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Original Article

Comparison of Blood Glucose Levels in Caesarean and Vaginally Delivered Newborns at Lagos University Teaching Hospital, Nigeria

Elizabeth Onazahi Ajogun[1], *Elizabeth Eberechi Oyenusi[2], Abiola Olufunmilayo Oduwole[2], Maryann Ugochi Ibekwe[3].

[1]Maidstone and Tunbridge Wells NHS Trust,Kent, UK/Paediatric Endocrinology Training Centre for West Africa, Lagos, Nigeria [2]Endocrinology and Metabolism Unit, Department of Paediatrics, College of Medicine, University of Lagos (CMUL)/Lagos University Teaching Hospital (LUTH), Lagos, Nigeria/ Paediatric Endocrinology Training Centre for West Africa, Lagos, Nigeria, [3]Department of Paediatrics, Alex Ekwueme Federal University Teaching Hospital, Abakaliki, Ebonyi, Nigeria.

Abstract

Background: Normal blood glucose supply and metabolism are of utmost importance for growth and normal brain development in the foetus and newborn. Disorders in glucose supply or metabolism can result in hypoglycaemia or hyperglycaemia. Considering the increasing trend of caesarean section (CS) worldwide, including Nigeria, it is important to determine the incidence and type of dysglycaemia in neonates delivered by CS. The study objective was to compare the blood glucose (BG) levels of newborns delivered by CS with those by vaginal delivery (VD).
Methodology: This was a prospective observational study of 164 neonates, of which 85 were delivered through CS and 79 through VD. A pretested questionnaire was used to obtain information on sociodemographic variables, gestational age, feeding time of the new-born and maternal fasting time, while BG was determined using Accu-chek Multiclix. Every tenth sample was also tested in the laboratory for quality control.
Results: The mean (SD) cord blood glucose level was lower in the CS (68.7(10.1) mg/dl) than VD neonates (80.9(11.5) mg/dl, p = <0.001). The mean (SD) blood glucose level at 2 hours of life was also lower in CS (62.5(10.0) mg/dl) than VD neonates (71.2(10.9) mg/dl, p = <0.001). Factors that were significantly associated with cord BG levels were gestational age, maternal fasting time and mode of delivery. At two hours of life, cord blood, neonatal feeding time, gestational age and birth weight were significantly associated with neonatal BG levels.
Conclusion: Cord and neonatal BG were significantly lower in neonates who were delivered via CS compared to those delivered vaginally.

Keywords: Newborn; Neonate; Blood Glucose; Vaginal Delivery; Caesarean Section.

***Correspondence:** Elizabeth Eberechi Oyenusi. Endocrinology and Metabolism Unit, Department of Paediatrics, College of Medicine, University of Lagos, Lagos, Nigeria. **Email:** eoyenusi@unilag.edu.ng

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Introduction

Normal blood glucose supply and metabolism are of utmost importance for growth and normal brain development in the foetus and newborn. [1] Disorders in glucose supply or metabolism can result in hypoglycaemia or hyperglycaemia. Hypoglycaemia is a common metabolic problem in the newborn period and may be associated with both acute decompensation and long-term neuronal loss. [2] The neonatal brain develops rapidly; therefore, persistent or recurrent hypoglycaemia may lead to long-term visual disturbance, hearing impairment, cognitive abnormalities, secondary epilepsy and other disorders in the central nervous system. [3]

After birth, the normal newborn infant's plasma glucose concentration falls quickly to levels lower than those prevalent in foetal life. [4] Labour is a form of stress both for the mother and the foetus. Labour stimulates pain, fatigue, physiologic alterations and maternal anxiety, a form of stress in the mother which leads to an increase in both maternal and foetal catecholamines. [5,6]

