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Term And Premature Infants: Dietary, Glycemia, Insulinemia, Lipid Profile At 6 Months Of Age

Claudia Silveira Viera
Universidade Estadual do Oeste do Paraná, Cascavel, PR, Brasil

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***Corresponding author:** Claudia Silveira Viera, Universidade Estadual do Oeste do Paraná, Cascavel, PR, Brasil

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Abstract

Background: Children born prematurely are subject to metabolic complications that lead the early onset of chronic diseases such as hypertension and diabetes. Phenotype expression in adulthood is closely related to lifestyle, particularly eating habits.

Aim: to correlate the dietary profile of premature and term infants and their relationship with plasma biochemical parameters from birth to six months of life.

Method: secondary data analysis study, based on the variables collected at birth (T0) and 6-month follow-up (T1) of term infants (n=73) and premature infants (n=39). Analyzed variables: weight, type of food intake, adequacy of birth weight, gestational age, biochemical tests (triglycerides, cholesterol, glucose, and insulin).

Results: Glucose and triglyceride values were influenced to born preterm or term ($p<0.01$). Premature infants have higher triglycerides concentration (T0–T1=57.97±87.65). Adequacy of birth weight and dietary types did not influence glucose and triglyceride variation. Baby's diet based on vegetables ($p=0.047$) and to born premature ($p<0.01$), exerted influence on the variation of insulin and cholesterol. The intake of vegetable soup showed an increase in insulin and cholesterol concentrations, regardless of a preterm or term birth.

Keywords: Premature infant; infant; lipids; blood glucose; insulin; diet

Statement of Significance:

It is recommended in evaluations of children during the postnatal follow-up, to check their lipid and glycemic profiles based on premature infants tended to have significantly higher mean total cholesterol variation compared to the term infant.
Vegetable-based diet influenced the values of insulin and total cholesterol, independently to born preterm or term.

Introduction:

Prematurity is a global problem to contribute for the infant mortality, being the most frequent cause of neonatal morbidity[1]. In 2016, 11.1% of all births in Brazil were premature [2].

Consequently, in the last decades, the survival rate of Premature (PT) infant has been increasing, especially for those with very low birthweight and a high degree of prematurity [1]. This fact influences long periods of hospitalization in the Neonatal Intensive Care Unit (NICU). There is a significant portion of children born prematurely who will, throughout their development, manifest metabolic or physiological complications resulting from prematurity. Notably, premature birthed seem to have a greater tendency to develop obesity and overweight in adolescence, with a higher risk for arterial hypertension, glucose intolerance, and dyslipidemia in adolescence and adulthood [3].

The relationship between prematurity and the onset of diseases in adulthood refers to the concept of metabolic programming [4], considered an event that occurs in critical stages of development (intrauterine, lactation, and adolescence) favoring the installation of comorbidities in adulthood.

These repercussions can be reduced by making use of continuous care strategies,

from hospitalization to home, one of them refers to the maintenance of exclusive breastfeeding until the sixth month of corrected age, considered a protective factor for the PT infant, since it provides adequate weight gain, harmonic growth, and prevents problems such as Metabolic Syndrome - MS [5].

Additionally, breast milk contains high concentrations of docosahexaenoic acid (DHA), which is related to better neuro psychomotor performance [6]. Therefore, it is desirable that at six months of age, children are still exclusively breastfeeding. However, PT infants are significantly more likely to be introduced to complementary foods early compared with term infants [7].

Another strategy is the monitoring of PT infants after hospital discharge for early detection of possible complications from prematurity. In particular, the assessment of the metabolic conditions of this group, as the literature points out that PT and low-birthweight babies are more vulnerable to developing cardiovascular changes and insulin resistance [8,9].

Studies carried out recently with term [10] and PT [11] infants in south of Brazil, show that the lipid profile in both groups were altered at six months of age. In both of them, the triglyceride values were above what was indicated by the consensus of clinical analyzes of 85mg/dl without fasting [12,13].

