nutrición clínica y Dietética Hospitalaria

Artículo Original

Nutr Clín Diet Hosp. 2023; 43(1):12-19
DOI: 10.12873/431santos

Influence of prematurity on the nutritional, metabolic and inflammatory aspects of pre-school children

Simone RAPOSO MIRANDA, Camila Yandara Sousa VIEIRA DE MELO, Nathalia Fidelis LINS VIEIRA, Ana Célia OLIVEIRA DOS SANTOS

Institute of Biological Sciences, Universidade de Pernambuco, Recife, Pernambuco, Brazil.

Recibido: 17/noviembre/2022. Aceptado: 30/diciembre/2022.

ABSTRACT

Objective: To identify an association between prematurity and the nutritional, metabolic and inflammatory aspects of pre-school children.

Methods: This was a case-control study with 32 preterm children and 32 full-term children. A nutritional diagnosis was obtained through the anthropometric indexes of height/age (H/A) and BMI/Age (BMI/A) using the WHO AnthroPlus® program. Metabolic assessment was performed through the levels of fasting glucose, fasting insulin, total cholesterol, triacylglycerides, high-density lipoprotein and low-density lipoprotein. The inflammatory profile was identified through the serum levels of interleukin 6 (IL-6) and C-reactive protein (CRP).

Results: The assessment age of preterm children was 81 months ± 23.8. A shorter gestation time was associated with an increased waist circumference (p=0.035), and total cholesterol levels (p=0.031), and tended toward an association with higher interleukin 6 levels (p=0.062). Waist circumference was associated with higher adiposity (p=0.003) and with increased blood pressure (p=0.010).

Conclusion: Preterm birth was related to increased levels of total serum cholesterol and increased waist circumference, thereby suggesting a higher risk of future cardiovascular events. No association was observed between gestational age and birth weight with other nutritional, metabolic or inflammatory aspects in the pre-school children assessed.

Correspondencia:
Ana Célia Oliveira dos Santos
ana.oliveira@upe.br

KEYWORDS

Premature. Waist circumference. Hypercholesterolemia.

INTRODUCTION

The intrauterine period and the first years of an infant's life are sensitive to nutritional and metabolic factors, which may have both short- and long-term effects on their health, extending into adulthood. Metabolic disorders, such as insulin resistance, diabetes, hypertension and dyslipidemia, in addition to an increased risk of death from coronary artery disease, are associated with prematurity and low birth weight[1–3].

The hypothesis known as "metabolic imprinting" can be related to an early nutritional experience, which occurs during a specific, critical period of development, thereby causing a predisposition to certain diseases. Among the events that may influence "metabolic imprinting", catch-up growth has been identified as an important risk factor for excess weight in future life[4]. Catch-up growth occurs during the period between 6 months and 1 year of life and enables these individuals to attain weight, height or head circumference above 2 standard deviations (SD) in relation to the initial parameter for age or above percentile 10[5-6].

Studies have suggested that infants who experience catch-up growth in early infancy, especially in weight gain, are more prone to obesity at around 6 years of age[3,4,6]. This fact may be justified since events that occur during an infant's fetal life and in the immediate postnatal period are closely associated with being overweight in adulthood and with the metabolic disorders associated with obesity[7].

After a period of inadequate nutritional support in early life, such as in prematurity, the body responds with a hypersecre-

tion of growth hormone and a reduction in insulin-like growth factor type 1 (IGF-1). These endocrine alterations favor modifications in the adipose reserves, with a reduction in the subcutaneous adipose tissue and an increase in the visceral adiposity, thus leading to insulin resistance (IR)[6], which, together with oxidative inflammatory reactions, may be the focal point between obesity, metabolic syndrome and chronic diseases in adults[8-10].

Inflammation is associated with insulin resistance and central obesity. Increased levels of serum C-reactive protein (CRP), for example, demonstrate an association with these conditions[11,12]. However, due to its nonspecific response to different inflammatory conditions, it should be used with caution. Other markers are also characteristic of inflammatory conditions, including Interleukin 6 (IL-6), given its association with CRP synthesis, its correlation with hyperglycemia, systemic arterial hypertension (SAH) and cardiovascular events[11,12].

The aim of this study is to identify an association between prematurity and nutritional, metabolic and inflammatory aspects.