Caesarean section (CS) is among the package of emergency obstetric care (EmOC), designed to manage potentially life-threatening complications and leads to a reduction in maternal and perinatal mortality. [7] The World Health Organization (WHO) documented that as countries increase their CS rates up to 10%, maternal and neonatal mortality are reduced. [8] In data from 154 countries, the rates of CS ranged from 5% to 42.8% [9] while in Nigeria, the overall prevalence rate of CS was 2.1% with South-West recording the highest prevalence of 4.7%. [10] In the Lagos University Teaching Hospital, the overall prevalence of C/S recorded over a 10-year period (2008-2017) was 51.3% with a statistically significant increase in C/S rate from 47% in 2008 to 56% in 2017. [11] Despite the increasing rate of CS globally and in Nigeria, studies comparing blood glucose levels in neonates delivered through CS and vaginally are few, with available ones showing varying results. [12-16] Therefore, the study compared the blood glucose levels of neonates delivered via CS to neonates exposed to the stress of labour through VD. This could inform policies and protocols for blood glucose monitoring and early intervention to reduce morbidity and mortality associated with dysglycaemia.

Subjects and Methods

This was a prospective, observational study carried out at the Lagos University Teaching Hospital (LUTH), Idi-Araba, Mushin Local Government Area of Lagos State, Nigeria. The study population was derived from mother-child pairs in the labour ward and the inborn neonatal unit. Newborns delivered by either vaginal delivery or elective caesarean section (CS) from gestational age of 37 complete weeks were included in the study. Exclusion criteria included newborns delivered by emergency CS, newborns of mothers with any medical disorder, diabetes, ante/intrapartum complications, newborns with Apgar Scores ≤ 7 or newborns with chromosomal and congenital defects.

Ethical Consideration

Ethical approval for the study was obtained from LUTH Health Research Ethics Committee (HREC no: ADM/DSCST/HREC/APP/363) prior to commencement of the study. Written informed consent was obtained from the mothers prior to delivery, and a pretested questionnaire was administered to them afterwards. Information obtained was treated as confidential, and feedback on the test results was given to participating mothers. All positive results were communicated to the managing physicians for appropriate management. The study participants did not bear the financial cost of investigations.

Sample Size Determination

The sample size estimation approach for testing hypotheses concerning two independent sample means was used for the study:

n = $2\sigma^2(Z_{\alpha/2} + Z_{1-\beta})^2 / \delta^2$

Where n = required sample size for each group

$Z_{\alpha/2}$ and $Z_{1-\beta}$ = the values of the standardized normal deviate corresponding to specified confidence and power levels, respectively

and α = type I error while ß is type II error

δ is the detectable difference between the two groups (vaginal vs caesarean delivery)

The level of confidence was specified at 95% and the power was fixed at 80%. Specifications for σ and $\delta(0.58)$ were based on information from available literature. A pooled standard deviation of 0.86 was determined from a study conducted by Hussein *et al*. [13]. From the above specifications, the minimum sample size for each group was 76 and for the two groups the combined size was 152. In order to compensate for invalid samples and invalid laboratory results, the sample size was adjusted upwards by 5% thus, the final minimum sample size came to between 152 - 160 (Between 76 - 80 CS and 76 - 80 VD).

Data Collection

Mothers who fulfilled the inclusion criteria and had been admitted either into the labour ward or the antenatal ward were identified before delivery. Every recruited newborn had 0.5 mls of venous cord blood sample obtained at delivery and measured for blood glucose, as well as capillary blood obtained by heel prick at 2 hours of life. Blood glucose levels were measured using the bedside device *Accu-chek Multiclix* (Roche Diagnostics, Mannheim Germany), which was standardized. For quality control, every tenth blood sample was also tested in the main laboratory and blood glucose levels that were considered hypoglycaemic and hyperglycaemic were confirmed in the laboratory.

For interventional purposes, blood glucose levels of less than or equal to 40 mg/dl were considered hypoglycaemic [17] and blood glucose levels of greater than or equal to 125 mg/dl were considered hyperglycaemic.[18,19] The managing paediatrician was informed of any dysglycaemia. A pretested questionnaire was administered to the mothers as soon as it was convenient for them after delivery. Gestational age, start of feeding time of the new-born, neonatal sex, weight, length and occipito-frontal circumference, Apgar score, duration of labour, duration of mother's fasting, and maternal fluids during labour were recorded.

