

# Correlation between extremes birth weight and current metabolic status in overweight pubertal patients

Correlação entre extremos de peso ao nascimento e avaliação metabólica atual em pacientes púberes com excesso de peso

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## Abstract

**Objectives:** To correlate birth weight and current metabolic condition in overweight pubertals. **Methods:** A retrospective cross-sectional study of 125 pubertal patients (85 females / 40 males) with overweight, categorized into three groups according to birth weight (<2500 g, 2500-3999 g and >4000 g). The following data were evaluated: chronological age, zBMI, Waist circumference (WC)/H, zHeight and lipid profile. **Results:** Low birth weight was observed in 16 patients (12.8%) and high birth weight in 15 (12.0%). At the time of the evaluation, the mean (SD) of the chronological age was 13.3 years (2.3), Body Mass Index z score (zBMI) + 2.60 (0.6), WC/height 0.59 (0.09), height z score + 0.44 (1.15) and HOMA-IR 4.37 (3.07), Glycemia 85.3 mg/dL(8.4), Insulin Sum 500.4 (306.4), Total Cholesterol 166 mg/dL (37.3), Low Density Lipoprotein (LDL) 100.5 mg/dL (28.9), High Density Lipoprotein (HDL) 41.4 mg/dL (8.8), triglycerides (TG) 119.8 (63.3) mg/dL and TG /HDL ratio 3.1 (1.97). There was only difference of the zBMI ( $p < 0.05$ ) between the groups, being the low birth weight group with higher zBMI. The other metabolic parameter compared showed no difference. **Conclusions:** It was observed a high frequency of low birth weight, insulin resistance and inadequacy of the lipid profile. Birth weight should be considered a risk factor for

only overweight, but as of the moment of weight gain, this fact, by itself, already increases the metabolic risk.

**Keywords:** Birth weight, Puberty, Obesity, Metabolic syndrome, Risk factors

## Resumo

**Objetivos:** Correlacionar peso ao nascer e condição metabólica atual em púberes com sobrepeso. **Métodos:** Estudo transversal retrospectivo de 125 pacientes (85 meninas /40 meninos), categorizados em grupos pelo peso ao nascer. Dados avaliados: idade cronológica, zIMC, CA /E, zEstatura e perfil lipídico. **Resultados:** Baixo peso ao nascer em 16 (12,8%) e alto peso em 15 (12,0%). Média (DP) de idade cronológica 13,3 anos (2,3), zIMC + 2,60 (0,6), Circunferência Abdominal / Estatura 0,59 (0,09), zEstatura + 0,44 (1,15), HOMA-IR 4,37 (3,07), Glicemia 85,3 mg /dL (8,4), Soma de Insulina 500,4 (306,4), Colesterol Total 166 mg/dL (37,3), LDL 100,5 mg/dL (28,9), HDL 41,4 mg /dL (8,8), triglicérides (TG) 119,8 ( DP 63,3) mg/dL e TG/ HDL 3,1 (1,97). Diferença do zIMC ( $p < 0,05$ ) entre grupos, com maior valor no baixo peso ao nascer. **Conclusões:** Alta frequência de baixo peso ao nascer, resistência à insulina e inadequação do perfil lipídico. O peso ao nascer deve ser considerado fator de risco para sobrepeso, mas a partir do momento do ganho ponderal, esse fato, por si só, já aumenta o risco metabólico.

**Descritores:** Peso ao nascer, Puberdade, Obesidade, Síndrome metabólica, Fatores de risco

## Introduction

The first 1000 days of life highlighted the importance of genetic programming by environmental factors and birth weight on health during childhood and adult life. The World Health Organization (WHO) defines low birth weight to be less than 2500 g, and high birth weight to be more than 4000 g, regardless of gestational age or other demographic variables<sup>(1)</sup>.

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Among the several complications associated with weight extremes at birth, both low weight and macrosomia, there is the effect on the development of chronic diseases typical of adulthood, mainly related to the metabolic syndrome<sup>(2-4)</sup>. Moreover, a direct association has been demonstrated between extremes of birth weight and being overweight during childhood and adulthood<sup>(2,5-6)</sup>.

Despite the range of evidence on the influence of birth weight on adult health, little is known about its possible effect on the metabolic profile of children and adolescents, particularly in the Brazilian population. Therefore, the present study aimed to assess any possible correlation between birth weight and current cardiovascular condition in overweight pubertal patients.

## Methods

This was a retrospective cross-sectional study with a sample comprising 125 pubertal overweight patients (85 females and 40 males with zBMI score above +1SD) who underwent follow-up at the outpatient Endocrinology clinic at the Irmandade da Santa Casa de Misericórdia of São Paulo hospital. The sample was of convenience, by retrospective study.

Inclusion criteria: overweight patients of both genders, pubertal and presenting data available in the medical record.

Patients with a clinical diagnosis of chronic or endocrine/metabolic diseases, genetic syndromes, short stature, chronic use of glucocorticoids and with conditions that made it impossible or to accurately measure height, such as bone dysplasias, rickets, severe scoliosis, were excluded from this study. The clinical and laboratory data were collected in the 1st evaluation of the patients in the service.

