemia or slow decline in blood glucose level) include headache, visual disturbance, lethargy, lassitude, restlessness, irritability, inability to concentrate, confusion, somnolence, stupor, loss of consciousness, hypothermia, twitching, convulsion, personality changes etc. [1, 16, 17] These symptoms, thus, vary from central nervous system to cardiopulmonary disturbances depending on the age of the child and the severity of hypoglycaemia. [14]

The prevalence of hypoglycaemia varies from place to place and even within the same geographic location could vary over time. A study in the United States of America [18] documented a prevalence of 7.5% while in various parts of Africa, prevalence rates ranged from 3.1% - 7.3%. [4, 8, 19, 20] In Nigeria however,

prevalence rates reported ranges from 5.1% - 22.1%. [3,9, 11, 12,21] These variations could also be attributable to the varying definition of hypoglycaemia, as well as methods employed in the various studies.

Studies have shown that hypoglycaemia is a major indicator of poor prognosis in many disease conditions and is a significant predictor of fatal outcome. [4, 22-27] No study of this kind has been carried out in the Children emergency room of Rivers State University Teaching Hospital since its inception. Thus, the present study was carried out to evaluate the prevalence, pattern and outcome of children presenting with hypoglycaemia in the emergency unit. Findings of this study will thus, contribute to the body of knowledge on hypoglycaemia in Nigeria and may also help in the formulation of policies that will improve health care in the hospital and in Rivers State.

METHODS

This prospective cross-sectional study was carried out over 3 months in the Children Emergency Room (CHER) of the Rivers State University Teaching Hospital (RSUTH) from January 20th 2023 to April 19th, 2023.

The Rivers State University Teaching Hospital, a government owned tertiary hospital in the south-south geopolitical zone in Nigeria, is a 375-bed hospital which receives referral from all the Primary Health care centres and general hospitals in the 23 local government areas of the State (as well as other peripheral hospitals within the state and from neighbouring states). The hospital consists of both non-clinical and clinical departments including the Department of Paediatrics. The Children Emergency Room which is one of the units in the Department of Paediatrics is a 11-bed unit open 24 hours manned by resident doctors, house officers with supervising consultants. All emergency cases irrespective of the age of the child are seen in the emergency room and are thereafter admitted in the emergency room if between 1 month to 17 years or are transferred to the Special Care Baby Unit if within the neonatal age. Children are usually admitted in the CHER for not more than 48 hours to allow for clinical stabilization, and are thereafter either discharged home from the emergency room if clinically stable, or transferred to the children's ward to continue treatment.

Sample size was calculated using the formula for proportion [27] at 95% confidence interval and a prevalence rate of 6.4% from the study by Elusiyan et al [11]: $n = pq(e/1.96)^2$ where p = prevalence of hypoglycaemia, q = 100-p, e = margin of error tolerated (5%). Ethical approval was obtained from the Ethics Review Committee of the institution and informed consent was obtained from parents/caregivers and assent from children > 6years of age.

All patients aged 1 month to 17 years admitted into the CHER were eligible for the study and were consecutively recruited until the calculated sample size was met. Inclusion criteria were all children aged 1 month to 17 years admitted into the CHER and whose parents/caregivers gave verbal consent after the study and procedure was explained to them in clear words and in the language they could understand. Children who were not within this age bracket or whose parents/caregivers did not give consent, as well as known diabetics, were excluded from the study.

Four research assistants (house officers) were recruited for this study. They were duly educated about the study and trained on the proper administration of the research proforma; as well as the proper method of collection of blood from the patients and how to perform random blood sugar using a point of care machine. A total of 94 children ages 1 month to 15 years were recruited for this study.

A pretested research proforma was used to record information which included sociodemographic characteristics, clinical features, diagnosis, management and outcome of management. Socio-economic status was according to Oyedeji's classification system. [28]

Random blood sugar (RBS) was determined for every child once admitted using Accu-

Chek Active Blood glucose meter (Roche diagnostics, Mannheim, Germany). Blood glucose levels were classified as hypoglycaemia (<3.3mmol/l), normo-glycaemia (3.4-8-9mmol/l), hyperglycaemia-prediabetic range(>8.9-11mmol/l) and hyperglycaemia-diabetic range(>11mmol/l).[10] A test strip was inserted into the glucometer thus switching it on. For children below 1 years, capillary blood was collected from the lateral aspect of the heel after the area was cleaned with an alcohol swab, air-dried and area pricked gently with a lancet while in older children, capillary blood sample was taken from the thumb in similar manner. A drop of blood (0.3µl) was allowed to drop on the glucometer strip test area and the blood glucose level displayed read within 30 seconds. Thereafter, a dry swab was used to secure haemostasis for about a minute by applying gentle pressure and reinforced with a plaster.

