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Original Article

Blood glucose levels in healthy, term, appropriate for gestational age, exclusively breastfed infants

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ABSTRACT

Objective This study aimed to determine blood glucose levels of healthy, term, appropriate for gestational age (AGA), exclusively breastfed infants at the age of 6, 12, 24, 48, and 72 hours of life, and to investigate the incidence of hypoglycemia in those infants.

Methods All healthy, term, AGA infants born in Cipto Mangunkusumo General Hospital, Jakarta, who were exclusively breastfed during the recruitment period of December 2003 until February 2004, were included in this study. These infants were subjected to blood glucose level determination at the age of 6, 12, 24, 48, or 72 hours of life, and the clinical signs of hypoglycemia were monitored.

Results Two hundred and fifteen blood samples taken from 137 newborns were studied. There was no incidence of hypoglycemia observed, whether symptomatic or asymptomatic. The range of blood glucose levels was between 41 mg/dl and 115 mg/dl. The means and the standard deviations (SD) of the blood glucose levels of the 6-, 12-, 24-, 48- and 72-hour old infants were 59.7 (11.98) mg/dl, 64.1 (13.51) mg/dl, 65.9 (14.42) mg/dl, 67.0 (14.95) mg/dl, and 78.6 (16.51) mg/dl, respectively.

Conclusions The current concern for hypoglycemia in the population of healthy, term, AGA, exclusively breastfed infants during the first few days of life was not proven to exist. Therefore, there is no reason to resort to prelacteal feeding in such infants **[Paediatr Indones 2005;45:7-13].**

Keywords: *blood glucose level, hypoglycemia, healthy, term, appropriate for gestational age, exclusively breastfed*

The growing concern for hypoglycemia in the population of healthy, term, appropriate for gestational age (AGA), exclusively breastfed infants during the first few days of life, has been the main reason to justify giving prelacteal feeding to these infants in our hospital, particularly to those who were born to primiparous mothers or delivered by caesarean section. This practice is against the sixth step of the Ten Steps to Successful Breastfeeding of the World Health Organization and the recommended breastfeeding practices from the American Academy of Pediatrics, which recommend giving newborn infants no food or drink other than breast milk, unless medically indicated.[1-2] Besides, prelacteal feeding is potentially harmful as it may introduce infection, sensitize the gut to foreign proteins, delay the onset of lactation, or shorten the duration of exclusive breastfeeding.[3-6]

The aims of this study were to determine blood glucose levels of healthy, term, AGA, exclusively breastfed infants at the age of 6, 12, 24, 48, and 72 hours of life, and to investigate the incidence of hypoglycemia in these infants.

Methods

This cross sectional study was performed in the transitional and postnatal wards of Cipto Mangunkusumo General Hospital, Jakarta, from December 2003 to February 2004. We included all healthy, term, AGA infants born in this hospital who

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were exclusively breastfed. We excluded infants who were at risk for hypoglycemia, such as those who suffered from respiratory distress, perinatal asphyxia (5-minute Apgar score of ≤7), hypothermia (temperature of <36°C), meconium aspiration syndrome, sepsis or suspected sepsis, hyperviscosity (hematocrit >70%), erythroblastosis foetalis, and those with signs of intrauterine growth retardation, congenital anomalies, weight of ≤2,500 grams, and discordant twins weighing 10% less than the larger twin. Infants born to mothers who suffered from hypertension, pre-eclampsia, diabetes mellitus, or mothers who received intrapartum intravenous glucose infusion or drug treatment such as terbutaline, ritodrine, propranolol, and oral hypoglycemic agents were also excluded.

Blood glucose levels were determined at the age of 6, 12, 24, 48, or 72 hours using the Medisense Optium glucose meter (Abbott laboratories) with the G3 point of care glucose strips and the results presented in mg/dl. Blood samples were collected by heel prick and each subject was examined once or more, to represent the blood samples of different age groups.

A blood glucose level of less than 40 mg/dl was considered as hypoglycemia. Changes in consciousness level (irritability, lethargy, stupor, coma), apnea, cyanotic spells, irregular breathing patterns, poor sucking, hypothermia, hypotonia, tremor, jitteriness, exaggerated Moro reflex, high-pitched cry, seizure, and vasomotor instability, were the clinical signs associated with hypoglycemia monitored in each subject. Infants were considered to have symptomatic hypoglycemia if the low blood glucose concentrations were associated with those clinical signs and asymptomatic hypoglycemia if the low blood glucose concentrations were not accompanied by any of those clinical signs.