The establishment of metabolic parameters in early age groups is contradictory in the literature. Therefore, a more detailed analysis implies characterizing the child's entire development, including the dietary profile, with the metabolic and health condition.

Furthermore, these studies [10,11] did not evaluate the relationship among the infant's feeding and their lipid and glycemic profile. The influence of food, especially breastfeeding, is evidenced as a protector against the development of metabolic changes such as diabetes mellitus [5]. So, there are a correlation between the glycemic and lipid profile of term infants and premature infants with feeding received from birth to six months of life?

This study proposed to analyze secondary data from the primary research database [10,11], aiming to correlate the dietary profile of PT and term infants and their relationship with plasma biochemical parameters from birth to six months of life.

Method and Results:

The study was quantitative research, with secondary data analysis [14]. The database was generated from two primary studies carried out in a public teaching hospital in southern Brazil, named: "Glycemic and lipid profile in term newborns and their correlations with maternal clinical and metabolic conditions"[10] and "Growth and biochemical markers of premature infants" [11].

The PT infant group includes those with less than 37 weeks of Gestational Age (GA), child birthed in the field study hospital, who remain in the NICU for a period equal to or superior to seven days and returned to the outpatient clinic during follow-up visits scheduled.

The group of term infants (TI) included every newborn birthed in the hospital under study, with mothers without metabolic changes or underlying diseases diagnosed until delivery, who attended the follow-up appointment scheduled for the sixth month of life.

All the newborn babies with some congenital malformation and born from adolescent mothers were excluded. A new database was created in Excel for Windows. The sample consisted of 82 term and 115 PT infants, included in primary studies at birth. At six months, there was a loss in the follow-up and the sample consisted of 73 term and 39 PT infants, of both sexes.

The variables collected were related to the birth moment (Time zero - T0) and the follow-up at six months after birth (Time 1 - T1), including: body weight (g), type of food intake (fruit-based diet; sweet-based diet; vegetable-based diet; protein-based diet; carbohydrate-based diet), birthweight adequacy, gestational age (GA in weeks) and biochemical tests - glucose (mg/dL), triglycerides (mg/dL), total cholesterol (mg/dL) and insulin (UI/mL).

In both primary studies, biochemical tests followed the same methodology: glucose, triglycerides, cholesterol, and insulin blood samples were collected from 24 to 72 hours after birth and at six months. For PT infants they were collected at six months of corrected age.

These samples were analyzed by dry chemistry method with 10mg/dL of sensibility for the triglycerides, 20mg/dL for glucose and 50mg/dL for cholesterol. The insulin exam was analyzed by electrochemiluminescence method with 0,03nUI/mL of sensibility. The data regarding food introduction was obtained through interviews with mothers in the follow-up consultation.

The birthweight and GA ratio was classified using the Fenton online calculator (http://www.ucalgary.ca/fenton/2013chart). PT and TI evaluated were classified as Adequate for Gestational Age (AGA), considered those among the percentiles 10 and 90; Small for Gestational Age (SGA), classified as less than the 10th percentile and Large for Gestational Age (LGA), those greater than the 90th percentile. PT infants were assessed in the follow-up according to the corrected gestational age to enable comparison with the group of TIs.

The sample was characterized by descriptive statistics when comparing both groups. Once this procedure was carried out, statistical tests were applied to measure the effect of predictors (the type of diet, adequacy of birth weight and birth GA) in the variation of glucose, triglycerides, cholesterol, and insulin. The average variation was performed by the equation:

Variation = (value of the variable in Time 1 - value of the variable in Time 0).

Due to the lack of homoscedasticity of such values (Bartlett's test) and the normality of the residues (Shapiro-Wilk test), Analysis of Variance (ANOVA) was used. Followed by the multiple comparison test of Boostrap averages, with 1000 permutations [15]. For all tests used, the level of significance considered was 5%. The hypothesis tested at Anova were presented in Table 1

Table 1:

Predictors considered for effect under the variable's lipid and glycemic responses. Cascavel, Paraná, Brazil, 2018.

