

Early Glycaemic Derangement in Newborn: A Cross-Sectional Analysis of Babies Born in an Urban Private Hospital in Benin City, Nigeria

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ABSTRACT

The transition from fetal to extra-uterine life in neonates is characterized by often dramatic physiological, metabolic and endocrine changes in order to maintain homeostasis. Glycaemic disturbance are frequently noted in the early post-natal period in neonates. Abnormal glucose levels have been shown to have negative impact on neurologic outcome in term and preterm babies as well as increased risk of death. This study therefore sought to describe the glycaemic status of newborn infants delivered in a private hospital in Benin City. The birth record of all babies delivered at the hospital from January 2020 to December 2020 was retrospectively reviewed. The data on random blood glucose concentration of all neonates was collected which had been measured within three hours of delivery using Accu-Check® Active (Roche) device after obtaining blood by heel prick over the period. The associations between glucose level and independent variables such as mothers age, parity, type of gestation, gestational age, mode of delivery and baby's gender, were investigated using Chi square statistics and fisher's exact correction where necessary. A multivariate regression analysis was done to identify factors that are independently associated with glycaemic derangement. A p value of less than 0.05 was accepted as the level of statistical significance. Four hundred and seventy-two mothers were included in the study. The mean age (SD) of mothers was 31.07 ± 5.3 years. Most (410; 82.0%) of neonates were delivered at term with about half (269 ;53.8%) being males. 63(12.6%) of the babies had low birth weight, 405 (81.0%) had normal birth weight while 32 (6.4%) had high birth weight. Hypoglycaemia was noticed in 36(7.2%), hyperglycaemia in 7 (1.4%) and majority(457 ;91.4%) had normal blood glucose levels at birth. Glycaemic status was significantly associated with birth weights (p = 0.013) and preterm gestational age at delivery (p = 0.025). There was no significant statistical association between parity and glycaemic status (p = 0.914). Our study revealed high prevalence of hypoglycaemia (7.2%) and hyperglycaemia (1.4%) in newborns. Prematurity and abnormal birth weights were significantly associated with hypoglycaemia in newborns.

Key words: Hyperglycaemia, Hypoglycaemia, Newborn

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INTRODUCTION

The transition from fetal to extra-uterine life in neonates is characterized by often dramatic physiological, metabolic and endocrine changes in order to maintain homeostasis.¹ Fetal glucose concentration is entirely dependent on maternal glucose levels through facilitated diffusion across the placenta.¹ This process maintains the fetal plasma glucose levels at approximately two-third of maternal levels with minimal fetal gluconeogenesis.² The onset of labour induces transient hypoxic stress necessitating anaerobic metabolism and increased glucose consumption. Similarly, with cord clamping post-delivery, maternal supply of glucose stops while the secretion of insulin continues resulting in a decline in the neonatal blood glucose concentration.³ To overcome the decline, counter-regulatory hormones like glucagon and cortisol are released. Also, endogenous glucose production through the process of gluconeogenesis and glycogenolysis ensues.⁴ Failure of neonatal metabolic adaptations can lead to hypo- or hyperglycaemia.

Glycaemic disturbance are frequently noted in the early post-natal period in neonates. Hypoglycaemia is largely the commonest metabolic abnormality of neonate.⁵ It is estimated to occur in 5-15% of healthy term babies and even higher in preterm babies. Factors that increase the risk of hypoglycaemia in neonates includes prematurity, perinatal stress, being an infant of a diabetic mother and small size for gestational age.⁶⁻⁸ The definition of hypoglycaemia has remained controversial.⁹⁻¹⁰ General consensus however appears to accept the definition of hypoglycaemia to be a glucose concentration less than 47mg/dl, although for practice purpose, blood glucose concentration less than 50mg/dl is generally considered as hypoglycaemia.¹² Similarly, the prevalence of hypoglycaemia varies from centre to centre depending on the cut-off values used to make the diagnosis.¹³ Neonatal hyperglycaemia on the other hand is another common metabolic

