ORIGINAL ARTICLE

Abnormal blood glucose concentrations on admission to a rural Kenyan district hospital: prevalence and outcome

F H A Osier, J A Berkley, A Ross, F Sanderson, S Mohammed, C R J C Newton

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See end of article for authors' affiliations

Correspondence to: Dr F H A Osier, Kenya Medical Research Institute (KEMRI), Centre for Geographic Medicine Research, Coast, Kilifi District Hospital, PO Box 230, Kilifi, Kenya; fosieruk@yahoo.co.uk

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Aims: To determine the prevalence, clinical characteristics, and outcome of hypoglycaemia on admission in children at a rural Kenyan district hospital.
Methods: Observational study of 3742 children (including 280 neonates) in Kilifi District Hospital, Kenya. Main outcome measures: hypoglycaemia (blood glucose <2.2 mmol/l) and hyperglycaemia (blood glucose >10.0 mmol/l).
Results: *Non-neonates*: the prevalence of hypoglycaemia on admission was 7.3%. Severe illness, malnutrition, last meal >12 hours ago, and a positive malaria slide were independently associated with hypoglycaemia. Overall, mortality in hypoglycaemic children was 20.2% compared to 3.8% in normoglycaemic children ($p < 0.001$). The brunt of mortality in hypoglycaemic children was borne by those who were severely ill or malnourished (31.8%) as opposed to those who were neither severely ill nor malnourished (9.0%). *Neonates*: 23.0% of neonates were hypoglycaemic on admission. Inability to breast feed and weight <2500 g were independently associated with hypoglycaemia. Mortality was 45.2% compared to 19.6% in normoglycaemic neonates ($p < 0.001$). Hyperglycaemia was present in 2.7% of children and was associated with a higher mortality than normoglycaemia, 14.0% versus 3.8% respectively ($p < 0.001$).
Conclusions: Hypoglycaemia is common in children admitted to a rural Kenyan district hospital and is associated with an increased mortality. Apart from features of severe illness and poor feeding, clinical signs have a low sensitivity and specificity for hypoglycaemia. Where diagnostic facilities are lacking, presumptive treatment of severely ill children is recommended. For other children, the continuation of feeding (by nasogastric tube if necessary) should be part of standard management.

Hypoglycaemia is the most common metabolic abnormality in childhood and is associated with neurological damage and death.[1] Children are particularly prone to develop hypoglycaemia in a wide variety of diseases and it may be difficult to detect clinically. In resource poor countries, poor nutritional status,[2] infectious diseases,[3] delay in presentation to hospital,[3] the use of potentially toxic herbal preparations,[3–5] and the lack of diagnostic facilities may aggravate hypoglycaemia. Previous African studies have been conducted in urban referral hospitals,[5 6] yet most children live and are treated in rural areas. Importantly, hypoglycaemia is amenable to inexpensive and widely available treatment.

The main aim of this study was to determine the prevalence and outcome of hypoglycaemia, in children requiring admission to a rural district hospital. A secondary aim was to identify the clinical characteristics of hypoglycaemic children.

PARTICIPANTS AND METHODS

Study site

The study was conducted in the paediatric ward of Kilifi District Hospital, situated 60 km North of Mombasa on the Kenyan coast. Approximately 5000 children are admitted each year. The hospital serves a mainly rural population consisting predominantly of the Giriama ethnic group. There are two seasonal peaks of malaria transmission following the rains from May to July and from November to December. The study was conducted between February and September 1999.

Patients and consent

All children admitted to the paediatric ward were eligible for recruitment into the study unless for elective surgery, minor trauma, diabetes mellitus, or if consent was refused. Parents were informed about the study in their own language and written consent was sought. The Kenyan National ethical committee approved the study.

