Concentration of Serum Lipids and Apolipoprotein B in Newborns

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Objective

To determine the concentrations of serum lipids and apolipoprotein B (apo-B) in a population of normal full-term and preterm newborns in a city in Southern Brazil, and assess the impact of gestational age and birth weight on these values.

Methods

Two hundred and twelve newborns of both genders were studied, 142 of whom were full-term (>37 weeks of gestation) and 70 preterm (<37 weeks of gestation). According to their birth weights, the full-term and preterm newborns were classified as small for gestational age or appropriate for gestational age. Umbilical cord blood was collected for biochemical analysis.

Results

The total cholesterol, LDL-C, HDL-C and apo-B values were higher in preterm newborns (79±34, 26±6, 45±15 and 36±14 mg/dL, respectively) than in full-term newborns (58±19, 20±10, 31±14 and 28±7 mg/dL, respectively; $p < 0.0001$). Inversely, triglyceride values were lower in preterm newborns (36±14 mg/dL) than in full-term newborns (43±25 mg/dL; $p < 0.0018$). Gender and size at birth did not have any impact on the values of total cholesterol and fractions, triglycerides, and apo-B.

Conclusion

Plasma concentrations of lipids and apo-B in the population of newborns studied are similar to those in newborns from other countries and continents reported in medical literature and, as expected, are markedly lower than the values mentioned in literature for infants over two years of age. Fetal maturity has an impact on the concentration of lipids in newborns, but birth weight does not have any effect on these parameters.

Key words

Newborns, cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein.

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Coronary heart disease is the leading cause of morbidity and mortality in the adult population in the Western world[1]. In Brazil, cardiovascular diseases and other manifestations of atherosclerosis account for one-third of all causes of mortality among adults[2], and dyslipidemia, which is one of the main risk factors for atherosclerosis, may have its onset during childhood[3]. Generally, clinical sequelae of atherosclerosis occur in adulthood, but several experimental and clinical studies have shown that these lesions may have their onset at a very early age. In their multicentric study named PDAY (Pathobiological Determinants of Atherosclerosis in Youth), McGill and McMaham made important remarks about the progression of fatty striae, the initial atherosclerotic lesions that may be detected in aortas of children and coronaries of adolescents. In this study, the transition from fatty striae to atherosclerotic plaques detected in young people from 25 years of age on, was associated to the increase in serum concentrations of LDL-C (low-density lipoprotein cholesterol) and VLDL-C (very low-density lipoprotein cholesterol), and decrease in HDL-C (high-density lipoprotein cholesterol) levels[3]. Over the last decade there was a great deal of interest about whether the lipid changes observed during the fetal period could result in permanent changes in the structure and functions of the organs that would be reflected in adult life. Some experimental and clinical studies have shown the presence of fatty striae in the aorta during the fetal development period[4-6], while other epidemiological investigations tried to link weight and lipid changes at birth to CHD in adult life; however, the results remain inconclusive[7-12].

Several clinical conditions may have an impact on serum lipid concentrations in newborns. Gestational age has an important effect on serum lipid and apolipoprotein concentrations, since as the fetus matures total cholesterol concentrations are reduced, while those of triglycerides increase[13,14]. Low birth weight associated with prematurity and alterations in intrauterine development, irrespective of gestational age, may be associated with increased total cholesterol and apolipoprotein B (apo-B) serum concentrations[8,15]. Other changes, such as perinatal infections and congenital malformations, may also affect the lipid profile of newborns[16]. As to the effect of maternal cholesterol serum concentration on fetal cholesterol concentration, the conclusions are controversial. Some authors concluded that this phenomenon could be potentialized by the mother's hypercholesterolemia[5], whereas others did not observe any correlation, even when the mother has hypercholesterolemia[17].

In our environment, the lipid profile of newborns is not known, but this is not the case in other countries. Knowledge of reference values for the lipid profile at the start of life may broaden the understanding of dyslipidemias and their associations with atherosclerosis, and help the preventive management of the disease even at very early age. Our objective was to determine the serum concentrations of lipids and apolipoprotein B (apo-B) in the umbilical cord blood of a population of normal full-term and preterm newborns in a city in Southern Brazil, and assess the influence of gestational age and birth weight on the lipid parameters.