MATERIAL AND METHODS

This was an unpaired analytical and observational case-control study, with one case to one control. The study was carried from november 2015 to June 2016, out at an outpatient clinic exclusively for preterm children born in a referral hospital in the state of Pernambuco, Brazil, and which constituted the case group. The control group consisted of children from a general outpatient clinic. Both groups were composed of children of both sexes.

A total of 178 children were monitored at the preterm clinic. Former preterm infants with a gestational age of up to 36 weeks with no presence of malnutrition during the nutritional assessment were included in the study. Children were excluded if they were born twins; were diagnosed with down syndrome or other genetic syndromes; presented cerebral palsy or pathologies directly associated with being overweight/obese and/or that make anthropometric assessment impossible; presented with type 1 diabetes mellitus; were on enteral nutritional therapy; or presented with any infectious processes. After applying the exclusion criteria, 126 (78.8%) children remained in the study. An active search was carried out (via telephone), inviting parents and/or guardians to participate in the research. A total of 32 (25.4%) agreed to participate in the study. The control group was formed by taking into account the sex and chronological age of those who sought care at the outpatient clinic, totaling 32 children.

To collect the variables: weight, height and waist circumference (WC), anthropometric parameters were used following the techniques recommended by the World Health Organization (WHO, 1995)[13], performed exclusively by a trained nutritionist. The nutritional diagnosis was performed based on the anthropometric indexes height/age (H/A) and BMI/age (BMI/A), according to sex, based on the reference standard of the World Health Organization[14] and using the WHO AnthroPlus® program. The results were expressed in Z-Scores, and considered that children below two SDs presented nutritional deficits and those presenting above one SD for the indicator BMI/A were overweight or obese[13].

Participants were divided into three groups, such as small-for-gestational-age (<10th, SGA), appropriate-for-gestational-age (≥10th and <90th, AGA,), and LGA (≥90th,), based on birthweight and number of weeks of pregnancy[14], Blood samples were collected through peripheral puncture of the forearm vein, performed after a 12-hour overnight fasting, using dry tubes. Levels were analyzed of fasting glucose (FG), fasting insulin (FI), total cholesterol (TC), triacylglycerides (TG), high density lipoprotein (HDL) and low density lipoprotein (LDL), Interleukin 6 (IL- 6) and C-Reactive Protein (CRP).

Fasting glucose, total cholesterol, triglycerides and high-density lipoprotein dosages were determined by the automated enzymatic method (COBAS INTEGRA, ROCHE®). LDL was calculated using the Friedewald formula. Serum insulin and IL-6 were determined by electrochemiluminescence using specific reagents by Roche® E 4011 automated equipment. The CRP level was detected with the Cobas Integra 400 – Roche® equipment, using the Roche kit through the immunoturbidimetric method. Rigorous quality control criteria were adhered to.

Normal levels of FG ≤ 99 mg/dL[16] and TC ≤ 170 mg/dL were considered as desirable, borderline between 170 and 199 mg/dL and high > 199 mg/dL. TG was considered normal up to 100 mg/dL for children under 10 years of age and up to 130 mg/dL for children over 10 years of age. Levels of HDL cholesterol of >40 were considered normal for children under 10 years and of >35 mg/dL for those aged over 10 years[15]. For comparison between the case and control groups, normal cholesterol was considered as ≤170mg/dL) and borderline and high as >170mg/dL. The dyslipidemia classification was considered when a child presented total cholesterol and/or low HDL. Insulin levels between 3 and 25 mU/L [16], CRP levels below 3.0 mg/L [17] and IL-6 levels below 5.9 pg/ml [18] were considered normal. A child was considered to be suffering an inflammatory process with an elevated CRP and/or IL-6. Blood Pressure (BP) was measured using the auscultatory method with an aneroid sphygmomanometer or a mercury column, with systolic and diastolic blood pressure measured in millimeters of mercury (mmHg)[19].