Children with hypoglycaemia were treated according to standard protocols with either 2mls/kg of 10%DW or 4mls/kg, depending on whether they were symptomatic or asymptomatic, followed by maintenance with 6-8mg/kg/minute of 10% Dextrose water (DW) given over 24 hours. [11,27] Random blood sugar was thereafter monitored 30 minutes after, then 1hourly; if normal x 3 it was checked 2 hourly; if normal x 3 it was checked 4 hourly for 24 hours. Subjects received management appropriate for their clinical diagnosis according to standard protocols.

Patient outcome following management was recorded as discharged, dead, discharged against medical advice (DAMA) and referred.

Data was entered in an Excel spread sheet and subsequently analysed using Statistical package for social sciences (SPSS) version 23.0. Results were presented as frequencies, percentages and bar charts. Test of association was done using χ^2 test and Fishers' Exact test. Statistical significance was set at *P* value <0.05.

RESULTS

A total of 94 children aged 1 month to 15 years were recruited over 3 months (January- April 2023). There were 52 boys (55.3%) and 42 girls (44.7%) with a male: female ratio of 1.24:1. Majority (75 children) were under-fives (79.8%). Majority of mothers are 30-39 years old (52 mothers, 55.3%) with secondary education (46 mothers, 48.9%). Commonest socio-economic status is Class 3(41,43.6%) as shown in Table I.

Table I: Sociodemographic characteristics of subjects

Variable	Frequency(n=94)	Percentage (%)
Sex of child		
Male	52	55.3
Female	42	44.7
Age Group of children (months)		
0 – 11	38	40.4
12 – 60	37	39.4
5 – 10 years	9	9.6
>10 years	10	10.6
Median age(IQR): 18.5 (45.5) months		
Mother's age group (years)		
20 – 29	24	25.5
30 – 39	52	55.3
≥ 40	18	19.2
Mean age (years) 34.29 ± 7.73		
Socio-economic Status		
Class 1	6	6.4
Class 2	14	14.9
Class 3	41	43.6
Class 4	26	27.7
Class 5	7	7.4

The presenting complaints of the subjects are as shown in Table II. The commonest symptoms were fever (78.3%), vomiting (47.8%), cough (38%), weakness (32.6%) and poor appetite (31.5%). The subjects' diagnoses are shown in Table III. Most common diagnosis seen were Malaria (35.1%), Sepsis (29.8%), Bronchopneumonia (24.5%), anaemia (17%) and Meningitis (16%).

Table II: Presenting complaints of the subjects

Presenting complaints (multiple response)	Frequency (n = 340)	Percent (%)
Fever	72	78.3
Cough	35	38.0
Vomiting	44	47.8
Poor appetite	29	31.5
Weakness	30	32.6
Abdominal pain	13	14.1
Weight loss	5	5.4
Convulsion	21	22.8
Loss of consciousness	7	7.6
Watery stool	15	16.3
Pain	5	5.4
Fast Breathing	15	16.3
Catarrh	10	10.9
Difficulty in breathing	5	5.4
Swelling	11	12.0
Colored urine	3	3.3
Headache	3	3.3
Others	17	18.5

Table III: Diagnoses of subjects

Diagnosis (multiple response)	Frequency (n = 173)	Percent (%)
Bronchopneumonia	23	24.5
Malaria	33	35.1
Sepsis	28	29.8
Gastroenteritis	8	8.5
Anemia	16	17.0
Meningitis	15	16.0
RVD	5	5.3
Tonsillitis	8	8.5
Appendicitis	2	2.1
SCD	4	4.3
Diarrhea	3	3.2
Convulsion	3	3.2
Others	25	26.6

Prevalence of hypoglycaemia

Of the 94 children, 11(11.7%) had hypoglycaemia, 76(80.9%) had normoglycaemia while 7(7.4%) had hyperglycaemia as shown in Figure 1 below. Hypoglycaemia was more common in females and those less than 5 years although this finding was not statistically significant (Table IV). Hypoglycaemia was however significantly associated with a diagnosis of Sepsis and Gastroenteritis (Table V).

