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ORIGINAL ARTICLE

Evolution of the lipid, glycemic and blood pressure profile of premature infants: a longitudinal study

Evolução do perfil lipídico, glicêmico e pressórico de prematuros: estudo longitudinal

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ABSTRACT

Objective: To relate the evolution of the lipid, glycemic and blood pressure profile of premature infants from birth to 2 years corrected age with the classification of birth weight and sex. **Methodology:** Longitudinal study, initial sample of 71 premature infants, of which 31 completed outpatient follow-up. Evaluated at birth, discharge, 6 months and 2 years corrected age (weight, gestational age, lipid, glycemic, blood pressure profile). **Results:** Blood glucose, total cholesterol, blood pressure and triglycerides were not statistically significant in relation to birth weight nor throughout follow-up. Total cholesterol (p=0.18) and blood glucose underwent interaction with sex. Blood pressure was higher than expected at 2 years old. Growth was uniform regardless of sex. **Conclusion:** The lipid, glycemic and blood pressure profile of premature infants during follow-up was not influenced by the birth weight classification. The cholesterol and blood glucose concentrations were influenced by sex.

Descriptors: Infant, Premature; Continuity of Patient Care; Lipid Metabolism; Blood Glucose; Neonatal Nursing.

RESUMO

Objetivo: Relacionar a evolução do perfil lipídico, glicêmico e pressórico de prematuro do nascimento aos 2 anos de idade corrigida com a classificação de peso ao nascer e sexo. **Metodologia:** Estudo longitudinal, amostra inicial de 71 prematuros, destes, 31 completaram o acompanhamento ambulatorial. Avaliados ao nascer, alta, 6 meses e 2 anos de idade corrigida (peso, idade gestacional, perfil lipídico, glicêmico, pressão arterial). **Resultados:** Glicemia, colesterol total, pressão arterial e triglicerídeos, não foram estatisticamente significantes em relação ao peso ao nascer e ao longo do seguimento. Colesterol total (p=0,18) e glicemia sofreram efeito de interação com o sexo. Pressão arterial acima do esperado aos 2 anos. Crescimento foi uniforme independente do sexo. **Conclusão:** O perfil lipídico, glicêmico e pressórico dos prematuros ao longo do acompanhamento não foi influenciado pela classificação de peso ao nascer. O sexo influenciou as concentrações de colesterol e a glicemia.

Descritores: Recém-nascido Prematuro; Continuidade da Assistência ao Paciente; Metabolismo dos Lipídeos; Glicemia; Enfermagem Neonatal.

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INTRODUCTION

Premature birth is considered a public-health problem, since in the last decades there has been an increase in rates both in the world and in Brazil. Consequently, there was an increase in the survival of Premature (PT) infants, with increasingly lower birth weight and a higher degree of prematurity, that is, Small for Gestational Age (SGA). This caused an increase in the number of children with special health needs due to the repercussions of prematurity[1].

These consequences result in complications for PT infants at birth in hospitalization, such as: infections, hyaline membrane disease, intraventricular hemorrhage, bronchopulmonary dysplasia and retinopathy of prematurity[2]. After hospital discharge, these repercussions can be seen in changes in growth speed, as well as in the oral motor sensory system, in this case exposing PT infants to greater risk of early weaning and feeding difficulties[3].

Other changes are related to the metabolic profile, such as the development of diabetes mellitus, heart disease and obesity[4], can be observed in later periods of the PT infant's life, such as adolescence and adulthood. The association of these changes in relation to the degree of prematurity and birth weight has been evidenced in studies, which reveal that the lower the GA and being born small for GA, the greater the risk of accelerated weight gain in the postnatal period[5]. Furthermore, the type of food offered during this period has been causing long-term consequences such as cardiovascular problems, obesity and Metabolic Syndrome (MS)[6,7].