Clinical definitions

Severe illness was defined as prostration (inability to sit unsupported, or breast feed[7]), or abnormally deep breathing (Kussmauls respiration).[8] Other clinical definitions were: hypothermia, an axillary temperature of <36°C; hypoxia, an oxygen saturation <90% in air; tachypnoea, a respiratory rate of >40 per minute in children between 1 and 5 years, and >50 per minute in infants greater than 2 months old[9]; and severe malnutrition, weight for age z score (WAZ) of <−3, calculated using reference data from the American National Centre for Health Statistics with Epi Info version 6.04b (CDC, Atlanta, USA). Severe anaemia was defined as a haemoglobin of <50 g/l.[10] Hypoglycaemia and hyperglycaemia were defined as a blood glucose <2.2 mmol/l[6 11 12] and >10.0 mmol/l[13] respectively. Previously undiagnosed diabetes was excluded in children found to have hyperglycaemia. Data were recorded on standard proforma on admission and at discharge, including final diagnosis. Hypoglycaemia in severely ill children was treated with intravenous dextrose 25% at 2 ml/kg.

Laboratory methods

A venous blood sample was taken on admission for: malaria parasites (Giemsa stain), a full blood count (Coulter Micro Diff II, UK), and blood glucose estimation. Blood glucose samples were collected into fluoride oxalate bottles and analysed by the glucose oxidase method (GM6 Analox instruments, UK). Samples were processed urgently on the request of the admitting clinician, guided by the following criteria: all neonates, severe disease, severe malnutrition, or symptoms of hypoglycaemia (drowsiness, agitation, feeding difficulties, hypothermia, jitteriness, and seizures on admission). Other samples

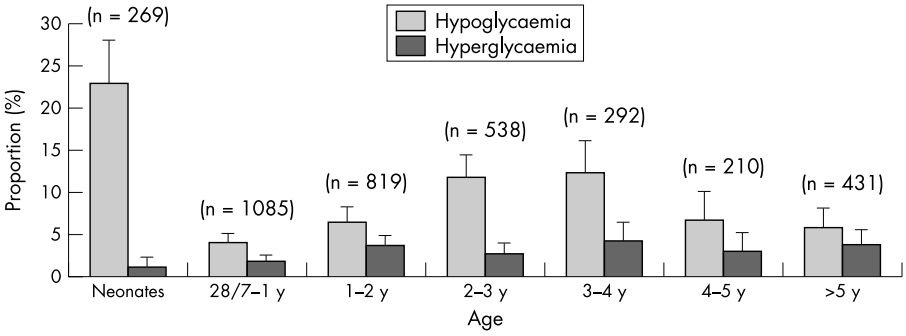

Figure 1 Prevalence of hypoglycaemia and hyperglycaemia with age.

were stored at –4°C and processed in twice weekly batches. Other investigations were performed as clinically indicated.

Statistical methods

Children were allocated into three categories: hypoglycaemia, normoglycaemia, and hyperglycaemia. Separate analyses were performed for neonates and non-neonates. We compared hypoglycaemia to normoglycaemia, and hyperglycaemia to normoglycaemia, separately. Initially, χ^2 tests were used to assess the univariate associations between abnormal glycaemic status and binary clinical variables. Logistic regression was then employed to estimate the associations between the clinical signs and presence of hypoglycaemia, adjusting for other variables.

RESULTS

During the study, 3742 children were admitted, including 280 neonates. The median age was 19 months (interquartile range (IQR) 9 to 37). The mean WAZ was –1.83, standard deviation (SD) 1.74. Severe illness was present on admission in 518 (13.8%) children. The median duration of illness and subsequent length of hospital stay were both 3 days (IQR 2 to 5). Blood glucose data was unavailable for 163 (4.4%) children who either fulfilled the exclusion criteria (n = 22), refused consent (n = 20), died before sampling (n = 2), or in whom the blood glucose sample was overlooked or impossible to obtain (n = 119). Nutritional data were missing for seven children.

Prevalence of hypoglycaemia

Hypoglycaemia was present in 295 (8.2%) children overall. Neonates, and children aged between 2 and 4 years had the highest prevalence of hypoglycaemia (fig 1).

