Prevalence of hyperglycaemia in children seen at a paediatric emergency unit

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Abstract

Hyperglycaemia is known to be of common occurrence in paediatric emergency units, particularly in patients with severe disease. This study aimed to determine its prevalence and describe the disease conditions and clinical features associated with hyperglycaemia among children presenting to an emergency unit. A total of 1000 children aged 1 month to 14 years were enrolled in a cross-sectional study of prevalence of hyperglycaemia in two paediatric emergency units. In all cases, blood glucose (BG) level was determined, as well as clinical information. Hyperglycaemia was defined as blood glucose ≥7.8 mmol/l. The BG levels ranged between < 0.6 and 27.4 mmol/l (mean±standard deviation (SD): 6.5±3.0 mmol/l). Fever was seen in 84%, polyuria and polydypsia in 3%, cough in 33%, vomiting in 35%, and diarrhoea in 33% of patients. Hyperglycaemia was observed in 16.5% of the study children. The mean age of hyperglycaemic patients was 56±48 months. Children older than 6 years had the highest frequency of hyperglycaemia (33%), while infants had the lowest (14%). The only factor significantly associated with hyperglycaemia was a history of fever (p=0.001). Study subjects with gastroenteritis had the highest frequency of hyperglycaemia (4.4%), followed by severe malaria with 2.7%, and protein energy malnutrition (PEM) 2.3%. The mortality in hyperglycaemic children was higher than that in children with no hyperglycaemia (22.4% vs 7.5%, p=0.001). In conclusion, hyperglycaemia is not uncommon in emergency paediatric admissions, and it occurs more in patients with severe acute diseases. Children with hyperglycaemia should be monitored closely since they are at increased risk of death.

Introduction

Hyperglycaemia is a condition in which an excessive amount of glucose circulates in the blood, and it can occur as a transient or persistent problem.[1] It could be attributable to stress of an illness, impaired glucose tolerance, or diabetes mellitus.[2,3] However, it has been documented that a wide variety of illnesses form part of the stressful states that evoke a common metabolic endocrine response leading to stress hyperglycaemia.[4] The severity of hyperglycaemia is significantly associated with the severity of the illness rather than a particular diagnostic category.[5–8]

The International Diabetes Federation (IDF) and the International Society for Pediatric and Adolescent Diabetes (ISPAD) define pre-diabetes hyperglycaemia as impaired glucose tolerance (IGT) of 7.8–11.1 mmol/l or impaired fasting glucose (IFG) of 5.6–6.9 mmol/l,9 although various studies have used different cut-off values to represent hyperglycaemia.[10,11] The global burden of IGT and diabetes is increasing, and incidental hyperglycaemia is known to be of common occurrence in paediatric emergency units.[5,12] The prevalence reported from studies varies from as low as 3% to as high as 86%.[10,13,14]

Prolonged hyperglycaemia in critically ill patients has been shown to be associated with a number of deleterious consequences,[15] contributing to greater risks of morbidity and mortality, even in the absence of pre-existing diabetes.[16–18]

Some clinical conditions like fever, respiratory illnesses, and neurological diseases (which are very common in our setting) are found to be associated with a high prevalence of hyperglycaemia in several studies.[1,2,5,19] The aim of this study, therefore, was to determine the prevalence and describe the disease conditions associated with hyperglycaemia among children presenting to an emergency unit in our environment.

Patients and methods

This study was carried out at the Children's Emergency Units of Aminu Kano Teaching Hospital (AKTH) and Hasiya Bayero Paediatric Hospital in Kano, Nigeria over a nine-month period (July 2014–March 2015). The subjects were consecutively admitted

Age group (months)	Total
≤12	203 (20%)
13–23	206 (21%)
24–30	197 (20%)
31–72	224 (22%)
≥73	170 (17%)
Total	1000 (100%)

