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ORIGINAL ARTICLE

Prenatal growth and metabolic syndrome components among Chilean children

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The association of prenatal growth with metabolic syndrome (MS) components and insulin resistance (IR) in children has not been studied in Chile and most developing countries. Some associations found in developed countries are controversial. A retrospective cohort study was designed linking present information on MS components and IR in children with register-based information on birth weight (BW), birth length (BL) and gestational age (GA). Examinations included anthropometry and blood pressure (BP), as well as self-report of pubertal status. A fasting blood sample was taken to determine lipids, glucose, insulin and homeostasis model assessment (HOMA)-IR was calculated. The study cohort of 2152 children was on average 11.4 ± 1.0 years old. The prevalence of MS, IR and overweight were 7.6%, 24.5% and 34%, respectively. Elevated BP was negatively associated with dichotomized risk categories of the perinatal factors studied (BW, BL and GA). Contingency tables showed that high waist circumference (WC) and elevated BP had a U-shaped association with various categories of BW and BL, respectively. Stepwise linear regressions selected: (a) WC as inversely associated to GA and directly associated to BW, (b) BP as inversely associated to GA and (c) HOMA-IR as inversely associated to BL. Non-optimal prenatal growth seems to predispose to high WC, elevated BP and IR in school-age children, supporting the early life origin of several non-communicable diseases. Those associations were rather weak as estimated by the slopes of the regressions and probably reduced by their U-shaped nature; they would reasonably become stronger with a longer follow-up.

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Introduction

The metabolic syndrome (MS) represents a set of risk factors that are closely linked to insulin resistance (IR).[1] The National Cholesterol Education Program Adult Treatment Panel (NCEP-ATP III) indicates that factors such as overweight, especially abdominal obesity and physical inactivity promote the development of IR. It also establishes the MS diagnostic criteria when three or more of the following five components are present: high waist circumference (WC), elevated blood pressure (BP), low high-density lipoprotein cholesterol (HDL-C), elevated triglycerides (TG) and high fasting glucose (GLU).[1] The use of adapted criteria for children has been proposed by Cook *et al*.[2]

Mainly based upon European studies the importance of nutrition during pregnancy, infancy and early childhood in the origin of chronic adult diseases such as obesity, diabetes and cardiovascular disease, has been established.[3] Barker and coworkers have shown that malnutrition during pregnancy favors the incidence of infants with low-birth weight (BW) as well as macrosomia; both groups have a greater predisposition to develop various components of MS and IR.[4,5]

Although many Chilean studies have shown the influence of maternal nutritional status on fetal growth[6,7] and there have also been some reports about the presence of components of MS and IR in Chilean children and adolescents, none of these included the association between components of MS and fetal growth.[8–14]

The objective of this study was to investigate for the first time in Chile, the association between prenatal growth and the components of MS, including IR, in schoolchildren.

Methods

During the years 2009 and 2010, a retrospective cohort study of children attending fifth and sixth grades at 14 public primary schools in the county of Puente Alto, located in the

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city of Santiago, Chile, was conducted. All 3521 children attending school were invited to participate with a letter addressed to their parents.

The information of the children who entered this study was linked to the perinatal data using the national individual identification number; perinatal data was collected by the Civil Registry and later refined by the Statistics Unit of the Ministry of Health of Chile.[15]

The perinatal variables used in this study were: BW, birth length (BL) and gestational age (GA) of delivery. They were determined in maternity hospitals immediately after delivery by trained personnel.[6,16] Newborns were weighed, in most cases, using an electronic balance Tanita 1583 (Tanita Corporation, Arlington Heights, IL, USA) with an accuracy of 10 g, or an electronic scale, Seca® 345 (Secacorp, Hamburg, Germany) with an accuracy of 20 g. Crown–heel length was measured on a custom-made neonatometer to the nearest 1 mm. GA was estimated with the date of the last menstrual period; when this data was inaccurate, an early obstetric ultrasound was used. This ultrasound examination is available for most women before 20 weeks gestation in Chile. The majority of these scans are performed with a Voluson® 730 PRO ultrasound machine (GE Healthcare, Chalfont St Giles, UK) or a Acuson® 120 XP (Acuson Inc., Mountain View, CA, USA).[6] Ultrasound examinations are sometimes not available in primary health care; in those situations GA is usually estimated by a postnatal clinical examination of the newborn performed by the physician.