Hypoglycaemia in non-neonates

In children over 28 days old, hypoglycaemia was present on admission in 233/3214 (7.3%). The proportion of children with hypoglycaemia varied significantly with the primary diagnosis ($p = 0.001$, χ^2 test). The highest proportion was observed in children with meningitis, 5/14 (36.0%). The proportions of hypoglycaemic children in the other major diagnostic categories were: anaemia of any cause, 15/150 (10.0%); malaria, 123/1420 (8.4%); respiratory tract infections, 22/558 (3.9%); gastroenteritis, 18/325 (5.5%); and protein calorie malnutrition, 21/318 (6.6%). Hypoglycaemia also complicated unknown encephalopathy (n = 5), HIV related illnesses (n = 3), septicaemia (n = 2), rabies (n = 2), sickle cell crises (n = 2), hepatitis (n = 2), abdominal tumour (n = 1), cerebral palsy (n = 1), intestinal obstruction (n = 1), and poisoning (n = 1); the diagnosis was undetermined in five hypoglycaemic children.

Eleven clinical variables were significantly associated with hypoglycaemia (table 1). Not having had a meal in the 12 hours preceding admission was strongly associated with hypoglycaemia; however, duration of illness and vomiting were not. Other important univariate associations included a history of seizures and jaundice. Multiple logistic regression analysis identified prostration, deep breathing, severe malnutrition, last meal >12 hours ago, and a positive malaria slide as independent indicators of hypoglycaemia (table 2). The presence of at least one of these variables had a sensitivity of 79% with a specificity of 33%. The sensitivity and specificity of our existing indications for urgent blood glucose estimation on admission were 41.6% and 88.2% respectively.

Figure 2 shows the association between blood glucose concentration and the proportion of children who died. Overall, the mortality in hypoglycaemic children (47/233, 20%) was higher than in normoglycaemic children (114/2981, 3.8%, $p < 0.001$). Mortality was especially high (41/129, 31.8%) in hypoglycaemic children with signs of severe illness (prostration or deep breathing) on admission or severe malnutrition. In normoglycaemic children in the same category the mortality was 78/864, 9.0%. Few deaths occurred in hypoglycaemic children with neither severe illness on admission nor severe malnutrition (3/98, 3.1%). In normoglycaemic children without severe illness or malnutrition, 34/2106 (1.6%) died. An interaction test provided no evidence that the association of hypoglycaemia with mortality was different in children with severe illness or severe malnutrition ($p = 0.17$).

Hyperglycaemia in non-neonates

Ninety six (2.9%) children outside the neonatal period were hyperglycaemic on admission. The main primary diagnoses were malaria (49.4%), gastroenteritis (12.9%), lower respiratory tract infection (11.8%), and burns (7.5%). None of these children had insulin dependent diabetes mellitus. On univariate analysis, a history of fever, a history of seizures, duration of illness ≥5 days, cough, hypothermia, hypoxia, prostration, and deep breathing were associated with hyperglycaemia (table 1). On multivariate analysis, hypothermia, hypoxia, prostration, and deep breathing were independently associated with hyperglycaemia (table 2). The mortality in hyperglycaemic children was higher than that in normoglycaemic children, 13/92 (14.0%) versus 112/2963 (3.8%) respectively ($p < 0.001$) (fig 2).

Neonates

Of the 280 neonatal admissions, 62 (23.0%) were hypoglycaemic, three (0.9%) were hyperglycaemic, and 11 (3.9%) had no admission blood glucose. Eighty one per cent of the hypoglycaemic neonates were <7 days old compared to 48% in normoglycaemic neonates ($p < 0.0001$). The main diagnoses were neonatal sepsis (55%), prematurity (12%), respiratory tract infections (8%), neonatal tetanus (6%), meningitis (5%), and birth asphyxia (3%). On univariate analysis, nine clinical variables were significantly associated with hypoglycaemia (table 3). A history of fever and cough were associated with a lower prevalence of hypoglycaemia. There was no evidence of an association between jaundice and hypoglycaemia. Logistic regression identified the inability to breast feed and an admission weight <2500 g to be associated with hypoglycaemia (table 2), adjusting for the confounders. The mortality