Although a sedentary lifestyle, a diet rich in fats, obesity, smoking, and alcohol are considered to be predisposing factors to atherosclerotic cardiovascular diseases in adults, it was identified that the genesis of atherosclerotic lesions begins while still intrauterine, according to a hypothesis created by Barker in 1995[8]. In this hypothesis, adaptations occur in the malnourished fetus between the middle and the end of pregnancy, adaptations which can be seen in the form of cardiovascular, biochemical or endocrine changes related to cholesterol metabolism, insulin responses to glucose, and structural and functional changes in the internal organs, leading to inadequate growth of the fetus. For Barker[8], the series of these events during the initial phase of life can trigger the development of atherosclerotic heart diseases in adulthood. The recognition of this hypothesis highlights the importance of assessing the lipid profile in the pediatric age group, since, if the premature development of the disease can be anticipated in childhood, cardiovascular events can be effectively prevented by taking appropriate measures.

Considering that PT infants usually present low birth weights, they would be subject to a greater risk of developing cardiovascular changes in the long term. Therefore, the continuous and accurate ambulatory follow-up of PT infants after hospital discharge is a necessary goal, viewing early identification of risks for possible changes in their growth, development, or markers for metabolic changes.

In Brazil, investigations about these repercussions among PT infants are still new. Recently in the south of the country, a study[9] on the prevalence of MS in this group of children evaluated after 2 years corrected age, showed that 15.1% of this group had MS. Of the total sample, 57.5% had changes in Blood Pressure (BP), 29.2% had low HDL values, 22.6% had high Triglycerides (TG) and 18.8% had abdominal obesity.

Another study[10] highlighted the concern with PT infants and the repercussions for their metabolisms, focusing on the development of future cardiovascular, endocrine and obesity problems. This study in the western region of Paraná identified 30% of premature-born adolescents with excess weight. Of these, 22% were overweight and 8% were obese, of which 8% had developed MS identified by the presence of altered waist circumference, BP and TG; 30% had altered blood pressure, 22% had higher Total Cholesterol (TC), and 41% had elevated TG[11].

Although the aforementioned Brazilian studies address the metabolic profile of PT infants, there are still few longitudinal studies. Thus, long-term follow-up is lacking in the literature of national studies. Therefore, there is a need to invest in research that evaluates PT infants during follow-up, with a view to promote the health of this group and reducing the risks of future changes as chronic health conditions become relevant. It is believed that lower birth weight may be related to changes in their lipid, glycemic, and blood pressure profiles at 2 years corrected age. In this context, the objective of this study was to relate the evolution of the lipid, glycemic, and blood pressure profile of premature infants from birth to 2 years corrected age with the classification of birth weight and sex.

METHODS

Quantitative, longitudinal, prospective study with analysis of primary and secondary data. In this study, the database produced by the field research of Barreto, 2017[12], with 71 PT infants, was used in the first stage, which aimed to evaluate the growth of these children from birth to 6 months corrected age (CA) and metabolic profile according to the adequacy of birth weight.

In the second stage, data from the PT infants that comprised the primary research sample were collected when they were at 2 years CA. They were approached when they attended the return visit to the outpatient clinic. As this is a longitudinal investigation and, in this study design, losses are imminent throughout the follow-up, the sample at 2 years

CA was reduced. It should be noted that based on the sample collected in the primary study[12], which refers to all PT infants included in the primary study and returned to the follow-up appointment at 2 years CA.

The inclusion criteria in the study were: having a GA less than 37 weeks, delivery at the hospital under study, and stay in the neonatal Intensive Care Unit (NICU) of at least seven days. In the follow-up study, they were to return to the outpatient clinic for appointments scheduled during the specified periods. All PT infants with congenital malformations and/or adolescent mothers without a legal guardian present at the appointments were excluded.

From the primary research database[12], a new database was created, composed of the following variables: birth weight (g), sex, GA, chronological age, lipid (triglycerides – mg/dL and total cholesterol – mg/dL) and glycemic (glucose – mg/dL) profiles, blood pressure (BP in mmHg). These variables were evaluated in four periods: birth, discharge from the NICU, 6 months CA, and the data collected about the same variables at 2 years CA were added.