The criteria of Cook *et al.*[2] were used to define MS, when at least three out of five of its components were present, as defined by the following cut-off points: WC $\geqslant$90th percentile;[17] BP, either systolic (SBP) or diastolic (DBP) $\geqslant$90th percentile;[18] HDL-C $\leqslant$40 mg/dl; TG $\geqslant$110 mg/dl and GLU $\geqslant$100 mg/dl. Recently proposed cut-off points of homeostasis model assessment (HOMA)-IR, according to sex and pubertal maturation, were used to classify IR.[19]

The evaluation at each school was made by a Nurse and a Nutritionist. Height and weight were measured using a stadiometer and a beam-scale Seca®, with an accuracy of 50 g, while being barefoot and lightly clothed. The final height and weight were the respective averages of three measurements; in the latter, the average weight of their clothes was deducted. We calculated body mass index (BMI = weight in kg/height^2 in m) expressed in percentiles and *z*-scores.[20] Nutritional status was classified according to BMI percentiles as; normal: 5 to 84, overweight: 85 to 94, obesity: $\geqslant$95 and underweight: $<$5.[20] WC was measured with inextensible tape on the upper lateral border of the right ilium in the mid-axillary line at the end of an exhalation;[21] three measurements were averaged and we used $\geqslant$90th percentile as cut-off value.[17] The triceps and subscapular skinfolds were measured with a Harpenden® caliper using a standard technique;[21] both were used to calculate the percentage of fat mass (%FM) using slaughter equations,[22] previously validated in Chilean children.[23,24] A Critikon® Dinamap Pro 100 BP monitor was used according to international norms and the averages of three measurements of SBP and DBP were obtained and classified as abnormal using the $\geqslant$90 percentile of the same reference.[18] A voluntary private self-report of pubertal status was requested by observation of standardized photos of breast development in girls and genitalia in boys, including the presence of pubic hair.[25]

Venous blood samples were collected for determination of GLU (Gluco-quant method, glucose/hexokinase, Roche Diagnostics GmbH, Mannheim, Germany) and insulin (immunoassay direct luminometer chemotherapy, ADVIA Centaur® XP, Bayer HealthCare LLC, Kyowa Medex Co., Japan), this method measures concentrations of insulin from 0.5 to 300 mUI/ml (sensitivity 0.5 mUI/ml) with a coefficient of variation of 3.48% and 6.17% for concentrations of 23.51 and 62.49 mUI/ml, respectively. The formula developed by Mathews *et al.*[26] was used to calculate HOMA-IR = [(GLU (mmol/liter) $\times$ insulinemia (mUI/ml))/22.5].

Student's *t* test for independent samples to compare averages and Pearson's χ^2 test for proportions comparison were used. Contingency tables were used to assess significant associations between children presenting MS components and IR with risk categories of dichotomized perinatal variables, that is, BW $<$ 2500 g, BL $<$ 50 cm and GA $<$ 37 weeks. A χ^2 test was also applied to assess possible U-shaped associations between MS components and IR with perinatal variables, that is, either BW or BL or GA, divided in various categories in the contingency tables; the Bonferroni correction was used to compute statistically significant differences of the proportions with the presence of MS components between the extreme categories and the lowest value found in an intermediate category. Poisson regression was used to model count data from those contingency tables for testing linear and quadratic behaviors. Stepwise linear regression models ascertained the joint associations of BW, BL and GA on the MS components, including the IR. After selecting MS components, including IR, with a significant association, covariance analysis (ANCOVA) was used to determine the effects of the same perinatal variables now adjusted for sex, pubertal age according to Tanner and %FM; all or part of those variables could be confounders that potentially influence the components of MS, including IR.[1,19,27–29] For all analysis SPSS 17.0 was used. Significant *P*-value was defined as $\leqslant$0.05.