A minimum sample size of 18 for each age group was calculated based on a standard deviation of 11 mg/dl,[7-8] a 95% confidence interval for the mean, and a desired precision of the interval of 5 mg/dl. To compare the means of blood glucose levels among the different age groups, a minimum sample size of 36 for each age group was needed.[9]

Written informed consent was obtained from subjectys' parents. Ethical approval for this study was granted by The Committee for Medical Research Ethics of the Medical School, University of Indonesia.

Unpaired Student's t test, analysis of variance, and chi-square tests were applied where necessary using SPSS version 11.5 for Windows.

Results

Two hundred and fifteen blood samples were taken from the 137 newborns examined. Thirty-nine, 42, 47, 48, and 39 samples were examined at the age of 6, 12, 24, 48 and 72 hours, respectively. The demographic data of the subjects (**Table 1**) shows no difference in sex, birth weight, gestational age, maternal age, and parity, except for the mode of delivery among the different age groups.

There was no incidence of hypoglycemia, whether symptomatic or asymptomatic, found in this

TABLE 1. DEMOGRAPHIC DATA OF SUBJECTS IN EACH AGE GROUP

Demographic data	Age group				
	6 hours n=39	12 hours n=42	24 hours n=47	48 hours n=48	72 hours n=39
Sex (n)					
Male	18	23	26	25	20
Female	21	19	21	23	19
Weight (grams)	3071.5	3181.9	3168.1 (346.06)	3047.1 (307.34)	3075.1 (305.85)
Mean (SD)	(311.27)	(333.55)			
Maternal age (years)			28.7 (6.13)	30.3 (5.31)	30.7 (5.56)
Mean (SD)	28.6 (5.69)	29.5 (5.50)			
Gestational age (weeks)			39.5 (1.30)	39.4 (1.32)	39.2 (1.34)
Mean (SD)	39.5 (1.21)	39.5 (1.29)			
Mother's parity n (%)			22 (46.8)	16 (33.3)	13 (33.3)
Primiparous	17 (43.6)	23 (54.8)	25 (53.2)	32 (66.7)	26 (66.7)
Multiparous	22 (56.4)	19 (45.2)			
Delivery method n (%)			31 (66.0)	21 (43.8)	11 (71.8)
Vaginal	32 (82.1)	26 (61.9)	16 (34.0)	27 (56.2)	28 (28.2)
Caesarean Section	7 (17.9)	16 (38.1)			

TABLE 2. BLOOD GLUCOSE LEVELS (MG/DL) OF SUBJECTS AT THE AGE OF 6,12, 24, 48, AND 72 HOURS

Age (hours)	Number of subjects	Range	Mean (SD) blood glucose	SEM	p value
6	39	42 – 88	59.7 (11.98)	1.92	
12	42	41 - 97	64.1 (13.51)	2.08	
24	47	42 - 114	65.9 (14.42)	2.10	
48	48	41 - 108	67.0 (14.95)	2.16	
72	39	53 - 115	78.6 (16.51)	2.64	0.0001*

* One way ANOVA

study. The mean (SD) and the range of blood glucose levels of each age group were presented in **Table 2**. There was a difference in the mean blood glucose levels among the age groups according to the one-way ANOVA test. The unpaired Student's t-test later showed that the mean blood glucose level of the 72-hour-old infants was significantly higher compared to that of the other age groups. **Figure 1** shows the mean with 2 standard errors of the mean (mean ± 2SEM) and the range of blood glucose levels in each age group.

Within each age group, no significant difference in the mean blood glucose levels was found between infants born to primiparous mothers and those born to multiparous mothers. The range and the mean ± 2SEM blood glucose levels according to parity in different age groups are presented in **Figure 2.**

There was no significant difference within each age group in the mean blood glucose levels according to the mode of delivery, except in the 6-hour old infants. In this age group, infants born by caesarean section had a higher mean blood glucose level than those delivered vaginally. **Figure 3** shows the range and the mean ± 2 SEM blood glucose levels according to delivery method within each age group.