The data collection period related to the second year of CA occurred between August 2017, and September 2018. Anthropometric data collection, BP verification and collection of biochemical tests followed the data collection protocol proposed in the study by Barreto[12]. Biochemical tests were requested by the neonatologist during the follow-up appointment and performed using the dry chemistry method, with a sensitivity of 10 mg/dL for triglycerides, 20 mg/dL for glucose and 50 mg/dL for cholesterol. Insulin was analyzed using the electrochemiluminescence method with sensitivity of 0.03nIU/mL. For anthropometric evaluation, weight (g) was measured with the PT infants unclothed, on a digital scale (Filizola®), with a sensitivity of 5 g, authorized by Inmetro. Length (cm) was obtained with the PT infants in the supine position by means of an anthropometric aluminum ruler (100 cm). The measurement of the head circumference (HC) was obtained using an inextensible millimeter tape (mm), positioned over the occipital protuberance and the arch of the eyebrows.

To calculate the Z-score of weight, length and head circumference, as well as the classification of weight adequacy for CA, the neonatal growth curves of Fenton and Kim (2013), available on the online calculator (http: //www.ucalgary.ca/fenton/2013chart), up to 40 weeks CA were used. After this, the curves recommended by the World Health Organization (WHO) (WHO/2006) and version 3.2.2 of the WHO Anthro program, available online (https://www.who.int/childgrowth/en/) were used.

The biochemical test and blood pressure values were compared to the reference values, according to the Brazilian Consensus for the Standardization of the Laboratory Determination of the Lipid Profile[13], as follows: Glycemia 80–126 mg/dL (postprandial); triglycerides <85 mg/dL (without fasting); Total Cholesterol <170 mg/dL (without fasting); Minimum BP:55/30 mmHg; Maximum BP: 77/56 mmHg.

To achieve the objective proposed in the study, the PT infants were grouped according to the ratio of birth weight versus gestational age, thus allowing the compared groups to be homogeneous regarding this variable. Data analysis was performed using STATISTICA 7. The data were described using mean (standard deviation) and median (minimum and maximum values). The distribution of residues was verified by the Shapiro-Wilk test, as well as the homogeneity of variances by the Cochran test. According to the relationship between birth weight and lipid, glycemic and blood pressure profile, the sample was divided into two groups: Premature Infants Small for Gestational Age (SGA, n=3) and Premature Infants Adequate for Gestational Age (AGA, n=28). The PT infants were also evaluated in the referred periods in relation to sex. It should be noted that among the PT infants included in the primary study in the classification of birth weight, 12.64% (9) were SGA and 87.36% (62) were AGA. In the follow-up sample, 9.67% (3) were SGA and 90.33% (28) were AGA. Losses over the two-year follow-up were 56% and occurred for the following reasons: death after 6 months of life of the PT infant; moved to another city; non-attendance of appointments scheduled by the outpatient team; phone number change that prevented contact to schedule an appointment at the clinic.

To measure the effect of predictors (sex and time; AGA and SGA) on the means of weight variation, systolic pressure, diastolic pressure, glucose, triglycerides and cholesterol, analysis of variance (ANOVA) was applied, followed by Fisher's LSD multiple comparison test. For all tests used, the level of significance considered was 5%.

This study is part of the project entitled Repercussions of prematurity: maternal stress and metabolic programming after hospital discharge, approved by the National Council for Scientific and Technological Development (CNPq), process no. 457109/2014-9, which was approved by the Ethics and Research Committee of Unioeste under ruling no. 1,134,712.

RESULTS

Of the final study sample at 2 years CA, which totaled 31 PT infants, 18 were male and 13 were female. They remained in continuity of care in outpatient follow-up for at-risk newborns of a university hospital in Paraná. The data are displayed first in a descriptive manner, showing the minimum and maximum values of each variable that make up the PT infants' blood pressure profile, serum concentrations of total cholesterol, blood glucose and triglycerides, from birth to 2 years CA (Table 1). To follow is the evolution of the variables: weight, total cholesterol,

glycemia, triglycerides and insulin, according to birth weight classification in AGA and SGA, separately.