Mean variation	Predictors	Answer variables
Mean variation = Time 0 (birth) - Time 1 (6 months after leaving the hospital)	Birth (term or preterm) Adequacy of birthweight - Food: fruit-based diet, sweet-based diet, vegetable-based diet, protein-based diet, carbohydrate-based diet	Glucose, Triglycerides, Cholesterol, Insulin

The statistical software used was R [16], with the ExpDes.pt packages [17,18]. The primary studies were approved by the Research Ethics Committee under process No. 1.134.712. The

informed consent form was read and signed by parents or guardians prior to the study.

Results:

Related to sex in the 82 TI, 44 (53.66%) were male and 38 (46.34%) females. Among the 115 PT, 48 (41.74%) were male and 67 (58, 26%) female at birth. At the sixth month, 18 (46%) PT and 39 (56,5%) of the TI were exclusively breastfed. Therefore, most had already introduced complementary feeding.

Comparing the average variation of glucose (F = 10.96, GL = 1, p <0.01) and triglycerides (F = 10.68, GL = 1, p <0.01) between the predictors, only the birth variable was statistically significant (Table 2).

Children in the TI group tended to increase glucose values between T0 and T1, with an average variation of 15.77 ± 20.35 (Table 2). On the other hand, in the PT group, there was drop-in blood glucose between T0 and T1 with a variation of -0.23 ± 30.11mg/dL (Table 2). Therefore, term infants tend increase their glycemic averages, in contrast to PT infants, who did not show vast variance during the follow-up.

The PT infants presented significantly higher triglyceride variation averages than in the TI group (Table 2).

Table2:

Mean ± Standard deviation (n-1) of the variable glycemia and triglyceride in relation to the variable birth and six months. Cascavel, Paraná, Brazil, 2018.

Evaluation periods	**Blood Glucose Average (mg/dL)**		**p-value**
	PT	**TI**	
	n= 39	n = 73	
T0 (Birth)	86,31 ± 29,08	63,15 ± 18,68	
T1 (6 month after birth)	86,08 ± 14,33	78,92 ± 9,56	
Average variation (T1– T0)	-0,23 ± 30,11[a]	15,77 ± 20,35[b]	<0,01
Evaluation periods	**Triglicerydes average(mg/dL)**		**p-value**
	PT	**TI**	
	n= 39	n = 73	
T0 (Birth)	97,72 ± 56,93	123,178 ± 49,89	
T1 (6 month after birth)	155,69 ± 75,79	131,15 ± 49,30	
Average variation (T0 – T1)	57,97 ± 87,65b	7,97 ± 68,66a	<0,01

Reference values: Glucose – 145 mg/dL (hyperglycaemia); <45 mg/dL (hipoglycaemia); Triglicerydes - <75mg/dL (fasting); 85mg/dL (no fasting), for age between 0 to 9.

Letters “a” and “b” indicate that the meanings are different in the line.

Regarding the insulin variable, the predictive variables 'birth' (F = 17.29; GL = 1; p <0.01) and 'vegetable-based diet' (F = 4.01; GL = 1; p = 0.047) were statistically significant. No other diet (exclusive breastfeeding, mixed or formula) or adjustment of birthweight had any effect on the variation of insulin.

In general, PT infants showed a decline in insulin values from T0 to T1 when compared to the TI, which showed an increase in means for this variable (Table 3). Independently of being born term or preterm, children who did not consume a vegetable-based diet tended to decrease their insulin values when compared to ones who ate such feeding. That variation showed stability over the analyzed period (Table 3).

