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Point-of-admission neonatal hypoglycaemia in a Nigerian tertiary hospital: incidence, risk factors and outcome.

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Abstract *Background* Neonatal hypoglycaemia is a major metabolic problem. It may result in mortality or severe handicap among survivors. Many babies admitted for neonatal care are at high risk for hypoglycaemia. The present study set out to determine its point-of-admission prevalence, clinical presentation and outcome.
Methods: Consecutive neonates who met the study criteria had plasma glucose determined at admission into the special care baby unit of Wesley Guild Hospital. Hypoglycaemia was defined as plasma glucose of ≤ 2.5mmol/L. Babies with and without hypoglycaemia were compared for risk factors, clinical features and outcome.
Results: A total of 150 neonates were studied out of which 49 (32.7%) had hypoglycaemia. The mean age, 38.3 ± 71.6 in hours was significantly lower among neonates with hypoglycaemia than those without hypoglycaemia [p = 0.006]. Low socioeconomic class (p = 0.034), admission weight less than 2500g (p = 0.009), hypothermia (p = 0.001) and preterm birth (p = 0.020) were significantly more common in babies with hypoglycaemia. Poor suck (p = 0.010), cyanosis (p = 0.020), convulsion (p = 0.040) and pallor (p = 0.048) were also more common among babies with hypoglycaemia. The mortality rate in babies with hypoglycaemia was 32.7%, higher than 18.8% in babies without hypoglycaemia but the difference was not statistically significant (p = 0.060).
Conclusion: Hypoglycaemia is common among high-risk neonates and is often associated with morbidity and mortality. Routine monitoring of blood glucose is therefore recommended for this class of babies

Key Words: Prevalence, Point-of-admission, Neonatal Hypoglycaemia, Morbidity and Mortality, Nigeria.

Introduction

Neonatal hypoglycaemia (NNH) is one of the most common metabolic problems in contemporary neonatal medicine.[1] It is defined either as whole blood glucose of less than 2.2 mmol/L or plasma glucose of less than or equal to 2.5 mmol/L.[1]

Outcome of NNH depends on the rapidity of onset; associated co-morbidities and adequacy of therapy.[2] Long-term sequelae include poor neurological development, poor intellectual function, motor deficits (especially spasticity and ataxia) and seizure disorders.[3]

Risk factors for NNH include maternal diabetes

mellitus, corticosteroid administration during pregnancy, toxaemia of pregnancy, prematurity, intrauterine growth restriction (IUGR), septicaemia, polycythaemia and erythroblastosis.[4] Other factors include adverse perinatal events like prolonged labour, birth asphyxia, cold stress, severe respiratory distress (due to increased energy utilisation).[4]

While several studies have been done on neonatal hypoglycaemia in the developed world, reports from Nigeria and perhaps many other developing countries on NNH are sparse. Specifically, there has been no previous documentation on the prevalence of neonatal hypoglycaemia at the Wesley Guild Hospital (WGH), Ilesa, Nigeria, a tertiary health facility which had been in existence for close to a century. Wesley Guild Hospital is a unit of the Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife. The hospital provides general and specialist paediatric care to the adjourning communities of at least four states in Nigeria. The objective of the present study was to determine the prevalence, risk factors, clinical presentations at time of admission, and outcome of NNH in a population of hospitalized Nigerian newborn babies.

Methodology

This was a prospective study, conducted over a six-month period. Institutional Ethical Clearance and parental informed consent were obtained. All consecutive neonates admitted into the unit during the study period were included except those who had intravenous infusion of fluid(s) that contained dextrose prior to admission into the unit.

Information obtained and entered into a proforma included demographic characteristics of the mothers and their babies, past medical history and illnesses during pregnancy especially that of diabetes mellitus and hypertension, antenatal booking status, the mode of delivery, duration and details of the management of labour and place of delivery (for referred babies), birth asphyxia as well as history of feeding prior to admission. Anthropometry, rectal temperature and clinical features were documented.

One millilitre of blood was taken into dry fluoride oxalate-containing specimen bottle and immediately processed in the laboratory for plasma glucose estimation using the glucose oxidase reaction method. Other investigations were done as indicated. Hypoglycaemia, for this study was defined as plasma glucose of = 2.5 mmol/l.[1] Babies with hypoglycaemia were managed initially with a bolus of 10 percent intravenous Dextrose-in-water at 2 ml/kg. This was followed with 10 percent Dextrose-in-water at a rate of 6 mg/kg/min (86 ml/kg/24hrs). Babies who had no contraindications to oral feeding were commenced on feeding while monitoring blood glucose levels.

Data analysis was done using the Computer Package for Epidemiologists (PEPI). Tests of statistical significance was done using Chi-square analysis for discreet and Student t-test for continuous variables respectively. Statistical significance was set at p values less than 0.05.

