ORIGINAL ARTICLE

Higher Metabolic Dysfunction in Adolescents Who Were Born Very Preterm: Case Control Study

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Abstract

Introduction: Literature has shown an increase in cardiovascular risk and metabolic changes in adolescents and young adults who were born preterm. In this regard, the present study aimed to assess metabolic dysfunction in adolescents who were born at less than 32 weeks of gestational age.

Methods: This case-control study was performed on adolescents within the age range of 10-17 years and born in a level III maternity, with gestational age of < 32 weeks. Controls were healthy adolescents with gestational age of ≥ 37 weeks. Demographic data, cardiovascular risk history, and clinical data were evaluated and blood tests were performed.

Results: In total, 110 preterm and 48 controls were enrolled in the study. Based on the results, mean systolic (118.8 *vs* 112.6 mmHg, $p = 0.001$) and diastolic (61.7 *vs* 58.5 mmHg, $p = 0.014$) blood pressures were statistically higher in preterm infants, compared to the controls. The preterm adolescents had a higher waist-to-height ratio, fat mass, fasting blood glucose, insulin, homeostasis model assessment for insulin resistance, total cholesterol, low-density lipoprotein, and apolipoprotein B100, compared to the controls. However, none of these differences were statistically significant. It was found that preterm adolescents had more metabolic dysfunction risk factors, compared to the controls ($p = 0.007$).

Discussion: Prematurity contributes to higher cardiovascular risk and metabolic dysfunction. Moreover, higher arterial blood pressure seems to be the most important clinical finding in this study. Close monitoring of risk factors, particularly blood pressure, in adolescents who were born at less than 32 weeks is important for the prevention and early diagnosis of metabolic and cardiovascular comorbidities in adulthood.

Keywords: Adolescent; Infant, Extremely Premature; Metabolic Diseases/etiology; Premature Birth/epidemiology; Prevalence; Risk Factors

Keypoints

What is known:

- Adolescents and young adults born preterm have higher systolic and diastolic arterial blood pressure, compared to those born at term.
- There is no consensus about other clinical and laboratory parameters (*eg*, body mass index, fat mass, lipid profile, and fasting glucose).

What is added:

- In a global assessment considering clinical, biometric, and laboratory parameters, adolescents who were born very preterm (< 32 weeks of gestational age) had a higher number of metabolic dysfunction risk factors, compared to controls.
- Adolescents who were born very preterm had higher systolic and diastolic blood pressure, compared to the controls, and this seems to be the most important clinical finding in adolescents.
- Pediatricians and general practitioners should be aware of the importance of close monitoring of cardiovascular and metabolic risk factors in adolescents and young adults who were born very preterm to prevent comorbidities in adulthood.

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Introduction

Worldwide, about 15 million preterm neonates are born annually, 700 000 of which are in Europe. It has been estimated that about one in 10 newborns are premature and in Europe, 16% of preterm newborns are born at less than 32 weeks of gestational age (GA).[1] As is known, very preterm neonates have more complications not only in the neonatal period but also in childhood, adolescence, and adulthood.

International literature has shown an increase in cardiovascular risk and metabolic changes in adolescents and young adults who were born preterm, with higher statistical evidence for those born with lower gestational age or those who were small for gestational age (SGA).[2-9] Published meta-analyses demonstrate higher arterial blood pressure (BP), systolic and diastolic, in adolescents born preterm, compared to those born at term. However, there is no consensus about the total cholesterol, low-density lipoprotein (LDL), fasting glucose levels, insulin, and percentage of fat mass.[6-9]

Furthermore, some differences have been observed between genders as adolescent females have a higher prevalence of elevated blood pressure, compared to adolescent males and adolescent males have a more atherogenic lipid profile, compared to adolescent females.[2] Moreover, the timing of postnatal catch-up growth seems to be critical in childhood obesity.[10]

Most published studies analyze these risk factors at young adult age, but some authors have already demonstrated that these metabolic dysfunction factors can be identified since preschool age.[11,12] In addition, most studies compare those born prematurely (GA < 37 weeks) to those born at term, while the described differences are more evident for adolescents who were born very preterm and SGA.[2-4]

Given this metabolic dysfunction risk, some authors have suggested emphasizing the promotion of healthy lifestyle habits and screening for metabolic risk factors in adolescents and young adults who were born prematurely.[2,13] This study aimed to evaluate metabolic dysfunction in adolescents who were born very preterm (GA < 32 weeks).