For statistical analysis, data were entered into Microsoft Excel and analyzed in SPSS 25.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were tested for normality of distribution using the Kolmogorov-Smirnov test and presented as

mean and standard deviation the variables with normal distribution and as median and interquartile ranges the variables with non-normal distribution. Categorical variables were described as proportions. Associations between the categorical variables was tested using Pearson's X^2 tests or Fisher's Exact Test. The difference between two means was identified using the Student's t test or Mann Whitney test. To assess the existence of linear correlation, the Pearson Correlation test was performed. Measures were also adopted for the coefficients, in order to measure the degree of relationship between the variables. Thus $r < 0.4$ (weak correlation); $r \geq 0.4$ and < 0.6 (moderate correlation); $r \geq 0.6$ (strong correlation). The level of significance was set at $p < 0.05$.

The study was approved by the Human Research Ethics Committee at the Instituto de Medicina Integral Professor Fernando Figueira (IMIP), in accordance with resolution No. 466 from December 12, 2012, of the National Health Council under CAAE 25231414.0.3001.5201. Written informed consent was obtained from all parents/guardians in both groups.

RESULTS

The mean (SD) gestational age of preterm infants participating in the study was 31 (26-36) weeks, with a mean (SD) birth weight of 1527 (± 347) grams., of which 56.3% were female. Of the total, 40.6% were classified as small for gestational age (SGA), 37.5% appropriate for gestational age (AGA) and 21.8% large for gestational age (LGA). The current mean age among preterm infants was 81 months (± 23.8 SD), corresponding to approximately 6.7 years. There was no difference between a family history for hypercholesterolemia and for cardiovascular disease between the groups. The comparison with the control group of children born at term is described in Table 1. All children presented blood glucose levels within the normal range.

The general condition of both the case and control groups was similar at the time of assessment with a current average age of 88 months (± 28.8 SD). Differences were observed only in the data referring to the differentiation of the groups (gestational age and birth weight). In relation to the current nutritional status of term and preterm children, a significant

Table 1. Nutritional and metabolic parameters of case and control groups at a referral hospital, Brazil

Variables	Birth				Total		p-value
	Term		Preterm				
	N	%	N	%	N	%	
Sex							
Male	18	56.3	14	43.8	32	50.0	
Female	14	43.8	18	56.3	32	50.0	0.317*
Gestational age (mean ± standard deviation)	39 ± 1.2		31 ± 3.0		35 ± 4.5		**< 0.001***
Birth weight, in kg (mean ± standard deviation)	3.3 ± 0.3		1.5 ± 0.3		2.4 ± 0.9		**< 0.001***
Current height							
Normal height	30	93.8	29	90.6	59	92.2	
Short height	2	6.3	3	9.4	5	7.8	1.000*
BMI/Age							
Eutrophic (-2 to +2)	27	84.4	24	75.0	51	79.7	
Overweight (> +2)	5	15.6	8	25.0	13	20.3	0.351*
Waist Circumference							
Normal	25	78.1	17	53.1	42	65.6	
High	7	21.9	15	46.9	22	34.4	**0.035***

* Chi-squared Test, or Fisher's Exact Test.

Table 1 continuation. Nutritional and metabolic parameters of case and control groups at a referral hospital, Brazil

Variables	Birth				Total		p-value
	Term		Preterm				
	N	%	N	%	N	%	
Insulinemia							
Low	4	12.5	8	25.0	12	18.8	
Normal	27	84.4	22	68.8	49	76.6	
Elevado	1	3.1	2	6.3	3	4.7	0.399*
Total Cholesterol							
Normal	26	81.3	18	56.3	44	68.8	
High	6	18.7	14	43.7	20	31.3	0.031*
HDL Cholesterol							
Normal	21	65.6	23	71.9	44	68.8	
Low	11	34.4	9	28.1	20	31.3	0.590*
Triglycerides							
Normal	26	81.3	25	78.1	51	79.7	
High	6	18.8	7	21.9	13	20.3	0.756*
Insulin Resistance							
Absent	31	96.9	30	93.8	61	95.3	
Present	1	3.1	2	6.3	3	4.7	1.000*
IL-6							
Normal	7	21.9	14	43.8	21	32.8	
High	25	78.1	18	56.3	43	67.2	0.062*
CRP							
Normal	22	68.8	25	78.1	47	73.4	
High	10	31.3	7	21.9	17	26.6	0.396*

* Chi-squared Test, or Fisher's Exact Test.

difference was observed in the waist circumference (p=0.035). With regard to the metabolic state, total cholesterol (p=0.031) presented a significant difference. Excess weight was observed in 20.3% of the sample, and was higher in the preterm group, in which 25% of children presented excess weight.