The serum concentrations of triglycerides, cholesterol and glycemia, from birth to 2 years CA presented values above the reference for age. Although BP at 6 months CA showed higher values, there was a reduction in the parameters at 2 years CA.

Assessment of weight evolution

The evolution of weight over the 2 years corrected age of the PT infants did not show a statistically significant difference in the interaction of the groups classified by the adequacy of birth weight (AGA and SGA) and assessment periods ($F_{3,57}$=0.712; p=0.548). When mean weights of both groups were evaluated over time, adequate growth of the PT infants was observed, with only a significant reduction in values at discharge (p<0.05) (Figure 1).

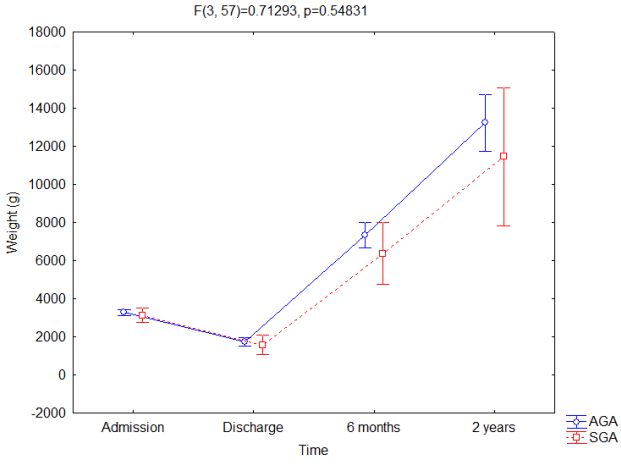
Regarding sex, the mean variation in weight values only had an influence in terms of age (p<0.001), thus indicating the uniform growth of children regardless of sex (Admission – Male= 1.975±849; 2 years= 12.041±2.124; Admission – Female= 1.534±483; 2 years= 13.919±3.403).

Assessment of the evolution of blood pressure, glycemia, triglyceride and total cholesterol during follow-up

In regard to the evolution of glycemia ($F_{3,48}$=4.921; p=0.004), triglycerides ($F_{3,48}$=0.814; p=0.492), and total cholesterol ($F_{3,48}$=0.551; p=0.650), the relationship between birth weight and the AGA and SGA groups was not statistically significant. When analyzing the comparison for the three biochemical variables in each of the follow-ups, there were no statistically significant differences (p>0.05).

Regarding glycemia and its relation to birth weight, despite the low number of SGA newborns at the beginning of the assessments (admission and discharge), there was a wide variation in blood glucose values, which stabilized afterwards. When evaluating the mean variation of glycemia values in relation to sex and age (Figure 2), it was found that there was a statistically significant effect (p=0.004). Thus, male children, at birth and upon discharge from the NICU, had significantly higher blood glucose values when compared to females. Observing a decrease in values at 6 months CA (Male= 79.35±7.13; Female= 85.50±12.92), becoming equivalent between sexes at up to 2 years CA.

Regarding the evolution of triglycerides, it was identified that when the means of both groups (AGA and SGA) were evaluated throughout follow-up, there was an increase in the values of serum TG concentrations at 6 months when compared to the other evaluation periods (p<0.05) with a gradual decrease until 2 years CA (Figure 3). Again, it is worth mentioning that there is a wide variation in triglyceride values