Anthropometry

The measurements of the mothers were taken prior to delivery. The weight was measured with a portable electronic weighing scale (Seca Alpha, model 770, Germany) after checking for zero error at each measurement, to the nearest 0.1 kg. The height was measured using the Leicester height measure (Seca) stadiometer, with the reading to the nearest 0.1cm. The body mass index (BMI) was calculated using the standard formula, Weight (kg)/Height^2 (m^2).The birth weight of the neonates was measured in grams using an electronic weighing scale, length was measured in centimetres (nearest 0.1cm) using an infantometer and the occipito-frontal circumference in centimetres (nearest 0.1cm) by an inelastic tape measure.

Data Analysis

The data was recorded and analysed using SPSS 21. Means and proportions of the basic socio-demographic, clinical data and blood glucose levels were compared between women who delivered by caesarean section and those who delivered vaginally using the student's t-test and Chi test, respectively.

Blood glucose levels were also analysed using different cut-offs that have been used previously in literature.

Linear regression was performed where blood glucose levels (cord, neonatal) were the dependent variable, and other variables (maternal and perinatal) were independent variables. A p-value of less than 0.05 was accepted as statistically significant.

Results

General characteristics of the study participants

One hundred and sixty-four neonates and their mothers, made up of eighty-five neonates delivered by caesarean section (CS) and seventy-nine neonates delivered vaginally (VD), were recruited into the study. Table 1 shows the socio-demographic characteristics of the study participants. Mothers aged 30 – 39 years accounted for 61.2% of neonates delivered by CS and for 57.0% of neonates delivered vaginally. The male-to-female ratio of neonates delivered by CS and VD was 1.8:1 vs 1:1, respectively.

Table 1: Socio-demographic characteristics distribution of mothers and neonates involved in the study

Variables	**CS** n = 85	**VD** n = 79	χ^2	**p-value**
Age				
15 - 19	1(1.2)	0(0.1)	2.592	0.459
20 - 29	30(35.3)	25(36.7)		
30 - 39	52(61.2)	45(57.0)		
40 - 49	2(2.4)	5(6.3)		
Tribe				
Yoruba	37(43.5)	29(36.7)	2.792	0.425
Igbo	41(48.2)	37(46.8)		
Hausa	3(3.5)	5(6.3)		
Others	4(4.7)	8(10.1)		
Maternal level of education				
No formal	1(1.2)	0(0.0)	6.11	0.106
Primary	2(2.4)	4(5.1)		
Secondary	26(30.6)	36(45.6)		
Tertiary	56(65.9)	39(49.3)		
Socioeconomic status				
High	62(72.9)	57(72.2)	2.19	0.334
Middle	22(25.9)	18(22.8)		
Low	1(1.2)	4(5.1)		
Neonatal gender				

Male	55(64.7)	40(50.6)	3.33	0.082
Female	30(35.3)	39(49.4)		

(Figures in parentheses are percentages of the total in columns)

The two groups of women (85 vs 79) were well matched in their basic characteristics, as shown in Table 2. However, the time of fasting was significantly longer in women who delivered by caesarean section compared to those who delivered vaginally (15.0(2.8) vs 9.7(3.3) hours, p = <0.001). Table 3 shows the characteristics of neonates. The mean (SD) birth weight was comparable (3260.8(391.4) g in neonates delivered by CS vs 3264.4(401) g in the VD group). The only statistically significant feature was the APGAR score at 5 mins, which was lower in the CS group (p<0.001) as shown in Table 3. About 16.5% of neonates delivered via CS were fed in the first 2 hours compared to 22.8% in the VD group, though the difference did not reach statistical significance (p=0.308)