Methods

A group of 212 newborns, 107 females and 105 males, was consecutively studied at the maternity ward of the *Hospital Universitário Regional Norte do Paraná da Universidade Estadual de Londrina (HURNP-UEL)*, out of a total of 496 births recorded over the period.

Inclusion criteria: The population studied included only full-term (≥ 37 weeks of gestation) and preterm (<37 weeks of gestation) newborns of both genders, born by normal delivery and c-section, without evident malformations or perinatal complications.

Exclusion criteria: Post-term newborns (>41 weeks of gestation) born to diabetic eclamptic mothers, and those who suffered fetal stress such as perinatal infections, respiratory distress syndrome, conditions that may have an effect on lipid concentrations, were excluded of the study[15].

Gestational age was calculated according to the date of the mother's last menstrual period. After the birth, all newborns were weighed and classified as full-term and preterm according to their gestational age. Later, the newborns were divided into two subgroups according to their birth weight: small for gestational age (SGA), when the birth weight was below the 10th percentile adjusted for the gestational age, and appropriate for gestational age (AGA) when the birth weight was between the 10th and 90th percentiles, according to criteria set by Alexander et al[18].

Table 1 shows data for newborns' gestational age and weight. Out of the population of 212 newborns, 77% were full-term and 33% preterm; as to their weight for

Table 1 - Distribution of newborns according to gestational age and weight

Total=212 (m)	Preterm newborns			Full-term newborns		
	AGA (56)	SGA (14)	Subtotal (70)	AGA (124)	SGA (18)	Subtotal (142)
Mean gestational age, wks* ± SD	34.4 ± 2.1	34.4 ± 1.8	34.4 ± 1.9	38.8 ± 1.0	37.8 ± 1.1	38.3 ± 1.0
Mean weight, kg ± SD	2385 ± 505	1706 ± 380	2200 ± 607	3241 ± 412	2260 ± 593	3124 ± 50

Wks - weeks; AGA - Appropriate for gestational age; SGA - Small for gestational age; SD - Standard deviation*

the gestational age, 85% were classified as AGA and 15% as SGA.

The research protocol was approved by the Research Ethics Committee of the HURNP-UEL. After having received all necessary information to participate in the research and authorized the procedures, the mothers signed the informed consent form.

Biochemical determinations: Newborns' blood samples were obtained by puncture of the umbilical cord vein. Six milliliters of blood were drawn from the proximal end of the umbilical, immediately after it had been clamped to avoid possible contamination with maternal blood[19].

Serum concentrations of total cholesterol, LDL-C, HDL-C, and triglycerides (TG) were determined from the samples. In 130 newborns, the serum concentration of apolipoprotein B was also obtained.

Blood samples were analyzed by the Dimension AR autoanalyzer (Dade Behring, Newark, USA), with reagent kits and protocols supplied by the manufacturer. Serum determinations of total cholesterol and triglycerides were obtained by endpoint colorimetric assays; to determine HDL-C, a precipitation method with sodium-magnesium phosphotungstate was used. LDL-C concentrations were calculated by the Friedewald equation[20] which is also used in newborns[21,22]. On the other hand, the assay for apo-B was performed by nephelometry with a Behring Nephelometer 100 Analyzer® (Dade Behring, Newark, USA).

Statistical Analysis: Data were transferred to an electronic spreadsheet (Excel, 2000 version) and later analyzed with SAS and SPSS software, 8.0 and 10 versions, respectively. Serum concentrations of lipoproteins were expressed as means and standard deviations.

The differences between the full-term and preterm newborns, and the SGA and AGA subgroups, were calculated using variance analysis for each value of serum concentration, considering a gamma distribution (non-normal), McCullagh & Nelder, 1989[23]. The level of statistical significance was established as $p < 0.05$.

Results

Table 2 shows serum concentrations of total cholesterol and fractions, triglycerides and apo-B of full-term and preterm newborns, also illustrated in Figure 1. TC, LDL-C, HDL-C and apo-B values were higher in preterm than in full-term newborns ($p<0.0001$). Inversely, triglyceride values were lower in preterm newborns than in full-term newborns ($p<0.0018$).

