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Original Article

Prevalence and risk factors for hypoglycemia in acutely ill children seen at the emergency pediatric unit of the Federal Teaching Hospital Katsina, Northern Nigeria

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Abstract

Hypoglycemia is a common metabolic problem seen in children presenting with acute illnesses. It may be part of the presentation and portends the illness's severity, contributing to morbidity and mortality. This study aimed to evaluate the prevalence and risk factors for hypoglycemia in children seen at the Emergency Paediatric Unit of the Federal Teaching Hospital Katsina. The study was descriptive and cross-sectional and was conducted in the Emergency Paediatric Unit (EPU) of the Federal Teaching Hospital Katsina. Of the One hundred and forty-six children screened for hypoglycemia, 6.2% had (plasma glucose less than 3 mmol/l). Patients whose last feed was taken 12 hours or more were more likely to have hypoglycemia at presentation (OR 51; CI=7.5–358). There were more deaths among hypoglycemic subjects compared to those without hypoglycemia. Children have a limited capacity for gluconeogenesis and are thus at higher risk of morbidities and mortalities related to hypoglycemia. Hypoglycemia should, therefore, be sought in all patients presenting with acute pediatric emergencies, particularly in those with a history of prolonged fasting.

Keywords: hypoglycemia, children, emergency pediatric unit, risk factors.

Introduction

Glucose has a central role in metabolism and is a source of energy storage in the form of glycogen, fat, and protein [1]. Hypoglycemia occurs when blood glucose falls below the optimal level for cellular metabolism. It is defined as a whole blood glucose value of less than 3 mmol/l (55 mg/dl) [1]. It is common in clinical practice. Its prevalence among children seen in emergency pediatric units ranges between 3.2% to 7.3% [2–7]. In studies by Elusiyan *et al.* in Ile-Efe and Oyenusi *et al.* in Lagos, the prevalence was 6.4% and 5.6%, respectively [5, 6]. Compared to those with euglycemia, morbidity and mortality is higher in acutely ill children with hypoglycemia [4–7]. Therefore, measuring blood glucose in all acutely ill children presenting to emergency pediatric units has become standard practice.

Certain factors increase the risk of hypoglycemia. Due to limited resources, identifying these factors is particularly important when triaging. They include age less than 5 years, low weight-for-age z-score (WAZs), diarrhea, prolonged fasting and a history of

ingestion of traditional medication or poisoning [5, 8, 9]. In the tropics, most childhood killer diseases, including meningitis, malaria, pneumonia, protein-energy malnutrition, and gastroenteritis, are complicated by hypoglycemia [4–6].

Clinical features of hypoglycemia are commonly non-specific and can be missed with attendant consequences [10]. Routine screening of all acutely ill children presenting to the Hospital will reduce misdiagnosis and mortality.

Data on the prevalence of hypoglycemia and the outcome of related morbidities in acutely ill children is scarce in Northern Nigeria. This study aimed to determine these rates in Katsina. The study has added to existing knowledge on the subject matter and has contributed to filling a data gap in northern Nigeria. The working hypothesis was that hypoglycemia was not common in acutely ill children and did not significantly increase the risk of mortality in children admitted into the children's emergency unit.

Material and methods

The study was descriptive and cross-sectional and was undertaken in the Emergency Paediatric Unit (EPU) of Federal Teaching Hospital Katsina. The Hospital is a tertiary referral center with a 500-bed capacity. On average, 35 patients were admitted every week to the 15-bed unit.

Katsina State has an estimated population of 7,831,300 and a landmass of 24,192 square kilometers. It is located in the northwest geopolitical zone at latitude 11°8'N 13°22'N and longitudes 6°52'E and 9°20'E [10].

Ethical clearance was obtained from the Ethics and Research Committee of the Federal Teaching Hospital Katsina. After full disclosure, written informed consent was also obtained from the parents/guardians of participating children. Parents also signed or thumb-printed the consent form. All children between the ages of 1 month and 14 years admitted into the emergency unit were consecutively recruited for the study until the sample size was attained. Children who received oral rehydration solution (ORS) or intravenous dextrose fluids within 6 hours of admission were excluded.