Results

A total of 150 babies were studied. They consisted of 88 males and 62 females giving a male: female ratio of 1.42: 1. Table 1 compares the socio-demographic data between babies with and without hypoglycaemia. Of the 150 babies studied, 49 (32.7%) had hypoglycaemia at the time of admission. Of the remaining 101 (67.3%), 93 (92.1%) babies had normal glucose levels while eight (7.9%) had hyperglycaemia (plasma glucose > 8.3 mmol/l). Of the 49 babies with hypoglycaemia, 29 (59.2%) were males and 20 (40.8%) were females giving a male: female ratio of 1.45: 1 similar to overall male: female ratio of 1.42: 1. A significantly higher proportion [43 (37.1%) of 116] of babies from lower social class had hypoglycaemia compared with six (17.6%) of 34 babies from higher social class ($p = 0.034$).

A higher proportion of referred babies compared with inborn babies experienced hypoglycaemia but the difference was not statistically significant [$p = 0.16$].

Babies who experienced hypoglycaemia were significantly younger than their counterparts who did not ($p = 0.033$). The admission weights ranged between 600g and 4,100g with a mean of 2,100 ± 900g. Hypoglycaemia occurred in 30 (43.5%) of 69 babies who were of low birthweight (birth weight less than 2,500g) compared with 19 (23.5%) of 81 who weighed 2,500g or more [$p = 0.009$].

The gestational age of babies with hypoglycaemia ranged between 26 to 44 weeks. Hypoglycaemia was significantly commoner among preterm babies than term babies ($p = 0.000$). The number of post term babies was remarkably smaller than those with normal or low values. The frequency of hypoglycaemia was more among post-term than term babies but the difference was not statistically significant ($p = 0.071$). Hypoglycaemia was recorded more commonly among twins (13 (41.9%) of 31 compared with 36 (30.1%) of 119 singletons though the difference was not statistically significant ($p = 0.217$).

Three (6.1%) of the 49 babies were infants of mothers with toxaemia of pregnancy.

Table 1: Comparison of Socio-demographic Data of Babies with and without Hypoglycaemia

Parameters	Babies with hypoglycaemia (49)	Babies without hypoglycaemia (101)	Total 150	Statistics
Age in hrs (mean ± SD)	38.3 (71.6)	106.0 (162.1)	150	t = 2.79, p = 0.006
Sex:				
Male	29 (33.0)	59 (67.0)	88	χ^2 = 0.01, p = 0.929
Female	20 (32.3)	42 (67.7)	62	
Social Class:				
Higher classes I and II	6 (17.6)	28 (82.4)	34	χ^2 = 4.51, p = 0.034
Lower classes III-V	43 (37.1)	73 (62.9)	116	
Gestational age (wk):				
< 37	30 (44.1)	38 (55.9)	68	χ^2 = 7.42, p = 0.006
37 to 42	15 (20.3)	59 (79.7)	74	χ^2 = 10.20, p = 0.001
> 42	4 (50.0)	4 (50.0)	8	χ^2 = 0.47, p = 0.492+
*Maternal age (years):				
< 20	3 (25.0)	9 (75.0)	12	χ^2 = 0.07, p = 0.788+
20–35	41(32.8)	84 (67.2)	125	χ^2 = 0.01, p = 0.938
>35	5 (38.5)	8 (61.5)	13	χ^2 = 0.22, p = 0.641
*Maternal parity:				
Primipara	14 (23.7)	45 (76.3)	59	χ^2 = 3.53, p = 0.060
Multipara	31 (37.4)	52 (62.6)	83	χ^2 = 1.85, p = 0.173
Grandmultipara	4 (50.0)	4 (50.0)	8	χ^2 = 0.47, p = 0.492+
Inborn (WGH)	16 (26.2)	45 (73.8)	61	χ^2 = 1.94,
Referred	33 (37.1)	56 (62.9)	89	p = 0.164

Keys:
The 150 babies were delivered by 136 mothers
Yates correction applied
Wk=weeks

Clinical features

The distributions of the clinical features among babies with and without hypoglycaemia are compared in Table 2. Twenty-nine (59.2%) of the 49 babies with hypoglycaemia were symptomatic compared with 28 (27.7%) of the 101 babies without hypoglycaemia (p = 0.000). The mean plasma glucose of asymptomatic babies was slightly less than that of symptomatic babies (1.47 ± 0.57 versus 1.51 ± 0.64) but the difference was not statistically significant (p = 0.823). The rectal temperature of babies with hypoglycaemia ranged between 33.70 and 38.70°C with a mean (SD) of 35.70 (1.10) °C. There was a significantly higher prevalence of hypoglycaemia among babies with hypothermia (χ^2 = 10.31, p = 0.001). Floppiness, poor suck, cyanosis and respiratory distress were the commonest clinical Features identified in hypoglycaemic as well as non-hypoglycaemic babies. In comparison however, hypoglycaemia was significantly more commonly associated with poor suck, cyanosis, convulsions and pallor.