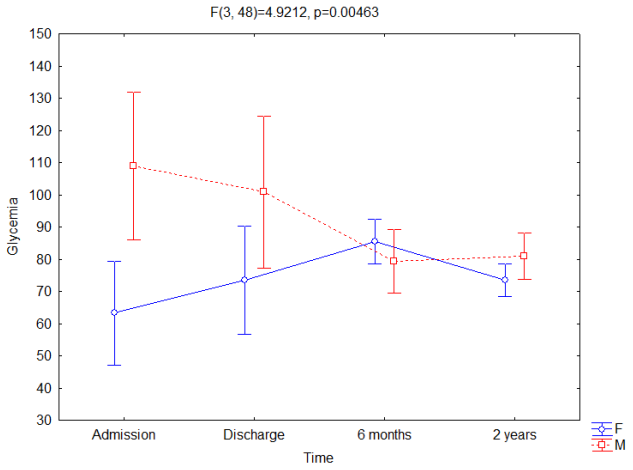
AGA: adequate for gestational age; SGA: small for gestational age.

Figure 1. Mean weight gain (g) and confidence interval (95%) over two years of assessment of the groups Premature Infants Adequate for Gestational Age and Premature Infants Small for Gestational Age (n=31). Cascavel, PR, Brazil, 2018.

Table 1. Means and confidence intervals (95%CI) of serum triglyceride concentrations, total cholesterol, glycemia, and systolic and diastolic blood pressure, from birth to 2 years corrected age. Cascavel, PR, Brazil, 2018.

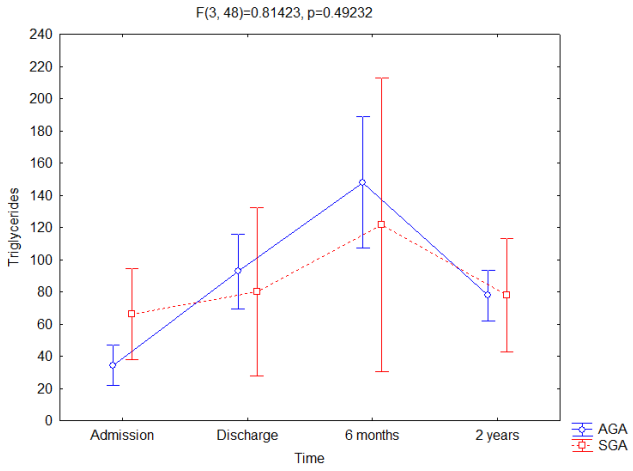
	Birth (n=71)	6 months CA (n=50)	2 years CA (n=28)
TG	47.70 [40.48–54.92]	146.7 [126.32–167.08]	77.50 [66.88–88.12]
TC	85.20 [72.88–87.64]	140.08 [131.25–148.91]	148.32 [135.71–160.94]
GLY	79.75 [68.23–89.36]	85.10 [81.29–88.91]	77.81 [74.21–81.42]
SAP	65.30 [61.78–68.82]	103.96 [97.01–110.91]	87.40 [84.03–90.82]
DAP	36.40 [33.15–39.63]	69.24 [62.27–76.21]	60.12 [57.20–63.03]

TG: triglyceride; TC: total cholesterol; GLY: glycemia; SAP: systolic arterial pressure; DAP: diastolic arterial pressure; CA: corrected age.



F: female; M: male.

Figure 2. Means and confidence intervals (95%CI) of female and male glycemia throughout admission, discharge, 6 months and 2 years of life.



AGA: adequate for gestational age; SGA: small for gestational age.

Figure 3. Mean and confidence interval (95%) of triglycerides over two years of evaluation of the Premature Infants Adequate for Gestational Age and Premature Infants Small for Gestational Age groups (n=31). Cascavel, PR, Brazil, 2018.

among newborns classified with SGA. This can be related to the low n sample (n=3).