Blood samples were taken from the finger prick site. After cleaning with a sterile swab, the finger was pricked with a lancet soaked in clean water and allowed to dry under free air. A drop was allowed on the *Accu-chek Active* glucometer, and the result was obtained within a minute. The result determines the response's urgency to correct blood glucose levels. Glucometer readings may be less sensitive for hypoglycemia (blood glucose less than 3 mmol/l) than the laboratory glucose oxidase method. With this fact, therefore, for every blood glucose that was less than 4 mmol/l, 1.5 ml of blood was obtained from a peripheral vein and transported in a fluoride oxalate-containing specimen bottle for immediate plasma glucose test by the glucose-oxidase method in the main laboratory [11]. For subjects with hypoglycemia, a 200 mg/kg mini-bolus of dextrose was administered by a slow intravenous push over three minutes (2 ml/kg of 10% dextrose) [1]. This was followed by a continuous intravenous infusion of 6 mg/kg/min (4 ml/kg/hour) using 10% dextrose solution or feeding as appropriate [12]. Blood glucose was monitored subsequently according to existing unit guidelines until the patient was fully stabilized. The urine specimen was collected from the first voided sample in all patients with blood glucose <4 mmol/l or >7.8 mmol/l. This was tested immediately for glucose and ketones using urinalysis dipsticks and recorded. Readings were taken for ketones and glucose after 30 and 45 seconds, respectively.

After stabilization, physical examination and anthropometry measurements were conducted, and a questionnaire was administered to the caregiver/subject. Information concerning the time of last feed-in hours, history of ingestion of traditional herbs, previous episodes of hypoglycemia, and other relevant socioeconomic history were collected and recorded in the semi-structured proforma developed for the study.

The data collected was analyzed using SPSS version 23 and Excel 2016. The raw data was tested for normality. Numerical variables were presented in tables and expressed in percentages and charts. Categorical variables were expressed in rates and proportions. Statistical significance was assessed using Chi-square for discrete variables and Student t-test for continuous variables at 95% confidence interval [13].

Results

Samples were obtained from 150 recruited patients. Of these, 146 were analyzed. Three were excluded due to incomplete data, and one was excluded due to the inappropriate handling of specimens.

The median age was 48 months, with an interquartile range of 13–108 months. Slightly more males, 75 (51%), were recruited compared to females, 71 (49%), giving a male-to-female ratio of 1.1:1. Two-thirds of

the patients were of low socioeconomic status. Forty-five percent had moderate to severe malnutrition with weight-for-height z-scores (WHZs) less than -2SD.

Of the 146 patients, only 9 had hypoglycemia (random plasma glucose <3 mmol/l). The prevalence of hypoglycemia was thus 6.2%. The mean random blood glucose (RBS) was 6.4 mmol/l±3.35. Table 1 compared the socio-demographic data between hypoglycemic and non-hypoglycemic subjects [14].

Risk factors for hypoglycemia

Several factors were evaluated for contribution to the risk of hypoglycemia in the study subjects. These include age, nutritional status, duration from the last feed, ingestion of traditional medication, and subnormal body temperature. The interval of more than 12 hours from the last feed was a significant factor for presenting with hypoglycemia than other children with a less prolonged feeding interval (OR 51; CI=7.5–358).

Clinical diagnosis

The commonest diagnoses among all patients were septicaemia, sickle cell disease (SCD) crisis, meningitis, severe pneumonia and malnutrition, representing 12.3%, 12.3%, 9%, 7.5%, and 6.1% of the total admissions, respectively. Four (2.7%) patients had typhoid fever, out of whom two had hypoglycemia, which was statistically significant ($\chi2=13.66$; p=0.019). Although hypoglycemia was identified as a complication in severe malaria, sepsis, typhoid fever, severe protein energy malnutrition (PEM), malignancy and acute nephritis syndrome, it was a significant finding in only Typhoid fever (Table 2).