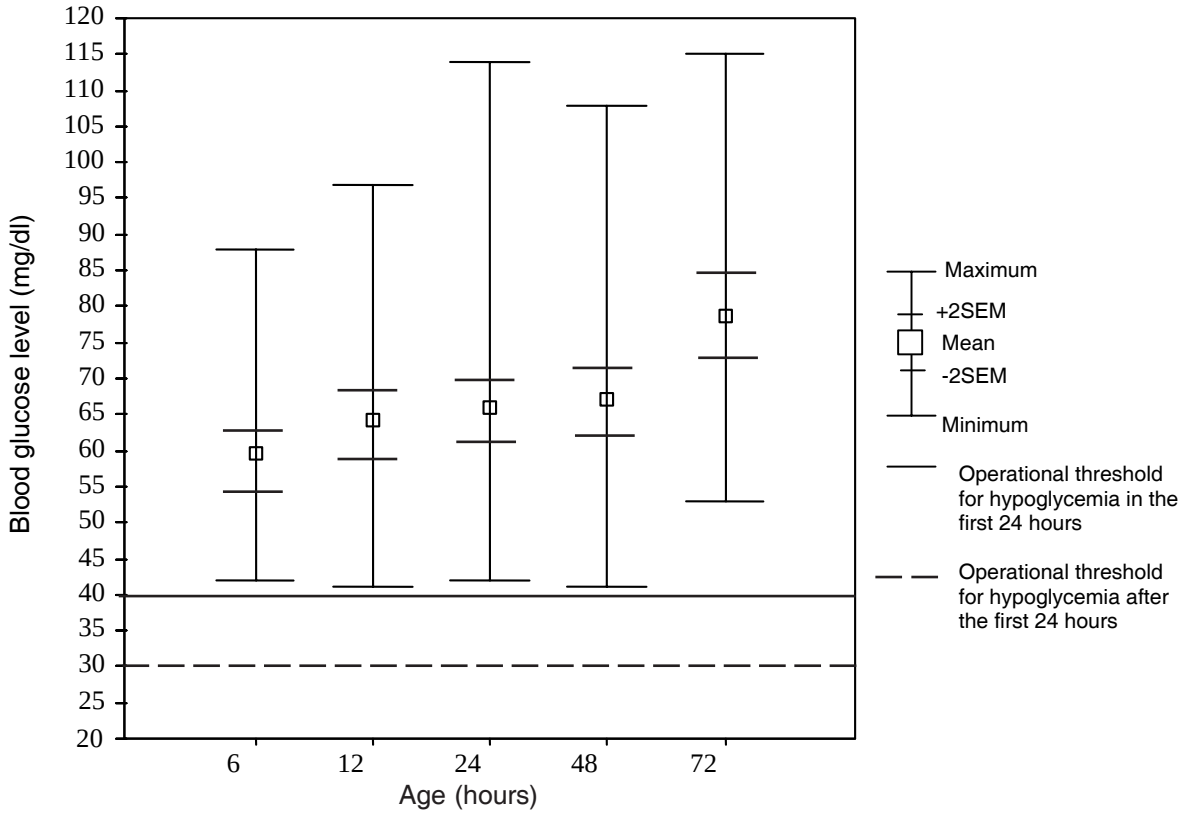

FIGURE 1. BLOOD GLUCOSE LEVELS OF SUBJECTS IN DIFFERENT AGE GROUPS

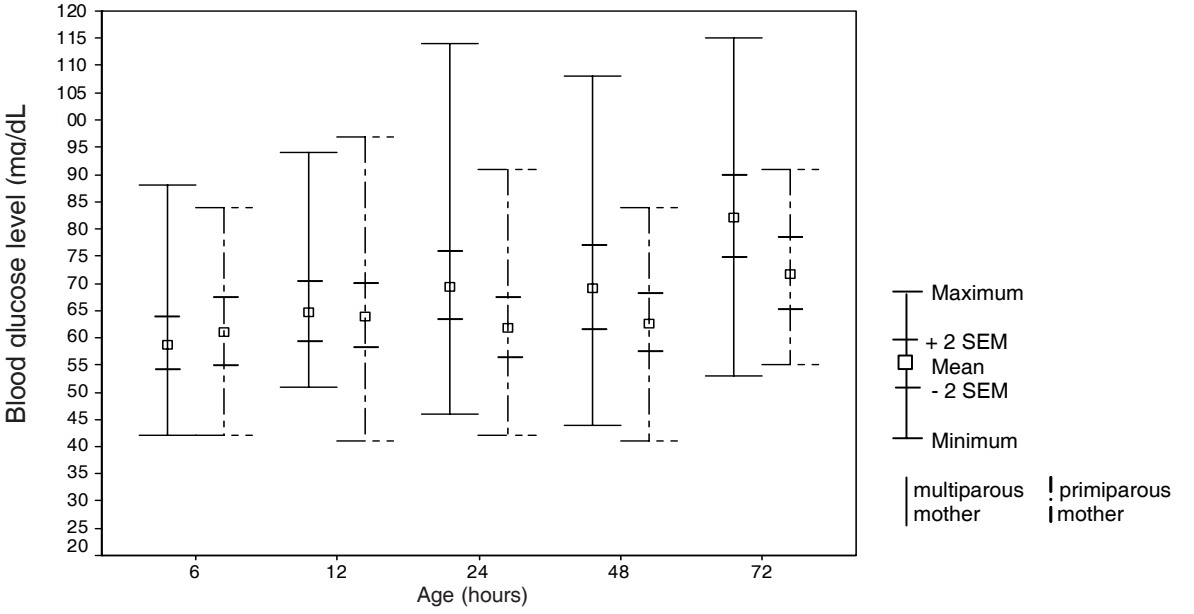

FIGURE 2. BLOOD GLUCOSE LEVELS OF THE SUBJECTS ACCORDING TO PARITY IN DIFFERENT AGE GROUPS

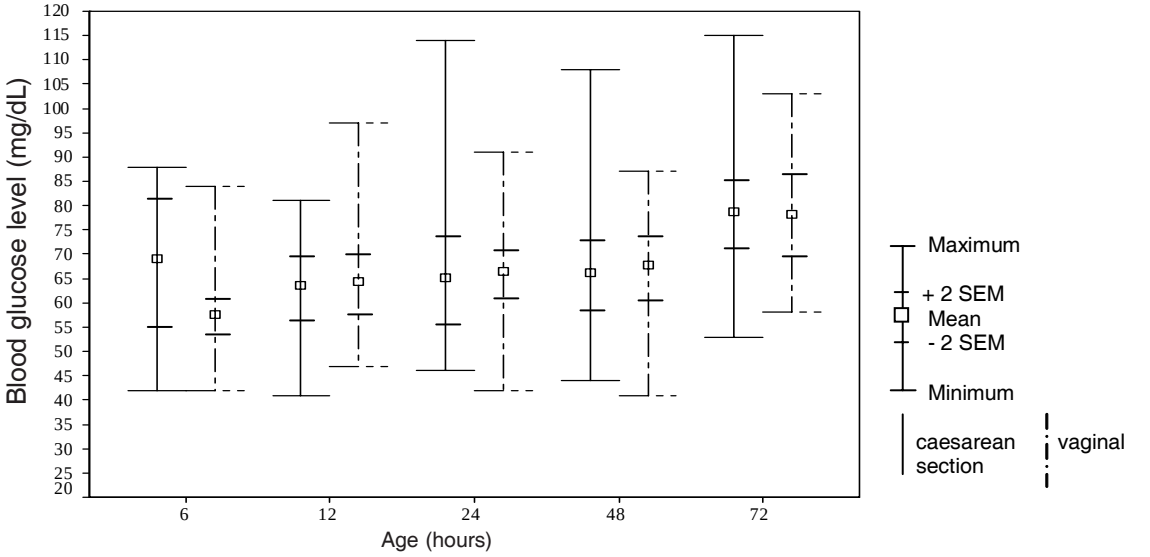

FIGURE 3. BLOOD GLUCOSE LEVELS OF THE SUBJECTS ACCORDING TO THE MODE OF DELIVERY IN DIFFERENT AGE GROUPS

Discussion

The absence of symptomatic hypoglycemia in this study had also been found in several previous studies which determined the blood glucose levels in healthy, term, AGA, exclusively breastfed infants.[8,10-12] This supports the statement of the World Health Organization that healthy, term, AGA infants who are exclusively breastfed will not experience symptomatic hypoglycemia.[12]

The blood glucose levels of the samples were all above 40 mg/dl, a value recommended by most text-

books of neonatology as the cut-off level for hypoglycemia.[13-16] The possibility that healthy, term, AGA, exclusively breastfed infants may have lower blood glucose levels and yet remain asymptomatic was shown by some other studies. In a cross-sectional study on 223 infants whose blood samples were collected at birth, the age of 1, 2, 4, 6, 12, 24, 48, 72, or 96 hours, Hoseth *et al*[11] found that 4% of the subjects had blood glucose levels below 40 mg/dl. In line with that finding, Diwakar and Sasidhar[12] in a longitudinal study on 200 infants whose blood samples were collected at the age of 3, 6, 24, and 72 hours found that 11.6% of the subjects had blood glucose levels below 40 mg/dl. In both studies, none of the subjects presented any clinical sign of hypoglycemia.