Methods

Study design

This observational, transversal, and analytic case-control study was performed on adolescents between 10-17 years of age, born in a level III maternity with a gestational age < 32 weeks in Coimbra, Portugal. It should be mentioned that cerebral palsy patients were excluded. Controls were healthy adolescents between 10-17 years of age, with a gestational age ≥ 37 weeks. They were selected from volunteers or people who had undergone elective surgeries at our hospital (*eg*, adenotonsillectomy, tympanoplasty, septoplasty, phimosis, and minor surgery to remove lipomas or nevi). Exclusion criteria for the control sample were adolescents with:

- Severe chronic disease (kidney, liver, endocrine, neurological, or tumor);
- Systemic inflammatory disease (rheumatological and inflammatory bowel);
- Acute infectious disease;
- Congenital and/or syndromic malformations;
- Chronic therapy (*eg*, oral corticosteroid therapy).

Clinical evaluation of the control sample was performed in a second hospital appointment.

Data collection

Demographic (age, gender, and race), pregnancy (gestational diabetes, hypertension with or without preeclampsia, maternal obesity, and maternal smoking), and perinatal data (gestational age, weight at birth, maternal age, twin pregnancy, and prenatal corticotherapy) as well as family cardiovascular risk history and their own lifestyle habits (physical activity, smoking, and alcohol consumption) were collected.

On clinical assessment, weight, height, body composition assessed by bioimpedance (fat mass percentage), waist and hip circumference, and blood pressure and presence or absence of axillary or cervical acanthosis nigricans were evaluated. Blood tests were collected with at least eight hours of fasting for glucose, insulin, hemoglobin A1c (HbA1c), total cholesterol, LDL, high-density lipoproteins (HDL), triglycerides, apolipoprotein A1 (ApoA), and B100 (ApoB). Moreover, body mass index (BMI), homeostasis model assessment for insulin resistance (HOMA-IR), atherogenic index, and ApoB / ApoA index were calculated.

All measures were evaluated twice and the average value was calculated. The blood pressure assessment was performed through the oscillometric method (digital) with an appropriate cuff size in the right upper limb after five minutes of sitting at rest. Weight, height, waist circumference, and hip circumference were measured as recommended by the World Health Organization.[14] The assessment of body composition by bioimpedance was performed with a four-hours fast on a day when the participant had not performed physical activity and had no sun exposure or other factors that cause dehydration. Furthermore, females were not

menstruating and they were required to urinate before the evaluation.

Risk factors of metabolic dysfunction studied to compare both groups included BMI z-score > 1, waist-to-height ratio > 0.5, high blood pressure for age, borderline-high total cholesterol (≥ 4.40 mmol/L), borderline-low HDL (≤ 1.17 mmol/L), borderline-high LDL (≥ 2.85 mmol/L), borderline-high triglycerides (≥ 1.02 mmol/L), HOMA-IR > 3, and high-fat mass percentage for age and gender.

Statistical methods

The statistical analysis was performed in SPSS® software (version 26.0). In addition, a descriptive analysis of the variables was performed. Categorical variables were presented as frequencies and percentages. Moreover, continuous variables were presented as means and standard deviations whenever they presented a gaussian distribution, or as medians and quartiles 1 and 3 when the sample distribution was not normal according to the Shapiro-Wilk test. The test used in each statistical analysis was specified by the type of variables and their distribution. Finally, the preterm samples were compared with the controls. All *p* values presented are for two-sided tests and the level of significance was considered 0.05.

Results

In total, a sample of 110 adolescents born preterm and 48 adolescents born at term (21 who underwent elective surgery and 27 volunteers) was obtained. It should be noted that gender distribution was similar between groups. Median age at clinical assessment was 14.6 years old (range 13.6-16.4 years old) in the preterm group and 13.3 years old (range 11.1-14.7 years old) in the control group ($p < 0.001$). All participants were Caucasian, except one in the preterm group who was black.