Outcome

Sixteen patients died, giving a mortality of 11 percent. Two among whom (12.5%) had hypoglycemia. Patients with hypoglycemia had a higher proportion of death, 22 percent (2/9), compared to 10 percent (14/137) among patients without hypoglycemia. However, this difference was not statistically significant ($\chi2=1.247$; p=0.257).

Discussion

The definition of hypoglycemia in this study was based on the new cut-off placed at random plasma glucose of <3 mmol/l [1]. Since most previous studies were based on lower values, comparison will be difficult. The prevalence of hypoglycemia in this study

Table 1: Demographic and nutritional characteristics of the 146 patients.

Clinical variables	Hypoglycemic (%)	Non-hypoglycemic (%)	P-value
Age			
Infants	1 (3)	33 (97)	
Under fives	3 (5.7)	49 (94.3)	0.206
Older children	5 (8.3)	55 (91.7)	
Sex			
Male	3 (4)	72 (96)	0.221
Female	6 (8.5)	65 (91.5)	
Social status *			
Upper	1 (2)	49 (98)	0.123
Lower	8 (8.3)	88 (91.7)	
Nutritional status			
Normal	3 (5.5)	52 (94.5)	
Mild malnutrition	2 (8.7)	21 (91.3)	0.463
Moderate malnutrition	2 (4.4)	43 (95.6)	
Severe malnutrition	2 (8.7)	21 (91.3)	

Note: * – The social classification was done as described by Oyedeji [14].

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Table 2: Comparison of hypoglycemic and non-hypoglycemic patients with respect to final diagnosis.

Final diagnosis	Frequency n=146 (%)	Hypoglycemic, n=9 (%)	Non-hypoglycemic, n=137 (%)	P-value
Severe malaria °	6 (4)	1 (17)	5 (83)	NS
Cerebral malaria	1 (0.7)	0 (0)	1 (100)	NS
Septicemia °	18 (12.3)	3 (17)	15 (83)	NS
SCA with crises °	18 (12.3)	0 (0)	18 (100)	NS
Malignancies	7 (4.8)	1 (14)	6 (86)	NS
Typhoid fever	4 (2.7)	2 (50)	2 (50)	0.019*
Nephrotic syndrome	4 (2.7)	0 (0)	4 (100)	NS
ANS	4 (2.7)	1 (25)	3 (75)	NS
Bacterial pneumonia °	11 (7.5)	0 (0)	11 (100)	NS
Severe PEM °	9 (6.2)	1 (11)	8 (89)	NS
Acute tonsillitis °	11 (7.5)	0 (0)	11 (100)	NS
Tuberculosis	2 (1.4)	0 (0)	2 (100)	NS
UTI ²	4 (2.7)	0 (0)	4 (100)	NS
Gastroenteritis	2 (1.4)	0 (0)	2 (100)	NS
Bacterial meningitis	13 (8.9)	0 (0)	13 (100)	NS
Status epilepticus	4 (2.7)	0 (0)	4 (100)	NS
Others	28 (19)	0 (0)	28 (100)	NS
Total	146 (100)	9	137	

Note: * – Statistically significant ($\chi 2=13.66$; df=1; p=0.019); ANS – Acute nephritis syndrome; SCA – Sickle cell anaemia; UTI – Urinary tract infection; NS – Not statistically significant; ° – unspecified; ² – site not specified.

was 6.2 percent. Earlier figures of 6.4% and 5.6% by Elusiyan *et al.* [5] and Oyenusi *et al.* [6], respectively, were based on plasma glucose <2.5 mmol/l. Since the current study used <3 mmol/l, the prevalence using the previous definition would be relatively less than these studies. Another study from Abia by Okoronkwo *et al.* [7] found 10%, which is much higher than the present study. Prevalence is also lower than that reported by Osier *et al.* in Kenya [5]. Allowing for little difference in methods, this study is also lower than the findings of 18.5% by Kupper *et al.* [15] from California. The study was conducted on patients in the PICU using the higher definition of 3.6 mmol/l. These will explain the observed high prevalence.

