## Screening of blood glucose levels in healthy neonates

Kayıran S M, Gürakan B

#### ABSTRACT

<u>Introduction</u>: This study aimed to screen the blood glucose levels in healthy term and nearterm neonates, and to assess the influence of mode of delivery, birth weight and gestational age on blood glucose levels.

<u>Methods</u>: The blood glucose concentrations of 1,540 healthy term and near-term neonates in the first hour of life were retrospectively evaluated from the clinical charts. Glucose levels were estimated from heel prick capillary samples. The glucose concentration was correlated with the mode of delivery, birth weight and gestational age.

<u>Results</u>: Vaginally delivered neonates had higher glucose levels. The glucose concentrations were not significantly different between infants in the different birth weight groups. However, glucose concentration was significantly correlated with gestational age, and the levels were observed to rise with increasing gestational age.

<u>Conclusion</u>: Screening asymptomatic, healthy term and near-term neonates for hypoglycaemia in the first hour following birth is unnecessary. Glucose strips and glucose meters are useful only as screening devices for neonatal hypoglycaemia, and a screening cut-off value must be established.

# Keywords: birth weight, gestational age, glucose, neonate, screening

Singapore Med J 2010;51(11):853-855

## INTRODUCTION

Glucose is very important for the body, especially for brain metabolism. As hypoglycaemia is one of the common metabolic problems in neonatal medicine, the assessment of blood glucose has consequently become a significant part of basic neonatal care in many hospitals.<sup>(1)</sup> It is classically known that in most healthy newborns, the frequently observed low blood glucose concentrations are not related to any significant problem, and only reflect the normal processes of metabolic adaptation to extrauterine life.<sup>(1,2)</sup> Blood glucose levels fall immediately after birth but rise after a few hours, either spontaneously or in response to feeding, in almost all healthy term infants.<sup>(2)</sup> On the other hand, when the low blood glucose levels are prolonged or recurrent, they may result in acute systemic effects and neurologic sequelae.<sup>(3)</sup> In this retrospective study, we evaluated the charts and files of 1,540 healthy term and near-term neonates, as well as determined their blood glucose levels in the first hour after birth and investigated the relationship of glucose levels with the mode of delivery, birth weight and gestational age.

## METHODS

The study population included 1,540 healthy term and near-term neonates delivered at a private hospital from January 2005 to May 2007. The clinical charts of the neonates were retrospectively evaluated. All of the neonates were born at term or near-term gestation, were healthy on physical examination, entirely asymptomatic and were being nursed by their mothers. Formula was given when the mothers were unable to breastfeed. We defined 'term' as delivery at 37–42 weeks' gestational age and 'near-term' as 36 weeks' gestational age, based on maternal dates.

Neonates with respiratory distress, perinatal asphyxia, any disease or malformation, meconium aspiration syndrome or polycythaemia, those who were either small or large for their gestational age, and those born to mothers with a history of hypertension, anaemia or diabetes mellitus were excluded from the study. Blood was collected by heel prick (after the heel had been warmed), and the blood glucose was evaluated within one hour after birth and before the infant was breastfed. The capillary blood glucose was tested with a reagent stripbased bedside test utilising modern biosensor technology (Accu-Check Active, Roche Diagnostics, Mannheim, Germany).

All statistical analyses were performed using the Statistical Package for the Social Sciences for Windows 11.0 (SPSS Inc, Chicago, IL, USA). A p-value  $\leq 0.05$  was considered statistically significant. Data on blood glucose levels were expressed as mean

Department of Paediatrics, American Hospital, Güzelbahce Sokak, No. 20 Nisantası Sisli, İstanbul, Turkey

Kayıran SM, MD Paediatrician

Gürakan B, MD Professor

Correspondence to: Dr Sinan Mahir Kayıran Tel: (90) 212 3112000 Fax: (90) 212 3112390 Email: sinanmahir@ gmail.com

Birth weight (g)	No. of neonates	Mean blood glucose level ± SD (mg/dl)
≥ 2,500-< 3,000	322	49.9 ± 12.5
≥ 3,000-< 3,500	754	49.8 ± 11.4
≥ 3,500-< 4,000	464	50.8 ± 12.3

Table I. Comparison of blood glucose levels according to birth weight.

p = 0.493

SD: standard deviation

Table II. Comparison of blood glucose levels according to gestational age.