Table 2: Comparison of characteristics of mothers

Variables	**CS** **n = 85**	**VD** **n = 79**	**t**	**p**
The mean (SD) of				
Maternal age (years)	30.9(4.6)	31.8(4.8)	-1.213	0.227
Maternal weight (kg)	84.0(9.3)	84.5(8.9)	-0.385	0.701
Maternal height(cm)	160.8(4.8)	158.9(17.1)	-0.970	0.334
Maternal BMI	32.2(3.5)	32.7(3.2)	-1.013	0.313
Parity	1.3(1.1)	1.5(1.4	1.17	0.246
Gestational age (Wks)	38.5(1.3)	38.8(1.3)	-1.58	0.117
Fasting time, hours	15.0(2.8)	9.7(3.3)	11.10	<0.001

Table 3: Comparison of characteristics of neonates

Variable	**CS** **n = 85** **Mean (SD)**	**VD** **n = 79** **Mean (SD)**	**t**	**p**
Neonatal Weight(g)	3260.8(391.4)	3264.4(401)	-0.058	0.954
Neonatal Length(cm)	50.1(2.8)	50.6(3.3)	-0.876	0.383
Neonatal OFC (cm)	35.3(2.5)	34.9(1.4)	1.067	0.288
APGAR score-1	7.7(0.8)	8.1(0.8)	-2.820	0.05
APGAR score-5	9.0(0.5)	9.4(0.7)	-4.805	<0.001*
Time of neonatal first feed (min)	13.5(31.9)	19.4(37.2)	-1.104	0.271

*Statistically significant

The mean (SD) cord and 2 hours of life blood glucose levels in neonates delivered by C/S were significantly lower (68.7mg/dl & 62.5mg/dl) compared to their counterparts born vaginally (80.9mg/dl & 71.2 mg/dl) [p = <0.001] as shown in figures 1 and 2. The change in blood glucose levels over the first 2 hours of life did not differ significantly between the babies born through VD and those born by CS (p = 0.093).

Figure 1: Cord blood glucose levels in vaginal and caesarean deliveries.