Table 1 Univariate analysis of clinical variables associated with hypoglycaemia or hyperglycaemia in non-neonates

	Hypoglycaemia				Hyperglycaemia			
	Hypoglycaemic, n (%) n=233	Normoglycaemic, n (%) n=2980	Odds ratio (95% CI)	p value	Hyperglycaemic, n (%) n=97	Normoglycaemic, n (%) n=2980	Odds ratio (95% CI)	p value
History								
Last meal >12 hours	47 (20.8)	215 (7.3)	3.3 (2.3 to 4.7)	<0.001	6 (6.5)	215 (7.3)	0.9 (0.3 to 1.9)	0.771
Duration of illness ≥5 days	54 (23.7)	855 (28.9)	0.8 (0.6 to 1.0)	0.090	10 (10.8)	855 (28.9)	0.3 (0.2 to 0.6)	<0.001
Fever	197 (86.4)	2490 (84.0)	1.2 (0.8 to 1.8)	0.345	64 (68.8)	2490 (84.0)	0.4 (0.3 to 0.7)	<0.001
Cough	86 (37.7)	1332 (45.0)	0.7 (0.6 to 0.97)	0.034	32 (34.4)	1332 (45.0)	0.6 (0.4 to 0.98)	0.043
Difficulty breathing	80 (35.1)	896 (30.2)	1.2 (0.9 to 1.7)	0.125	27 (29.4)	896 (30.2)	0.9 (0.6 to 1.5)	0.858
Vomiting	81 (35.5)	1014 (34.2)	1.1 (0.8 to 1.4)	0.689	34 (36.6)	1014 (34.2)	1.1 (0.7 to 1.7)	0.642
Diarrhoea	53 (23.3)	656 (22.1)	1.1 (0.8 to 1.5)	0.699	21 (22.6)	656 (22.1)	1.0 (0.6 to 1.7)	0.921
History of seizures	66 (29.0)	616 (20.8)	1.6 (1.2 to 2.1)	0.004	38 (40.9)	616 (20.8)	2.6 (1.7 to 4.0)	<0.001
Uncountable seizures	8 (3.6)	27 (0.96)	3.9 (1.8 to 8.4)	<0.001	2 (2.2)	27 (0.96)	2.3 (0.0 to 8.9)	0.241
Admhosp1*	6 (2.7)	81 (2.8)	0.96 (0.4 to 2.2)	0.927	6 (6.6)	81 (2.8)	2.4 (1.1 to 5.7)	0.031
Antibiotics	21 (9.7)	365 (13.1)	0.7 (0.5 to 1.1)	0.150	6 (6.7)	365 (13.1)	0.5 (0.2 to 1.1)	0.079
Antimalarials	57 (26.4)	761 (27.4)	0.95 (0.7 to 1.3)	0.752	25 (28.1)	761 (27.4)	1.0 (0.6 to 1.6)	0.884
Aspirin	40 (18.6)	595 (21.4)	0.84 (0.6 to 1.2)	0.332	10 (11.2)	595 (21.4)	0.5 (0.2 to 0.8)	0.021
Observations								
Hypothermia	22 (9.8)	92 (3.1)	3.4 (2.1 to 5.5)	<0.001	15 (16.9)	92 (3.1)	6.3 (3.5 to 11.3)	<0.001
Hypoxia	26 (12.3)	137 (4.8)	2.8 (1.8 to 4.3)	<0.001	21 (24.7)	137 (4.8)	6.6 (3.9 to 11.0)	<0.001
Tachypnoea, <1 year old	19 (8.4)	272 (9.3)	0.9 (0.5 to 1.4)	0.611	7 (7.5)	272 (9.3)	0.8 (0.4 to 1.7)	0.570
Tachypnoea, >1 year old	58 (25.8)	448 (15.3)	1.9 (1.4 to 2.6)	<0.001	18 (19.4)	448 (15.3)	1.3 (0.8 to 2.2)	0.279
WAZ <–3	49 (25.8)	463 (19.0)	1.5 (1.1 to 2.1)	0.023	10 (13.0)	463 (19.0)	0.6 (0.3 to 1.2)	0.183
Examination								
Pedal oedema	36 (15.8)	318 (10.7)	1.6 (1.1 to 2.3)	0.019	4 (4.3)	318 (10.7)	0.4 (0.1 to 0.98)	0.046
Jaundice	9 (4.0)	50 (1.7)	2.4 (1.2 to 4.9)	0.015	2 (2.2)	50 (1.7)	1.2 (0.0 to 4.8)	0.734
Unconscious	60 (26.3)	148 (5.0)	6.8 (4.8 to 9.5)	<0.001	30 (32.3)	148 (5.0)	9.1 (5.7 to 14.5)	<0.001
Prostration	83 (36.4)	250 (8.4)	6.2 (4.6 to 8.4)	<0.001	41 (44.1)	250 (8.4)	8.6 (5.6 to 13.1)	<0.001
Deep breathing	45 (19.7)	125 (4.2)	5.6 (3.9 to 8.1)	<0.001	25 (26.9)	125 (4.2)	8.3 (5.1 to 13.6)	<0.001
Chest in-drawing	69 (30.3)	639 (21.6)	1.6 (1.2 to 2.1)	0.002	28 (30.1)	639 (21.6)	1.5 (0.9 to 2.4)	0.050
Stiff neck	1 (0.44)	35 (1.2)	0.4 (0.0 to 2.1)	0.305	0 (0)	35 (1.2)	0.0 (0.0 to 3.5)	0.291
Skin infection	9 (4.0)	124 (4.2)	0.9 (0.5 to 1.8)	0.863	2 (2.2)	124 (4.2)	0.5 (0.0 to 1.9)	0.331
Basic investigation								
Malaria slide positive	156 (67)	1719 (57.9)	1.5 (1.1 to 2.0)	0.006	51 (52.6)	1719 (57.9)	0.8 (0.5 to 1.2)	0.312
Severe anaemia	49 (21.3)	469 (15.8)	1.4 (1.0 to 2.0)	0.029	10 (10.3)	469 (15.8)	0.6 (0.3 to 1.2)	0.142