The peri- and neonatal characteristics of both groups are summarized in Table 1. The median gestational age and median birthweight of the preterm population were 29.9 weeks (range 28.0-30.9 weeks) and 1208 g (range 980-1508 g), respectively. About 22% of our preterm sample were extremely preterm (< 28 weeks). Maternal hypertension and preeclampsia were significantly more frequent in the preterm group (25.5% and 17.3%, respectively), compared to the controls (6.4% and 2.1%, respectively). However, no differences were observed between the groups in terms of gestational diabetes, maternal obesity, maternal smoking, and maternal age. Besides, the preterm infants were breastfed for a shorter period (2.75 months) than the controls (6.0 months) ($p = 0.005$).

Table 1. Peri- and neonatal characteristics of the sample comparing preterm and controls

Peri- and neonatal characteristics	Preterm (n = 110)	Controls (n = 48)	*p value*
Gender (male)	56 (50.9%)	26 (54.2%)	0.732*
Gestational age (weeks) min - max ≥ 28 weeks < 28 weeks	29.9 [28.0, 30.9] 24w+0d - 31w+6d 86 (78.18%) 24 (21.82%)	39.1 [38.0, 40.0] 37w+1d - 42w+0d	**< 0.001**†
Birth weight (g) min - max - SGA (< p10) - AGA - LGA (> p 90)	1208 [980,1508] 460 - 2130 10 (9.1%) 96 (87.3%) 4 (3.6%)	3325 [3069, 3545] 2500 - 3915 4 (8.3%) 42 (87.5%) 2 (4.2%)	**< 0.001**†
Twin pregnancy	33 (30.0%)	0 (0%)	-
Maternal age (years) min - max	30 [25.00, 34.00] 17 - 39	30 [27, 32.75] 22 - 40	0.605†
Maternal morbidity - Gestational diabetes - Hypertension - Preeclampsia - Obesity - Smoking	 8 (7.3%) 28 (25.5%) 19 (17.3%) 15 (13.6%) 15 (13.6%)	 4 (8.5%) 3 (6.4%) 1 (2.1%) 8 (17.0%) 4 (8.5%)	 0.753‡ **0.006*** **0.009*** 0.583* 0.367*
Prenatal corticosteroids	91 (82.7%)	0 (0.0%)	-
Breastfeeding (months) min - max	2.75 [0.73, 6.00] 0 - 24	6.0 [1.63, 9.75] 0 - 48	**0.005**†

AGA - appropriate for gestational age; d - days; LGA - large for gestational age; max - maximum; min - minimum; SGA - small for gestational age; w - weeks.
* Pearson chi-square test.
† Mann-Whitney U test.
‡ Fisher's exact test.
Values are given as absolute value (%) or medians [quartile 1, quartile 3].

Table 2. Family and personal history comparing preterm and controls

Family and personal history	Preterm (n = 110)	Controls (n = 48)	*p value*
Family cardiovascular risk			
1-2 family members	44 (40.0%)	27 (56.3%)	0.102*
3-4 family members	32 (29.1%)	13 (27.1%)	
≥ 5 family members	34 (30.9%)	8 (16.7%)	
Physical activity (hours / week)			
< 1	50 (45.5%)	15 (31.3%)	
1-2	18 (16.4%)	0 (0.0%)	
2-4	19 (17.3%)	14 (29.2%)	**0.005***
4-6	9 (8.2%)	8 (16.7%)	
6-8	8 (7.3%)	6 (12.5%)	
> 8	6 (5.5%)	5 (10.4%)	
Active / passive tobacco use			
No	81 (73.6%)	40 (83.3%)	
~ once / month	2 (1.8%)	0 (0%)	0.453†
~ once / week	6 (5.5%)	4 (8.3%)	
~ twice to four times / week	6 (5.5%)	1 (2.1%)	
Every day	15 (13.6%)	3 (6.3%)	
Alcohol Consumption			
No	102 (92.7%)	44 (91.7%)	
~ once / month	4 (3.6%)	3 (6.3%)	0.781†
~ once / week	4 (3.6%)	1 (2.1%)	
~ twice to four times / week	0 (0%)	0 (0%)	
Every day	0 (0%)	0 (0%)	

*Pearson chi-square test.
†Fisher's exact test.
Family cardiovascular risk (in parents, grandparents, or cousins) includes cardiac pathology, stroke, type 2 diabetes, hypertension, and obesity.
Values are given as absolute value (%).