problem.^{13,14} It is likely due to elevated stress hormones and decreased glucose uptake by the neonatal brain in addition to impaired hepatic, pancreatic and peripheral tissue glycaemic balance. It is particularly a major cause of morbidity and mortality in extreme low birth babies.¹⁵ Risk factors for neonatal hyperglycaemia include low birth weight, birth asphyxia and neonatal sepsis.^{15,16} Neonatal hyperglycaemia and the patterns of brain injury seen in babies with hyperglycaemia have been largely understudied.¹⁴ Recent studies suggest predominant basal ganglia or global injury compared to neonates with normal glucose levels.¹⁴ Other retrospective studies have reported increased risk of death and major disability in babies with hyperglycaemia and glucose variability.^{13,16} This study therefore sought to describe the glycaemic status of newborn infants delivered in a private hospital in Benin city. An understanding of the pattern and the factors associated with derangement may help in the management of modifiable factors and the prevention of neurodevelopmental complications associated with early glucose impairment in newborn.

MATERIALS AND METHODS

Setting

This was a retrospective study conducted at the delivery suite of the Lily Hospitals Limited, Benin City, Nigeria. The hospital is a 48-bed capacity multi-specialty private hospital established in 2015. Most of its clients are from the high- and middle-income socio-economic class. The hospital has its headquarter in Warri, Delta state with branches in other parts of Nigeria. Specialties available include obstetrics, gynecology, pediatrics, neonatology, general surgery, pediatric surgery, orthopedics, otorhinolaryngology, family Medicine, anesthesia, radiology, physiotherapy and public health. The delivery suite consists of one delivery bed and three beds in the active phase room. The obstetric unit is run by three consultants and two medical officers. The

unit provides twenty-four hour coverage ensured by a complement of 10 nurses and other support staff. All babies delivered are examined by medical officers and/or the paediatrician within 24 hours after delivery. About 450 deliveries are supervised yearly in the hospital.

Study design and data collection

This was a retrospective study of newborn babies delivered between January 1st 2020 to December 31st 2020. The birth record of all babies delivered at the hospital from January 1st, 2020, to December 31st, 2020 was retrospectively reviewed. The random blood glucose concentration of all neonates was measured within three hours of delivery using Accu-Check® Active (Roche) device after obtaining blood by heel prick. The documented random blood glucose level was further categorized into hypoglycaemia (<50mg/dl), normal (50-125mg/dl) and hyperglycaemia >125mg/dl. Blood glucose level was considered as the outcome while factors like birth weight, gestational age at delivery, mother's age, parity, mode of delivery, type of gestation and sex of the baby were considered as possible predictors of the random blood glucose concentration (independent variables). Blood glucose sample was obtained before commencement of feeding for all the babies.

Ethical approval

Ethical approval, both for the study usage of the hospital data was granted by the Lily Hospital limited Ethics and Research committee. Personal identifiers like name and address were not extracted from the delivery records.

Statistical analysis

The statistical analysis was done using the International Business Machine Statistical Package for Social Sciences (IBM SPSS) for window-version 21.0. Frequency tables were used for descriptive statistics and cross tabulations for relationship between

variables. The associations between glucose level and independent variables such as mothers age, parity, type of gestation, gestational age, mode of delivery and baby's gender, were investigated using Chi square statistics and fisher's exact correction where necessary. A multivariate regression analysis was done to identify factors that are independently associated with glycaemic derangement. A p value of less than 0.05 was accepted as the level of statistical significance.

RESULTS

Four hundred and seventy-two mothers were included in the study. Majority (458 ;97.0%) of them were within age group 40 years and below. The mean age (SD) was 31.07 ± 5.3 years. Multiparous paturients constituted a higher proportion; 277 (58.0%) of mothers while majority ;461 (96.4%) had singleton gestation. Of 517 newborns delivered during the study period, 500 were analyzed after excluding 17 who had missing data. Majority (410 ;82.0%) of neonates were delivered at term with slightly more than half (269; 53.8%) being males. Low birth weight neonates constituted slightly above one-tenth (63 ;12.6%) while majority (405 ;81.0%) had normal birth weight. Hypoglycaemia was recorded in 36 (7.2%) of neonates at birth with majority having normal blood glucose level.