Parents or their representatives signed an informed consent form and boys/girls an informed acceptance form. The study was approved by the Ethics Committees of the School of Medicine (Pontificia Universidad Católica de Chile) and FONDECYT.

Results

Of the total of 3521 eligible subjects, 1602 were girls and 1919 were boys. 31.5% of the girls and 44.5% of the boys refused to participate ($P < 0.0001$). 2174 children and adolescents signed the informed acceptance forms and entered the study. There were no significant differences between those who participated or those who did not with respect to their mean values of BW, BL, GA and maternal years of education; *P*-values were: 0.074, 0.15, 0.15 and 0.072, respectively.

Complete information at birth was obtained for 2152 children (98.9%), of which 50.9% were girls and 49.1% boys. Table 1 shows mean age for the entire sample, which was 11.4 years, and the anthropometric characteristics by sex. Weight was significantly higher for girls and the opposite was true for height. Prevalence of overweight in the entire sample was 37.6% while obesity reached 14.8%; 80.3% of the children self-reported being pubertal.

The prevalence of MS and IR were 7.6% and 24.7%, respectively. Regarding the MS components frequency distribution in the total sample, TG $\geqslant$110 mg/dl was the most common with 25.6%, followed by 18.8% for WC $\geqslant$90th percentile, 17.2% for HDL-C $\leqslant$40 mg/dl, 13.9% for BP $\geqslant$90th percentile (SBP reached 99% of those cases) and 8% for GLU $\geqslant$100 mg/dl.

Table 2 shows the mean values of the MS components by gender. Significantly higher concentrations were found for HDL-C and GLU in boys, whereas mean values for TG and HOMA-IR were significantly higher in girls. Results of Table 2 for each sex were also adjusted for BMI and for age. *P*-values for non-adjusted and adjusted for BMI and age comparisons gave similar results and are not presented. With regard to perinatal variables, BW and BL were significantly higher among boys (Table 3).

In contingency tables, BP was negatively associated with dichotomized categories of perinatal factors (Table 4). The proportions of children with BP $\geqslant$90th percentile were significantly higher in BW < 2500 g, BL < 50 cm and GA < 37 week categories.

The presence of MS was not associated with perinatal factors. Figures 1 and 2 show the only two U-shaped

Table 1. *Anthropometric measures (mean ± S.D.) by gender in 2152 children from Puente Alto, Chile, 2009–2010**

Variable	Total ($n = 2152$)	Girls ($n = 1095$)	Boys ($n = 1057$)	*P*-value
Age (years)	11.4 ± 0.98	11.4 ± 0.96	11.5 ± 1.00	0.006
Weight (kg)	43.8 ± 11.14	43.7 ± 11.0	43.3 ± 11.2	0.021
Height (cm)	146.6 ± 8.2	147.0 ± 7.8	146.2 ± 8.5	0.02
BMI (kg/m^2)	20.18 ± 3.9	20.3 ± 3.8	20.0 ± 3.9	ns
z-BMI	0.58 ± 1.05	0.58 ± 0.99	0.57 ± 1.10	ns
WC (cm)	72.7 ± 10.4	73 ± 10.1	72.3 ± 10.7	ns

*BMI, body mass index; *z*-BMI, *z*-score for body mass index; WC, waist circumference.