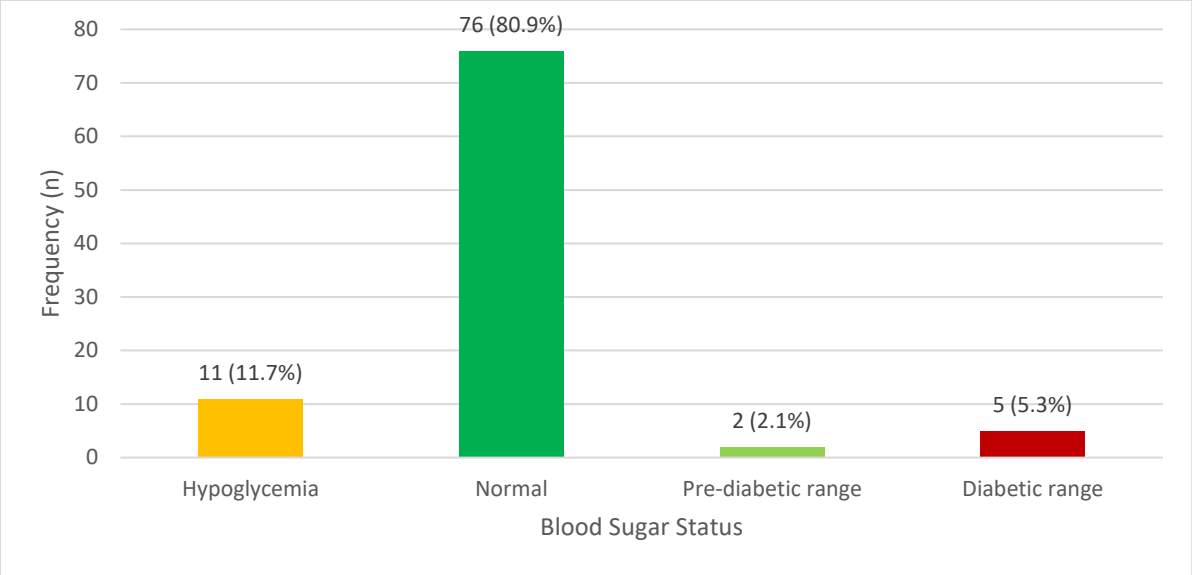

Figure 1: Random Blood Sugar levels of the Children

Table IV: Association between Hypoglycaemia, Sex and Age of children

	Hypoglycemic status		Statistical Significance
	Yes n (%)	No n (%)	Fisher's Exact
Sex			
Male	4 (36.4)	48 (57.8)	0.210
Female	7 (63.6)	35 (42.2)	
Age Group of children (months)			
0 – 11	4 (36.4)	34 (41.1)	
12 – 60	7 (63.6)	30 (36.1)	0.327
5 – 10 years	0	9 (10.8)	
>10 years	0	10 (12.0)	

Table V: Association between Hypoglycaemia and Diagnosis

Diagnosis	Hypoglycemic status		Statistical Significance
	Yes n (%)	No n (%)	Fisher's Exact
Bronchopneumonia	1 (9.1)	22 (26.5)	0.284
Malaria	6 (54.5)	27 (32.5)	0.185
Sepsis	8 (72.7)	20 (24.1)	0.002
Gastroenteritis	3 (27.3)	5 (6.0)	0.049
Anemia	0	16 (19.3)	0.201
Meningitis	2 (18.2)	13 (15.7)	1.000
RVD	0	5 (6.0)	1.000
Tonsillitis	0	8 (9.6)	0.590
Appendicitis	0	2 (2.4)	1.000
SCD	0	4 (4.8)	1.000
Diarrhea	0	3 (3.6)	1.000
Convulsion	0	3 (3.6)	1.000
Others	3 (27.3)	22 (26.5)	1.000

Of the 11 children with hypoglycaemia, following appropriate correction (with either 2mls/kg of 10%DW or 4mls/kg followed by maintenance with 10%DW depending on whether they were symptomatic or asymptomatic); 4(44.4%) had their blood glucose level restored after 1 hour, 3(33.3%) had hypoglycaemia persisting and 2(22.3%) had hyperglycaemia. Out of the 3 children who had hypoglycaemia persisting, 2(66.7%) died while the 3rd (33.3%) was discharged. Mortality rate among those with

hypoglycaemia was 27.3%. Hypoglycaemia was found to be significantly associated with patient mortality (table VI).