Bivariate analysis

There was no significant difference in the prevalence of abnormal glycaemic status and sex ($p=0.401$) or parity ($p=0.914$). However, a higher proportion(22 ;8.2%) of male neonates had hypoglycaemia as opposed to 14 (6.1%) female-newborns with hypoglycaemia. Bivariate analysis showed statistically significant association between glycaemic status and birth weight ($p=0.013$) and gestational age at delivery ($p=0.025$). 10 (15.9%) and 4 (12.5%) of neonates with low and high birth weight respectively had hypoglycaemia. Also, a higher proportion (11 ;12.2%) of hypoglycaemic neonates were delivered preterm compared to 25

Table 1: Sociodemographic and obstetric characteristics of mothers

Variable	Frequency (n = 472)	Percent
Age group (years)		
≤ 30	227	47.5
31 – 40	231	48.3
41 – 50	17	3.6
≥ 51	3	0.6
Mean age + SD	31.07 ± 5.3 years	
Parity		
Primipara	197	41.2
Multipara	277	58.0
Grand multipara	4	0.8
Type of gestation		
Singleton	461	96.4
Multiple	17	3.6

Key: SD: Standard Deviation

Table 2: Gestational age at delivery, sex, birth weight and glycaemic status of neonates

Variable	Frequency (n = 500)	Percent
Gestational age at delivery		
Preterm	90	18.0
Term	410	82.0
Sex		
Male	269	53.8
Female	231	46.2
Birth weight		
LBW	63	12.6
NBW	405	81.0
HBW	32	6.4
Glycaemic status		
Hypoglycaemia	36	7.2
Normoglycemia	457	91.4
Hyperglycemia	7	1.4

Key: LBW- low birth weight; NBW-normal birth weight; HBW-high birth weight

Table 3: Association between glycaemic status and maternal parity, gestational age at delivery, sex and birthweight of neonates

Variable	Glycaemic status			Test statistics	P value
	Hypoglycaemia (n = 36) Freq (%)	Normal (n = 457) Freq (%)	Hyperglycemia (n = 7) Freq (%)		
Sex					
Male	22 (8.2)	242 (90.0)	5 (1.8)	Fischer’s exact = 1.781	0.401
Female	14 (6.1)	215 (93.1)	2 (0.8)		
Birth weight					
LBW	10 (15.9)	51 (81.0)	2 (3.1)	Fischer’s exact = 12.504	0.013
NBW	22 (5.4)	378 (93.3)	5 (1.3)		
HBW	4 (12.5)	28 (87.5)	0 (0.0)		
GA at delivery					
Preterm	11 (12.2)	76 (84.4)	3 (3.4)	$\chi^2 = 7.356$	0.025
Term	25 (6.1)	381 (92.9)	4 (1.0)		
Parity					
Primipara	12 (6.1)	182 (92.4)	3 (1.5)	Fischer’s exact = 1.725	0.914
Multipara	21 (7.6)	252 (91.0)	4 (1.4)		
Grand multipara	0 (0.0)	4 (100.0)	0 (0.0)		

Key: GA-Gestational age; LBW-Low birth weight; NBW-Normal Birth Weight; HBW-High Birth Weight.

Table 4: Evaluation of possible determinants of hypoglycemia among neonates

Predictors	B (regression co-efficient)	Odds ratio	95% CI for OR		p-value
			Lower	Upper	
Maternal age	0.053	1.054	0.989	1.124	0.104
Maternal parity					
Grand multipara	-18.532	0.001	0.001	0.001	0.999
Multipara	0.238	1.269	0.572	2.814	0.558
Primipara*	1				
Gestational age					
Preterm	0.283	1.327	0.404	4.360	0.641
Term*	1				
Birth weight					
Low birth weight	0.113	1.119	0.220	5.689	0.892
Normal birth weight	-1.072	0.342	0.106	1.105	0.073
High birth weight*	1				
Sex					
Male	0.462	1.587	0.722	3.490	0.251
Female*	1				

*Reference category, $R^2 = 33.0\% - 85.0\%$, CI= Confidence Interval

(6.1%) delivered at term.

