

## **Point of Care Blood Glucose Profile of Neonates in a Lagos State Owned Tertiary Health Facility in Ikeja, Lagos, Nigeria**

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### **Abstract**

**Background:** Blood glucose abnormality is a well-recognized problem among sick neonates but its diagnosis is overlooked because of the similarity in its clinical presentation to that of the primary disease of the affected neonates. The objective of this study was to determine the blood glucose profile of sick neonates at the point of admission into the pediatric ward of Lagos State University Teaching Hospital, Ikeja, Lagos.

**Methods:** At point of admission venous sample was taken from peripheral vein of the neonates whose parents consented to be part of the study for blood glucose concentration estimation. Detailed history, general and physical examination was carried out.

**Results:** The prevalence of hypoglycaemia, normoglycaemia and hyperglycaemia were 32.7%, 60.8% and 6.5% respectively. The prevalence of hypoglycaemia and hyperglycaemia were significantly higher among neonates with gestational age at delivery <37 weeks compared to those 37–42 weeks ( $p = 0.041$ ). The prevalence of hypoglycaemia and hyperglycaemia were also significantly higher among neonates with weight on admission of >1.5–2.5Kg compared with their counterparts with weight 1.5Kg or >2.5Kg ( $p = <0.0001$ ) as well as neonates that were large for gestational age and those with preterm delivery as their clinical diagnosis on admission.

**Conclusion:** Dysglycaemia was common among hospitalized sick neonates with hypoglycaemia being the most common. Prevalent clinical conditions associated with dysglycaemia were preterm delivery and low gestational age at birth.

**Keywords:** Dysglycaemia, Hypoglycaemia, Normoglycaemia, Hyperglycaemia, Neonates

## Introduction

Glucose is the major energy source for the neonates.<sup>1</sup> The new-borns' brain depends upon glucose almost exclusively.<sup>2</sup> It has been estimated that up to 60% of total body glucose requirement is consumed by the brain.<sup>3</sup> Alternate fuels (e. g, ketones, lactate) can be used by new-borns' brain in condition of hypoglycaemia.<sup>4</sup> The usual rate of glucose utilization by the new born is 4 - 6 mg/kg/min to keep the plasma glucose levels within the normal range.<sup>5</sup> The glucose regulatory mechanism are reported to be sluggish at birth.<sup>5</sup> During pregnancy, glucose is passed from the mother to the fetus through the placenta and umbilical cord.<sup>1</sup> Some of this transferred glucose is stored in the placenta, and later in the fetal liver, heart, and muscles.<sup>1</sup> These stores are important for supplying the baby's brain with the necessary glucose during delivery, and for nutrition immediately after the baby is born.<sup>1</sup> Until exogenous supply of glucose is provided, either by enteral feedings or intravenous fluid administration, endogenous hepatic production of glucose remain the most significant source of glucose to meet the neonate's metabolic requirement.<sup>1</sup> The maintenance of normoglycaemia depends upon adequacy of glycogen stores, maturation of glycogenolytic and gluconeogenic pathways, and an integrated endocrine response.<sup>6</sup> The endocrine events believed to trigger the release of glucose and the mobilization of fat from peripheral stores are an increase in adrenaline secretion and a rapid fall in the insulin: glucagon ratio during the first few hours of life, attributed to both a fall in the plasma insulin concentration and a surge in glucose concentration.<sup>6</sup> These blood glucose control mechanism may be impaired for a variety of underlying reasons.<sup>6</sup> Neonates are generally born with plasma glucose of 70% of maternal glucose.<sup>7</sup> There is transient reduction after birth which resolves within the first 48 – 72 hours of life.<sup>8</sup> Maintenance of plasma glucose requires the interplay of several systems. As the primary regulator, insulin stimulates the uptake of glucose by cells.<sup>5, 8</sup> Its counter regulatory hormones, specifically cortisol, glucagon, epinephrine, and growth hormone, are prevalent in times of starvation to encourage glycogenolysis and lipolysis.<sup>5, 8</sup> The liver both synthesizes glucose from