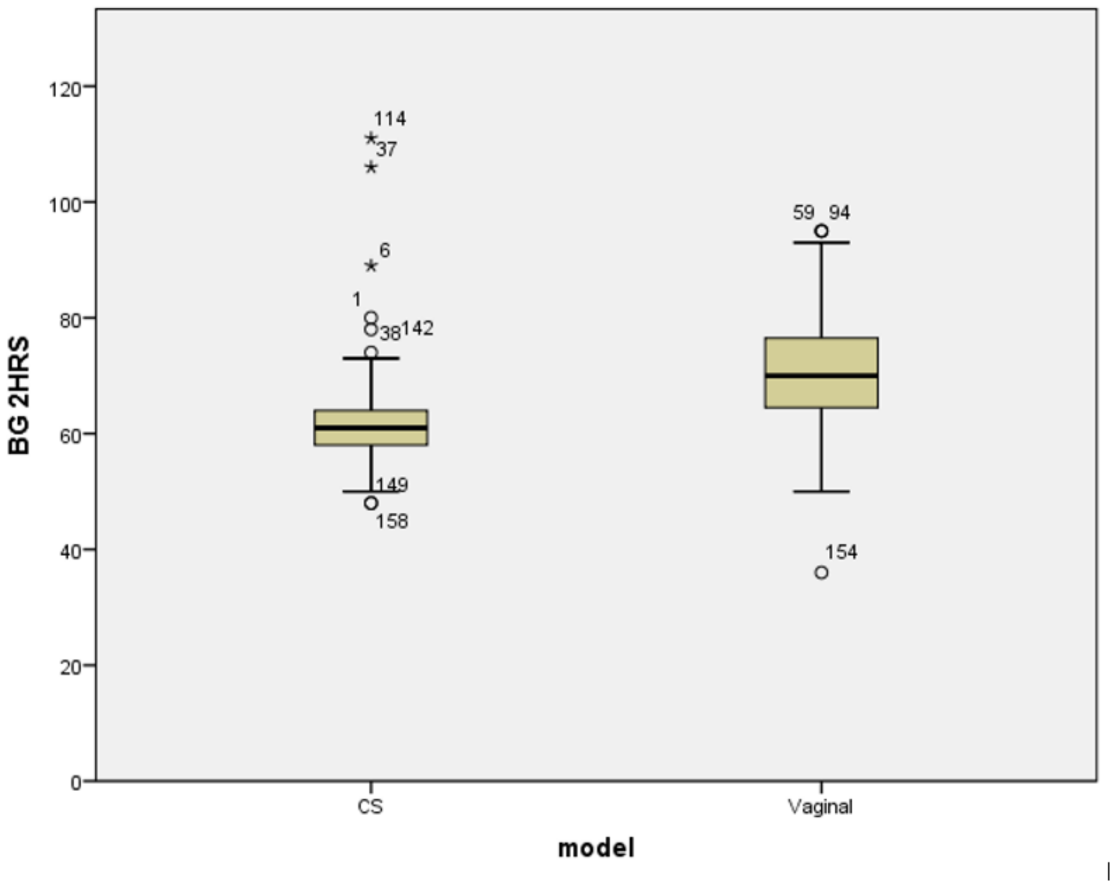

Figure 2: Neonatal blood glucose levels at 2 hours of life in caesarean and vaginal deliveries.

Neonatal blood glucose levels in caesarean and vaginal deliveries

Table 4 shows the blood glucose stratification. At delivery, only one neonate (1.2%) had hypoglycaemia when the blood glucose cut-off was ≤ 40mg/dl, ($p = 0.518$), four (4.7%) had hypoglycaemia when ≤45mg/dl ($p = 0.05$) was used as cut-off while five neonates (5.9%) had hypoglycaemia when ≤47 and 50mg/dl ($p = 0.03$) were used as cut-offs, in the CS group. None of the neonates delivered via VD had hypoglycaemia at delivery. Two neonates had hyperglycaemia, both in the vaginal delivery group ($p = 0.482$). At 2 hours of life, hypoglycaemia was found in both neonates delivered via CS and VD. The incidence of hypoglycaemia in this study at delivery was 0.6%, 2.4%, 3.0% and 3.0% while at 2 hours of life, it was 0.6%, 0.6%, 0.6% and 4.3%, when the cut-off for neonatal hypoglycaemia was placed at ≤40mg/dl, 45mg/dl, 47mg/dl and 50mg/dl respectively.

Table 4: Neonatal blood glucose levels in caesarean and vaginal deliveries regarding hypoglycaemia and hyperglycaemia

Cord blood glucose level	Caesarean delivery n = 85	Vaginal delivery n = 79	Total n = 164	p - value
At birth –				
≤ 40mg/dl	1(1.2)	0(0.0)	1(0.6)	0.518
≤45mg/dl	4(4.7)	0(0.0)	4(2.4)	0.05
≤47mg/dl	5(5.9)	0(0.0)	5(3.0)	0.03
≤50mg/dl	5(5.9)	0(0.0)	5(3.0)	0.03
2 Hr of life				
≤ 40mg/dl	0(0.0)	1(1.3)	1(0.6)	0.482
≤45mg/dl	0(0.0)	1(1.3)	1(0.6)	0.298
≤47mg/dl	0(0.0)	1(1.3)	1(0.6)	0.298
≤50mg/dl	5(5.9)	2(2.5)	7(4.3)	0.289
At birth - ≥ 125mg/dl	0(0.0)	1(1.3)	1(0.6)	0.482
At 2 hours of life - ≥ 125mg/dl	0(0.0)	0(0.0)		n/a

Factors affecting blood glucose obtained from the cord and two hours of life

Factors that were significantly associated with mean cord blood glucose levels were gestational age (p = 0.036), maternal fasting time (p = <0.001) and mode of delivery (p = 0.009). This is shown in Table 5. The factors that were significantly associated with mean neonatal blood glucose levels at two hours of life were cord blood glucose (p = <0.001), neonatal feeding time (p = <0.001), gestational age (0.039) and neonatal birth weight (p = 0.029) as shown in Table 6. The blood glucose level at two hours of life was significantly lower in neonates who had not been fed.