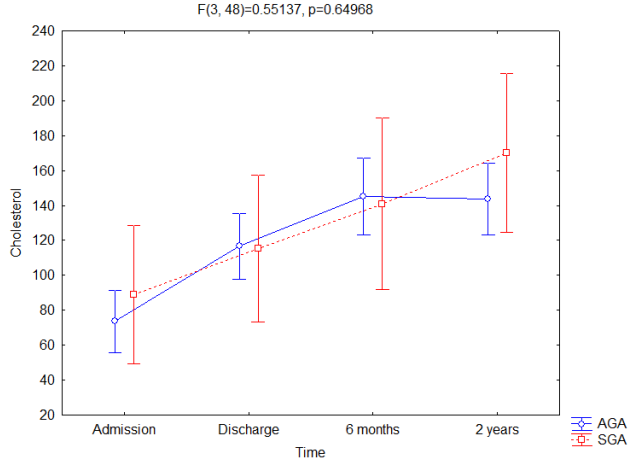
When evaluating the mean variation of triglyceride values, it was found that there was only an effect on age ($p<0.001$), indicating, therefore, a uniform increase in triglyceride values up to 6 months of age, and subsequent reduction at 2 years of life, regardless of sex (Admission – Male= 50±40; 2 years= 76±32; Female= 37±22; 2 years= 76±26).

Concerning the assessment of the evolution of total cholesterol, the means of AGA and SGA over time showed a gradual increase in values from six months onward when compared to the values obtained at admission and at discharge for SGA ($p<0.05$), while the AGA maintained stable concentrations beginning at sixth months (Figure 4).

The mean variation in total cholesterol values (Figure 4) showed an effect of the interaction of sex and lifetime ($F_{3.48}=0.551$, $p=0.650$). Thus, male children, at birth, tended to have lower cholesterol values (53±14) when compared to females (86±34), values that were equivalent at 6 months (Male=161±44; Female=138±33) and 2 years of age (Male=150±36; Female=148±40).

Considering the assessment of the evolution of systolic pressure (Figure 5), it was found that there was no statistically significant difference in the interaction of the groups regarding birth weight and assessment periods ($F_{3.45}=0.236$; $p=0.871$). When the means of both groups were evaluated over time, a significant increase in values was observed after 6 months when compared to the values obtained at admission and at discharge ($p<0.05$).

Regarding the assessment of the evolution of diastolic pressure, it was found that there was no statistically significant difference in the interaction of the groups and evaluation

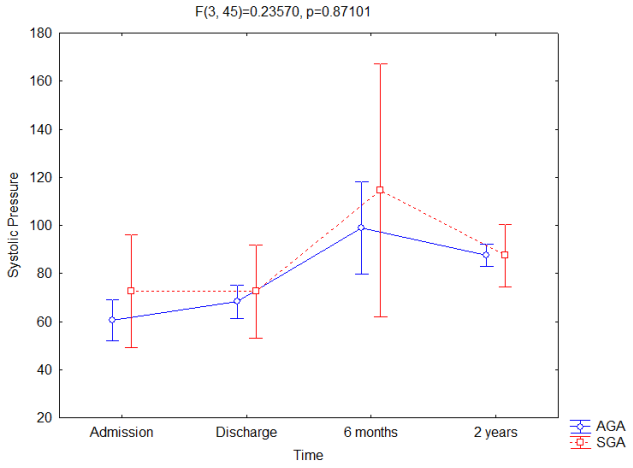


AGA: adequate for gestational age; SGA: small for gestational age.

Figure 4. Mean cholesterol and confidence interval (95%) over two years of assessment of the Premature Infants Adequate for Gestational Age and Premature Infants Small for Gestational Age groups (n=31). Cascavel, PR, Brazil, 2018.

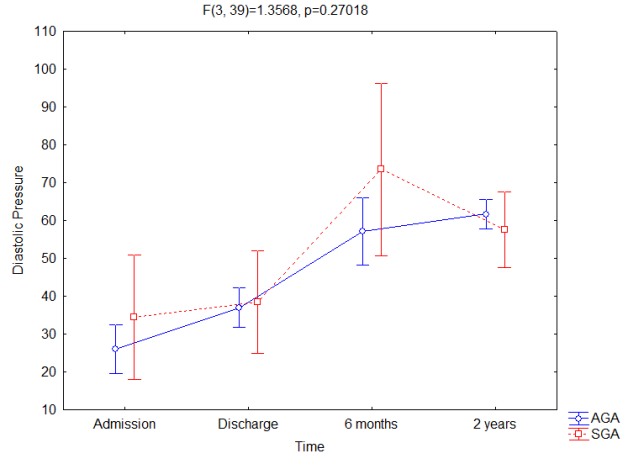
periods ($F_{3.39}=1.357$, $p=0.270$). When evaluating the means of both groups over time, a significant increase in the values at 6 months was observed when compared to the values obtained at admission, discharge, and at 2 years ($p<0.05$) (Figure 6).