For the total cholesterol variable, the predictors T0 (F = 27.45; GL = 1; p <0.01) and 'vegetable-based diet' (F = 3.88; GL = 1; p = 0.035) were statistically significant. No other diet (exclusive breastfeeding, mixed or formula) or adequacy of birthweight, had any effect on the cholesterol variation (Table 3).

Table3:

Mean ± Standard deviation (n-1) of the variable insulin and total cholesterol in relation to the variable birth and six months after birth and the variable vegetable based-diet. Cascavel, Paraná, Brazil, 2018.

Evaluation periods	**Insulin (uIU/mL)**		**p-value**
	PT	**TI**	
	n= 39	n = 73	
T0 (Birth)	10,08 ± 12,95	2,00 ± 1,77	
T1 (6 month after birth)	5,17 ± 4,58	3,95 ± 3,74	
Average variation (T1–T0)	-4,91 ± 13,28[a]	1,95 ± 3,58[b]	<0,01
Evaluation periods	**Vegetable based-diet**		**p-value**
	PT	**TI**	
	No (2) n= 38	Yes (1) n= 73	
T0 (Birth)	6,15 ± 10,88	4,05 ± 7,04	
T1 (6 month after birth)	3,36 ± 3,02	4,90 ± 4,45	
Average variation (T1–T0)	-2,79 ± 10,92[a]	0,85 ± 7,34[b]	0,047
	Total Cholesterol (mg/dL)		
Evaluation periods	**PT**	**TI**	**p-value**
	n= 39	n= 73	
T0 (Birth)	122,77 ± 34,16	86,53 ± 20,04	
T1 (6 month after birth)	138,82 ± 26,74	140,36 ± 26,69	
Average variation (T1–T0)	16,05 ± 44,30a	53,82 ± 31,22b	<0,01
Evaluation periods	**Vegetable based-diet**		**p-value**
	PT	**TI**	
	No (2) n= 38	**Yes (1)** n= 73	
T0 (Birth)	105,40 ± 35,90	95,95 ± 27,87	
T1 (6 month after birth)	135,45 ± 25,91	142,07 ± 26,84	
Average variation (T1–T0)	30,05 ± 46,89[a]	46,12 ± 35,73[b]	0,035

Reference values: Insulin - 2,6 a 24,9 uUI/mL; Total Cholesterol - <170mg/dL, independently of fasting or not for the age of 0 to 2years.

Letters “a” and “b”, indicate that the means are different in the line.

Children in the PT group tended to have significantly higher

averages of variation in the serum concentration of total cholesterol compared to the TI. Regarding vegetable-based diet, independently of the group, those who presented this diet also showed significantly higher variation averages when compared to those who did not receive it.

Discussion:

When correlating the glycemic and lipid profile of term and preterm infants with the kind of food received from birth to six months of life, the researchers observed that to be a PT or TI at birth influenced the glucose and triglycerides values.

Also, insulin was only influenced by the type of complementary diet. Besides, total cholesterol was affected by premature birth and the introduction of a vegetable-based diet. Independently of being a PT or TI infant, those who were on complementary feeding with the introduction of vegetable-based diet were more susceptible to having their serum total cholesterol values higher than those who were exclusively breastfeeding, mixed or with formula.

Thus, being born term or preterm was a statistically significant predictor of the glucose and triglyceride variation. Being born SGA or AGA did not influence the concentrations of this exams. Similar data was shown in another studies [18,20]. In contrast, this relationship was identified as a predictor for changes in triglycerides at earlier periods, such as at birth or one year of age [21,22].

The TI tend to increase their glycemic averages from T0 to T1, in contrast to PT infants. Possibly, it may occur due to the immaturity of the PT infant enzyme and endocrine mechanism, in which hypoglycemia can commonly occur at birth [23].

In addition, neonates have poorly developed regulatory mechanisms to combat hypoglycemia. In a hypoglycemic state, the protective effect of the newborn will occur, generating a reduction in insulin secretion and an increase in glucagon, epinephrine, growth hormone and cortisol secretion. This reaction will lead to the production of glucose and the mobilization of fatty acids from adipose tissues [24].

