Influence of altered maternal lipid profile on the lipid profile of the newborn

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ABSTRACT

Objective: To evaluate whether there is an association between altered maternal lipid profile and the lipid profile of the newborn in a maternity hospital. **Subjects and method:** Cross-sectional study with 435 parturients and their respective newborns. Blood samples from the newborns were collected during delivery by venipuncture of the umbilical cord close to the placenta. Blood samples from the parturients were collected in the pre-delivery room or right after delivery. The concentrations of total cholesterol, triglycerides and HDL-c were determined by an enzymatic colorimetric method and LDL-c was calculated by the Friedewald formula. **Results:** There was no significant difference in mean concentrations of total cholesterol, LDL-c, HDL-c and triglycerides in neonates according to altered or non-altered maternal total cholesterol, LDL-c, HDL-c and triglycerides. **Conclusions:** Change in maternal lipid profile is not significantly associated with the mean concentrations of total cholesterol, LDL-c, HDL-c and triglycerides in newborns. Arch Endocrinol Metab. 2015;59(2):123-8

Keywords
Total cholesterol; LDL-C; HDL-C; triglycerides

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INTRODUCTION

Pregnancy is a condition that involves a metabolic adaptation to satisfy the nutritional support and development of the fetus (1). Since it is a moment of intense maternal hormonal change, the maternal lipid profile (total cholesterol and cholesterol fractions) undergoes physiological changes, increasing throughout the pregnancy (2,3). The pituitary-stimulating hormones released by the hypothalamus – gonadotropin-releasing hormone (GnRH), corticotropin-releasing hormone (CRH), growth hormone releasing hormone (GHRH), thyrotropin-releasing hormone (TRH) and prolactin – act directly on the pregnancy and reach high circulating levels due to placental stimulation (2). Some studies have shown that significant changes may occur in overweight or obese women (4,5). The normal physiological increase in circulating lipids allows the mother to have a valuable source of energy for her and for the baby and keeps their metabolic rate steady, enabling the healthy development of the newborn (6). However, during intrauterine development, pathophysiological processes can occur in the metabolism of the lipids leading to abnormal serum concentrations in fetal circulation (7-11).

The understanding of how the maternal/newborn lipid transport occurs allows us to find out whether lipid alterations are capable of generating permanent changes in the structures and functions of the organs, which may reflect on their metabolism and post-uterine life (3). Some authors consider the placenta a transport channel for the lipid portions from the mother to the fetus, and this transport can be influenced by maternal diseases associated with lipid metabolism (12,13). Several clinical conditions can influence the serum concentrations of lipids in neonates, and some authors disagree in relation to the transport via placenta (14). Changes in circulating lipids – total cholesterol (TC), high-density lipoprotein (HDL-c), low-density lipoprotein (LDL-c) and triglycerides – may be related to maternal/fetal transport mechanisms, in which the supply of fatty acids can be favored or restricted causing serious problems for fetal organs and tissues (15-19).

The aim of this study was to evaluate whether there is an association between altered maternal lipid profile and the lipid profile of the newborn in a public maternity hospital in Joinville, Santa Catarina.

SUBJECTS AND METHODS

Design and study population

This is a cross-sectional study, conducted with 435 pairs (mothers and children) attending a public maternity hospital in the city of Joinville-SC, between January and February of 2012. The sample was calculated with the software OpenEpi version 3.02. Based on a prevalence of 6% of macrosomic infants (20-22), for a 95% confidence interval, absolute precision of 2.5% and a population of 7,200 newborns, the estimated sample size was 331 individuals. Assuming a 20% loss, a total of at least 397 participants was required.

This study is part of a larger project which included investigation of socioeconomic, demographic, obstetric, anthropometric and reproductive data of mothers and their newborns. We included in the study all pregnant women in labor, aged 18 years or more, with gestational age classified as "term" (37 to 42 weeks), who did not follow any specific type of diet before or during pregnancy, or at the time of delivery, with a single pregnancy and live births who delivered in the maternity ward. We excluded mothers diagnosed with infectious and contagious diseases (syphilis, human immunodeficiency syndrome, toxoplasmosis and hepatitis) and preeclampsia, and those newborns who presented morphological changes at the time of birth. The study was approved by the Research Ethics Committee of Univille under the number 107/2011.