Table 5: Factors affecting cord blood glucose levels using Multiple linear regressions

Variable	Coefficient	Std Error	F-test	P-Value
Maternal age	-0.158	0.185	0.73	0.394
Maternal BMI	-0.016	0.257	0.00	0.950
Socioeconomic class	0.612	1.486	0.16	0.681
Parity	-0.065	0.694	0.00	0.925
Gestational age	1.391	0.658	4.46	0.036

Neonatal gender	-0.221	1.570	0.01	0.888
Maternal fasting time	-1.314	0.256	26.40	<0.001
Mode of delivery	5.390	2.042	6.97	0.009
Birth weight	0.001	0.002	0.11	0.741

Table 6: Factors affecting new-born blood glucose levels at 2 hours of life using multiple linear regressions

Variable	Coefficient	Std Error	F-test	P-Value
Cord blood glucose	0.377	0.073	26.59	<0.001
Feeding time	0.164	0.021	60.02	<0.001
Maternal age	-0.124	0.167	0.55	0.459
Maternal BMI	-0.071	0.229	0.10	0.758
Parity	0.173	0.626	0.08	0.782
Gestational age	-1.248	0.600	4.32	0.039
Gender	-0.757	1.417	0.29	0.594
Maternal fasting time	-0.072	0.248	0.08	0.771
Mode of delivery	3.118	1.877	2.76	0.098
Birth weight	0.005	0.002	4.89	0.029

Comparison of blood glucose levels and sociodemographic variables between CS and Vaginal deliveries

When the sociodemographic variables of mother-infant pairs (outlined earlier in tables 5&6), were compared with blood glucose levels between the modes of delivery, multiple logistic regression analysis showed that in the group delivered by CS, only the maternal fasting time was associated with cord blood glucose levels ($p<0.001$) while the feeding time ($p<0.001$) and the birthweight ($p=0.04$) were significantly associated with the blood glucose at two hours of life. Similarly, in the neonates delivered by VD, only the maternal fasting time was significantly associated with cord blood glucose ($p=0.008$), while cord blood glucose and infant feeding time were significantly associated with blood glucose levels at two hours of life (both p values <0.001).

Discussion

The current study noted that the mean (SD) Cord blood glucose level was lower in the babies delivered by CS than those by vaginal delivery (VD). This is similar to an Indian-based study by Dias et al [20] among 100 mothers and their neonates, which documented high mean blood glucose levels in babies delivered vaginally, at all the time points tested, compared to babies delivered by CS. Likewise, other studies from Israel, involving 37 newborns [12] Khartoum, Sudan, of 110 mother-infant pairs [13] and Ethiopia, comprising 60 newborns[14], all documented the same pattern of BG.

Studies have documented that production of catecholamines is higher during normal vaginal delivery than during caesarean section, which can be explained by the increased stress in vaginal delivery. [21,22] This labour-induced foetal catecholamine surge is presumed to provide the neonate with an important mechanism of adaptation to the extra-uterine life. This catecholamine surge is thought to be responsible for the increased level of blood glucose in new-borns delivered vaginally compared to their counterparts delivered through elective CS. [12]

With regards to the neonatal blood glucose levels at 2 hours of life, in the current study, these were also significantly lower in the CS new-borns than the VD new-borns. However, the Israel [12] and Sudan [13] based studies (mentioned earlier) did not find a significant difference at two hours of life in both groups of new-borns.