Family and personal history of preterm and controls are summarized in Table 2. The preterm sample practiced physical activity for fewer hours per week, compared to the controls (p = 0.005). There was no statistically significant difference between preterm and term adolescents in terms of family cardiovascular risk.

Table 3 tabulates the clinical assessment results of adolescents who were born preterm and term. Mean systolic (118.8 *vs* 112.6 mmHg, p = 0.001) and diastolic blood pressure (61.7 *vs* 58.5 mmHg, p = 0.014) values were statistically higher in preterm adolescents, compared to the controls. Through the application of linear regression, it was found that the difference between preterm and term adolescents in terms of systolic blood pressure is not explained by age (preterm b = 2.633, R^2 = 0.190, p < 0.001; controls b = 1.730, R^2 = 0.169, p = 0.004).

In the sample, preterm female adolescents had a higher systolic blood pressure mean (p = 0.033, Student t-test) and diastolic blood pressure mean (p = 0.010, Student t-test) in comparison to the female adolescents in the control group. Among male adolescents, systolic and diastolic blood pressure were also higher, compared to the male adolescents in the control group; however, there was no statistical difference (p = 0.099 and p = 0.538, respectively, Student t-test).

Although the preterm group had a higher BMI, waist-to-height ratio, fat mass, and nigricans acanthosis there was no statistical significance (Table 3).

Blood analysis results are summarized in Table 4. The preterm group had lower HbA1c and triglycerides and also higher ApoA, compared to the controls (p < 0.05). Despite the lack of statistical significance, fasting blood glucose, insulin, HOMA-IR, total cholesterol, HDL, LDL, and ApoB were higher in the preterm group, compared to the control group.

Given the metabolic dysfunction risk factors of both groups (Table 5), it was found that the preterm group had a higher number of risk factors than the controls and that this difference was statistically significant (p = 0.007).

Discussion

The main finding of this study was that adolescents who were born very preterm (GA < 32 weeks) had a higher number of metabolic dysfunction risk factors, compared to those born at term. Among analyzed maternal diseases during pregnancy, hypertension was the only one with a significantly higher frequency in the preterm group. Besides the fact that preterm newborns were born smaller and more immature than term newborns, the lifestyle differences of adolescents, in particular a

sedentary lifestyle, might influence their cardiovascular risks. In the sample of this study, it was highlighted that the group of term adolescents practiced more physical activity than adolescents who were born preterm. Therefore, a range of physiopathological pathways might have had an influence on a higher metabolic dysfunction risk in preterm adolescents.

Clinical parameters

Based on the findings, the mean systolic and diastolic blood pressure values of adolescents who were born very preterm were 6.2 and 3.2 mmHg higher than those of controls. This difference was not explained by the difference in age between the preterm and control groups. This finding is consistent with the literature.[2-9] However, the difference between values is slightly higher than those reported in published meta-analyses.[6-9] This perhaps can be explained by the younger gestational age of the samples of the present study. The difference found in systolic and diastolic blood pressure was higher in females than in males, as described by other authors.[2,6,8]

Only half of the preterm adolescents in this study had normal blood pressure for their age, stature, and gender, and around a quarter of them had values compatible with hypertension grade 1 or 2. These results emphasize the importance of screening and early diagnosis of hypertension at young ages and demonstrate the greater cardiovascular risk of this population in the long term.

Furthermore, it was revealed that there is a strong association between very preterm newborns and heart failure in childhood and young adulthood.[15] Moreover, recently, it was demonstrated that adolescents and young adults born prematurely had cardiac morphologic differences which may be associated with higher lifetime cardiovascular risk.[16] Therefore, it can be said that adolescents who were born preterm would benefit from a regular blood pressure evaluation and early referral for cardiovascular risk consultation if necessary.