Table 2: Comparison of Clinical Features among Babies with and without Hypoglycaemia.

Clinical features	Babies with hypoglycaemia No (%)	Babies without hypoglycaemia No (%)	Total	χ^2	p value
Floppiness	12 (24.5)	16 (15.8)	28 (18.7)	1.63	0.202
Poor suck	12 (24.5)	9 (8.9)	21 (14.0)	6.65	0.010
Cyanosis	11 (22.5)	9 (8.9)	20 (13.3)	5.23	0.022
Respiratory distress	8 (16.3)	28 (27.7)	36 (24.0)	2.35	0.125
Convulsions	8 (16.2)	6 (5.9)	14 (9.3)	4.21	0.040
Pallor	7 (14.3)	5 (5.0)	12 (8.0)	3.91	0.048
High pitched cry	6 (12.2)	4 (4.0)	10 (6.7)	2.43	0.119*
Jitteriness	5 (62.5)	3 (3.0)	8 (5.3)	2.14	0 .144*
Apnoea	4 (8.2)	2 (2.0)	6 (4.0)	1.87	0.171*
Hypothermia	22 (44.9)	20 (19.8)	42 (28.0)	10.31	0.001

* = Yates' correction applied
Figures in parenthesis are percentages of total in each row

Admission diagnoses

Table 3 shows that preterm delivery, birth asphyxia and septicaemia were the commonest admission diagnoses in hypoglycaemic and non-hypoglycaemic neonates. Hypoglycaemia was significantly more frequent among preterm babies (p = 0.006) and those who were small-for-gestational age (p = 0.022).

Table 3: Comparison of Diagnoses on Admission in Babies with and without Hypoglycaemia.

Diagnoses* on admission	Babies with hypoglycaemia No. (%)	Babies without Hypoglycaemia No. (%)	Total	χ^2	p value
Preterm	30 (61.2)	38 (37.6)	68	7.42	0.006
Birth asphyxia	19 (38.8)	36 (35.6)	55	0.14	0.709
Septicaemia	8 (16.3)	24 (23.8)	32	1.0\9	0.297
Neonatal jaundice	4 (8.2)	19 (18.8)	23	2.12	0.145**
Severe anaemia	6 (12.2)	10 (9.9)	16	0.19	0.663
Polycythaemia	7 (14.3)	6 (5.9)	13	2.90	0.088
SGA	8 (16.3)	4 (4.0)	12	5.28	0.022**
LGA	2 (4.1)	4 (4.0)	6	0.00	1.000**
Tetanus	1 (2.0)	4 (4.0)	5	0.02	0.897**
Rhesus Iso-immunisation	0 (0.0)	2 (2.0)	2	0.05	0.816**

* = Many babies had more than one diagnoses
**= Yates' correction applied
Figures in parenthesis are percentages of total babies with and without hypoglycaemia
SGA= Small for gestational age
LGA= Large for gestational age

Outcome

The outcome of study subjects is presented in Table 4. The prevalence of motor deficit among discharged hypoglycaemic babies (all spastic) was about ten times that in other babies (p = 0.009). There were a total of 35 (23.3%) deaths among the 150 babies studied. Mortality rate was higher among hypoglycaemic babies but the difference was not statistically significant (p = 0.060).

Table 4: Comparison of Outcome among Babies with and without Hypoglycaemia.

Outcome	Babies with hypoglycaemia No. (%)	Babies without hypoglycaemia No. (%)	Total No. (%)	χ^2	value
Discharged without motor deficit	27 (55.1)	79 (78.2)	106 (70.7)	8.51	0.004
Discharged with motor deficit	5 (10.2)	1 (1.0)	6 (4.0)	5.09	0.024*
Discharged against medical advice	1 (2.0)	1 (1.0)	2 (1.3)	0.00	1.000
Referred	0 (0.0)	1 (1.0)	1 (0.7)	0.00	1.000
Died	16 (32.7)	19 (18.8)	35 (23.3)	3.53	0.060
Total	49 (100)	101 (100)	150 (100)		