Table 1. Age and sex distribution of study subjects

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	Hyperglycaemia		Total		
	Present n (%)	Absent n (%)	Total (n)	χ^2	p-value
Fever					
Yes	123 (15%)	720 (85%)	843	14.206	0.000
No	42 (27%)	115 (73%)	157		
Headache					
Yes	17 (24%)	53 (76%)	70	3.312	0.069
No	148 (16%)	782 (84%)	930		
Convulsion					
Yes	28 (17%)	139 (83%)	167	0.010	0.919
No	137 (16%)	696 (84%)	833		
Cough					
Yes	42 (13%)	288 (87%)	670	5.088	0.024
No	123 (18%)	547 (82%)	330		
Vomiting					
Yes	72 (20%)	283 (78%)	355	5.713	0.017
No	93 (14%)	552 (86%)	645		
Diarrhoea					
Yes	67 (20%)	262 (80%)	329	5.315	0.021
No	98 (15%)	573 (85%)	671		
Abdominal pain					
Yes	17 (20%)	66 (80%)	83	1.042	0.307
No	148 (16%)	769 (84%)	917		
Body swelling					
Yes	10 (21%)	37 (79%)	47	0.817	0.366
No	155 (16%)	798 (84%)	953		
Polyuria					
Yes	7 (23%)	24 (77%)	31	0.859	0.354
No	158 (16%)	811 (84%)	969		
Polydipsia					
Yes	7 (23%)	24 (77%)	31	0.859	0.354
No	158 (16%)	811 (84%)	969		
Weight loss					
Yes	7 (19%)	30 (81%)	963	0.163	0.686
No	158 (16%)	805 (84%)	37		
Total	**165 (16%)**	**835 (84%)**	**1000**		

Table 2. Association between clinical features and presence of hyperglycaemia

children aged between one month and 14 years.

Written informed consent was obtained from the caregivers of all the recruited subjects, and written informed assent was also sought and obtained from all children old enough to give assent before enrolling them in the study. Ethical clearance was obtained from the Ethical and Research Committee of AKTH, and the Hospital Management Board of Kano State.

Demographic data, time of admission, interval of last meal, duration of illness before admission, presenting complaints, and blood glucose values were obtained. Patients who ingested food or glucose-containing fluids less than two hours prior to presentation, and referred patients who had received any intravenous infusion within the last six hours, were excluded from the study. All the patients had their blood glucose (BG) determined at admission (before any intervention) with a bed-side glucose meter (Accu-Chek Active) using the glucose oxidase method. For quality control, after every 50 testings, a blood sample was send to the laboratory for BG testing using photometric analysis. The bed-side meter testing was done by the principal investigator and trained assistants. Hyperglycaemia was defined as blood glucose ≥7.8mmol/l.[9]

Data generated were analysed using the statistical programme SPSS version 20. Qualitative variables were expressed in the form of frequencies and percentages. Categorical data were analysed using the Chi-square test. Continuous variables were summarised using means, medians, and standard deviations (SD). A p-value of ≤0.05 was considered significant using a 95% confidence interval. Data are expressed as means±1 standard deviation (SD), unless otherwise specified.

Results

During the study period, 1000 patients aged 1–168 months (mean of 41±38 months) were studied. There were 558 (66%) males and 442 (44%) females, giving a male to female ratio of 1.3:1.0. Most subjects (627 or 63%) were aged one–six years. Two hundred and three (20%) were infants and 170 (17%) were older than six years (see Table 1).

The BG levels in the study patients ranged between <0.6 and 27.4 mmol/l (mean, 6.5±3.1 mmol/l); 165 (16.5%) had hyperglycaemia. The hyperglycaemic patients consisted of 87 males and 78 females and were aged 2–168 months (mean, 56±48 months). Children over six years old had the highest frequency of hyperglycaemia (56 or 33%) while infants had the lowest (29 or 14%); this was a significant difference (p=0.001).