Biochemical analysis

The blood samples of the newborns, approximately 10 mL, were collected at the time of the delivery by aspiration of the umbilical vein close to the placenta up to 10 minutes after clamping to prevent coagulation. Blood samples of the parturients, approximately 10 mL, were collected by a nurse in the pre-delivery room or soon after the delivery (up to 24 hours). Immediately after collection, the blood was transferred to tubes containing separating gels, then identified and kept at room temperature for 30 minutes. After that, the tubes with the samples were placed in a refrigerator for up to four hours and subsequently centrifuged under 6°C refrigeration at 3,500 rotations per minute for 15 minutes. After separation of the serum, the samples were fractionated in aliquots of 0.5 mL for measurement of TC, HDL-c, LDL-c and triglycerides, and the remainder was stored in a freezer at -75°C.

The concentrations of TC, triglycerides and HDL-c were determined by an enzymatic colorimetric method with Advia Centaur (model 1650, Siemens), using the kits Cholesterol Liquiform (GOD-ANA 2009), Triglycerides Liquiform (GOD-ANA 2009) and D-HDL (Siemens Diagnostics, Tarrytown, USA), respectively. From the TC, triglycerides and HDL-c levels obtained, we determined the values of LDL-c using the Friedewald formula when triglycerides values were below 400 mg/dL (23). We considered as reference values for lipids in women above the age of 20 years, those proposed by the "V Brazilian Guideline on Prevention of Dyslipidemia and Atherosclerosis" of the Brazilian Society of Cardiology, which considers as high those values of TC ≥ 240 mg/dL, LDL-c ≥ 160 mg/dL and triglycerides ≥ 200 mg/dL (24). HDL-c was considered low when the values were below 40 mg/dL, according to the "V Brazilian Guideline on Prevention of Dyslipidemia and Atherosclerosis", which stratifies this variable according to gender (24). For women aged 19 years or younger, we adopted the reference values proposed by the "I Guideline on Prevention of Atherosclerosis in Childhood and Adolescence", which considers as high those values of TC ≥ 170 mg/dL, LDL-c ≥ 130 mg/dL, HDL-c < 45 mg/dL and triglycerides ≥ 130 mg/dL (25).

Gestational weight gain

Gestational weight gain (GWG) was calculated by subtracting from the weight at the time of hospitalization at the MDV, as evaluated by the screening staff and recorded in the medical chart, the weight reported by the mother before the pregnancy. The adequacy of the GWG was evaluated according to the new recommendations of the Institute of Medicine - IOM (26). Underweight women (BMI < 18.5 kg/m^2) should gain between 12.5 and 18 kg; women with adequate BMI (18.5-24.9 kg/m^2) between 11.5 and 16.0 kg, overweight women (25.0-29.9 kg/m^2) between 7.0 and 11.5 kg, and obese women (BMI ≥ 30.0 kg/m^2) between 5.0 and 9.0 kg (26).

Statistical analysis

The data were stored and analyzed by the software SPSS Inc. Released 2008. SPSS Statistics for Windows, Version 17.0. Chicago: SPSS Inc. We calculated measures of central tendency and dispersion for quantitative variables and frequency distributions for categorical variables. The statistical comparison was analyzed using

the Mann-Whitney *U* test for non-parametric variables. Biochemical variables were transformed into the binary modes "NOT ALTERED" and "ALTERED". Normality was verified using the Kolmogorov-Smirnov test and the significance level adopted was 5%.

RESULTS

Of 529 children born during the period of investigation, 46 did not fulfill the inclusion criteria and 12 were excluded from the study, yielding a total of 471 pairs. Of these, 36 (7.6%) were considered losses, resulting in 435 pairs.

The general characteristics of the 435 parturients and their children are presented in table 1. The mean age of the mothers was 25.9 (SD = 6.0) years and most (56.6%) were ≥ 24 years of age, with ≥ 8 years of education (75.2%), married/in a stable relationship (83.0%) and with a declared household income ≥ 3 times the minimum wage (57.5%). More than one third (37.9%) of the parturients reported having a BMI ≥ 25 kg/m² before the pregnancy. As for the newborns, the male gender was the most prevalent (51.5%), about one third (33.3%) were delivered by cesarean section and 24.4% were categorized as large for gestational age – LGA (Table 1).