amino acids, glycerol, and lactate, and converts glycogen to glucose during fasting. When compared with adults, infants have decreased glycogen stores and poorly matured glycogenolysis.<sup>9</sup> In the normal well - nourished neonate, by 2 to 3 hours following a meal, insulin is suppressed and counter regulatory hormones are high.<sup>10</sup> By 12 - 16 hours of fasting, the hepatic stores are depleted, and muscle and adipose begin to break down.<sup>10</sup> Muscle can use its own glycogen stores during fasting, and although the glucose created is not released systemically, amino acids are released to the liver.<sup>10</sup> Disorders of glucose metabolism can be classified as hyper and hypoglycaemia. In many neonates, hypoglycaemia is more common than hyperglycaemia.<sup>11</sup> Hypo- or hyperglycaemia may have a significant effect on the outcome in a sick neonate.<sup>2</sup> Hypoglycemia is a common condition in the neonatal population with significant prevalence among at risk group.<sup>8</sup> The prevalence is estimated to be 47% in Large-for-Gestational Age (LGA) infants, 52% in Small-for-Gestational Age (SGA) infants, 48% in infants of diabetic mothers, 54% in late preterm infants, and 34% in infants born before 33 weeks.<sup>8</sup> Hyperglycemia has been reported as a common condition among very preterm infants with an estimated incidence rate of between 45 – 80% among extremely low birth weight infants.<sup>12</sup>

The objective of this study was to describe the point of care blood glucose profile of neonates admitted into the Paediatrics wards of the hospital. As there is paucity of studies on neonatal dysglycaemia in our setting, it is hoped that the information derived from this study will help the clinicians to provide efficient and effective blood glucose management of neonates at point of hospital admission. The hypothesis of the study is that glucose abnormalities (dysglycaemia) is a frequent phenomenon among sick neonates in our setting.

## Methodology

This study was conducted in paediatric wards (children emergency room and the neonatal ward) of Department of paediatrics, Lagos State University Teaching Hospital (LASUTH), Ikeja, Lagos in South West Nigeria, LASUTH is an urban

tertiary health centre in Lagos State, Western Nigeria. It is a major referral centre serving the whole of Lagos State, which is a major point of entry into Nigeria from different parts of the world and the economic nerve centre of Nigeria. The study population consisted of all infants age 0 – 28 days admitted into the paediatric wards (children emergency room and the neonatal ward) of the Department of paediatrics, Lagos State University Teaching Hospital (LASUTH), Ikeja, Lagos during the study period. The inclusion criteria were all neonates admitted into the children emergency room and the neonatal ward of LASUTH whose parents consented to be part of the study. The exclusion criteria were admitted neonates whose parents did not grant consent to be part of the study. This study was a descriptive cross-sectional one conducted over a six month period on all consecutive neonates admitted into the paediatric wards (children emergency room and the neonatal ward) of LASUTH. Two millilitres of blood were drawn from a convenient peripheral vein and transferred into fluoride oxalate containing tubes. The vacuum tubes were labelled and were transported to the Chemical Pathology Laboratory of Lagos State University Teaching Hospital for analysis. The fresh blood samples collected was analysed for plasma glucose level using glucose oxidase reaction techniques in an auto-analyzer. The minimum sample size was calculated using the formula<sup>13</sup>  $(Z_{\alpha/2})^2(SD)^2/d^2$ , where  $Z_{\alpha/2}$  is critical value of the normal distribution at 95% type I error (1.960), SD is the standard deviation of RBS values from a previous study,<sup>14</sup> which is 37.8mg/Dl (2.1mmol/l) and d is the desired margin of error of 5%. Substituting these figures into the formula the calculated sample size was 220, an additional 10% (22 subjects) of the calculated sample size were added to accommodate possible attrition or unforeseen errors and also to increase the power of the study to bring the calculated minimum study sample size to 242, and therefore, two hundred and forty - five neonates were conveniently recruited, except those who did not give consent. All consecutive neonates admitted into paediatric wards (children emergency room and the neonatal ward) of Department of paediatrics, LASUTH who satisfied the study inclusion criteria were conveniently enrolled. Data collection was by a

semi-structured questionnaire developed by the researchers. Detailed history, general and physical examination was carried out. A single observer did a physical examination of all the study subjects. The collected data was entered in Microsoft Excel and Statistical analyses were conducted using the Statistical Products and Service Solution (SPSS) version 17.0. Descriptive data were presented as mean  $\pm$  standard deviation (SD) or, in the case of a skewed distribution, as median and interquartile range (IQR).

Means of normally distributed data were compared using the Student's t-test. Categorical variables were compared using Pearson's chi-square test as indicated. Correlations between variables with normal and non-normal distribution were performed by Pearson's and Spearman's correlation, respectively. P values < 0.05 were considered significant.