No significant differences were found between preterm and term adolescents regarding BMI, waist-to-height ratio, and fat mass percentage, as also described in previously published meta-analyses.[7,8]

Blood analysis

In this study, no significantly higher fasting glucose, insulin resistance, or atherogenic lipid profile values

Table 3. Clinical parameters of preterm and control adolescents

Clinical parameters	Preterm (n = 110)	Controls (n = 48)	*p value*
BMI (kg/m²)	20.12 [18.01, 22.27]	19.22 [17.11, 21.77]	0.389*
min - max	14.10 - 36.52	13.96 - 27.81	
- z-score	0.10 (1.13)	0.27 (1.14)	0.398†
min - max	-2.99 - +3.06	-1.96 - +2.50	
- Excess weight (p 85-97)	15 (13.6%)	8 (16.7%)	0.431‡
- Obesity (p > 97)	6 (5.6%)	5 (10.4%)	
Waist / height ratio	0.44 [0.41, 0.47]	0.43 [0.40, 0.47]	0.602*
min - max	0.37 - 0.63	0.37 - 0.60	
Fat Mass (%)	21.81 (8.73), n = 103	20.23 (8.29)	0.293†
min - max	6.00 - 47.00	6.0 - 38.0	
- Normal	15 (14.6%)	6 (12.5%)	0.374‡
- Increased	63 (61.2%)	25 (52.1%)	
Systolic BP (mmHg)	118.83 (11.36)	112.56 (10.26)	**0.001**†
min - max	96.0 - 148.0	91.0 - 139.0	
Diastolic BP (mmHg)	61.70 (7.73)	58.52 (6.51)	**0.014**†
min - max	45.0 - 85.0	43.0 - 76.0	
BP classification			
- Normal	57 (51.8%)	35 (72.9%)	0.112§
- High	28 (25.5%)	7 (14.6%)	
- Hypertension grade 1	20 (18.2%)	5 (10.4%)	
- Hypertension grade 2	5 (4.6%)	1 (2.1%)	
Nigricans acanthosis			
- No	99 (90.0%)	48 (100%)	0.244§
- Cervical	6 (5.5%)	0 (0%)	
- Axillary	2 (1.8%)	0 (0%)	
- Both	3 (2.7%)	0 (0%)	

BMI - body mass index; BP - blood pressure; max - maximum; min - minimum; p - percentile.
* Mann-Whitney U test.
† Student t-test.
‡ Pearson chi-square test.
§ Fisher's exact test.
Values are given as absolute value (%), medians [quartile 1, quartile 3] or mean (standard deviation).

Table 4. Blood analysis results from preterm and control adolescents

Blood analysis	Preterm (n = 110)	Controls (n = 48)	*p value*
Glycemia (mmol/L) min - max	4.95 [4.80, 5.18] 3.30 - 5.90	4.90 [4.63, 5.10] 3.80 - 5.70	0.265*
Insulin (μUI/mL) min - max	7.45 [5.13, 12.55] 1.60 - 38.20	7.10 [4.23, 9.68] 1.90 - 23.70	0.298*
HbA1c (%) min - max	5.30 [5.10, 5.60] 1.60 - 6.20	5.50 [5.30, 5.70] 4.6 - 6.0	**0.018***
HOMA-IR min - max	1.66 [1.07, 2.80] 0 - 8.49	1.41 [0.95, 2.18] 0.39 - 5.58	0.297*
Total cholesterol (mmol/L) min - max - Borderline-high (≥ 4.40) - High (≥ 5.18)	4.00 [3.52, 4.43] 2.64 - 5.80 19 (17.3%) 9 (8.2%)	3.74 [3.39, 4.38] 2.41 - 5.44 8 (16.7%) 3 (6.3%)	0.145* 0.956†
HDL (mmol/L) min - max - Borderline-low (≤ 1.17)	1.39 [1.18, 1.59] 0.78 - 2.40 24 (21.8%)	1.32 [1.13, 1.52] 0.9 - 1.86 13 (27.1%)	0.103* 0.541†
LDL (mmol/L) min - max - Borderline-high (≥ 2.85) - High (≥ 3.37)	2.24 [1.92, 2.72] 1.02 - 4.34 11 (10.0%) 7 (6.4%)	2.19 [1.93, 2.66] 1.04 - 4.01 5 (10.4%) 4 (8.3%)	0.741* 0.887‡
Triglycerides (mmol/L) min - max - Borderline-high (≥ 1.02) - High (≥ 1.47)	0.73 [0.54, 0.91] 0.35 - 2.05 13 (11.8%) 6 (5.5%)	0.85 [0.56, 1.19] 0.32 - 2.1 10 (20.8%) 6 (12.5%)	**0.048*** 0.078†
Atherogenic index min - max	2.84 [2.52, 3.31] 1.75 - 5.14	2.87 [2.51, 3.36] 2.13 - 4.39	0.573*
ApoA (mg/dL) min - max - Borderline-low (≤ 120)	141.0 [130.00, 155.00], n = 107 100 - 208 7 (6.5%)	136.50 [121.50, 147.75] 113 - 210 11 (22.9%)	**0.048*** 0.003†
ApoB (mg/dL) min - max - Borderline-high (≥ 90) - High (≥ 110)	72.29 (16.02) 45 - 122 10 (9.4%) 2 (1.9%)	69.37 (16.70) 39 - 120 4 (8.3%) 1 (2.1%)	0.235§ 1.000‡
ApoB / ApoA ratio min - max	0.50 [0.44, 0.60] 0.23 - 0.95	0.50 [0.43, 0.59] 0.31 - 0.85	0.918*