Factors	β	OR (95% CI)	p-value
Fever			
No	-	1.000	
Yes	0.531	1.700 (1.110–2.605)	0.015
Cough			
No	-	1.000	
Yes	0.303	1.354 (0.912–2.009)	0.133
Vomiting			
No	-	1.000	
Yes	0.184	0.832 (0.526–1.316)	0.832
Diarrhoea			
No	-	1.000	
Yes	0.390	0.677 (0.417–1.099)	0.115

β, coefficient of regression; OR, odds ratio; CI, confidence interval. Group with OR=1.000 represents the reference group

Table 3. Logistic regression model of factors associated with hyperglycaemia

Table 2 shows the association between clinical features and the presence or absence of hyperglycaemia. Only 31 (3%) had a history of polydypsia and polyuria. The following factors were significantly associated with hyperglycaemia: fever (p=0.001), cough (p=0.024), vomiting (p=0.017), and diarrhoea (p=0.021). Most patients had a history of fever (84%), and 75% had a documented fever of >37.5°C. The result of multivariate analysis is shown in Table 3, and this showed that only fever (and not cough, vomiting, or diarrhoea) remained significantly associated with hyperglycaemia – odds ratio (OR) 1.700 (p=0.015).

Table 4 shows the association between hyperglycaemia and individual diagnostic categories. Hyperglycaemia was most common in patients with gastroenteritis: 44/1000, or 4.4% of the total group. Next most common was malaria at 27/1000 (2.7%), followed by protein–energy malnutrition (PEM) at 23/1000 (2.3%).

The overall mortality rate in hyperglycaemic children was 37/165 (22.4%), and this was higher than that of children without hyperglycaemia (63/835 (7.5%)). This difference was highly statistically significant (p=0.001).

Discussion

The prevalence of hyperglycaemia in children admitted to this emergency unit was found to be 16.5%. However, this is lower than the prevalance reported in India by Rakesh et al[6] (27%) and Deepak et al[20] (28%) in Washington. These two studies were carried out in the more stressful environments of paediatric intensive care units (PICUs) among critically ill and peri-operative patients with traumatic brain injury, respectively. The prevalence of hyperglycaemia is said to be more common in severely ill patients.[5–8] The stress of illness is known to induce hyperglycaemia by activation of neuro-endocrine phenomenon leading to activation of an inflammatory cascade causing the release of several hormones (e.g. cortisol) and inflammatory cytokines and humoral mediators, leading to inhibition of insulin release and its peripheral sensitivity.[21]

In this study, a history of fever was significantly associated with hyperglycaemia. This finding is similar to that reported by Bhisikul et al[5] in 1994 where it was found that the higher the temperature, the greater the risk of hyperglycaemia. Valerio et al[22] in 2001 also found that hyperglycaemia was 14% versus 4% among children with high and low temperatures, respectively. Fever, mainly due to infection, is known to cause stress responses and hormonal release likely to lead to hyperglycaemia (as discussed above).[23,24]

In the present study, a history of diarrhoea and vomiting was not associated with hyperglycaemia, although a study by Ronan et al[25] did find a significant association between hyperglycaemia and diarrhoea. All the hyperglycaemic patients in their study were severely dehydrated, while in the present study this was not the case.

Hyperglycaemia during diarrhoea has been attributed to a number of different causes. These include hypernatraemia,[26] acidosis,[27] or hypokalaemia; and a stress response caused by either infection[28] or marked hypovolaemia.[29] The findings of the Ronan study are consistent with a stress response to marked hypovolaemia as the cause of hyperglycaemia,[25] since in their study, compared with normoglycaemic patients, patients with hyperglycaemia had significantly increased concentrations of the hormones adrenaline, noradrenaline, cortisol, growth hormone, and glucagon; all of which have an anti-insulin effect.[30] A decrease in intravascular volume is one of the most potent stimuli for the release of catecholamines and cortisol.[31]

There was no association between gender and hyperglycaemia in this study, but there was a significant association between age and hyperglycaemia, with older children of more than six years being more likely to have hyperglycaemia. This finding is in contrast to a study in Washington by Deepak et al[20] in 2008, and another by Klein et al[7] in New York in 2008 where a strong association was found between age, gender, and hyperglycaemia. These workers reported that younger children less than four years and female children were more likely to have hyperglycaemia.

The current study identified a higher prevalence of hyperglycaemia among some specific diagnostic disease conditions, i.e. sepsis, gastroenteritis, protein energy malnutrition, seizure disorder, bronchopneumonia, severe malaria, and meningitis. Some previous studies, especially by Krinsley[32] and Osier et al,[2] found that hyperglycaemia was more prevalent among participants with similar disease conditions.