n is the total number of children in each category. Analysis for each clinical variable was done on the available data.
*Admitted to hospital in the preceding 14 days..

Table 2 Logistic regression models for hypoglycaemia and hyperglycaemia in non-neonates; and for hypoglycaemia in neonates

Clinical variable	Odds ratio (95% CI)	p value
Hypoglycaemia, non-neonates		
Prostration	3.3 (2.2 to 4.9)	<0.001
Deep breathing	2.6 (1.6 to 4.2)	<0.001
Last meal >12 hours	2.1 (1.4 to 3.1)	0.001
Positive malaria slide	1.5 (1.1 to 1.2)	0.013
WAZ <–3	1.5 (1.0 to 2.2)	0.034
Hyperglycaemia, non-neonates		
Prostration	4.7 (2.7 to 8.1)	<0.001
Deep breathing	2.5 (1.3 to 4.8)	0.005
Hypothermia	2.6 (1.4 to 4.8)	0.003
Hypoxia	2.4 (1.1 to 5.1)	0.026
Hypoglycaemia, neonates		
Unable to breast feed	3.4 (1.8 to 5.4)	<0.001
Weight <2500 g	2.6 (1.3 to 4.9)	0.003

with hypoglycaemia was 28/62 (45.2%) compared to 40/204 (19.6%) with normoglycaemia ($p < 0.001$).