There was an association between birth classification according to gestational age and variables related to the nutritional and inflammatory status. The mean IL-6 levels were 7.3 (±3.2) and 7.5 (±2.4) pg/m for the preterm and term groups, respectively, although there was no significant difference (p= 0.06).

When relating birth weight with different markers of nutritional status and inflammatory status, total cholesterol, HDL, CRP and the BMI/Age score demonstrated an inversely proportional relationship with birth weight, although with no statistically significant difference. Only fasting blood glucose revealed a statistically significant difference (p = 0.017), which is directly proportional to birth weight. This data is presented in Table 2.

By associating the WC with nutritional, metabolic and inflammatory aspects in children born preterm, we observed that the WC was associated with a nutritional diagnosis of obesity (p=0.003) and with blood pressure (p=0.010) in children born preterm, as presented in Table 3.

There was no association between birth weight for gestational age, classified as SGA, AGA, and LGA and the height/age index, BMI/age index, a diagnosis of dyslipidemia and CRP levels, however we observed an association with IL-6 levels, as presented in Table 4.

Table 2. Correlation between birth weight and biochemical profile, inflammatory marker and nutritional status, Brazil

Variables	Birth weight	p-value*
Total Cholesterol	-0.136	0.284
Triglycerides	0.134	0.291
HDL Cholesterol	-0.216	0.086
Fasting Glucose	0.298	0.017
Insulinemia	0.020	0.878
Insulin Resistance (HOMA-IR)	0.049	0.699
IL-6	0.015	0.904
CRP	-0.037	0.772
BMI/Age	-0.056	0.663

Pearson's Correlation Coefficient.
* Bilateral Test (H0: correlation=0; H1: correlation≠0).

Table 3. Association between waist circumference and nutritional, metabolic and inflammatory aspects, Brazil

Variables	Waist Circumference				Total		p-value*
	Normal		Large				
	N	%	N	%	N	%	
BMI/Age							
Eutrophic (-2 to +2)	16	94.1	7	46.7	23	71.9	
Overweight (> +2)	1	5.9	8	53.3	9	28.1	**0.003**
Blood Pressure							
Normal	17	100.0	10	66.7	27	84.4	
High	0	0.0	5	33.3	5	15.6	**0.010**
Insulin Resistance							
Absent	17	100.0	13	86.7	30	93.7	
Present	0	0.0	2	13.3	2	6.3	0.120
Dyslipidemia							
Present	11	64.7	7	46.7	18	56.3	
Absent	6	35.3	8	53.3	14	43.7	0.305
Inflammation							
Absent	6	35.3	8	53.3	14	43.7	
Present	11	64.7	7	46.7	18	56.3	0.538

* Chi-Squared Test, or Fisher's Exact Test.

Table 4. Association between of birth weight according to gestational age and nutritional, metabolic and inflammatory, Brazil

Nutritional Status	BW/GA						Total		p-value*
	SGA		AGA		LGA				
	N	%	N	%	N	%	N	%	
Height/Age									
Normal height	12	92.3	11	91.7	6.0	85.7	29	90.6	
Low height	1	7.7	1	8.3	1.0	14.3	3	9.4	0.879
BMI/Age									
Eutrophic (-2 to +2)	9	69.2	8	66.7	7.0	100.0	24	75.0	
Overweight (> +2)	4	30.8	4	33.3	0.0	0.0	8	25.0	0.287
Dyslipidemia									
Present	8	61.54	6	50	4	57.1	18	56.2	
Absent	5	38.46	6	50	3	42.9	14	43.8	0.899
IL-6									
Normal	3	23.1	9	75.0	2.0	28.6	14	43.8	
High	10	76.9	3	25.0	5.0	71.4	18	56.2	0.022
CRP									
Normal	9	69.2	11	91.7	5.0	71.4	25	78.1	
High	4	30.8	1	8.3	2.0	28.6	7	21.9	0.466

* Chi-Squared Test or Fisher's Exact Test.
Legends: Small for gestational age (SGA); Appropriate for gestational age (AGA); Large for gestational age (LGA); BW: birth weight; GA: Gestational age.