In our study, the mortality in hyperglycaemic patients was significantly higher than in non-hyperglycaemic patients, 37/165 (22.4%) versus 63/835 (7.5%), respectively (p<0.001). This is similar to the Kenyan study by Osier et al[2] where they found a significantly higher mortality in

Diagnosis	All cases n (%)	Hyperglycaemia n (%)	No hyperglycaemia n (%)
Sepsis	170 (17.0%)	19 (1.9%*)	151 (15.1%)
Gastroenteritis	169 (16.9%)	44 (4.4%)	125 (12.5%)
Seizure disorder	33 (3.3%)	6 (0.6%)	27 (2.7%)
Meningitis	49 (4.9%)	3 (0.3%)	46 (4.6%)
Sickle cell disease	72 (7.2%)	13 (1.3%)	59 (5.9%)
PEM	177 (17.7%)	23 (2.3%)	154 (15.4%)
Severe malaria	140 (14.0%)	27 (2.7%)	113 (11.3%)
Poisoning	11 (1.1%)	3 (0.3%)	8 (0.8%)
Bronchopneumonia	76 (7.6%)	16 (1.6%)	60 (6.0%)
Malignancy	31 (3.1%)	1 (0.1%)	30 (3.0%)
Tuberculosis	23 (2.3%)	1 (0.1%)	22 (2.2%)
UTI	17 (1.7%)	2 (0.2%)	15 (1.5%)
Others	32 (3.2%)	7 (0.6%)	25 (2.5%)
Total	**1000 (100%)**	**165 (16.5%)**	**835 (83.5%)**

*The % for patients with and without hyperglycaemia are proportions of all patients, not just those with particular diagnosis.
PEM, protein energy malnutrition; UTI, urinary tract infection.

Table 4. Comparison of presence of hyperglycaemia among the various diagnoses

hyperglycaemic children: 13/92 (14.0%) versus 112/2963 (3.8%), respectively ($p<0.001$). However, in both studies the prevalence was found to be higher among children with severe diseases – such as severe malaria, protein energy malnutrition, severe pneumonia, and poisoning. A study by Faustion and Apkon reported higher mortality in children admitted to intensive care units than emergency wards.[33] Therefore, the types of patients managed probably determines the overall outcome and prevalence of hyperglycaemia.[10,33]

Although hyperglycaemia could be a marker of stress, adult data support the theory that hyperglycaemia is directly injurious to critically ill patients.[34] Hyperglycaemia is known to activate different potentially deleterious pathways, such as protein kinase C, polyol, glycation, and reactive oxygen species.[10] Furthermore, the morbidity and mortality from hyperglycaemia may be explained partly by its ability to exacerbate ischaemic neurological injury.[35] This was shown in animal studies to be due to a reduction in brain adenosine production. Because adenosine, a cerebral vasodilator, can inhibit the release of neuronal excitotoxins as well as affect neutrophil–endothelial interactions, it has been proposed as an endogenous neuroprotector. Thus the attenuation of adenosine and its metabolites may be a factor in the pathogenesis of increased ischaemic brain injury associated with systemic hyperglycaemia.[35] Hyperglycaemia was also shown to be significantly related to distinct changes of humoral and cellular immune functions.[36]

This study and others have demonstrated that certain diseases are associated with hyperglycaemia, but why a particular diagnosis will be associated with hyperglycaemia in one patient and normoglycaemia in another is not fully understood. It may be related to the way individuals react to stress, and this may also be influenced directly or indirectly by hormonal and metabolic interplay. The overall effect of stress states on glucose metabolism is increased gluconeogenesis via cortisol and glucagon, increased glycogenolysis via adrenaline, and peripheral insulin resistance via glucagon and adrenaline.[11]

In conclusion, hyperglycaemia is a common occurrence in children admitted to emergency units in Africa. Where facilities for blood glucose estimation exist, it should be measured in all children sick enough to warrant admission, particularly those severely ill or malnourished. Children with hyperglycaemia should be the object of closer surveillance since they are at increased risk of mortality.

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Author declaration

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