As to serum concentrations of cholesterol, no gender differences were observed among full-term newborns (males 70±28, females 66±28, $p>0.05$), nor among preterm newborns (males 80±43; females 78±40, $p>0.05$).

Table 2 shows plasma lipid and apo-B values in newborns with appropriate weight for gestational age and small for gestational age, in the preterm and full-term groups. The weight at birth did not influence total cholesterol, LDL and HDL, triglyceride, and apo-B values, both in full-term and preterm newborns.

Discussion

This study documented the lipid profile and the serum concentration of apo-B in the umbilical cord blood of newborns in a city in Southern Brazil.

The values found for total cholesterol, LDL-C and HDL-C were similar to those described by other researchers in different populations of newborns in Chile[24], Europe[25,26], North America and Canada[27-29], Africa[30] and Japan[31]. However, Juarez et al[21] described lipoprotein values in Mexican newborns higher than those shown in this study and those previously reported, and this is an exception. This discrepancy may be due to a particularity of the Mexican population, since our values are compatible with those of most studies described. The triglyceride values obtained, which reflect mainly the serum concentration of VLDL (very low-density lipoprotein) particles, were also similar to those found by other authors[14,26]. It is worth mentioning that the lipid composition of the umbilical cord blood drawn immediately after birth corresponds exactly to that of blood drawn from a peripheral vein[19]. This procedure avoids the traumatism that venous punctures may cause to newborns.

Table 2 - Plasma lipid and apo-B concentrations (in mg/dL) of newborns participating in the study, divided into groups according to their fetal maturity and birth weight (AGA* and SGA). Values are means ± Standard deviations**

	Preterm newborns			Full-term newborns			Mean	p
	AGA	SGA	Subtotal	AGA	SGA	Subtotal	Total	(Preterm x Full-term)
Total cholesterol	76±30	90±47	79±34	57±19	63±19	58±19	65 (61-69)	<0.0001
LDL-C	26±14	27±14	26±6	19±8	21±11	20±10	22 (21-23)	<0.0001
HDL-C	44±19	54±33	45±15	30±14	34±11	31±14	36 (38-33)	<0.0001
TG	34±13	43±17	36±14	42±25	48±25	43±25	41(38-44)	<0.0018
Apo-B	34±12	44±20	36±14	27±7	28±5	28±7	30 (28-32)	<0.0001

AGA - Appropriate for gestational age; SGA - Small for gestational age; ( ) = 95% confidence interval

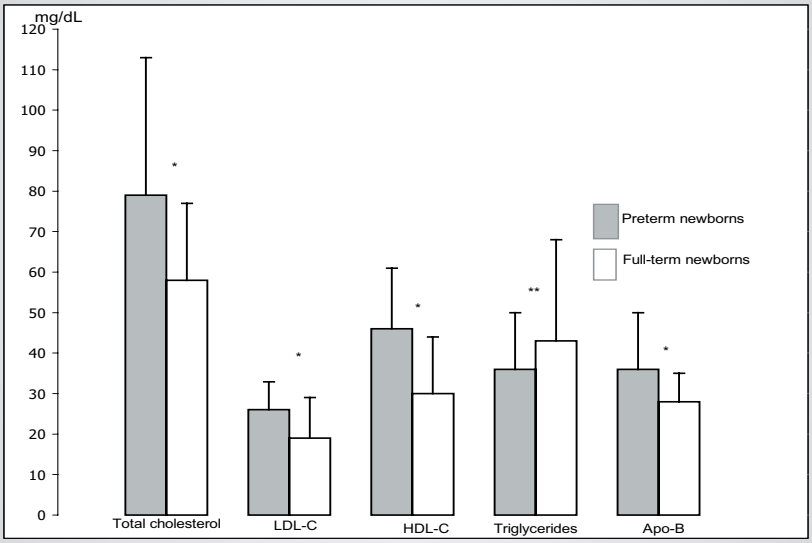

Fig.1 *- Means and standard deviations of the lipid profile of preterm AGA and SGA newborns, and full-term AGA and SGA newborns; * p<0.0001; ** p<0.001*