DISCUSSION

There was a high prevalence of overweight children irrespective of term or preterm birth. When moving from a situation of restrictive growth, due to hormonal or nutritional reasons, to one with an appropriate supply of nutrients, a child born preterm may present accelerated growth recovery (catch-up growth) to reach the genetically determined potential[18,20]. Accelerated weight gain, since it is associated with increased fat deposition, may explain the higher frequency of overweight children observed in the preterm group. Other authors have also reported greater adiposity at older ages among children born preterm[21,22]. A study conducted with 18,288 adolescents and adults presented an increase of 0.92 in the BMI score for every 1 kg of weight at birth, thereby demonstrating that when nutritional status is analyzed at older ages it may still be influenced by birth weight[22]. Evidence has illustrated that obesity in childhood and adolescence, if uncontrolled, tends to persist into adulthood, resulting in an increase in comorbidities and a decrease in life expectancy[21].

In the present study, the WC classification according to age demonstrated a statistical difference between children born term and preterm. A case-control study carried out by Ibañez (2008) observed greater abdominal adiposity in children born preterm. This variation was only observed in an assessment conducted from the age of four, indicating central obesity[23].

Two reviews that aimed to indicate the metabolic pathway that leads to increased adiposity in premature newborn babies, raised the hypothesis that insulin resistance and adiposity was derived from a variation of the glucocorticoid receptor gene, whereby preterm adults presented a greater response to stressors. This increased response leads to a greater production and concentration of glucocorticoids, activating the

hypothalamic-pituitary-adrenal axis, promoting greater food intake and, consequently, an increase in the deposition of abdominal fat[21]. Another hypothesis highlighted that the origins of these alterations are related to lower levels of leptin and greater insulin sensitivity at birth[24].

With regard to an association between gestational age at birth and total cholesterol levels, Huxley et al. (2004) demonstrated through a systematic review and meta-analysis that for every 1 kg increase in birth weight, there is a reduction in total cholesterol by 1.39 mg/dL [25]. However, according to the meta-analysis on metabolic changes associated with prematurity, there is no evidence that birth weight is associated with serum lipid levels at later ages[26].

Pecks et al. (2014), with the aim of identifying the causality of high cholesterol levels in preterm children, observed that the lipid profile of umbilical cord blood at birth is dependent on the gestational age at delivery. Both the TC and LDL appeared in higher concentrations in preterm children compared to full-term children, while HDL levels remained constant. Thus, the LDL/HDL ratio is higher in preterm children[27].

The literature indicates an association between low birth weight and IR, generally explained by changes in the adiposity of children born preterm[27]. A case-control study comparing children born prematurely and children born at term reported a higher prevalence of insulin resistance assessed by the HOMA-IR method in those born preterm, revealing that the determining factor for this change would be the presence of catch-up growth[28]. Moreover, Deng et al (2011) reported that there was a high BMI/Age score in preterm children who went through catch-up compared to children born at term, a fact that was not evidenced in the absence of this phenomenon[29].

Although no children with high blood glucose were observed in the study, those born preterm presented lower blood glucose levels. This finding differs from a systematic review with 48 studies on birth weight and changes in glucose metabolism, which reported an inverse relationship between birth weight and fasting blood glucose, post-load glucose, fasting insulin concentration, the prevalence of diabetes type 2 mellitus, and levels of insulin resistance and secretion[28].

Once inflammation has been recognized as a component of atherosclerosis, it is likely that, in the long term, the action of IL-6 may contribute to the risk of cardiovascular disease[29].

IL-6 has previously been associated with birth weight, especially in the perinatal phase, and is an important marker associated with brain injury in preterm newborn children. A study with 768 children weighing 401 to 1,000 g at birth observed that an increase in IL-6 during the first month of life was associated with lower growth velocity and weight at 36 weeks of postmenstrual age and concluded that this finding may have a direct effect on the energy balance and postnatal growth[30].

In the present study, WC was associated with nutritional diagnosis and with BP. Other studies have already demonstrated this association and have also managed to identify an association between abdominal obesity and insulin resistance[5,8], which was not observed in the present study.

The limitations of this study are: a low sample number, the follow-up of children at the institution's nutrition clinic, which may have contributed to the positive effect of the evaluated parameters. In addition, the nutritional habits of both groups were not analyzed.