Children were categorized into three groups according their blood glucose levels based on criteria previously reported in the literature.<sup>15</sup>

- Hypoglycaemia: <45 mg/ dL
- Normoglycaemia: 45 – 145 mg/ dL
- Hyperglycaemia: >145 mg/ d/L

Abnormal blood glucose, or dysglycemia, was defined as any of the two (2) categories which differ from normoglycemia.<sup>16</sup>

The study was carried out in compliance with the basic principles of research ethics (confidentiality, consent, justice, rights to decline enrolment and non-maleficence). The study was carried out in accordance with the ethical standards of the Declaration of Helsinki. Informed consent was obtained from each parent/caregiver prior to the selection of the newborn for the study after a detailed explanation of what the study entails. Consecutive neonates who required hospital admission were conveniently enrolled.

## **Results**

### **Characteristics enrolled neonates on admission**

The median age (Inter Quartile Range) of the neonates at recruitment was 3.0 (1.0 – 24.0) days. One hundred and sixty (65.3%) of study neonates were males and eighty-five (34.7%) females with a male to female ratio of 1.9:1. Table 1.

The most frequent age group at enrolment was >1 –

7 days while >7 days was the least. Four-fifth of all the study enrollees was delivered at the gestational age of 37 - 42 weeks. The most common weight on admission among all study neonates was >2.5kg. The admission weight of subjects ranged from 1.0 to 6.0kg with a mean ( $\pm$ SD) of 2.8 ( $\pm$ 0.79) Kg. The age at enrolment, gestational age at delivery and admission weight were not significantly different irrespective of gender ( $P>0.05$ ).

#### **Plasma glucose level among study subjects**

Table 2 shows that the median plasma glucose levels increase with increasing age group, but this finding was not statistically significant ( $p>0.05$ ). The median plasma glucose values for subjects delivered after 42 weeks of gestation was about triple the median plasma glucose values for subjects delivered before 42 weeks of gestation. However, the observation was not statistically significant ( $p > 0.05$ ). There was no consistent pattern with the weight of neonates on admission, the highest and lowest median values of plasma glucose levels were observed among neonates whose admission weight were 1.5kg and >1.5 – 2.5kg respectively. These findings were not statistically significant ( $p>0.05$ ).

#### **Association between blood glucose levels of neonates and variables on admission**

The prevalence of hypoglycaemia, normoglycaemia and hyperglycaemia were 80 (32.7 %), 149 (60.8%) and 16 (6.5%) respectively. Dysglycaemia was seen more commonly among neonates aged seven days and below at enrolment. This association between glucose abnormalities and age at enrolment was not statistically significant ( $p = 0.225$ ). The prevalence of dysglycaemia was higher among neonates with gestational age at delivery <37 weeks compared to those 37 weeks. However, this observation was not statistically significant ( $p = 0.167$  with Yates correction). The prevalence of dysglycaemia was significantly higher among subjects with weight on admission of 1.5Kg compared with those >1.5Kg ( $p = 0.004$ ). The prevalence of dysglycaemia was 96 (39.2%). Dysglycaemia was seen more commonly among neonates aged seven days and

below at enrolment. This association between dysglycaemia and age at enrolment was not statistically significant ( $p = 0.225$ ). Dysglycaemia occurred more commonly among subjects whose gestational age at delivery was <37 weeks. This relationship was not statistically significant ( $p = 0.09$ ). The prevalence of dysglycaemia significantly decreased with increasing weight on admission ( $p=0.004$ ). Table 3.

#### **Prevalence of glucose abnormalities among study neonates according to their clinical diagnosis on admission**

As shown in Table 4, most of the study neonates had more than one diagnosis on admission. Hypoglycaemia was most common among neonates who were large for gestational age and those with preterm delivery as their clinical diagnosis on admission while hyperglycaemia was predominantly seen among neonates who were preterm delivery at admission. The classification tagged others comprises of neonatal tetanus, congenital anomaly, transient tachypnoea of newborn, HIV exposed infant, abandoned baby, pneumonia, and haemorrhagic disease of newborn e.t.c.

#### **Correlation between glucose level and other variables**

There was a weak positive correlation between glucose level and other variables which was not statistically significant ( $p>0.05$ ). Table 5.