There is insufficient data to define a normal range for blood glucose levels in healthy, term, AGA, exclusively breastfed infants. Even if a normal range could be set, it would not establish a threshold blood glucose level at which to initiate treatment in asymptomatic infants, as they have the capability to mobilize and use alternative fuels (particularly ketone bodies, fatty acids, and lactate) as a normal adaptive response to transiently low nutrient intake during the establishment of breastfeeding.[17-19] As data correlating asymptomatic hypoglycemia with long-term neurological damage is too limited to set a safe cut-off blood glucose level,[17-20] WHO[17] and Cornblath *et al*[19] recommended that asymptomatic healthy, term, AGA, exclusively breastfed infants do not require routine monitoring of blood glucose concentration.

The higher mean blood glucose level in the 72-hour age group may point to the increased production of breast milk and mobility of the mothers at that particular postnatal period. Seventy-two hours postpartum is often used as the time associated with adequate breast milk production, especially for primiparous mothers whose onset of lactation were relatively delayed compared to multiparous ones.[3, 21]

Regarding mean differences between different age groups, previous studies on blood glucose levels of healthy, term, AGA, exclusively breastfed infants showed variable results. Hoseth et al[11] found that the mean blood glucose levels of 24-hour old infants were significantly lower compared to that of older infants, while the studies of Hawdon *et al*[10] and Diwakar and Sasidhar[12] showed no significant difference among different age groups.

The concern that infants born to primiparous mothers may not receive enough breast milk during the first several days, which may later cause hypoglycemia, was not proven to exist in this study. Moreover, the mean blood glucose level of infants born to primiparous mothers was not lower compared to those of multiparous mothers in all age groups. This finding was in accordance with those reported by Diwakar and Sasidhar.[12]

Infants of primiparous mothers normally will not have a full supply of breast milk for 72 to 96 hours, in contrast with those of multiparous mothers, who may obtain it earlier as the milk is produced more quickly.[3] Delayed onset of milk production, which was significantly associated with primiparity, was reported in the study of Dewey *et al*.[21] They also found that some multiparous mothers had difficulties in feeding the infants (termed as 'suboptimal infant breastfeeding behavior') on the first postnatal day but were able to improve the situation earlier than primiparous mothers could. This was presumed to be due to the past breastfeeding experience of the multiparous mothers.

Although Evans *et al*[22] in their study of the effect of caesarean section on breast milk transfer to the normal term newborn over the first week of life had found that the volume of breast milk transferred to infants born by caesarean section was less than the volume transferred to infants born by normal vaginal delivery over the first 6 days of life, our study showed that the mean blood glucose levels of the infants born by caesarean section was not lower than those delivered vaginally. This finding was in agreement with the results showed by previous studies.[11,12]

Despite the fact that infants born to primiparous mothers and those delivered by caesarean section received less breast milk compared to those born to multiparous mothers and those delivered vaginally, the result of our study showed that they did not have lower blood glucose levels. We presumed that most likely these infants had adequate metabolic adaptation that enabled them to maintain their blood glucose at an adequate level despite relatively minimum milk intake during the first few days of life.

There are some limitations in this study, including the period of sample collection which was not specific to the time of feeding and the failure to observe some subjects for clinical signs of hypoglycemia until the third day of life, as most of the vaginally delivered infants were discharged on the second day.

In conclusion, there was no incidence of hypoglycemia (symptomatic or asymptomatic) observed in this study. Therefore, the current concern for hypoglycemia in healthy, term, AGA, exclusively breastfed infants during the first few days of life was not proven to exist, and there is no reason to resort to prelacteal feeding in these infants.