Table 2. *MS and IR components (mean ± S.D.) by gender in 2152 children from Puente Alto, Chile, 2009–2010**

Measure	Total ($n = 2152$)	Girls ($n = 1095$)	Boys ($n = 1057$)	*P*-value
CHDL (mg/dl)	51.3 ± 11.8	50.3 ± 11.7	52.5 ± 11.8	<0.0001
TG (mg/dl)	91.5 ± 58.5	97.3 ± 58.3	85.5 ± 58.2	<0.0001
SBP (mmHg)	110.6 ± 8.3	110.8 ± 8.4	110.3 ± 8.3	ns
DBP (mmHg)	58.4 ± 7.1	58.6 ± 7.5	58.2 ± 6.8	ns
GLU (mg/dl)	90.5 ± 6.6	89.4 ± 6.6	91.6 ± 6.4	<0.0001
HOMA-IR	3.2 ± 2.3	3.6 ± 2.2	2.9 ± 2.3	<0.0001

*MS, metabolic syndrome; IR, insulin resistance; HDL, high-density lipoprotein; CHDL; HDL cholesterol; TG, triglycerides; SBP, systolic blood pressure; DBP, diastolic blood pressure; GLU, glucose; HOMA, homeostasis model assessment.

Table 3. *Perinatal characteristics (mean ± S.D.) by gender in 2152 children from Puente Alto, Chile, 2009–2010**

Variable	Total ($n = 2152$)	Girls ($n = 1095$)	Boys ($n = 1057$)	*P*-value
BW (g)	3343.3 ± 522.7	3292.3 ± 512.6	3396 ± 528.1	<0.0001
BL (cm)	49.6 ± 2.4	49.2 ± 2.3	49.9 ± 2.4	<0.0001
GA (weeks)	38.9 ± 1.7	38.9 ± 1.8	38.8 ± 1.7	ns

*BW, birth weight; BL, birth length; GA, gestational age.

Table 4. *Associations of abnormal values of BP with risk categories of perinatal factors in 2152 children from Puente Alto, Chile, 2009–2010 – values are n (%)**

	BW (g)			
BP	<2.500	⩾2.500	Total	*P*-value
<90	84 (78.5)	1768 (86.5)	1852 (86.1)	
⩾90 percentile	23 (21.5)	277 (13.5)	300 (13.9)	0.021
	107	2045	2152	
	BL (cm)			
	<50	⩾50		
<90	796 (83.5)	1056 (88.1)	1852 (86.1)	
⩾90 percentile	157 (16.5)	143 (11.9)	300 (13.9)	0.0024
	953	1199	2152	
	GA (weeks)			
	<37	⩾37		
<90	101 (79.5)	1751 (86.5)	1852 (86.1)	
⩾90 percentile	26 (20.5)	274 (13.5)	300 (13.9)	0.028
	127	2025	2152	

*BP, blood pressure; BW, birth weight; BL, birth length; GA, gestational age.

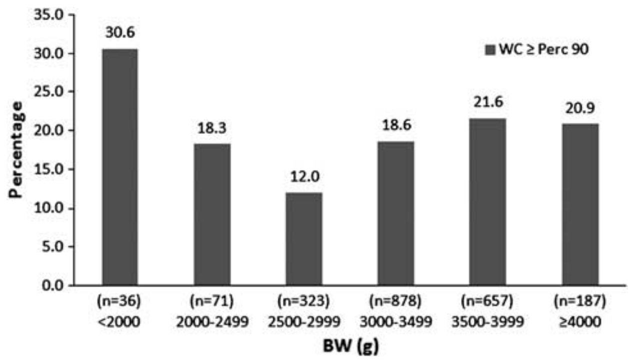

Fig. 1. Association of WC ⩾90th percentile with various categories of BW. Puente Alto, Chile, 2009–2010. BW, birth weight; WC, waist circumference.