CONCLUSION

The occurrence of excess weight was high in both groups studied. A shorter gestation period was associated with a higher waist circumference and higher total cholesterol, which indicates a higher risk of developing cardiovascular events in children born prematurely. Waist circumference was associated with the current nutritional status and arterial hypertension.

ACKNOWLEDGMENTS

This research it was funded by the Coordination for the Improvement of Higher Education Personnel - Brazil (CAPES) – Finance Code 001.

REFERENCES

1. Wachamo TM, Bililig Yimer N, Bizuneh AD. Risk factors for low birth weight in hospitals in North Wello, Ethiopia: A case-control study. PLoS One. 2019;14(3):e0213054. Publicado em 20 de março de 2019. doi:10.1371/journal.pone.0213054.
2. TORRES, R. M.; CHÁVEZ, A. M. C; OCÁDIZ, G. V; SÁNCHEZ, J. M. Food insecurity in homes of mothers of premature newborns with anthropometric alterations at birth. Nutr Clín Diet Hosp. 2020; 40(4):63-69 DOI: 10.12873/404.
3. Zeng M, Lamb KE, Grimes C, Laws L, Bolton K, Ong KK, et al. Rapid weight gain during infancy and subsequent adiposity: a systematic review and meta-analysis of evidence. Obesity Reviews. 2017;19:321–32.
4. Leroy JL, Frongillo EA, Dewan P, Black MM, Waterland RA. Can children recover the consequences of malnutrition? Evidence of infant linear growth, epigenetics of brain and neurocognitive development and development. Adv Nutr. 2020;11(4):1032-1041. doi:10.1093/advances/nmaa020
5. Deng H-Z, Deng H, Su Z, Li Y-H, Ma H-M, Chen H-S, et al. Insulin resistance and adiponectin levels are associated with height catch-up growth in pre-pubertal Chinese individuals born small for gestational age. Nutrition & Metabolism. 2012;09:107.
6. Belford MB, Brown RS. Fetal and pos natal growth: mechanisms, consequences and controversies. Current Opinion in Endocrinology, Diabetes and Obesity. 2007;(14):1–2.

7. Carreira ML. Grande Prematuridade: Nutrição e Crescimento. Nascer e Crescer. Set de 2010;19(3):202–3.

8. Hussid MF, Cepeda FX, Jordão CP, et al. Visceral Obesity and High Systolic Blood Pressure as the Substrate of Endothelial Dysfunction in Obese Adolescents. Obesidade Visceral e Hipertensão Sistólica como Substratos da Disfunção Endotelial em Adolescentes Obesos. Arq Bras Cardiol. 2021;116(4):795-803. doi:10.36660/abc.20190541.

9. García-Muñoz Rodrigo F, Figueras Aloy J, Saavedra Santana P, García-Alix A. Crecimiento posnatal hasta el alta hospitalaria en recién nacidos extremadamente prematuros españoles [Postnatal growth at hospital discharge in extremely premature newborns in Spain]. An Pediatr (Barc). 2017;87(6):301-310. doi:10.1016/j.anpedi.2016.10.011

10. Ferranti SD, Osganian SK. Epidemiology of paediatric metabolic syndrome and type 2 diabetes mellitus. Diabetes and Vascular Disease Research. 2007;4(Dec):285–96.

11. Grundy SM. Metabolic syndrome pandemic. Arteriosclerosis, Thrombosis, and Vascular Biology. Journal of American Heart Association. 2008;28:629–36.

12. Simental-Mendía, L., Hernández-Ronquillo, G., Gómez-Díaz, R. et al. O índice de triglicerídeos e glicose está associado a fatores de risco cardiovascular em crianças e adolescentes com peso normal. Pediatra Res, 2017; 82, 920-925. https://doi.org/10.1038/pr.2017.187

13. WHO. Physical Status: The Use and Interpretation of Anthropometry. Genebra: Organização Mundial de Saúde; 1995. (Technical Report Series). Report No.: 854.

14. Institute of Medicine - IOM; National Research Council (USA) Committee to Reexamine IOM Pregnancy Weight Guidelines. Weight gain during pregnancy: reexamining the guidelines. Rasmussen KM, Yaktine AL, editor. Washington, D.C.: National Academies Press; 2009 [cited 2020 Oct 5]. 868 p. Available from: https://doi.org/10.17226/12584 » https://doi.org/10.17226/12584

15. Brasil. V- DIRETRIZ BRASILEIRA DE DISLIPIDEMIAS E PREVENÇÃO DA ATEROSCLEROSE Sociedade Brasileira de Cardiologia • ISSN-0066-782X • Volume 101, Nº 4, Supl. 1, Outubro 2013.