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References

1. Naylor AJ. Baby-friendly hospital initiative: protecting, promoting, and supporting breastfeeding in the twenty-first century. Pediatr Clin North Am 2001;48:475-83.
2. The American Academy of Pediatrics, Work Group on Breastfeeding. Breastfeeding and the use of human milk. Pediatrics 1997;100:1035-9.
3. Lawrence RA. Breastfeeding: a guide for the medical profession. 4th ed. St. Louis: Mosby; 1994. p. 215-77.
4. Prasad B, Costello AM deL. Impact and sustainability of a baby friendly health education intervention at a district hospital in Bihar, India. BMJ 1995;310:621-3.
5. Ludvigsson JF. Breastfeeeding intentions, patterns, and determinants in infants visiting hospitals in La Paz, Bolivia. BMC Pediatrics 2003;3:5.
6. Perez-Escamilla R, Segura-Millan S, Canahuati J, Allen H. Prelacteal feeds are negatively associated with breast-feeding outcomes in Honduras [abstract]. J Nutr. 1996;126: 2765-73.
7. Srivasan G, Pildes RS, Cattamanchi G, Voora S, Lilien LD. Plasma glucose values in normal neonates: a new look. J Pediatr 1986;109:114-7.
8. Heck LJ, Erenberg A. Serum glucose levels in term neonates during the first 48 hours of life. J Pediatr 1987;110:119-22.
9. Madiyono B, Moeslichan Mz S, Sastroasmoro S, Budiman I, Purwanto HP. Perkiraan besar sampel. In: Sastroasmoro S, Ismael S, editors. Dasar-dasar metodologi penelitian klinis. 2nd ed. Jakarta: Sagung Seto; 2002. p. 259-87.
10. Hawdon JM, Platt MPW, Aynsley-Green A. Patterns of metabolic adaptation for pretem and term infants in the first neonatal week. Arch Dis Child 1992;67:357-65.
11. Hoseth E, Joergensen A, Ebbesen F, Moeller M. Blood glucose levels in a population of healthy, breastfed, term infants of appropriate size for gestational age. Arch Dis Fetal Neonatal Ed 2000;83:F117-9.
12. Diwakar KK, Sasidhar MV. Plasma glucose levels in term infants who are appropriate size for gestation and exclusively breastfed. Arch Dis Fetal Neonatal Ed 2002;87:F46-8.
13. Ogata ES. Carbohydrate homeostasis. In Avery GB, Fletcher MA, MacDonald MG, editors. Neonatology: pathophysiology and management of the newborn. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 1999. p. 699-714.
14. Kliegman RM. Problems in metabolic adaptation: glucose, calcium, and magnesium. In: Klaus MH, Fanaroff AA, editors. Care of the high-risk neonate. 5th ed. Philadelphia: WB Saunders Company; 2001. p. 301-9.
15. Gomella, TL, Cunningham MD, Eyal FG, Zenk KE. Neonatology: management, procedures, on-call problems, diseases, drugs. 4th ed. New York: Lange Medical Books/McGraw-Hill; 1999. p. 247-51.
16. Sperling MA. Hypoglycemia. In: Behrman RE, Kliegman RM, Jenson HB, editors. Nelson textbook of pediatrics. 16th ed. Philadelphia: W.B.Saunders Company; 2000. p. 439-50.
17. World Health Organization. Hypoglycemia of the newborn: review of the literature. Geneva: WHO; 1997.
18. Eidelman AI. Hypoglycemia and the breastfed neonate. Pediatr Clin North Am 2001;48:377-87.
19. Cornblath M, Hawdon JM, Williams AF, Aynsley-Green A, Ward-Platt MP, Schwartz R, *et al*. Controversies regarding definition of neonatal hypoglycemia: suggested operational thresholds. Pediatrics 2000;105:1141-5.

20. Koh THHS, Aynsley-Green A, Tarbit M, Eyre JA. Neuronal dysfunction during hypoglycemia. Arh Dis Child 1988;63:1353-8.
21. Dewey KG, Nommsen-Rivers LA, Heinig MJ, Cohen RJ. Risk factors for suboptimal infant breastfeeding behavior, delayed onset of lactation, and excess neonatal weight loss. Pediatrics 2003;112:607-19.
22. Evans KC, Evans RG, Esterman AJ, James SL. Effect of caesaren section on breast milk transfer to the normal term newborn over the first week of life. Arch Dis Fetal Neonatal Ed 2003;88:F380-2.