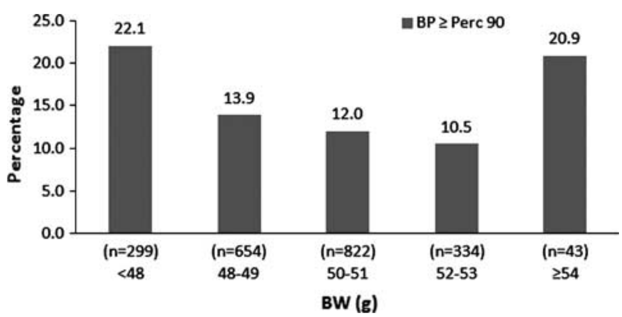

Fig. 2. Association of BP ⩾90th percentile with various categories of BL. Puente Alto, Chile, 2009–2010. BL, birth length; BP, blood pressure.

associations found. They were between BW with WC ⩾90th percentile and between BL with BP ⩾90th percentile. Differences of WC ⩾90th percentile proportions between extreme BW categories, < 2000 g and ⩾4000 g, with an intermediate category (2500–2999) were significant ($P < 0.001$; Fig. 1). Differences of BP ⩾90th percentile proportions between extreme BL categories, < 48 cm and ⩾54 cm, with an intermediate category (52–53 cm) were significant ($P < 0.001$; Fig. 2).

The Poisson regression that analyzed the association between BW and WC ⩾90th percentile confirmed a quadratic positive term with P-value = 0.001; the model with a linear term was not significant. The Poisson regression also analyzed the association between BL and BP ⩾90th percentile and resulted in two behaviors: a linear negative term and a quadratic positive term, having P-values of 0.001 and 0.01, respectively. When including the linear and quadratic behaviors together, both remained significant meaning that the general tendency is negative but allowing a relevant curve or quadratic component.

The stepwise linear regression selected the following components of MS, including IR, as associated with perinatal factors: (a) WC inversely associated with GA and directly associated with BW, (b) BP inversely associated with GA and (c) HOMA-IR inversely associated with BL (Table 5).

Table 5. *Perinatal variables selected by a stepwise linear regression on WC, BP and HOMA-IR in 2152 children from Puente Alto, Chile, 2009–2010**

	Coefficient β mean ± S.E.	P-value
WC variation (cm)		
Per 100 g of BW increment	0.31 ± 0.05	<0.0001
Per 1 week of GA increment	−0.463 ± 0.158	0.0003
BP variation (mm/Hg)		
Per 1 week of GA increment	−0.028 ± 0.11	0.007
Unit HOMA-IR variation		
Per 1 cm of BL increment	−0.06 ± 0.02	0.005

*WC, waist circumference; BP, blood pressure; HOMA, homeostasis model assessment; IR, insulin resistance; BW, birth weight; GA, gestational age; BL, birth length.

Table 6. *Perinatal variables selected by a stepwise linear regression on WC, BP and HOMA-IR, after adjustment by gender, %FM and pubertal maturation, in 2152 children from Puente Alto, Chile, 2009–2010**

	Coefficient β mean ± S.E.	P-value
WC variation (cm)		
Per 100 g of BW increment	0.11 ± 0.02	<0.0001
Per 1 week of GA increment	−0.24 ± 0.08	0.0018
BP variation (mm/Hg)		
Per 1 week of GA increment	−0.33 ± 0.10	0.0012
Unit HOMA-IR variation		
Per 1 cm of BL increment	−0.06 ± 0.02	0.0007

*WC, waist circumference; BP, blood pressure; HOMA, homeostasis model assessment; IR, insulin resistance; FM, fat mass; BW, birth weight; GA, gestational age; BP, blood pressure; BL, birth length.

Table 6 presents the same associations as shown in the previous analysis (Table 5) but now adjusted for gender, %FM and self-report of pubertal maturation, which did not influence the direction of the findings. Furthermore, P-values did not change markedly. However, there were some effects detailed below.

In the WC model the slope of the association with BW was reduced to one-third; meanwhile, the association with GA was reduced to one-half. In that case the slopes for %FM and self-reported pubertal status on WC were positive and negative, respectively, with an important effect in both cases; significant slope values were 0.80 cm of WC change for one percent of FM, −5.72 cm of WC change for pubertal status 1, −4.75 cm of WC change for pubertal status 2 and −3.20 cm of WC change for pubertal status 3.