Table 1. General characteristics of the mothers and their newborns according to absolute (n) and relative (%) frequencies. Joinville, SC, Brazil, 2012

Characteristics (n = 435)	n	%
Mothers		
Age		
< 24	189	43.4
≥ 24	246	56.6
Years of education		
≥ 8	327	75.2
<8	108	24.8
Marital status		
Married/stable relationship	361	83.0
Others	74	17.0
Family income		
<3	177	42.5
≥ 3	239	57.5
Pre-gestational BMI (kg/m²)		
Underweight (< 18.5)	19	4.4
Normal weight (18.5 – 24.9)	251	57.7
Overweight (25 – 29.9).	108	24.8
Obese (≥ 30)	57	13.1
Newborns		
Gender		
Male	224	51.5
Female	211	48.5
Type of delivery		
Normal	290	66.7
Cesarean section	145	33.3
Weight status		
Small for gestational age (SGA)	4	0.9
Appropriate for gestational age (AGA)	325	74.7
Large for gestational age (LGA)	106	24.4

Table 2 lists the values of GWG of the 435 investigated parturients. Although the average GWG decreased with increasing BMI, the parturients categorized as being overweight or obese (n = 165; 39.9%) gained more weight than the recommended maximum by the IOM classification (26). When we analyzed only women with BMI ≥ 25 kg/m² (overweight and obese), Spearman's correlation analysis showed no association between GWG and the lipid profile of the newborns (TC: rho = -0.058, p = 0.467; LDL-c: rho = -0.071, p = 0.376; HDL-c: rho = 0.031, p = 0.701; triglycerides: rho = -0.052, p = 0.518).

Table 2. Minimum, maximum and mean values and standard deviations (SD) for gestational weight gain (GWG) of 435 parturients. Joinville, SC, Brazil, 2012

Gestational weight gain (kg)[a]	Minimum	Maximum	Mean	SD
Low weight (12.5 - 18.0)[b], (n = 19)	8.0	27.0	15.2	4.4
Normal weight (11.5 - 16.0), (n = 251)	1.6	39.0	14.8	5.9
Overweight (7.0 - 11.5), (n = 108)	-9.1	43.0	13.7	6.9
Obesity (5.0 - 9.0), (n = 57)	-7.0	32.9	10.4	7.7

[a] According to Rasmussen and Yaktine, 2009.
[b] Minimum and maximum values in kilograms of recommended weight gain according to the nutritional classification.

The values of the lipid profile of the mothers and their children are presented in table 3. The mean concentrations of TC (208.1 mg/dL) and triglycerides (197.8 mg/dL) of the mothers were classified as altered and borderline, respectively, according to the "V Brazilian Guideline on Prevention of Dyslipidemias and Atherosclerosis" (24).

Table 3. Mean values and standard deviations (SD) of plasma lipid concentrations of the mothers and their newborns. Joinville, SC, Brazil, 2012

Characteristics	n	Mean	SD
Mothers			
Total cholesterol (mg/dL)	414	208.1	33.9
LDL-c (mg/dL)	404	112.7	27.6
HDL-c (mg/dL)	414	56.3	9.7
Triglycerides (mg/dL)	413	197.8	76.4
Newborns			
Total cholesterol (mg/dL)	412	57.7	14.7
LDL-c (mg/dL)	412	29.9	10.2
HDL-c (mg/dL)	412	21.7	6.9
Triglycerides (mg/dL)	412	30.3	17.9

LDL-c: low-density lipoprotein cholesterol; VLDL-c: very-low-density lipoprotein cholesterol; HDL-c: high-density lipoprotein cholesterol.

Table 4 shows the mean values and standard deviations of the concentrations of TC, LDL-c, HDL-c and triglycerides of newborns according to the maternal lipid profile, whether not altered (N) or altered (A). There was no significant difference in the plasma lipid concentrations in newborns in relation to the maternal lipid profile.

DISCUSSION

In this study we demonstrated that with the exception of the maternal variable LDL-c, the other maternal biochemical variables (TC, HDL-c and triglycerides) are not significantly associated with the lipid profile of the newborn.

The relationship of the maternal lipid profile to the lipid profile of the newborn is still not well understood in the scientific literature. Several authors report the occurrence of lipid transport across the placenta, but this transport is not enough to influence the infant's plasma lipid concentration (1,6,7,13). The physiological and biochemical mechanisms of the transport of nutrients across the placenta is rather complex (9-11). According to some authors, triglycerides are not transferred from the mother to the fetus (7), however, when the placenta presents lipase enzymatic activity and membrane receptors to lipoproteins, essential fatty acids are transported as triglycerides bound to lipoproteins, becoming thus available to the fetus (1,6,7).