The patients in the study had a mean chronological age of  $13.3 \pm 3.3$  years and were categorized into 3 groups according to birth weight (<2500g, 2501-3999g and 4000g). The birth weight (BW) assessment was based on the data contained in the participants' birth record. In the present study, we used birth weight between 2.501 and 3.999 g as adequate.<sup>(1)</sup>

Weight was measured with a digital scale and height (H) with a fixed wall stadiometer (Tonelli model). Weight and height were used to calculate body mass index (BMI) and both height and BMI were expressed as z scores. Patients with zBMI between +1 and +2 SD were considered as overweight and those with zBMI above +2 SD were considered as obese (WHO, 2007)<sup>(7)</sup>. Pubertal staging was verified by a physical examination, being established according to the Tanner scale<sup>(8-9)</sup>.

A tape measure was used to assess waist circumference (WC) at the midpoint between the upper border of the iliac crest and the last costal border, with the patient standing without clothing, arms positioned along the body and in the expiratory phase of breathing. The ratio of waist circumference to height (WC/H) was calculated, with a cut of 0.5<sup>(10)</sup>.

Measurements of total cholesterol (TC), high density lipoprotein-cholesterol (HDL-c), low density lipoprotein-cholesterol (LDL-c), very low density lipoprotein (VLDL) and triglycerides (TG) were performed using automatic enzymatic colorimetric analysis. Serum glucose was analyzed by the enzymatic colorimetric method (hexokinase) (Siemens Medical Solutions Type spectrophotometric Chemistry) and insulinemia was obtained by chemiluminescence (Siemens IMMULITE200).

As a criterion for the diagnosis of insulin resistance, the HOMA-IR index, described by Matthews et al 1985<sup>(11)</sup>, was used, and calculated as the product of fasting insulin (mIU/mL) and fasting glucose (mmol/L) divided by 22.5. The cutoff point of HOMA-IR was > 2.5.<sup>(12)</sup> The sum of insulin (SI) was assessed by performing an oral glucose tolerance test (OGTT), which can also be used as a parameter for insulin resistance, based on the sum of insulin levels.<sup>(12)</sup>

The percentage of abnormal lipid values was based on the First Brazilian Guideline for the Prevention of Atherosclerosis in Childhood and Adolescence<sup>(13)</sup>. The ratio of triglycerides divided by HDL-c (TG/HDL-c) was calculated, considering the cutoff value for the ratio of 2<sup>(14)</sup>.

The data averages obtained from the three groups were compared using the one-way ANOVA test and, when necessary, the Kruskal-Wallis test using the SigmaStat 3.5 program for Windows (SPSS, Point Richmond, CA, USA). The Z test was also performed to compare the proportions of abnormal percentages of lipid values among the three groups. The results were considered statistically significant when  $p < 0.05$ .

The project was approved by the Research Ethics Committee of the institution, (certificate No. 01937412.7.0000.5479), and a free and informed consent form was signed by the parents and/or guardians.

## Results

16 patients (12.8%) had low birth weight (LBW), 15 (12%) had high birth weight (HBW) and the remaining 94 (75.2%) were considered to have adequate birth weight (ABW). The percentage of individuals with obesity in the groups was 81% in LBW, 80% in ABW and 93% in HBW.

Table 1

Anthropometric and laboratorial data in each group according to birth weight, expressed as mean (standard deviation) and p value.

Variables	LBW	Adequate	High BW	p values
CA	14.4 (2.1)	13.2 (2.4)	12.9 (1.8)	0.113
Gender	11 F; 5 M	69 F; 25 M	10 F; 5 M	>0,05#
ZBMI	3.11 (0.64)	2.59 (0.68)	2.38 (0.58)	0.025*
WC/H	0.64 (0.59)	0.59 (0.08)	0.60 (0.05)	0.184
zHeight	0.07 (0.01)	0.41 (1.82)	0.41 (0.89)	0.617
HOMA-IR	3.30 (2.66)	4.06 (2.51)	2.44 (5.66)	0.990
Blood glucose (mg/dl)	85.06 (11.93)	84.64 (7.46)	89.33 (9.39)	0.139
SInsulin	486.41 (188.98)	433.50 (273.11)	342.70 (544.58)	0.431
Total Cholesterol (mg/dl)	160.00 (38.27)	164.50 (38.87)	151.00 (23.95)	0.636
LDL-c (mg/dl)	89.50 (31.73)	100.00 (30.06)	93.00 (15.89)	0.669
HDL-c (mg/dl)	38.50 (11.96)	40.00 (8.49)	40.00 (7.28)	0.785
Triglycerides (TG) (mg/dl)	86.50 (67.01)	109.00 (64.61)	90.00 (52.73)	0.696
TG/HDL	2.23 (2.61)	2.45 (1.91)	2.57 (1.65)	0.950

CA: chronological age, F: female, M: male, BMI: body mass index, WC/H: waist circumference to height, SInsulin: Sum of insulin. #z test, p>0.05. \*ANOVA test and the Kruskal-Wallis test. zBMI LBW x ABW: p = 0.025 (Kruskal-Wallis test).

