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Original Research Article

Dysglycaemia in Nigerian neonates with hypoxic ischemic encephalopathy

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ABSTRACT

Background: To investigate the prevalence and associated outcomes of dysglycaemia in neonates with hypoxic ischemic encephalopathy (HIE).
Methods: This was a retrospective analysis of neonates with HIE over one year. The point of admission blood glucose level was measured. Dysglycaemia is defined as a blood glucose level <45 mg/dl or >145 mg/dl, and its association with short-term outcomes was determined.
Results: Dysglycaemia was observed in 4/22(18%) of the neonates with stage 1 HIE, 6/32 (28.1%), and 1/5(20%) with stage 3 (p>0.05). Thirty-eight neonates survived, while 21 (35.6%) died. Death was observed in 15 (33.3%) normoglycemic neonates, and 6/14 (42.9%) with dysglycaemia (*p*>0.05). After controlling for birth weight, hypothermia, hypoxia, and HIE stage, dysglycaemia was not significantly related to mortality (AOR=0.64, 95% CI= 0.16–2.63, p=0.537).
Conclusions: Dysglycaemia occurred in about one in four neonates with HIE. They were associated with higher mortality, though the association was not significant. Continuous glucose monitoring during treatment of asphyxiated neonates will enable early detection and prompt treatment of glucose alterations, thereby improving outcomes. Expanding access to advanced neuroprotective care, such as therapeutic hypothermia, could further reduce mortality in similar settings.

Keywords: Dysglycaemia, Neonates, Hypoxic ischemic encephalopathy, Hypoglycaemia, Hyperglycaemia, Nigeria, Outcome

INTRODUCTION

Hypoxic ischemic encephalopathy (HIE) is the most typical central nervous system complication of birth asphyxia, which is defined as inability of the newborn to establish and sustain respiration at birth.[1] Birth asphyxia is an important cause of morbidity and mortality in Nigeria, with HIE case fatality rate (CFR) in excess of 25%.[2-5] The primary energy source of the fetal brain is the glucose; it switches to alternative energy sources, such as ketones, lactate, and fatty acids, during transition from fetal to the neonatal life due to the transient neonatal hypoxia during labor.[6] This adaptive mechanism is affected in asphyxiated infants, in whom glucose supplies are rapidly depleted.[6] Furthermore, glucose homeostasis in the first few hours after birth, which is mainly driven by the liver and endocrine organs, is compromised in newborns with HIE.[7] HIE is associated with significant metabolic and hormonal dysfunction, including dysglycaemia. Dysglycaemia is a term used to describe variations in plasma glucose levels, encompassing both elevated (hyperglycemia) and reduced (hypoglycemia) levels.[8] Most studies on dysglycaemia were conducted in neonates with HIE undergoing therapeutic hypothermia, and the reported incidence varies significantly across the literature, ranging from 21% to 48% for hyperglycemia and 9% to 35% for hypoglycemia, both of which were associated with the worst outcome.[9-13] Additionally, these

studies were conducted in the developed world, where the standard of care for neonates is therapeutic hypothermia; hence, these findings may not be generalizable, especially in resource-limited settings. Literature is scarce on the prevalence and outcome of dysglycaemia in children with HIE in Nigeria, where there is an increasing incidence of HIE and high CFR.[3-14] Furthermore, HIE is an important contributor to neonatal morbidity and mortality. Dysglycaemia has been reported to be 6.1% to 6.5% and significantly associated with mortality, and Hypoglycemia of 15.2% to 32.6% respectively at the point of admission among Nigerian newborns.[15-17]

Furthermore, 4 to 16.6% of asphyxiated babies were reported to be hypoglycemic and significantly associated with mortality.[18,19] Therefore, this study hypothesizes that dysglycaemia is uncommon and not associated with adverse outcomes in babies managed for HIE. Alternatively, dysglycaemia is common and associated with adverse outcomes. The findings from this study will equip physicians caring for babies to make evidence-based decisions in managing such cases, thereby improving outcomes.

METHODS

This was a hospital-based cross-sectional study (retrospective analysis) of a prospective cohort of babies with HIE admitted to the SCBU of Federal Medical Centre, Birnin Kudu, between Jan 1 and Dec 31, 2023.

Inclusion criteria

Term babies with complete records with diagnosis of HIE 1, 2, OR 3. Preterm babies, infants of Diabetic mothers, or those with congenital abnormalities were excluded. The following variables were extracted from the medical records: gender, age at presentation, temperature in degrees celsius, oxygen saturation, weight in kilograms, clinical symptoms, HIE stage, and outcome.

Demographics and data related to pregnancy and delivery were also retrieved from the medical notes. Clinical grade of encephalopathy was assigned using the Sarnat score (20) at admission. The primary outcome measures are survival (discharge) or an adverse outcome (death). A point-of-care glucometer was used to measure blood glucose levels. Hypoglycemia and hyperglycemia were defined as blood glucose levels < 45 mg/dl (2.6 mmol/l) and > 145mg/dl (8 mmol) respectively.[21] Neonates with Hypoglycemia were treated with an intravenous bolus of 2 ml/kg of 10% dextrose over 1 minute and maintained on D10. Random Blood glucose levels were monitored every 30 to 60 minutes to maintain levels> 50 mg/dl (2.8 mmol/l). Dextrose infusion rate or concentration was adjusted. In infants with hyperglycemia, the rate or concentration of glucose infusion was adjusted to maintain blood glucose within normal levels.

Data analysis

The data was entered in SPSS version 20. Continuous data were expressed as mean and median, along with standard deviation. Categorical data was expressed as numbers and percentages. Different groups of continuous variables were compared using an independent-samples Student's t-test. In contrast, categorical variable groups were compared by applying the chi-square test and Fisher's exact test. Multiple logistic regression models were built to investigate the association between dysglycaemia and death. Statistical significance for the final models was assessed at the 0.05 level.