Table VI: Association between Hypoglycaemia and Hospital Outcome of Children

Hospital outcome	Hypoglycemic status		Statistical Significance
	Yes n (%)	No n (%)	Fisher's Exact
Discharged	6 (54.5)	77 (92.8)	
Dead	3 (27.3)	2 (2.4)	0.002
DAMA	2 (18.2)	2 (2.4)	
Referred	0	2 (2.4)	

DISCUSSION

The prevalence of hypoglycaemia in the present study was found to be 11.7%. This finding is comparable to the findings of Azuka et al [10] in a study done at the teaching hospital in Nnewi (prevalence of 12.9%) and Ameyaw et al [29] (prevalence of 13%) but higher than the findings of Jaja et al,[3] Elusiyan et al[11] and Ugege et al[27] with prevalence reported as 5.1%, 6.4% and 2.1% respectively. This difference may be due to the fact the authors for these 3 studies used lower cut-offs for the definition of hypoglycaemia: <2.5mmol/l in plasma for the study by Jaja et al[3] and Elusiyan et al[11] and then <2.8mmol/l in whole blood for the study by Ugege et al. [27]

Musa et al[9] however reported much higher prevalence of 22.1%. The reason for this difference is not clear, however may not be unrelated to the fact that this study was done in Gusau in the far north of the country, an area recently troubled by insurgency and the associated challenges of poverty, difficulty accessing care on time due to security concerns. Wintergerst et al[30] also reported a higher prevalence of 18.6% in California, USA. This study however involved children in an intensive care unit and thus were likely more ill.

Hypoglycaemia was found to be more common in females and in children under five years. This is similar to that reported by Elusiyan[11] who also reported hypoglycaemia being more common in children <3years. This finding is not surprising as children under five are more vulnerable to severe illnesses that predispose them to hypoglycaemia by causing anorexia and interfering with glucose uptake and are also more dependent of their anxious parents for feeding.[3,6] Infants and young children are also known to have a less efficient glucose homeostasis because of a lower reserve of liver glycogen/muscle protein and a higher level of glucose utilization due to a higher brain to body mass ratio.[10] This association, however was not found to be statistically significant.

Hypoglycaemia was found to be significantly associated with Sepsis and Gastroenteritis. This finding was not surprising as these diagnoses are associated with poor intake, accelerated tissue metabolism, increased fluid/calorie losses via vomiting and passage of loose stools.[6] This is similar to findings of several authors who also in addition reported hypoglycaemia as being more common in children with severe malaria, bronchopneumonia, malnutrition and coma.[3, 6, 9-11, 20, 27] The risk for hypoglycaemia is often worsened by the fact that some parents ignorantly withhold feeds from very ill children especially those stooling or vomiting for fear of worsening their symptoms.[3] Fever, an inflammatory response frequently seen in patients with Sepsis, may cause an increase in peripheral glucose utilization thus leading to the development of hypoglycaemia.[10] Hypoglycaemia in patients with Sepsis has also been reported to be likely due to production of endotoxins which may stimulate insulin secretion and also inhibit gluconeogenic pathways.[11] The study by

Elusiyan et al[11] in contrast to the finding of this present study, however, reported no hypoglycaemia in all 14 children admitted for Gastroenteritis in the Paediatric emergency ward at Ife, Osun state. This observation was attributed to the judicious use of Oral rehydration therapy in these patients. This highlights the need for further enlightenment of parents, hospital workers and the public at large about the need for proper address of nutritional requirements of ill children, particularly those with gastroenteritis, by encouraging adequate oral feeds when possible and the judicious use of oral rehydration therapy.

Mortality rate was significantly high amongst children with hypoglycaemia (27.3%) and even higher in those with hypoglycaemia persisting beyond the first hour despite appropriate corrective measures (66.7%). Hypoglycaemia was shown by this study to be significantly associated with patient outcome. This is similar to the findings of several other authors. [3,6,9-11, 20, 31] Jaja et al[3] also reported a high mortality rate of 36.8% amongst hypoglycaemic children suggesting hypoglycaemia is a poor prognostic feature of many childhood diseases. Azuka et al[10] reported hypoglycaemic children as being three times more likely to die than normoglycaemic children. Elusiyan et al[11] reported that whenever hypoglycaemia was present, especially with severely ill children, the risk of dying was higher. Thus, the importance of prevention of hypoglycaemia, it's prompt diagnosis and appropriate treatment cannot be over-emphasized for the reduction of morbidity and mortality amongst sick children.

CONCLUSION

Hypoglycaemia is common in children presenting in the emergency room and may be associated with increased mortality. Blood glucose levels should be monitored closely in all sick admitted children and hypoglycaemia corrected appropriately. The need for prompt diagnosis and treatment cannot be over emphasized to reduce morbidity and mortality among these children.

Declaration by Authors

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