Figures in parenthesis are percentages of total in each column

$\chi^2 = 13.0$, df = 4, p = 0.01

*With Yates's correction

Discussion

The point-of-admission prevalence of neonatal hypoglycaemia in the present study was 32.7 percent. This was high, especially when compared with the 6.6 percent reported in 1977 by Omene from Benin,[5] Mid-western Nigeria and 9.5 percent reported in 1994 by Njokanma and Fagbule in Sagamu.[6] Sagamu, like Ilesa, is located in South-western Nigerian. The prevalence observed in the present study was also higher than the 20.6 percent reported by Sexson[7] from the USA and 23.0 percent reported by Osier *et al*[8] from Kenya, an East African country. The earlier cited Nigerian reports of 1977 and 1994 would suggest a rise in prevalence of NNH and the later works from Kenya and USA, though from different populations give credence to this trend. The difference between the observed prevalence in the present study and the values cited from the more recent USA and Kenyan studies may also be a reflection of higher predisposing factors to NNH in the locality in which the present study was done as suggested by Koh *et al.*[9] Indeed, much higher figures of 38 percent was reported from Nepal, an Asian country and 38.4 percent Lahore in Pakistan.[10,11]

However, one major reason that may partly account for the higher prevalent rates of NNH in the present study is the use of higher plasma glucose level in the definitions of NNH. For example, using cut-off blood glucose levels of 1.1 mmol/L or 1.7 mmol/L,[5] will give lower prevalent rates than using blood glucose levels of 2.2 mmol/L[6-8] or plasma level of 2.5 mmol/L.[10] Even in the same population using lower glucose levels will exclude babies with higher plasma glucose levels making fewer babies being diagnosed as having hypoglycaemia. Another possible reason for the difference between the prevalent rates of hypoglycaemia may be in the selection of the babies studied. Whilst in the present study high-risk babies who required hospitalisation for major illnesses were studied, the Nepalese study recruited apparently healthy babies from a post-natal ward within the first 50 hours of life while Hamid *et al* in Lahore, Pakistan recruited neonates with known risk factors or suggestive clinical feature.[10,11]

The relatively higher blood glucose cut-off value used in the present study has the advantage of providing management opportunities for many more babies who were at risk of hypoglycaemia. This is clinically beneficial in view of the damaging effect of symptomatic hypoglycaemia on the brain and the fact that the critical blood glucose level at which damage can occur has not been clearly defined.[2,12] Koh *et al* [12] showed reversible disturbances in evoked potentials at glucose level below 2.6 mmol/L in asymptomatic term babies, although no similar studies have been reported from Nigeria.

Findings of higher proportion of babies with hypoglycaemia among referred babies than inborn babies in the present study is in agreement with the previous reports of Njokanma and Fagbule.[6] This could partly be explained on the basis of delay in arrival of referred high-risk babies to the hospital; for example, the mean age of outborn babies with hypoglycaemic was significantly higher when compared with that of the inborn babies with hypoglycaemia. Very ill babies while waiting to be referred or during transfer are hardly fed adequately, if at all fed. Such babies are usually subjected to cold injury (from lack of transfer incubators or proper wrappings) and may therefore develop hypoglycaemia. Moreover, the high index of suspicion and better high-risk neonate identification and interventions may be contributory to the lower prevalent rate of hypoglycaemia among inborn babies.

Although, hypoglycaemia is a common finding among infants of diabetic mothers (IDM),[13] none of the two infants of diabetic mothers seen in the present study developed hypoglycaemia, a finding consistent

with that of another Nigerian study.[5] However, the number of infants of diabetic mothers in this study is too small to have a meaningful conclusion.

The proportion of babies with symptomatic hypoglycaemia in the present study was higher than 35.7 percent previously documented in Benin[5] and 40.2 percent in India.[14] The comparison of occurrence of symptoms and signs suggestive of NNH between studies is rather difficult since these features are not specific for hypoglycaemia and different blood glucose levels have been used to define hypoglycaemia. However, babies with features suggestive of hypoglycaemia such as hypothermia, cyanosis, convulsion, refusal to suck, and non-anaemic pallor deserve prompt estimation of blood glucose. Empirical treatment for hypoglycaemia is advised if estimation of blood glucose is not available or likely to be delayed.

About a third of the babies with hypoglycaemia in the present study died. This was almost twice the mortality rate in non-hypoglycaemic babies. The implication is that hypoglycaemia to some extent contributes to neonatal mortality.

The high prevalent rate of NNH and high mortality rate among babies with NNH in the present study is an indication that blood glucose estimation should be routine in the care of high-risk neonates. Where standard laboratory facilities are sparse, cheap but sensitive and reliable strip methods of glucose estimation may be used. Most of the major risk factors for NNH in the present study like LBW, hypothermia, birth asphyxia, septicaemia and polycythaemia are highly preventable and treatable. Effort to reduce these factors must be pursued vigorously. There is need to train and re-train health workers, particularly those in the lower tiers of health care system on the prevention of NNH. Public awareness on the immediate post-delivery care of the newborn and provision of suitable transfer medium for referred babies should also be intensified to reduce the burden of NNH among out-born babies. Affordable and easily accessible maternal and child health services with improved referral facilities for high-risk pregnancies will prevent most of the co-morbidities and therefore reduce the high morbidity and mortality rates reported in the present study.

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