ApoA - apolipoprotein A1, ApoB - apolipoprotein B100; HbA1c - hemoglobin A1c, HDL - high density lipoprotein; HOMA-IR - homeostasis model assessment for insulin resistance; LDL - low density lipoprotein, max - maximum; min - minimum.
* Mann-Whitney U test.
† Pearson chi-square test.
‡ Fisher's exact test.
§ Student t-test.
Values are given as absolute value (%), medians [quartile 1, quartile 3] or mean (standard deviation).

Table 5. Risk factors for metabolic disfunction from preterm and control adolescents

Risk factors*	Preterm (n = 110)	Controls (n = 48)	*p value*
0	8 (7.3%)	11 (22.9%)	
1	36 (32.7%)	8 (16.7%)	**0.007**†
≥ 2	66 (60.0%)	29 (60.4%)	

* Risk factors: body mass index z-score > 1, waist / height ratio > 0.5, high blood pressure, borderline-high total cholesterol, borderline-low high density lipoproteins, borderline-high low density lipoproteins, borderline-high triglycerides, homeostasis model assessment for insulin resistance > 3, high fat mass percentage.
† Pearson chi-square test.
Values are given as absolute value (%).

were in the preterm group. Results of previously published meta-analyses and studies were not in line with this finding.[7,8,11,17] Nonetheless, the most recently published meta-analysis concluded that there were no significant differences between preterm and term adolescents, young adults, and even adults.[6]

Some potentially protective parameters were found in the preterm population, namely, lower HbA1c and triglycerides as well as higher ApoA levels. These results were not in agreement with what was expected; however, the published scientific evidence regarding these parameters is still scarce. According to the findings of previously published studies, triglycerides did not present a statistical difference between preterm and term adolescents or young adults.[2,3,6-8] Moreover, according to other authors, ApoA levels were lower in females who were born early preterm.[3] We are aware that HbA1c is not a recommendable diagnostic tool for screening glucose intolerance and type 2 diabetes in obese children and adolescents.[18] It should also be mentioned that it was not analyzed in other studies.

Metabolic dysfunction risk factors

Given the most important metabolic dysfunction parameters (high BMI, waist-to-height ratio, blood pressure, fat mass, HOMA, and atherogenic lipid profile), preterm adolescents presented a greater association of risk factors than the controls, more than 90% of whom had at least one risk factors for metabolic dysfunction in adolescence. Similarly, other authors found that children who were born preterm, already had higher systolic and diastolic blood pressure, fasting glucose levels, HOMA, and cholesterol levels at preschool age, compared to the children born at term.[11]

In an evaluation of preterm infants with a birth weight of < 1500 g, it was found a 15.1% prevalence of metabolic syndrome-like symptoms at 2 years of corrected age.[12] Therefore, pediatricians and general practitioners who are responsible for child and adolescent health surveillance should be aware of this metabolic dysfunction risk to implement counseling and prevention strategies and improve monitoring and early diagnosis of these conditions.