Gestational age (wk)	No. of neonates	Mean blood glucose level ± SD (mg/dl)
36–37	220	46.6 ± 9.7
38–39	1,270	50.1 ± 11.8
≥ 40	50	58.6 ± 14.1

p < 0.001

SD: standard deviation

 $\pm$  standard deviation (SD). Kolmogorov-Smirnov test was employed for analysing the distribution of data, Levene F test was used for examining the homogeneity of variances, and the one-way ANOVA and independent samples *t*-test were applied for further analysis. Tukey's b test was used for the results of parametric tests that exhibited significant differences as well as to determine the groups showing significant differences.

### RESULTS

Blood glucose was determined in each of the 1,540 neonates in the first hour of life. A total of 225 infants were born vaginally, while 1,315 were delivered by caesarean section, with a male to female ratio of 659:881. This high rate of caesarean section in our hospital may be due to the attitudes of pregnant women and obstetricians regarding caesarean section. The mean blood glucose level for the whole study group was  $50.2 \pm 12.0$  mg/dl and the birth weight was  $3,319 \pm$ 206 g. A subgroup of 87 neonates, who were all healthy and had appropriate gestational ages, were found to have low glucose levels (< 36 mg/dl). On analysis, no significant differences based on the different birth weight and gestational age categories were observed for this subgroup of neonates. Vaginally delivered infants were found to have a significantly higher mean blood glucose concentration (59.1 ± 14.3 mg/dl) compared with those delivered via caesarean section (48.5  $\pm$  10.6 mg/dl) (p < 0.001). The infants were categorised into three groups based on their birth weights (Table I). Glucose concentrations were not significantly different between infants in the different birth weight groups ( $p \ge 1$ 0.05). Based on gestational age, the infants were divided into three groups (Table II). A statistically significant difference was found between the mean blood glucose levels of babies who were born at 36-37 weeks and 38-39 weeks gestational age, those born at 36-37 weeks and  $\geq 40$  weeks gestational age, and those born at 38–39 weeks and  $\geq 40$  weeks gestational age (p < 0.001). The blood sugar level was observed to rise with increasing gestational age.

DISCUSSION

At birth, the umbilical venous plasma glucose is at 60%-80% of the maternal venous plasma glucose concentration. There is a rapid decline in plasma glucose concentration in the first 30-60 minutes after birth, followed by a rise which reaches a steady level by 2-4 hours.<sup>(3,4)</sup> The accurate measurement of blood glucose levels is essential in the diagnosis of hypoglycaemia. Glucose reagent strips, considered a screen or an estimate, are often used in newborn nurseries.<sup>(3)</sup> In these neonates, glucose measurements are usually monitored at the bedside using glucose meters. In addition to requiring only a small amount of blood compared to laboratory glucose testing, they provide immediate quantitative results, allowing for more rapid intervention when required. Screening of all the neonates for blood glucose values after birth was conducted until the end of our study. Cornblath et al reported that measurements using glucose meters are not as accurate as those taken using laboratory methods, and confirmation of low levels are necessary for the diagnosis of neonatal hypoglycaemia.<sup>(5)</sup> Therefore, in our study, these strips were only used for screening purposes. Any abnormal values after breastfeeding were confirmed by accurate laboratory measurement.

Much controversy and confusion have surrounded the definition of hypoglycaemia.<sup>(3)</sup> For example, Koh et al demonstrated that the definition varied widely not only among standard paediatric textbooks but also among neonatologists, with values given ranging from below 18 mg/dl to below 72 mg/dl.<sup>(6)</sup> In the current study, the lowest value was 20 mg/dl, while the highest was 97 mg/dl. It is suggested that in an asymptomatic baby and in babies at risk for hypoglycaemia (irrespective of gestational age), plasma glucose values < 36 mg/dl should warrant close monitoring and intervention if the value remains below that level.<sup>(7)</sup> Therefore, the threshold value of 36 mg/dl was used in our study.

87 of the blood samples were below the threshold value, and as such, these babies were given their mother's milk as soon as she was able to breastfeed. The bedside tests of the 87 babies were confirmed by laboratory

plasma glucose test, with 56.7% of the laboratory values correlating with low initial glucose levels. After being fed breast milk or formula (some of the mothers were not able to breastfeed immediately after a caesarean section), new heel prick samples were reassessed after 30 minutes, and all the samples were found to be above the threshold value. Thus, no other interventions (e.g. intravenous dextrose) were required. Neonates delivered via caesarean section had lower plasma glucose levels (p < 0.001) because a caesarean section usually involves less stress for the baby and the possible impact of perinatal anaesthesia, compared to a vaginal delivery. After a caesarean section, mothers are often not ready to breastfeed for a relatively longer period of time compared to those after vaginal delivery. Therefore, perinatal anaesthesia for caesarean section may delay breastfeeding and result in lower plasma glucose levels compared to vaginal delivery. However, our findings were in contrast with those of some studies that included data from caesarean sections and vaginal deliveries; they did not show differences in the plasma glucose levels between these two methods of delivery.(8-10) In our hospital, all mothers, regardless of the mode of delivery, are placed on an intravenous dextrose drip.