Systolic and diastolic blood pressure only showed the effect of age ($p<0.001$), indicating, therefore, a uniform increase in blood pressure regardless of sex.



AGA: adequate for gestational age; SGA: small for gestational age.

Figure 5. Means and confidence intervals (95%CI) of systolic blood pressure of the Premature Infants Adequate for Gestational Age and Premature Infants Small for Gestational Age groups throughout admission; discharge, 6 months, and 2 years of life.



AGA: adequate for gestational age; SGA: small for gestational age.

Figure 6. Means and confidence intervals (95%CI) of diastolic blood pressure of the Premature Infants Adequate for Gestational Age and Premature Infants Small for Gestational Age groups throughout admission, discharge, 6 months, and 2 years of life.

DISCUSSION

The findings showed that the serum concentrations of glucose, triglycerides and total cholesterol, as well as, the blood pressure of PT infants assessed from birth to 2 years CA, were not influenced by birth weight (SGA or AGA) at any time of the evaluation. However, it was observed that the results of the obtained exams had values above the reference adopted for analysis. It should also be noted that the total cholesterol values gradually increased until 2 years of age among those born SGA. It was evidenced that glycemia and total cholesterol were influenced by sex and PT infant evaluation time.

Throughout the first two years of life, it was found that the PT infants had adequate growth, regardless of sex and birth weight classification. The weight of the evaluated PT infants showed a recovery above -2 Standard Deviation in the reference curves[14], indicating that there was longitudinal growth.

Blood glucose evolution did not show any significant difference in any of the evaluated periods. Male infants had higher blood glucose levels at birth and at discharge from the NICU, however, the values were equivalent to female PT infants at 2 years CA. Evidence found about the PT infant glycemic profile addresses this data while still in the neonatal period. Therefore, it is impossible to make comparisons with the findings in our study[15]. It should be noted that the blood glucose of PT infants at 2 years CA (77.81 mg/dL) was within the reference values (80–126 mg/dL)[13].

Although the evolution of triglycerides in our study demonstrated that the means of AGA and SGA were not statistically significant over the analyzed time, regardless of sex, it is evident that the values, especially at 6 months CA, were higher than those established by the referred parameters[13]. This situation puts PT infants at greater risk of developing MS, since high concentrations of triglyceride-rich lipoproteins in premature infants and low birth weight HDL cholesterol are potential risk factors for cardiovascular diseases later in life[16].

Among PT infants assessed in southern Brazil[9], changes in serum TG values at 2 years were identified in 22.6% of the sample. In Cuiabá[17], the values found among premature infants studied for TG were 26–176 mg/dL for children aged one year, and 27-135 mg/dL for children aged 2–5 years. Plasma concentrations were similar to those found in our study at 2 years of age, in which the TG varied between 38–141 mg/dL. Thus, children born prematurely should be monitored and evaluated in relation to this parameter with greater accuracy throughout their childhood, since intrauterine growth restriction contributes to atherosclerosis in adulthood. To that end, investigating the mechanisms of the origins of health and disease development, including the assessment of metabolic factors, may contribute to a new approach in consultations with PT infants in outpatient follow-up, with a view to prevent atherosclerosis and insulin resistance. Likewise, the adequate management of malnutrition during pregnancy and neonatal growth in the early postnatal period must be a theme present in the management of NICUs[18].