Serum concentrations of total cholesterol and fractions and triglycerides obtained from the newborns in this study were markedly low when compared to the reference values for school age children[32] and adopted by the Brazilian Society of Cardiology. Medical literature describes a sharp increase in serum levels of the lipid profile during the first week of life when breastfeeding starts, up until 6 months of age[14]. Hence, mean values of total cholesterol increase from 70 mg/dL to 150 mg/dL, of LDL-C from 30 mg/dL to 100 mg/dL, and triglycerides from 32 mg/dL to 58 mg/dL[26]. After the first year of life, these values rise slowly and, around the second year of life, come close to those observed in adolescents and adults[33]. For this reason, newborns have a peculiar lipid profile when compared to infants, children, or adolescents.

This study also showed that the LDL-C/HDL-C ratio in full-term newborns was 0.6, identical to those of preterm newborns (0.6). Therefore, from the total cholesterol value detected in newborns, only 34% corresponds to the LDL-C fraction and more than a half (56%) corresponds to the cholesterol present in the HDL-C fraction. It is interesting to observe that, according to international reference values[32] for children above two years of age and adolescents, the LDL-C/HDL-C ratio is 1.7, a lot different that of from newborns, and the LDL-C fraction is approximately twice as much (70%)[33]. In Brazil, in the two studies conducted with children from six years of age on, the LDL-C/HDL-C ratio was higher, 1.8, in Bento Gonçalves (RS) and 2.1 in Campinas (SP), as was the frequency of undesirable values of total cholesterol (>180 mg/dL) with 30% and 35%, respectively[34,35]. These results show that from the age of two an inversion takes place in the serum LDL-C and HDL-C fractions relative to the neonatal period, differentiating this period from the others even more. This inversion seems to be more striking among Brazilian children, probably because the atherogenic events in this population begin in childhood.

The determination of apo-B in full-term and preterm newborns was also very low when compared to reference values for children over two years of age. The tendency of its concentration being lower in the population studied followed the low levels of the circulating LDL-C fraction and the LDL-C/apo-B ratio in full-term and preterm newborns (0.7), similar to those described in medical literature[28,29,36]. This possibly happened because the serum concentration of apo-B is mainly related to the concentration of LDL particles, despite the fact that this determination also includes other classes of lipoproteins that contain apo-B, such as VLDL, IDL (intermediate-density lipoprotein) and Lp(a) (lipoprotein a).

In this study, we did not classify the newborns according to gender because no differences were found in the total cholesterol and fractions, and triglyceride values between males and females, results that are consistent with findings in medical literature[30]. We did not classify the newborns according to race either, since, according to Glueck et al[27], this factor does not influence the lipid profile and also because of the undeniable racial miscegenation that characterizes the Brazilian population.

Another important aspect in this study is the lipid profile of newborns according to their fetal maturity. The total cholesterol level was higher in preterm compared to full-term newborns. Inversely, triglyceride values were higher in full-term compared to preterm newborns, with a divergent tendency in total cholesterol and fractions and triglyceride values. This variation was also reported in other studies in literature[15,37] and is attributed to the consumption of nutrients, mainly fat, in order to accelerate fetal development close to birth date[17].

The lipid profile in these results was not affected by the newborn being considered small or appropriate for the gestational age. This characteristic generates controversy

in medical literature, as some works correlate prematurity and low birth weight with a higher incidence of coronary artery disease in adults, which, on the other hand, may be related to the lipid profile at birth[38,40]. However, these are hypothesis that need to be confirmed by better-controlled studies.

This study determined the plasma lipid and apo-B concentrations in newborns in a city in Southern Brazilian, and the impact of fetal maturity and birth weight on these parameters. Total cholesterol, LDL-C, HDL-C, triglyceride, and apo-B values were similar to those of newborn populations in other countries; fetal maturity had an impact on these values, but birth weight did not influence these parameters. Although scarce, national data from previous studies show that the frequency of undesirable levels of cholesterol in children 6 years of age or older is high. Therefore, knowledge of lipid profile values from the neonatal period has an intrinsic value from the epidemiological and pathophysiological point of view, broadens our understanding of their relationship with cardiovascular diseases, and helps to develop preventive planning in earlier phases of life.

Potencial Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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