**Table 1: Characteristics of enrolled neonates on admission**

Characteristics	Male	Female	ALL	p-value
<b>Age at recruitment (days)</b>				
=1	42 (66.7)	21 (33.3)	63	0.811
>1 – 7	86 (66.2)	44 (33.8)	130	
>7	32 (61.5)	20 (38.5)	52	
<b>Gestational age (weeks)</b>				
<37	29 (63.0)	17 (37.0)	46	0.359
=37 - 42	131 (66.2)	67 (33.8)	198	
>42	0 (0.0)	1 (100.0)	1	
<b>Weight on admission (Kg)</b>				
=1.5	11 (68.8)	5 (31.2)	16	0.603
>1.5 – 2.5	43 (60.6)	28 (39.4)	71	
>2.5	106 (67.1)	52 (32.9)	158	

NB: Values in parenthesis are in % of row total

**Table 2: Distribution of plasma sugar values among neonates studied**

Characteristics	Median (IQR) mg/dL	p – value
<b>Age at recruitment (days)</b>		
=1	57.0 (3.0 – 493.0)	0.095
>1 – 7	58.0 (4.0 – 233.0)	
>7	65.5 (15.0 – 151.0)	
<b>Gestational age (weeks)</b>		
<37	59.0 (5.0 – 233.0)	0.343
=37 - 42	59.0 (3.0 – 493.0)	
>42	129.0 (129.0 – 129.0)	
<b>Weight on admission (Kg)</b>		
=1.5	83.5 (10.0 – 233.0)	0.071
>1.5 – 2.5	52.0 (4.0 – 175.0)	
>2.5	60.0 (3.0 – 493.0)	

IQR = Inter Quartile Range

**Table 3 : Association between blood glucose levels of neonates and variables on admission**

Characteristics		Dysglycaemia	Normoglycaemia	p-value
<i>Age at recruitment (days)</i>	=1	26 (41.3)	37 (58.7)	0.225
	>1 – 7	55 (42.3)	75 (57.7)	
	>7	15 (28.9)	37 (71.1)	
<i>Gestational age (weeks)</i>	<37	24 (52.2)	22 (47.8)	0.167
	=37 - 42	71 (35.9)	127 (64.1)	
	>42	0 (0.0)	1 (100.0)	
<i>Weight on admission (Kg)</i>	=1.5	11 (68.7)	5 (31.3)	0.004
	>1.5 – 2.5	34 (47.9)	37 (52.1)	
	>2.5	51 (32.3)	107 (67.7)	

NB: Values in parenthesis are in % of row total

**Table 4: Prevalence of glucose abnormalities among study neonates according to their clinical diagnosis on admission**

Diagnosis	Normoglycaemia	Dysglycaemia
Sepsis	44 (62.9)	26 (37.1)
Asphyxia	43 (65.2)	23 (34.9)
Neonatal Jaundice	21 (72.4)	8 (27.6)
Preterm	10 (33.3)	20 (66.7)
LGA	2 (33.3)	4 (66.7)
Others	29 (65.9)	13 (29.6)

NB: Values in parenthesis are in % of row total

**Table 5: Correlation between glucose level and other variables**

Characteristics	Correlation Coefficient (r)	p-value
Age at recruitment (days)	0.081	0.204 <sup>S</sup>
Gestational age (weeks)	0.117	0.069 <sup>P</sup>
Weight on admission (Kg)	0.003	0.958 <sup>P</sup>
Pearson's correlation = <sup>P</sup>		Spearman's correlation = <sup>S</sup>

**Discussion**

The present study revealed that the median plasma glucose level increases with increasing age at recruitment. It has been documented that there is variation of blood glucose level postnatally due to termination maternal glucose supply, insufficient neonatal liver glycogen storage, and increased glucose consumption due to cold and neonatal activity after birth.<sup>17</sup> Thereafter, the blood glucose gradually increases by exogenous supply of

glucose either by enteral feedings or intravenous fluid administration, and maturation of gluconeogenesis.<sup>1,17</sup>

This study showed that the median plasma glucose values increase with gestational age with the highest being for subjects delivered after 42 weeks of gestation. Previous authors have documented positive correlation between plasma glucose level in neonates and gestational age with the preterm group having lower blood glucose level compared

to the term group.<sup>18</sup> In contrast to the finding in our study some authors have demonstrated that blood glucose levels increased with the gestational age up to term and then decreased in post-term neonates.<sup>19</sup> The comparison between this study and others is hampered by the blood sampling time, sample size and some characteristics of the study neonates such as delivery complications and feeding practices.<sup>19</sup> It was observed that children with admission weight of 1.5Kg or less had the highest median plasma blood glucose level. This finding suggested that the studied sick neonates were less likely to adjust to the cessation of intrauterine glucose supply compared to the older studied neonates. This may be due to the selection of more sick neonates with admission weight 1.5Kg who had complicated deliveries. The comparison of blood glucose concentrations across the admission weight groups maybe hampered by the heterogeneity of sick neonates studied.