DISCUSSION

More than 10% of children admitted to a Kenyan rural district hospital had an abnormal blood glucose concentration on admission. Hypoglycaemia (8.2%) was more common than hyperglycaemia (2.7%). Overall, there was a strong association between hypoglycaemia and mortality. Nearly a third of hypoglycaemic children with severe illness or malnutrition died, despite a protocol of urgent determination of blood glucose and treatment. The high prevalence of hypoglycaemia in children aged between 2 and 4 years was an unexpected finding. Neither differences in the nutritional status nor the presence of a positive malarial slide could explain this result, which needs further investigation.

One other study has investigated all children admitted to hospital. This was at an urban referral centre in Mozambique and reported a prevalence of hypoglycaemia of 7.1%.[5] A Tanzanian study[6] of children with severe illness also showed a high mortality despite treatment in hypoglycaemic children. In that study, time from last meal was also a strong association of hypoglycaemia, and the mechanism was thought to be glycogen depletion and impaired hepatic gluconeogenesis.

The World Health Organisation recommend that blood glucose estimation should be possible in all small hospitals that provide paediatric care,[14] but it is often unavailable. Thus, treatment of hypoglycaemia often depends on clinical suspicion. Presumptive treatment with intravenous or nasogastric dextrose is appropriate for children with severe illness. For children with non-severe illness, indicators of hypoglycaemia have a low specificity and oral treatment is recommended. Children who have not fed within the previous 12 hours are particularly at risk. Where children are able to feed normally, this should be actively encouraged while in hospital. For children who are unable to feed adequately, nasogastric milk or a glucose containing drink should be given until feeding is re-established.

In neonates, nearly a quarter were hypoglycaemic. A weight of less than 2500 g and the inability to breast feed identified 53 of 62 (85.4%) hypoglycaemic neonates. In practice, neonates who are unable to breast feed should be managed with nasogastric expressed breast milk (EBM) or intravenous 10% dextrose as a continuous infusion, and are therefore treated for hypoglycaemia. Mothers of neonates who are able to adequately breast feed should be encouraged to do so while in hospital. Where facilities for blood glucose estimation are available, it should be repeated one hour after treatment for hypoglycaemic neonates and older children.

We found that hyperglycaemia occurred in some children in the absence of insulin dependent diabetes mellitus. Non-diabetic hyperglycaemia in children has been described as part of the stress response to hypovolaemia,[13 15] acute illnesses,[16 17] and trauma.[18] In children with severe head injury it has been shown to be a significant indicator of severity and predictor of outcome.[18] The effect of treating non-diabetic hyperglycaemia is unknown but is unlikely to be beneficial.

Abnormal glucose concentrations are common in children admitted to a rural district hospital in Africa. Where facilities for blood glucose estimation exist, blood glucose should be measured in all children sick enough to warrant admission, particularly those severely ill or malnourished children and neonates who bear the brunt of mortality. Where facilities do not exist, we recommend presumptive treatment of hypoglycaemia in these groups of children. In non-severely ill children we recommend the continuation of feeding as part of standard management, using a nasogastric tube if necessary. There are

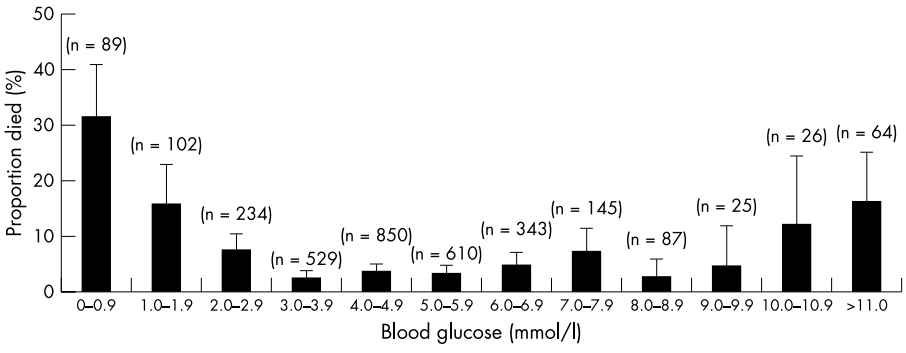

Figure 2 Association between blood glucose and mortality.