In the current study, the change in blood glucose levels in the first two hours of life did not differ between the two groups of neonates. However, the change within the individual groups revealed a significant decrease in blood glucose levels over the first two hours of life. This means that the mode of delivery does not affect the type of change that occurs in the first two hours of life. Physiologically, with loss of the continuous transplacental supply of glucose, plasma glucose concentration in the healthy term new-born falls during the first two hours after delivery, reaching a nadir that usually is no lower than 40mg/dl, which seems to be the case in this study. [23] This, however, contrasts with some studies which reported a striking difference between the two groups over the first two hours of life, with a slight increase in the caesarean-delivered group and a decrease in the VD group. [12,13]

In the present study, the factors that were significantly associated with mean cord blood glucose levels were gestational age, maternal fasting time and mode of delivery. This finding is similar to the report of Hussein *et al* [13] with regards to CS delivery, but in contrast, the study documented that maternal glucose at the time of delivery, but not maternal fasting time, was significantly associated with mean cord glucose levels. [13] However, maternal glucose at the time of delivery was not tested in the current study, so it is difficult to compare. Furthermore, we noted that cord blood glucose, neonatal feeding time, gestational age and neonatal birthweight were significantly associated with blood glucose levels at two hours of life. This strong association between neonatal feeding time and blood glucose level was also documented by Pal *et al*. [24]. This emphasises the need to promote early breastfeeding. Hussein *et al* [13] also reported the significant influence of cord blood glucose on neonatal blood glucose levels at two hours of life; however, no significant association was found with neonatal feeding time, gestational age or neonatal birth weight.

In this study, only the maternal fasting time influenced the cord blood glucose in both the CS and vaginally delivered neonates. Some authors have suggested that maternal prolonged fasting time may cause hypotension that reduces perfusion pressure, thus causing foetal hypoglycaemia if a critical level is reached.[25,26] However, other studies showed no correlation between maternal fasting time and neonatal blood glucose levels. [27,28]

At delivery, the prevalence of hypoglycaemia ranged from 1.2% to 5.9% in the neonates delivered by CS with the different cut-offs used in literature. None of the neonates delivered via VD had hypoglycaemia at delivery. In a study by Frank-Briggs *et al* [29] in Port-Harcourt, South-South Nigeria, the commonest factor associated with hypoglycaemia was CS delivery. The incidence of neonatal hypoglycaemia in this study was lower than that documented in previous studies in Nigeria. [29-32]This may be because the babies in the current study were all term neonates without perinatal asphyxia, unlike those previous studies.

Two neonates had hyperglycaemia, both in the vaginal delivery group. The gestational age (all term infants) in the present study may account for this low incidence of hyperglycaemia, which has been shown to be lower in term neonates. [19]

Limitation: Measurement of peripartum maternal blood glucose would have given more information. Previous studies had established that cord blood glucose concentrations correlate with maternal blood glucose concentrations, assumed to correlate with fasting time, but the Sudanese study [13] reported that maternal blood glucose at delivery correlated with neonatal blood glucose but not with maternal fasting time. This difference may be due to the population of mothers studied. Therefore, future studies should explore maternal blood glucose levels in addition. Despite this limitation, the study added information on other factors that affect blood glucose levels in new-borns in relation to mode of delivery.

Conclusion

Cord blood glucose and neonatal blood glucose levels at two hours of life were significantly lower in neonates who were delivered by CS compared to those delivered vaginally. The change in blood glucose levels over the first two hours of life did not differ significantly between the two groups. The maternal fasting time was significantly associated with cord blood glucose in CS and VD neonates, while neonatal feeding time was significantly associated with blood glucose levels at 2 hours of life in neonates delivered by caesarean section. Blood glucose levels of newborns delivered via CS should be monitored within two hours of life. Newborns should be fed within two hours of life, particularly those delivered via CS.When maternal fasting time is prolonged, irrespective of the mode of delivery, blood glucose levels should be monitored and neonates fed within two hours of life.Vaginally delivered neonates with lower cord blood glucose levels should be fed within two hours of life.

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