A third of the studied neonates were observed to have hypoglycaemia. This reported prevalence was comparable to prevalence reported in a group of sick Nigerian neonates in Ilesha, Oyo State.<sup>20</sup> The reported prevalence in the present study was higher than findings of earlier workers in Nigeria<sup>21-23</sup> and elsewhere<sup>24</sup> which were between 11.0% - 28.3%. Our study showed that hypoglycaemia is most prevalent among subjects with <37 weeks of gestation at delivery. This finding is consistent with other studies.<sup>19-21</sup> Preterm babies have low glycogen stores that should have occurred in the third trimester and as a result are more predisposed to hypoglycaemia.<sup>21,25</sup> The other means of maintaining blood glucose levels is by gluconeogenesis that is impaired in preterm infants.<sup>26</sup>

From the current study about one in twenty neonates had hyperglycaemia. The reported prevalence from current study was comparable to that reported among ill neonates at Wesley Guild Hospital Ilesa.<sup>14</sup> Our study revealed that hyperglycaemia was more prevalent among neonates with admission weight 1.5Kg as well as in those with length of gestation <37 weeks. Glucose uptake into tissues and organs are regulated by a protein called Glucose Transporters (GLUT) of which there are several types.<sup>27,28</sup> In fetal life, GLUT 1 which is found in most of the cells of the body is the most predominant type but its level

declines after birth while other types such as GLUT 2 and GLUT 4 increase. GLUT 4 levels increase with the growth of tissues where it is expressed such as skeletal muscle in response to insulin and this contributes to the insulin insensitivity experienced in preterm and low birth weight infants which is responsible for hyperglycaemia seen in them.<sup>27</sup> Abnormal blood glucose or dysglycaemia, was defined as presence of hypoglycaemia or hyperglycaemia.<sup>16</sup> In this study, plasma dysglycaemia was observed in about two-fifth of the study neonates. This finding shows that abnormal glucose concentration is a common occurrence among sick neonates in our setting. The clinical importance of this is that sick neonates require close monitoring of their blood glucose status. It was observed that dysglycaemia was most prevalent among sick neonates with weight on admission of 1.5Kg. This reported prevalence was higher than prevalence reported in a group of extremely low birth weight Italian neonates in Palermo.<sup>29</sup> The observed difference is possibly an effect of sample size. The small sample size of sixteen neonates with weight on admission of 1.5Kg in the study under reference may have produced exaggerated incidence rates. However, the disparity in hyperglycaemia cut off defining criteria may also account for this observed difference. While the cut off in the current study was >145mg/dL, it was >240 mg/dL in a single determination or >180 mg/dL in two determinations at 2-hour intervals in the Italian study.

In our study, majority of the admitted neonates with dysglycaemia had clinical diagnosis of either preterm or LGA baby. All the neonates with LGA clinical diagnosis had hypoglycaemia with none having hyperglycaemia. Hence, there should be cautious monitoring of blood sugar of these neonates. Prematurity was an equally common diagnosis on admission, associated with dysglycaemia. Therefore, strict monitoring of IV fluid and blood sugar should be emphasized during admission of preterm neonates. As there is a paucity of studies on neonatal dysglycaemia to compare these results, we believe that this association is mostly contributed by the transport status of the sick neonates to health facilities. The most common mode for transporting referred patients was public

bus followed by private vehicle in our country.<sup>30</sup> However, this high prevalence of dysglycaemia in our study is worrying as it is deleterious in case of premature and LGA neonates

### Conclusion

Dysglycaemia is a common problem among sick neonates in our setting. Blood glucose determination is important in all acutely ill neonates and therefore, the practice of empirical administration of intravenous bolus of glucose without plasma blood glucose estimation in all neonates should be discouraged especially among sick preterm and LGA sick neonates.

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