In the present study, no significant difference in the blood glucose levels was found between the birth weight groups (Table I). Pal et al reported a birth weight < 2.5 kg as an independent risk factor for moderate hypoglycaemia.<sup>(11)</sup> In our study, all the neonates were  $\geq$ 2.5 kg. Moreover, the evaluation of blood sugar levels in terms of gestational age revealed significant differences in the blood glucose levels (Table II). In the first hour after birth, there was a significantly greater decrease in blood glucose concentration for near-term infants, suggesting that they were less able to adapt to the cessation of intrauterine nutrition than full-term neonates. As the gestational age increases, the glucose concentration also rises. Similarly, Hawdon et al reported that the preterm group had a lower mean blood glucose concentration in the first few postnatal hours than the term group, and even healthy term newborns showed significantly lower values than healthy older children and adults.(8)

It is interesting to note that at birth, few metabolic differences seem to exist between full-term and nearterm neonates. This may be due to the selection of infants who all had uncomplicated deliveries and were of an appropriate birth weight for gestational age. The comparison of blood glucose concentrations between the present study and earlier studies was hampered by the heterogeneity of infants studied previously, the blood sampling time, assay methods and feeding practices.

We do not recommend that all asymptomatic term and near-term infants with blood glucose concentrations < 36 mg/dl be treated with intravenous glucose, but instead suggest encouraging mothers to continue breastfeeding. The normal pattern of early, frequent and exclusive breastfeeding meets the needs of healthy term and near-term neonates. Transient hypoglycaemia in the immediate newborn period is common, and routine blood glucose monitoring of term and near-term neonates with no additional risk factors is not necessary. Currently, we do not screen the blood glucose level of healthy term and near-term neonates in our newborn nursery. We also emphasise that glucose strips and glucose meters are useful only as screening devices for neonatal hypoglycaemia and that a screening cut-off value for the first hour following birth must be established.

#### REFERENCES

- Cornblath M. Neonatal hypoglycemia 30 years later: does it injure the brain? Historical summary and present challenges. Acta Paediatr Jpn 1997; 39 Suppl 1:S7-11.
- Hawdon J. Disorders of blood glucose homeostasis in the neonate. In: Rennie JM ed, Roberton's Textbook of Neonatology. 4th ed. Edinburgh: Churchill Livingstone, 2005: 851-8.
- Cornblath M, Hawdon JM, Williams AF, et al. Controversies regarding definition of neonatal hypoglycemia: suggested operational thresholds. Pediatrics 2000; 105:1141-5.
- Persson B, Gentz J, Kellum M. Metabolic observations in infants of strictly controlled diabetic mothers. Plasma levels of glucose, FFA, glycerol and B-beta-hydroxybutyrate during the first two hours after birth. Acta Paediatr Scand 1973; 62:465-73.
- Cornblath M, Schwartz R, Aynsley-Green A, Llyod JK. Hypoglycemia in infancy: the need for rational definition. A Ciba Foundation discussion meeting. Pediatrics 1990; 85:834-7.
- Koh TH, Eyre JA, Aynsley-Green A. Neonatal hypoglycemia the controversy regarding definition. Arch Dis Child 1988; 63:1386-8.
- Kalhan S, Peter-Wohl S. Hypoglycemia: What is it for the neonate? Am J Perinatol 2000; 17:11-8.
- Hawdon JM, Ward Platt MP, Aynsley-Green A. Patterns of metabolic adaptation for preterm and term infants in the first neonatal week. Arch Dis Child 1992; 67:357-65.
- Yamauchi Y. Hypoglycemia in healthy, full term, breast-fed neonates during the early days of life: preliminary observation. Acta Paediatr Jpn 1997; 39 Suppl 1:S44-7.
- Diwakar KK, Sasidha MV. Plasma glucose levels in term infants who are appropriate size for gestation and exclusively breast fed. Arch Dis Child Fetal Neonatal Ed 2002; 87:F46-8.
- Pal DK, Manandhar DS, Rajbhandari S, et al. Neonatal hypoglycaemia in Nepal 1. Prevalence and risk factors. Arch Dis Child Fetal Neonatal Ed 2000; 82:F46-51.