The factors associated with hypoglycaemia in the bivariate analysis as well as sex, parity and maternal age were entered into a multivariate logistic regression model. Sex, parity and maternal age were not significantly associated with hypoglycaemia;

DISCUSSION

The findings of our study indicate that glycaemic derangement occurs in about one in ten neonates delivered in our hospital setting. Hypoglycaemia was five times more common in newborn compared to hyperglycaemia. The prevalence in the present study is however lower than that reported by Ochoga and colleagues in Benue state (11.0%)¹⁷ and Frank-Briggs et al in Port Harcourt (28.3%).¹⁸ The difference in prevalence may be accounted for by the fact that all babies in our study were those delivered in the facility. The study in Benue and Port Harcourt, included babies delivered outside the facility. These babies may have been referred on account of clinical conditions associated with hypoglycaemia. Similarly, it is likely

that the period of transfer might have necessitated long fast in these babies whose capacity for gluconeogenesis is limited. Studies from Ghana¹⁹, Uganda²⁰ and Bangalore²¹ however reported lower prevalence of hypoglycaemia in new born. The lower values in these studies may be accounted for by the difference in cut-off value for defining hypoglycaemia. In our study, a higher cut-off for blood glucose (50mg/dl) was used to define hypoglycaemia.

Our results show that the occurrence of hypoglycemia in premature babies, neonates with low birth weight and in those with high birth weights was significantly higher than that in full-term babies and normal birth weight children. The American Academy of Paediatrics (AAP) have earlier identified prematurity, being an infant of a diabetic mother and weighs small or large for gestational age as significant risk factor for hypoglycaemia in infants²². Preterm and Low birth weight babies have small hepatic glycogen stores and limited capacity for gluconeogenesis.^{23,24} Delays in instituting breastfeeding or commencing dextrose

infusion may increase the chance of hypoglycaemia in these babies. Birth weight that is large for gestational age and high birth weight have been documented to be associated with hypoglycaemia in both term and preterm babies.²⁵ The presence of hypoglycaemia in these neonates might be in association with maternal gestational diabetes mellitus. Our study however did not determine the presence or otherwise of gestational diabetes in the mothers.

The prevalence of hyperglycaemia observed in our study (1.6%) is lower than what was observed in Turkey (2.9%) among newborns admitted in the neonatal unit.²⁶ The lower prevalence in our study may be explained by the fact that our study sample included all babies born in the hospital, whether they needed neonatal care or not. It is likely that neonatal morbidities necessitating admission into the neonatal unit might have been partly responsible for the higher prevalence of hyperglycaemia observed among Turkish babies. The association between neonatal morbidities like sepsis and asphyxia and hyperglycaemia is well documented.²⁷ Asphyxia and sepsis which are common causes of neonatal admissions are also associated with disordered glucose metabolism and abnormal glucose levels in neonates.

Regarding the factors associated with hyperglycemia, there was no significant association between hyperglycaemia and neonatal or maternal factors considered. Hyperglycaemia however was more common in preterm and low birth weight babies compared to other neonates. Kurt et al²⁶ in Turkey found similar observation in previous studies. They observed that the prevalence of hyperglycemia progressively increased with decreasing birth weight and gestational age of newborns. Generally, preterm babies have immature expression of glucose transporters, decreased ability to suppress endogenous glucose production and decreased insulin response to blood glucose^{27,28} thus increasing the risk of hyperglycaemia. The lack of significance in our study may be related to the small number of babies with hyperglycaemia. A

large cohort study may be needed to examine the observation.

One limitation of our study is that only one blood glucose test was done. This may have underestimated the prevalence of glycaemic derangement in neonates. Repeated blood glucose test is recommended to provide evidence for a trend in glucose concentration following delivery. Secondly, information on the maternal condition like pre-eclampsia, gestational diabetes and maternal perinatal glucose concentration which might have affected neonatal glucose levels was not available. In spite of these limitations, our findings provide evidence for burden and associated factors for glycaemic derangement in newborns.

CONCLUSION

Our study revealed the prevalence of hypoglycaemia (7.2%) and hyperglycemia (1.4%) in newborns. Hypoglycemia was associated with prematurity and abnormal birth weights. Considering the adverse impact of abnormal glucose levels on cognitive and neurodevelopmental outcome among neonates and children, we recommend that blood glucose check should be included in routine new born care especially for preterm babies and those with abnormal birth weights.

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