In the BP model the slope of the association with GA was increased more than 10 times in the adjusted model. In that case the slopes of the regressions on BP for sex and self-reported pubertal status were negative and much higher than the positive slope for %FM. Significant negative slope values were: −0.86 mm/Hg of BP change for female sex, −7.94 mm/Hg of BP change for pubertal status 1, −7.16 mm/Hg of BP change for pubertal status 2, −5.66 mm/Hg of BP change for pubertal status 3 and −4.53 mm/Hg of BP change for pubertal status 4. A significant positive value of 0.17 mm/Hg of BP change was found for one percent of FM.

In the HOMA-IR-adjusted model the slope of the negative association with BL was similar. In that case the slopes of the regressions on HOMA-IR for sex and self-reported pubertal status were non-significant and the positive slope for %FM was rather low reaching a value of just 0.09 HOMA-IR units for one percent of FM.

Discussion

The sample of children from 14 public schools from Puente Alto County represents the largest number of children studied in the last few years in Chile.[8–14,24] MS and IR prevalences were 7.6% and 24.7%, respectively, showing an important prevalence of metabolic risks; the latter almost joining the rather high prevalence of overweight (37.6%).

The main results of this study show that two of the three studied prenatal factors, BL and GA, were independently and inversely associated to HOMA-IR as well as with WC and BP, respectively. These results were consistently shown for the first time in our country in all multivariate analyses performed. On the other hand, it was also observed in the stepwise multiple regressions that BW was positively associated to WC. However, it is important to note that lower and higher BW categories presented a higher proportion of children with WC ⩾90th percentile than intermediate categories in the contingency tables showing a U-shaped association.

Mean values of weight, height, TG and HOMA-IR were higher for girls, whereas mean HDL-C was higher for boys, generally in correspondence with other recent national studies of anthropometry or MS components in children of similar ages.[12–14,24]

The most frequently observed MS components were TG, WC, HDL-C and BP, whereas GLU was the less frequently observed; this distribution of components has been considered characteristic for children.[28]

It has been suggested that the inverse association between BL and HOMA-IR may be explained by the observation that short BL babies have a higher ratio of fat to lean body mass; as muscle tissue is the most important tissue for the storage and oxidation of GLU, individuals with a higher fat to muscle ratio are at increased risk of the metabolic consequences of IR.[30,31] A negative association between birth size, as estimated by BW, and HOMA-IR has been shown but only after adjustment for weight.[32]

Regarding the independent negative association of GA with WC, recent reports from younger children have suggested a tendency for a higher central adiposity in pre-term children.[33,34] Our results in older children give further support for those publications; follow-up studies would lend more information on this aspect.

Some epidemiological studies have suggested that arterial hypertension is a chronic disease that begins in childhood, and that prematurity is potentially associated with the development of hypertension in childhood and adulthood. However, the possibility of an inverse association of GA with BP, which has been systematically reviewed for children in a small number of available studies, recently concluded that the majority of them failed to show that association;[35] our study supports this possibility.

Other studies support the idea that BW, rather than GA, can negatively influence BP. One study from Finland demonstrated that SBP was higher in children who were born at term but were small for their GA relative to full-term children who had an adequate weight for their GA, after adjusting for current BMI, meaning that an important influence of current body size was apparent;[36] in that study the most important differences in mean values between the two groups were in BW and BL rather than GA. Similar results were found in a cohort study that included five low- and middle-income countries; inverse and significant associations were found between BW and SBP and DBP.[37] A recent Chilean study in children between 4 and 16 years demonstrated an inverse exponential association between BW and BP, which persisted even after adjusting for BMI and pubertal status;[38] the authors concluded that the associations observed may be partially explained by fetal programming of the hypothalamic–pituitary–adrenal axis. Another multinational study, which included 3–6 year old Chilean children, first found a negative association between body size at birth and raised BP.[39] On the other hand, a study of Chinese adult found that SBP had an independent U-shaped relationship with BW.[40]