Table 3 Univariate analysis of clinical variables associated with hypoglycaemia in neonates

	Hypoglycaemic, n (%) n=62	Normoglycemic, n (%) n=204	Odds ratio (95% CI)	p value
History				
Last meal >12 hours	11 (20.0)	16 (8.3)	2.8 (1.2 to 6.3)	0.014
Days ill ≥5	4 (6.5)	21 (10.4)	0.6 (0.2 to 1.7)	0.354
Fever	17 (27.4)	89 (43.6)	0.5 (0.3 to 0.9)	0.022
Cough	4 (6.5)	53 (26.0)	0.2 (0.1 to 0.5)	0.019
Difficulty breathing	24 (38.7)	83 (40.7)	0.9 (0.5 to 1.6)	0.781
Vomiting	1 (1.6)	20 (9.8)	0.2 (0.0 to 0.9)	0.036
Diarrhoea	2 (3.2)	5 (2.5)	1.3 (0.0 to 6.1)	0.739
History of seizures	5 (8.1)	19 (9.3)	0.8 (0.2 to 2.3)	0.737
Uncountable seizures	0 (0)	2 (1.1)	0.0 (0.0 to 6.4)	0.435
Admhosp1*	0 (0)	5 (2.5)	0.0 (0.0 to 2.7)	0.228
Antibiotics	0 (0)	55 (24.9)	0.0 (0.0 to 0.7)	0.023
Antimalarials	0 (0)	12 (6.6)	0.0 (0.0 to 1.0)	0.051
Aspirin	1 (1.8)	8 (4.4)	0.4 (0.0 to 2.6)	0.381
Observations				
Hypothermia	20 (32.8)	28 (13.9)	3.0 (1.6 to 5.9)	0.001
Hypoxia	20 (33.9)	38 (19.6)	2.1 (1.1 to 4.0)	0.022
Tachypnoea >60/min	17 (27.4)	64 (31.5)	0.8 (0.4 to 1.5)	0.539
Weight <2500 g	41 (68.3)	85 (41.7)	3.0 (1.6 to 5.5)	<0.001
Examination				
Jaundice	18 (29.0)	67 (32.8)	0.8 (0.4 to 1.5)	0.513
Unconscious	3 (4.8)	7 (3.5)	1.4 (0.4 to 5.2)	0.615
Unable to breast feed	39 (26.2)	59 (8.9)	4.1 (2.3 to 7.5)	<0.001
Deep breathing	8 (12.9)	6 (2.9)	4.8 (1.7 to 14.1)	0.002
Chest in-drawing	22 (35.5)	73 (35.8)	0.98 (0.5 to 1.8)	0.965
Stiff neck	3 (4.8)	7 (3.4)	1.4 (0.4 to 5.3)	0.61
Skin infection	3 (4.8)	14 (6.9)	0.7 (0.2 to 2.3)	0.568
Basic investigation				
Malaria slide positive	1 (1.6%)	10 (4.9%)	0.3 (0 to 1.9)	0.254

n is the total number of hypoglycaemic and normoglycaemic neonates. Analysis of clinical variables done where specific data were available.
*Admitted to hospital in the preceding 14 days.

no data on the long term neurodevelopmental outcomes of hypoglycaemic in children in this setting, and further studies are therefore needed.

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Authors' affiliations

F H A Osier, F Sanderson, S Mohammed, Kenya Medical Research Institute (KEMRI), Centre for Geographic Medicine Research, Coast, Kilifi District Hospital, PO Box 230, Kilifi, Kenya
J A Berkley, A Ross, Centre for Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, The John Radcliffe Hospital, Oxford, UK
C R J C Newton, Neurosciences Unit, Institute of Child Health and Great Ormond Street Hospital, University College London Medical School, London, UK

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