The relatively lower prevalence found in this study was not surprising, considering the timing. The study was conducted in the harmattan months (November–March), coincidentally with when malaria incidence is at its lowest in Northern Nigeria [16]. Seasonal variation in the endemicity of malaria has been described in Northern Nigeria. This can be seen from the low prevalence of severe forms of malaria among the admissions when compared to other previous reports. Malaria was the leading diagnosis in the studies from Ile-Ife, Lagos and Abia [5–7].

There was no significant difference in prevalence of hypoglycemia between the various age groups, or by social and nutritional status. This was in keeping with findings of other researchers [5, 6].

Hypoglycemia was significantly higher among children presenting after a period of 12 hours from the last feed. Similar findings had been reported by other African and Nigerian authors, reflecting delayed presentation even in ardent emergencies [5–7]. The glycogen reserve in children can only last 6–12 hours without feeding, beyond which gluconeogenesis must be activated [1]. Childhood illness is associated with anorexia and gluconeogenesis dysregulation. The hypoglycemia may be due to abnormalities in hormone secretion, substrate interconversion, or mobilization of metabolic fuels [17].

Certain orthodox drugs and traditional herbs may predispose to hypoglycemia [7]. Drugs such as quinine, salicylates, propranolol, oral antihyperglycemic agents

(AHA), and insulin have been reported to be associated with hypoglycemia [18, 19]. Findings from a study in Southeast Nigeria showed a significantly higher rate of hypoglycemia among children given traditional concoctions prior to presentation [7]. Twenty-six patients (18%) used traditional remedies prior to presentation in the present study, with no statistically significant difference between hypoglycemic and non-hypoglycemics. The traditional herbs reported in this study included "sabara" (Guiera senegalensis), "hano" (Boswellia dalzielli), "neem tree" (Azadirachta indica), "rawaya" (Kigalia Africana) and "Habbatus saudaa" (black cumin). Available information shows that the neem tree has a hypoglycemic effect [20]. Many plants used as traditional medicine in northern Nigeria, such as garlic, onion, aloe vera, bitter lemon, and Madagascar periwinkle Moraceae, have blood-lowering effects [21]. Unfortunately, most of our patients, including two who had hypoglycemia, did not know the name of the remedies used, and this hindered any meaningful interpretation of potential effects. There is an urgent need to organize the traditional medicines in Nigeria for easy profiling.

Many childhood illnesses can present with hypoglycemia as a measure of severity or complication. Out of nine patients with hypoglycemia at presentation, 3 (33.3%) were subsequently diagnosed with septicaemia. Other clinical conditions that presented with hypoglycemia included typhoid fever, severe malaria, malignancy, acute nephritic syndrome (ANS), and severe PEM. Previous Nigerian studies found severe malaria as the leading clinical condition complicated by hypoglycemia in Emergency Paediatric Units admission [5–7]. In this study, septicaemia was the most common condition complicated by hypoglycemia. It had been reported among conditions presenting with hypoglycemia in other studies [5–7]. The mechanism of hypoglycemia in septicaemia involves increased metabolic requirement with increased peripheral glucose utilization, inhibition of gluconeogenesis and increased insulin secretion due to the effect of endotoxins [18, 22]. The finding of two out of four patients with typhoid fever presenting with hypoglycemia was rather unusual. There is a dearth of literature concerning the occurrence of hypoglycemia in typhoid fever. It can be assumed that similar mechanisms described above for sepsis are responsible for hypoglycemia. Since these patients presented with enteritis/perforation, impaired absorption may be a contributing factor.

Forty-four percent of the patients with hypoglycemia had unfavourable outcomes, compared to 17% among non-hypoglycemic patients. The model was not significant ($\chi 2=4.285$; df=1; p=0.06). It may be related to the power of the study. Thus, further studies with larger samples are needed.

Conclusion

Hypoglycemia is common among emergency paediatric admissions, with a prevalence of 6.2%. It is characteristically present in severely ill patients such as those with severe sepsis, severe malaria, malnutrition and typhoid fever. The risk of hypoglycemia is considerably increased in patients presenting after prolonged fasting. There is, therefore a need for families, communities and the government to intensify efforts in eliminating all factors that hinder prompt access to care in developing countries.

Conflict of interest

The authors declare no conflict of interest.

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