16. Müller JL. Fatores Predominantes Para Diagnóstico Da Síndrome Metabólica Em Crianças E Adolescentes: Uma Revisão Sistemática. Revista Brasileira de Obesidade, Nutrição e Emagrecimento. 2015;9(51):105–14.

17. Myers GL, Rifai N, Tracy RP, Roberts WL, Alexander RW, Biasucci LM, et al. CDC/AHA Workshop on Markers of Inflammation and Cardiovascular Disease. Circulation. 2004;110:545–9.

18. Junqueira CLC, SanfAnna PR, Junqueira ASN, Oliveira JMF, Romêo Filho LJM. Associação de Marcadores Inflamatórios e Níveis Tensionais em Indivíduos Hipertensos com Diabetes Mellitus Tipo 2. Revista da SOCERJ. 2005;18(5):392–6.

19. National High Blood Pressure Education Program Working Group on Hypertension Control in Children and Adolescents. Pediatrics; 1996 p. 649–58. (Task Force Report on High Blood Pressure Education Program.). Report No.: 98.

20. Leal VS, Lira PIC, Oliveira JS, Menezes RCE, Sequeira LAS, Arruda Neto MA, et al. Excesso de peso em crianças e adolescentes no Estado de Pernambuco, Brasil: prevalência e determinantes. Cad Saúde Pública. junho de 2012;28(6):1175–82.

21. Hong YH, Chung S. Small for gestational age and obesity related comorbidities. Ann Pediatr Endocrinol Metab. 2018;23:4–8.

22. Thomas EL, Saud NBA, Durighel G, Frost G, Bell JD. The Effect of Preterm Birth on Adiposity and Metabolic Pathways and the Implications for Later Life. Clin Lipidology. 2012;7(3):275–88.

23. Ibanez L, Suarez L, Lopez-Bermejo A, Diaz M, Valls CZ. Early development of visceral fat excess after spontaneous catch-up growth in children with low birth weight. The Journal of Clinical Endocrinology and Metabolism. 2008;93(3):925–8.

24. Beltrand J, Nicolescu R, Kaguelidou F, Verkauskiene R, Sibony O, Chevenne D. Catch up growth following fetal growth restriction promotes rapid restoration of fat mass but without metabolic consequences at one year of age. PLoS One. 2009;4: E5343–E5350.

25. Huxley R, Owen CG, Whincup PH, Cook DG, Colman S, Collins R. Birth weight and subsequent cholesterol levels: exploration of the "fetal origins" hypothesis. JAMA. 2004; 292(22):2755–64.

26. Liao L, Deng Y, Zhao D. Association of Low Birth Weight and Premature Birth With the Risk of Metabolic Syndrome: A Meta-Analysis. Front Pediatr. 2020;8:405. Published 2020 Jul 28. doi:10.3389/fped.2020.00405

27. Pecks U, Mohaupt MG, Hütten MC, Maass N, Rath W, Escher G. Cholesterol acceptor capacity is preserved by different mechanisms in preterm and term fetuses. Biochimica et Biophysica Acta. 2014;1841:251–8.

28. Iñiguez G, Ong K, Bazaes R, Avila A, Salazar T, Dunger D, et al. Longitudinal changes in insulin-like growth factor-1, insulin sensitivity, and secretion from birth to age three years in small-for-gestational-age children. J Clin Endocrinol Metab. 2006;91:4645–4649.

29. Deng HZ, Li YH, Su Z, Ma H-M, Huang YF, Chen H-S, et al. Association between height and weight catch-up growth with insulin resistance in pre-pubertal Chinese children born small for gestational age at two different ages. Eur J Pediatr. 2011;170:75–80.

30. Denson LA, McDonald SA, Das A, et al. Early Elevation in Interleukin-6 is Associated with Reduced Growth in Extremely Low Birth Weight Infants. Am J Perinatol. 2017;34(3):240-247. doi:10.1055/s-0036-1585419