The U-shaped association between BW and WC found in this study has scarcely been reported in the literature; only two recent studies with similar results were found.[32,40] The former observed this U-shaped association and in addition found a similar relation with FM index and subscapular skinfold.[32] The latter study found that subjects with the lowest and the highest BW categories had higher risks of developing abdominal obesity, compared with those in the category of BW 2500–3499 g, an observation that is highly similar to our results.[40] Following a study published in 1992,[41] recent studies have consistently shown an inverse association between BW and central obesity in children, adolescents and adults.[42,43] Oken and Gillman[44] concluded that there is a paradox of increased adiposity at both ends of the BW spectrum: higher BMI with higher BW and increased central obesity with lower BW; the latter association may be mediated through changes in the hypothalamic pituitary axis, insulin secretion and sensing and vascular responsiveness. BW has recently been shown to be inversely associated specifically with visceral fat rather than subcutaneous abdominal fat in adults;[45] this association was apparent only after adjustment for adult BMI, suggesting that rapid postnatal weight gain, rather than BW alone, leads to increased visceral fat.

One of the major findings in the present study was a U-shaped association between BL and BP and a negative association with HOMA-IR. In the contingency tables the BL risk category selected as significantly associated with BP $\geqslant$90 percentile was $<$ 50 cm, which reached 44.3% in the studied population, similarly to the national proportion.[15] The importance of maternal height, length at birth and length during infancy for the future health and productivity of the populations has recently been raised by different groups.[46–48]

The two U-shaped associations found in this study, that is, BW with WC $\geqslant$90th percentile and BL with BP $\geqslant$90th percentile, are similar to those found in previous studies,[4,5] and suggest that having a larger sample size may permit to ascertain similar associations with other MS components and IR. The latter can be derived from the observation that malnutrition during pregnancy, reflected by a higher proportion of cases with low BW as well as macrosomia, which shows a U-shaped association, can also be related to various components of MS and IR in the two extremes during childhood.[4,5]

The effects of the associations between the MS components and HOMA-IR with the perinatal factors, as estimated by the respective slopes observed in the stepwise regressions, were rather weak. For example, the change of 1 week in GA was associated with a change of -0.463 cm in WC. Observed effects were modified after adjustments in the first two models presented. In the case of the WC variation, the most important factor negatively adjusting BW and GA effects was pubertal status; it is well known that WC increases with age and pubertal status.[17] In the case of the BP variation, the most important factor negatively adjusting BW effect was pubertal status; non-pubertal status prevents from BP elevation as recently reported.[49] For HOMA-IR variation, the slope of the association with BL was similar, denoting a scarce influence of adjustment and supporting the above made comment on the important role of BL.

The original sample consisted of 3521 school-aged children, however, 31.5% of girls and 44.5% of boys did not accept to participate. This suggested a sample bias towards an over representation of girls. However, the final study sample included 50.9% of girls and 49.1% of boys, showing a similar gender distribution as the national distribution in Chile. Information at birth was complete for 98.9% of the included subjects, and their mean GA, BW and BL values were similar to the national live birth averages. This suggests that our study sample is representative of the national distribution.[15] Furthermore, there were no significant differences between participants and non-participants with regard to their mean values of BW, BL, GA and maternal years of education.

In summary, the linear associations found between the MS components and HOMA-IR with perinatal factors were rather weak. This fact may be partly explained by the young age of the study population. One alternative explanation could be the U-shaped nature of the associations. Strengths of the paper include a large representative sample size. The associations between prenatal and metabolic factors will probably become stronger with a longer follow-up.

A possible limitation of this study is that pubertal status was determined by self-report. However, this is a method widely used in population studies. Good correlations have been reported between self-report and scores given by health personnel for boys and girls.[50] Two studies done in China support the use of self-report in population studies when no specific individual evaluations are needed.[51,52]

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