Limitations

Limitations of this study include:

- Reduced sample of controls due to the difficulty in the identification of healthy adolescents who volunteered to collect blood samples;
- Lack of assessment of the growth curves of preterm adolescents to analyze the age of their catch-up growth;
- Unicentric nature of the study.

Despite these limitations, the results of this study are clinically relevant as few published studies have analyzed metabolic dysfunction in adolescents who were born prematurely at less than 32 weeks. Currently, most of the published papers refer to the analysis of young adults or adolescents who were born prematurely at less than 36 weeks, with small samples with gestational < 32 weeks. In addition, in this study, adolescents were analyzed globally, taking into account clinical, biometric, and laboratory parameters.

In conclusion, the results suggest that prematurity contributes to a higher cardiovascular and metabolic risk and higher arterial blood pressure seems to be the most important clinical finding in adolescence. Therefore, throughout health surveillance, close monitoring of metabolic risk factors, and blood pressure in particular, of adolescents who were born very preterm is important to prevent metabolic and cardiovascular comorbidities in adulthood. Nonetheless, further multicentric and prospective studies are necessary to better characterize the risk of this population and propose the best clinical practice for their follow-up.

Author Contribuitions

JBC, ID, BO, GM and SM participated in the study conception or design. JBC, GM and SM participated in acquisition of data. JBC, ID, BO, GM and SM participated in the analysis or interpretation of data. JBC participated in the drafting of the manuscript. ID participated in the critical revision of the manuscript. All authors approved the final manuscript and are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

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Protection of human and animal subjects

The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki 2013).

Provenance and peer review

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Confidentiality of data

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

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Disfunção metabólica em adolescentes nascidos grandes prematuros - estudo de caso-controlo

Introdução: A literatura tem demonstrado um aumento do risco cardiovascular e alterações metabólicas em adolescentes e adultos jovens que nasceram prematuros. Assim, este estudo teve como objetivo avaliar a disfunção metabólica em adolescentes que nasceram com menos de 32 semanas de idade gestacional.

Métodos: Este estudo de caso-controlo foi realizado em adolescentes com idades entre os 10-17 anos, nascidos numa maternidade de nível III com uma idade gestacional inferior a 32 semanas. Os controlos foram adolescentes saudáveis nascidos com idade gestacional igual ou superior a 37 semanas. Foram avaliados dados demográficos, história de risco cardiovascular e dados clínicos e foram realizadas análises sanguíneas.

Resultados: No total, foram incluídos neste estudo 110 prematuros e 48 controlos. Com base nos resultados, as pressões arteriais médias sistólica (118,8 *vs* 112,6 mmHg, p = 0,001) e diastólica (61,7 *vs* 58,5 mmHg, p = 0,014) foram significativamente superiores nos prematuros comparativamente aos controlos. Os adolescentes prematuros apresentaram maior relação cintura/altura, massa gorda, glicemia em jejum, insulina, avaliação do modelo de homeostase para resistência à insulina, colesterol total, lipoproteína de baixa densidade e apolipoproteína B100 em comparação com os controlos. No entanto, nenhuma dessas diferenças foi estatisticamente significativa. Verificou-se que adolescentes prematuros apresentaram mais fatores de risco para disfunção metabólica do que os controlos (p = 0,007).

Discussão: A prematuridade contribui para maior risco cardiovascular e disfunção metabólica. Além disso, o aumento da pressão arterial parece ser o achado clínico mais importante neste estudo. A monitorização rigorosa dos fatores de risco, principalmente da pressão arterial, em adolescentes nascidos com menos de 32 semanas é importante para a prevenção e diagnóstico precoce de comorbidades metabólicas e cardiovasculares na vida adulta.

Palavras-Chave: Adolescente; Doenças Metabólicas/etiologia; Fatores de Risco; Lactente Extremamente Prematuro; Nascimento Prematuro/epidemiologia; Prevalência