The BMI SDS showed a significant difference (p value <0.05) between groups. No significant differences between groups were found in the WC/H, H SDS, Insulin Sum, HOMA-IR, fasting glycemia, CT, HDL-c, LDL-c, TG and TG/HDL ratio. When comparing the sexes, the following data were found: in the LBW group, 68.7% were female and 31.3% male, in the ABW, 73.4% and 26.6% respectively, and 66.7% and 33.3% in the HBW, without any distinction between groups: LBW x ABW (p = 0.934), LBW x HBW (p = 0.609) and ABW x HBW (p = 0.201). The detailed variables of each group are shown in Table 1.

An increase in the percentage of inadequacy of the lipid profile was observed in the study, with no significant differences between the groups (table 2). When comparing the groups, there was no statistically significant difference between LBW x ABW (p = 0.759), LBW x HBW (p = 0.641) and ABW x HBW (p = 0.414).

Table 2

Lipid profile and degree of inadequacy of the values in the entire sample.

Lipid profile	Degree of inadequacy (%)
Total Cholesterol	41.60%
LDL-c	12.80%
HDL-c	44.80%
Triglycerides	35.20%

## Discussion/Conclusion

A higher prevalence of LBW was, therefore, observed in this group of overweight patients when compared to the national average (8.53%)<sup>(15)</sup>. The group of patients studied presented high frequency of insulin resistance and inadequacy of the lipid profile, with no significant difference associated with birth weight. A statistically significant relationship was found with regard to zBMI between the groups. This finding corroborates previous studies that show that patients with birth weight extremes present a relationship to overweight during their life and their potential complications<sup>(2,5-6)</sup>. However, the association between LBW and increased zBMI is not yet fully established<sup>(19)</sup>.

LBW and its association with increased zBMI can be explained by some physiological mechanisms: the change in phenotypic expression generated by insufficient cell replication, which seems to lead the body to store energy as an adaptive response; the change promoted in the metabolism through the expression of hormones, emphasizing the association between LBW and insulin resistance; individual predisposition that LBW leads to greater vulnerability to environmental influences present in later stages of the life cycle<sup>(20)</sup>. There are many studies showing the association between an adverse intrauterine environment and chronic diseases later in life, a concept termed "the developmental origins of health and disease"(DOHaD)<sup>(21)</sup>. However, the intrauterine environment theory is not able to explain all the

associations between birth weight and metabolic consequences. A recent study suggested a fetal genetic effect on later cardio-metabolic health, in particular, the association between lower birth weight and higher adult blood pressure<sup>(22)</sup>. The DOHaD theory has now expanded to neonatal period as well. This is especially important when considering preterm infants that emerge from the intrauterine environment more developmentally immature than term infants. So, the presence of an adverse intrauterine and/or neonatal environment significantly increases the risk of obesity, insulin resistance and leptin deficiency with major implications for metabolic regulation. Therefore, low birth weight itself should be considered a marker, rather than a cause of later diseases, with the varying etiologies of low birth weight encompassing relatively benign normal genetic variation and more life-threatening events including intrauterine growth restriction and preterm delivery<sup>(23)</sup>.

In this group, adolescents with LBW did not present worsening of the metabolic profile than the other groups. This factor suggests that excessive weight gain is the main risk factor for metabolic changes. However, it would be important to evaluate adolescents with LBW, but who remained eutrophic in order to determine if the frequency of metabolic changes is greater than in the ABW group. It is important to state the importance of proper feeding and weight management in this at-risk group.

In the last decades an increase in HBW frequency has been observed in several countries, ranging from 3% to 15% of normal pregnancies<sup>(16)</sup>, reaching 15% to 50% in pregnancies of patients with gestational diabetes mellitus (GDM) and 24% to 40% in type 1 and 2 diabetic pregnancies<sup>(17)</sup>. Medeiros et al, 2012<sup>(18)</sup>, in a study that evaluated the birth weight and metabolic risk factors in overweight children and adolescents, found a prevalence of 16% of HBW. Our study had a similar frequency of HBW (12.0%) of the literature.

However, it's important to highlight that, independent of the BW, there was a high frequency of metabolic abnormalities seen in this group of overweight patients. It could suggest that a close monitoring of nutrition and anthropometric measures must be done in patients with inadequate birth weight, in order to avoid overweight.

The study had limitations because it was a retrospective study, in which some data that would be important were not completely filled, such as blood pressure values. It is worth mentioning the absence of adequate documentation of the gestation data of the patients, such as maternal weight gain during pregnancy, use of medications during this period, and eventual perinatal interferences.

There was a higher frequency of LBW in the studied group of overweight patients than described in the general population. Therefore, BW should be considered a risk factor for only overweight, but from the moment of weight gain, this fact, by itself, already increases the metabolic risk.

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