During pregnancy, there is an increase in circulating lipids, leading to maternal hyperlipidemia. However, the lipoprotein-specific receptors for the transport of fatty acids in the placenta are metabolized in the fetal plasma (6,7,9-12). A study conducted with blood from the umbilical cord of newborns showed a lower concentration of TC and lipid fractions when compared with the concentrations obtained in the first days of life of these same individuals, probably due to the production of TC from the maternal milk. Maternal TC and lipid fractions are transferred to the fetus due to placental permeability (9-12). However, at the end of the pregnancy, cholesterol is no longer physiologically important, since it is then synthesized by fetal tissues. Ketone and small amounts of glycerol are also transferred across the placenta, because the fetus uses these elements in their metabolism (1).

Essential fatty acids are required for fetal development, and they are transferred to the fetus with the help of lipoprotein receptors present in the trophoblasts (6). Although the trophoblasts are responsible for the transport of cholesterol to the fetus, these cells express receptors for LDL-c and HDL-c in their membranes,

Table 4. Mean values and standard deviations (SD) of plasma lipid concentrations of newborns according to the maternal lipid profile – whether not altered (N) or altered (A). Joinville, SC, Brazil, 2012

Concentration of plasma lipids in newborns (mg/dL)	Maternal Lipid Profile											
	Total cholesterol			LDL-c			HDL-c			Triglycerides		
	N	A	*P**	N	A	*P**	N	A	*P**	N	A	*P**
	Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)	
Total cholesterol	57.1 (15.1)	59.1 (14.6)	0.221	57.7 (15.1)	56.7 (13.6)	0.605	57.4 (14.4)	59.2 (17.1)	0.614	57.3 (15.8)	58.1 (14.2)	0.452
LDL-c	29.7 (10.5)	30.7 (9.9)	0.155	29.9 (10.4)	29.6 (9.1)	0.883	29.9 (10.2)	30.5 (10.7)	0.695	30.1 (11.6)	29.9 (9.2)	0.424
HDL-c	21.3 (6.8)	22.3 (7.1)	0.261	21.7 (7.0)	21.4 (6.5)	0.613	21.4 (6.8)	22.6 (7.3)	0.273	21.0 (6.7)	22.2 (7.1)	0.180
Triglycerides	30.3 (18.5)	29.8 (17.0)	0.743	30.4 (17.8)	28.9 (21.1)	0.179	30.2 (18.3)	30.1 (16.7)	0.930	30.7 (21.1)	29.8 (15.0)	0.863

Altered Maternal Lipid Profile: ≤ 20 years: total cholesterol ≥ 170 mg/dL, LDL-c ≥ 130 mg/dL, HDL-c < 45 mg/dL, Triglycerides ≥ 130 mg/dL; > 20 years: Total cholesterol ≥ 240 mg/dL, LDL-c ≥ 160 mg/dL, HDL-c < 40 mg/dL, Triglycerides ≥ 200 mg/dL.

* Mann-Whitney U test.

which are responsible for the uptake and transport of cholesterol to the intracellular environment via lysosome. In the lysosome, cholesterol ester is hydrolyzed and then transported by the Niemann-Pick C1 (NPC1) protein, which regulates the transport of cholesterol from the lysosomes to other cellular compartments, making it available to the fetal plasma (9-11). Despite the occurrence of this transport of lipoproteins from the mother to the fetus, the maternal concentrations of TC, LDL-c, HDL-c and triglycerides seem not to affect the lipid profile of the newborn, as demonstrated in this study. Additionally, the GWG also showed no relationship with the lipid profile of the newborn, signaling that the nutritional status of the mother seems not to significantly change the lipid profile of the newborn.

Similarly to what has been reported by various authors, there is still limited information on the relationship between the lipid metabolism of the mother and the newborn. Mechanisms of synthesis, degradation and transport of fats, as well as carbohydrate metabolism, need to be better investigated in this group in order to enable the correct monitoring of the maternal plasma lipids during the gestational period.

To conclude, limitations of the present study include: 1) the fact that some parturients were not fasting when the blood was collected, which may have overestimated the values obtained for maternal TC and triglycerides; 2) the absence of a standard reference for the lipid variables TC and cholesterol fractions in children under the age of two years does not allow the assessment of a relationship between the altered lipid profile of the mother and the lipid profile of the child, hindering the understanding of the transport of these substances across the placenta.

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