Ethical consideration

Ethical approval was obtained from the Hospital Research Ethics Committee of the hospital.

RESULTS

We included 59 neonates who met the inclusion criteria in this study. Table 1 showed that teenagers and primiparas formed a third of the maternal population. It also showed that mothers had low antenatal care attendance and in-facility deliveries.

Table 1: Maternal characteristics (n=59).

Maternal characteristics	N (%)
Age <19 years	32 (54.2)
No formal education	35 (59.3)
Attended antenatal care	43 (72.9)
Prolonged labor	37 (62.7)
Hospital delivery	40 (67.8)
Spontaneous vertex delivery	50 (84.7)
Meconium-stained liquor	7 (11.6)

About 2/3 of the babies were male (13/59, 22%);22% were low birth weight. All the neonates were full term; the majority (39/59) were admitted within 24 hours of birth, with a third within the first 6 hours of life (Table 2).

Glycemic profile

All 59 had glucose RBS done at the point of admission. 14/59(23.7%) neonates had abnormal glucose reading as shown in Table3. Dysglycaemia was observed in 4/22(18%) of the neonates with stage 1 HIE, 6/32 (28.1%), and 1/5(20%) with stage 3. p>0.05.

Outcome

Thirty-eight neonates survived, while 21 (35.6%) died. Death was observed in 15 (33.3%) normoglycemic newborns, and 6/14(42.9%) with dysglycaemia (p > 0.01). After controlling for birth weight, hypothermia, hypoxia, and HIE stage, dysglycaemia was not

significantly associated with mortality (AOR=0.64, 95% CI=0.16-2.63, p=0.537).

Table 2: Neonatal characteristics (n=59).

Total number	N (%)
Males	37 (62.7)
Weight in kg mean (SD)	2.7 (0.5)
Presented in the first 6 hours of life	18 (31)
Respiratory distress	29 (49.2)
Convulsion	37 (62.7)
Feeding difficulty	34 (57.6)
Lethargy	37 (62.7)
Hypoxic	39 (66.1)
Hypothermic	34 (57.6)
O2 saturation in % mean (SD)	85.5 (12.7)
Blood glucose level in mmols/l mean (SD)	5.7 (2.9)
Temperature mean 0c (SD)	36.2 (1.5)
HIE staging (N, %)	Stage 1 (22,37.3)
	Stage 2 (32,54.2)
	Stage 3 (5,8.5)

Table 3: Glycemic profile and outcome.

Glycemic profile	Frequency (n=59)	Outcome death (n=21)
Normoglycemia	45 (76.3%)	15 (33.3%)
Hypoglycemia	8 (13.5%)	4 (50%)
Hyperglycemia	6 (10.2%)	2 (33.3%)
Total	59	21

DISCUSSION

The present study assessed the glycemic profile and its relationship with short-term outcomes in neonates diagnosed with HIE who received standard supportive care. Dysglycaemia was observed in 23.7% (13.5% hypoglycemia, 10.2% hyperglycemia) of neonates, with a mortality rate of 42.9% in this subgroup, compared to an overall mortality rate of 35.6%. While the association between glucose abnormalities and survival was not statistically significant, neonates with abnormal glucose levels exhibited lower survival rates.

Dysglycaemia is a common metabolic disturbance among neonates with perinatal asphyxia. Our finding is lower than the 32.9% reported by Anga and colleagues from Lagos state, Nigeria, amongst the subgroup of neonates with birth asphyxia.[16] The difference could be due to varied methodology. For instance, we excluded preterm babies and included only neonates with HIE. It is, however, lower than the previous researchers reported dysglycaemia among neonates undergoing therapeutic hypothermia in a range of 42.6 to 57%. [9,22,23] This study found the prevalence of hypoglycaemia to be 13.5%, which falls within the 4-16.6% range reported earlier in Nigeria and elsewhere.[8,9,24] Hypoglycaemia in neonates with HIE is multifactorial, including prolonged anaerobic glycolysis with subsequent glucose depletion, hyperinsulinism impaired response of counter-regulatory hormones, and impaired liver function due to impaired perfusion.[7,25] Additionally, asphyxiated babies are often not fed early and are on fluid restriction. Hyperglycaemia is observed in 10.2% of neonates with HIE in this study. However, about 21.2 to 48% prevalence was reported amongst neonates with HIE undergoing TH.[9,26,27] This is expected, as TH is linked to stress responses, along with decreased glucose uptake and utilization, which is the consequence.[28]

The case fatality rate in this study is 35.6%, and neonates with dysglycaemia show lower odds of survival compared to euglycemic babies. This is in keeping with the findings of previous researchers, that dysglycaemia is associated with adverse outcomes, including death. [23,29-33] This study may be limited by its retrospective design and small sample size, potentially compromising the accuracy of the findings. Also, we used a single blood sugar measurement, so we might have missed some neonates with dysglycaemia, as blood sugar levels in neonates are known to fluctuate. Nevertheless, it has added to the existing literature and to the pioneering study in Nigeria that documented the prevalence of dysglycaemia. A further prospective study with a larger sample size will provide robust evidence to guide clinical management of babies with HIE and dysglycaemia, thereby improving their outcomes.

CONCLUSION

Dysglycaemia occurred in about one in four neonates with HIE and was associated with higher mortality. Regular glucose monitoring and timely correction should be standard in the management of asphyxiated newborns. Expanding access to advanced neuroprotective care, such as therapeutic hypothermia, could further reduce mortality in similar settings.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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