It was evidenced in this study that the concentrations of TC among the AGA stabilized from the sixth month onward, while, in the SGA, they showed an increase from discharge of the NICU onward. Similar to the TG values, the TC also

has no reference value for children aged 0 to 2 years. In the Consensus[13] of 2016 the value set as a reference parameter is 170 mg/dL, regardless of whether fasting or not. A study[17] demonstrated minimum and maximum values of TC in an age group of 1 to 2 years, ranging from 62–225 mg/dL, similar to the value found in the present study (88–235 mg/dL). However, the evolution of cholesterol only presented statistical differences when the means were evaluated in both groups over time and according to sex, with a significant increase in values starting at 6 months old. Regarding the adequacy of birth weight and gestational age, the literature[19] confirms that SGA show less efficiency of cholesterol absorption between 8 to 12 years than those born AGA, in which the synthesis of predicted endogenous cholesterol was higher. Furthermore, the cholesterol absorption efficiency was lower in those who had a greater increase in the weight percentile between birth and follow-up. This was also observed in the present study, in which the SGA, as previously mentioned, had a gradual increase in TC up to the corrected age of two years, therefore, they have a higher risk of suffering metabolic changes in the long term.

In this context, both fetal growth and child growth are related to cholesterol metabolism programming in children born prematurely[19]. Thus, during the PT infant assessments, more specifically of those born SGA, in the follow-up after discharge from the NICU, attention should be paid to weight gain and the TC values of those children to prevent future damage to their health in adolescence and adult life.

The pressure profile of the studied sample, although not statistically significant in relation to sex and birth weight classification, showed a considerable increase during the follow-up, both in systolic and diastolic BP. These values are above the maximum indicated parameters of 77/56mmHg[13], starting at 6 months of age compared to the periods of birth and discharge. This finding is in agreement with evidence in literature that shows the prevalence of high BP in preterm children when compared to those born at term[20,21]. Studies have identified that PT hypertensive children, some diagnosed in the NICU and others in older age, the latter of whom are of a lower gestational age, spent longer in the NICU and have a higher incidence of perinatal risk factors for hypertension[22,23]. Thus, the need to routinely check BP in PT follow-up appointments emerges starting at 6 months CA.

From the convincing data that suggests cardiovascular diseases can be programmed in the womb[24], added to the fact that male and female fetuses may respond differently to the adverse intrauterine environment, resulting in sexual differences in cardiovascular diseases in later stages such as adolescence and adult life[25], it can be evidenced that PT infants in adverse intrauterine environments are more susceptible to developing cardiovascular problems throughout their lives.

Effects of this process are already identified at preschool age, such as the presence of systolic prehypertension, high glucose levels and hypercholesterolemia, showing an unfavorable cardiovascular risk profile the greater the degree of prematurity[20]. Thus, the implementation of routine cardiovascular programs for the follow-up of PT newborns beyond early childhood is suggested.

As this is a longitudinally designed study, in which losses from follow-up occur, the study sample was small, which is a limitation of the study, making generalizations impossible. This evidences the need for further research on this theme, with a larger sample to validate the data presented here. Likewise, in order to understand the early metabolic changes among PT infants, a study with a control group of full-term babies should be carried out. Another limitation refers to the non-crossing of the variable food profile with the lipid, glycemic, and blood pressure profile of PT infants. Thus, a suggestion for new studies is to include this aspect in their analyses and investigate the influence of food on these profiles, associated with prematurity.

CONCLUSIONS

The evolution of the lipid and glycemic profile of PT infants from birth to 2 years corrected age in relation to the adequacy of birth weight, indicated that the serum concentrations of glucose, triglycerides, and cholesterol from birth to two years showed values above the reference parameters. However, there was no influence of the weight classification in the referred profiles. BP in the sixth month of CA had higher values, which decreased at 2 years CA, regardless of sex.

Thus, based on the findings, it is suggested that postnatal monitoring of premature births should routinely assess their lipid, glycemic, and blood pressure profiles, further investigating the type of diet introduced to these children, so that cardiovascular changes in adulthood are prevented.

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