Related to triglycerides, being born prematurely was a predictor that influenced this concentration. Moreover, PT had higher serum values than TI. This may come from the type of nutrition that PT infants receives during hospitalization, which is rich in calories to promote and achieve growth catch-up [25].

Therefore, early nutrition is a key factor in growth, composition, and metabolism, but certainly not the only one, considering the complex interactions between endocrine factors, such as IGF-I and nutrition, a study [25] suggests the introduction a high protein diet but not more calories. In other words, enriched food before discharge, can prevent the excessive accumulation of fat and the long-term health risks of the PT infants.

Regarding the insulin variation, it was found that for PT infants the values were higher than for the TI. However, PT infants showed a decline in serum concentration from T0 to T1, while TI showed an increase in values at the same period. This drop-in serum insulin concentration in the PT infant group, according to a study by the Pediatric Endocrinology Society [26], occurs as a defense of the organism to maintain adequate glucose concentrations.

The findings showed that PT infants tended to have significantly higher mean total cholesterol variation compared to the TI. The initiation of breastfeeding can raise cholesterol levels during the first six months. Since breast milk has a higher concentration of cholesterol than formula milk, However, in long term, breastfeeding has benefits on lipid metabolism in adulthood [27]. Likewise, being born AGA for PT infant is a protective factor for metabolic changes at the age of two years corrected [28].

Furthermore, both fetal and child growth are related to cholesterol metabolism programming in premature children [29]. Besides, investigations correlating infant's type of diet to insulin and cholesterol concentrations are scarce or inconclusive. A study [30] suggests that research should be developed to assess the needs of TI and PT infants for long-chain polyunsaturated fatty acids, the sites of action and the clinical effects of lipid mediators on immunity and inflammation, its role in metabolic, neurological and immunological outcomes and the mechanisms by which lipids act in the short- and long-term health.

The serum concentrations of total cholesterol and insulin were related to the vegetable-based diet in the period evaluated. This relationship may be due to the type of feeding that PT infant receives at hospitalization. While TI infant usually receives only breast milk, considered protective for such metabolic changes, PT infant receives numerous interventions, such as the inclusion of catecholamine infusions to increase and hydrocortisone to promote blood pressure, which contribute significantly to the common physiological disorders in these infants [30].

These factors also produce a highly variable gastrointestinal function in the intestinal motility of the PT infants. Moreover, they make use of antibiotics, which contribute significantly to changes in the intestinal microbiota and in the ability to effectively manage enteric nutrients but still little analyzed [30].

Another point is the parenteral nutrition alone already promotes changes in enteral feeding, as it reduces gastrointestinal villous development, decreases the digestive enzymes production, reduces the exudation of incretins (intestinal hormones, such as glucagon-like peptides 1 and 2) that promote insulin secretion [31]. Thus, all these interventions happened during hospitalization could produce different effects on biochemical parameters during the PT infant follow-up.

Conclusion:

This study identified the complementary diet introduced based on vegetables, for both groups, proved to be statistically significant for the values of total cholesterol and insulin. In the follow-up of children, attention should be dedicated to the way diets are prepared, since the preparation with excess fat can influence the increase in total cholesterol.

It is noteworthy as a limitation of the study the total cholesterol fractions were not analyzed, the sample at T1 was small due to the significant loss in the follow-up. In this sense, more investigation on this subject need to be developed with a larger sample.

The significance for practice is to comprehend that prematurity is a predictive factor for glycemic and lipid changes (total cholesterol and triglycerides). Besides, vegetable-based diet influenced the values of insulin and total cholesterol, independently to be PT or TI. During the follow-up appointment the health professionals should ask mothers about the feeding. It is recommended in evaluations of children during the postnatal follow-up, to check their lipid and glycemic profiles and the type of diet introduced at six months.

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