

Accelerated Growth in Early Life and Obesity in Preschool Chilean Children

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In Chile, childhood obesity rates are high. The purpose of this article is to compare BMI growth characteristics of normal (N), overweight (OW), and obese (OB) 5-year olds from 0 to 5 years and explore the influence of some prenatal factors on these patterns of growth. The study was done on a retrospective cohort of 1,089 5-year olds with birth weight >2,500 g. Weight and height were obtained from records at nine occasions (0–36 months); at 52 and 60 months, we measured them. At 60 months, children were classified as N, OW, and OB. At each age, BMI and z-score of BMI (BMI Z) differences were compared among groups. The influence of birth weight, pre-pregnancy BMI, and prenatal variables (weight gain, smoking, and presence of diabetes and preeclampsia) on BMI Z differences between N and OB was also explored. Adiposity rebound (AR) was not observed for the N, although for the OW, it occurred ~52 months and for the OB at ~24 months. BMI Z differences between N and OB were significant from birth, but were greatest between 6–12 and 36–52 months. Additional adjustment by birth weight, pre-pregnancy BMI, and prenatal variables decreased the BMI Z differences for the first 24 months with virtually no effect after this age. Accelerated growth in OB children from post-transition countries occurs immediately after birth, much earlier than the AR. The influence of prenatal factors on adiposity acquisition may extend at most until 2 years of life, although BMI gains thereafter are more related to postnatal variables.

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INTRODUCTION

In most developing countries in transition, obesity constitutes an important public health concern (1). In Chile, dietary changes toward an increased consumption of high-energy density foods and a decrease in physical activity has led to high obesity rates in all age groups (2). In 6-year-old children, the prevalence of obesity has almost tripled in the past two decades, from 7% in 1987 to 19.4% in 2006 (ref. 3). The health consequences of this trend projects into higher prevalence of risk factors of chronic diseases, dyslipidemia, hypertension, and glucose intolerance; to some degree this is already present in childhood (4).

The development of childhood overweight may be due to multiple factors involving genetic, biological, social, and environmental factors. The life-course approach can be especially helpful in studying how these factors relate to the development of this condition because it considers health as a dynamic process beginning from the prenatal period (5). Maternal weight before and during pregnancy, smoking during pregnancy, birth weight, and postnatal weight gain have all been associated with the development of childhood obesity (6).

We are presently studying the interaction between parental obesity and child growth, on obesity at 5 years of age in a cohort of ~1,200 children. We have collected data on risk factors for

childhood obesity (weight gain during pregnancy and smoking during pregnancy and lactation, duration of breast feeding), as well as anthropometric data from birth till 5 years of age. In this article, our aim is to compare BMI growth characteristics of normal (N), overweight (OW), and obese (OB) 5-year olds from birth also taking into account the influence of some prenatal factors.

METHODS AND PROCEDURES

Subjects

We selected preschool children (2.6–4 years old) who were attending 54 nursery schools belonging to the National Association of Day Care Centers (JUNJI) in 2006. JUNJI is a nationwide program catering to middle-low and low-income children (6 months to 5 years), which provides free education and food for 4 or 8 h/day (presently ~90,000, 2- to 5-year-old children attend JUNJI nursery schools) (7). The inclusion criteria for our study were: (i) children attending JUNJI centers located in six counties of Santiago, (ii) single birth with birth weight >2,500 g, (iii) evidence of being enrolled the previous year in one of JUNJI's centers, and (iv) absence of physical or psychological conditions that could severely affect growth.

The mothers of 1,195 children (from a total of 1,953 eligible participants) accepted to participate in the study. **Figure 1** shows the flow of participants of the study. No significant differences were found in terms of age, gender, birth anthropometry, weight, and height at 4 years of those recruited compared to those not enrolled.

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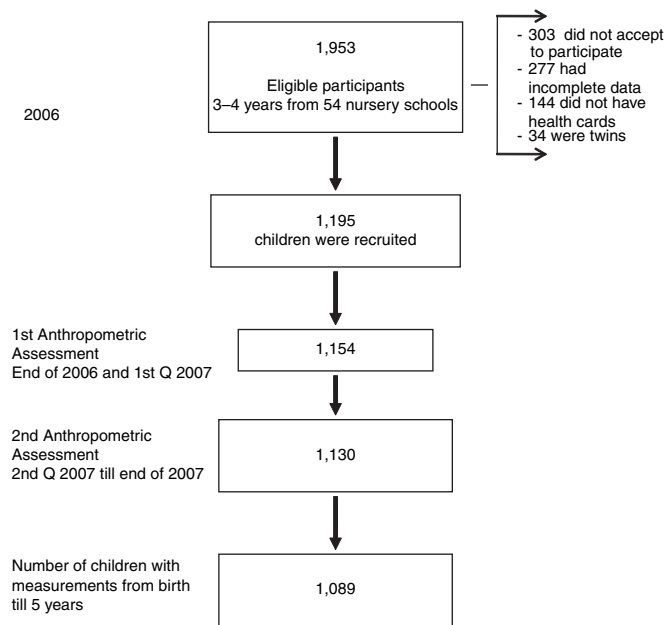


Figure 1 Flow of participants in the study.

Of the 1,195 children recruited, 1,089 (91%) have measurements from birth to 5 years; thus, our final sample size for these analyses is 1,089 children.

The study protocol was approved by the Executive Director of the JUNJI Program and the Institute of Nutrition and Food Technology (INTA) of the University of Chile. Informed consent was obtained from all parents or guardians of the children.

Anthropometric measurements

Weight and height measurements were obtained from birth until 36 months of age retrospectively from health records. Birth weight and birth length are determined at maternity hospitals immediately after delivery by trained personnel under standard procedure. After birth, weight and height are taken by nurses or nutritionists at the health center. Infant's weight up to 24 months is obtained using a pediatric balance-beam scale with a precision of 10 g, recumbent length is obtained with 0.1 cm accuracy. After 24 months, a balance-beam scale with a precision of 100 g is used, and height with the stadiometer (accurate to 0.1 cm). At 52 and 60 months of age, weight, height, and other anthropometric parameters were collected using standardized procedures by four trained registered dietitians of our team. Weight was measured with a portable electronic scale (Seca 770) with a precision of 0.1 kg, while height was measured with a portable stadiometer (Harpender 603) to the nearest 0.1 cm. Intra- and interobserver reliability on weight and height measurements were confirmed intraclass correlation ≥ 0.75 .

At 60 months, mothers of 754 children provided information on their pre-pregnancy weight (we measured them to determine height), gestational weight gain, smoking during pregnancy, presence of gestational diabetes, and preeclampsia. Mean pre-pregnancy BMI was 24.2 ± 4.3 , while mean weight gain during pregnancy was 12.4 ± 4.8 . The % of pregnant women who smoked during pregnancy was 15.2%, while the prevalence of gestational diabetes and preeclampsia was 4.8 and 9.1%, respectively. These are consistent with results reported in previous studies conducted in Chilean women (8–11).

Data analysis

Based on the established calendar of health visits, we considered the weight and height at: birth, 1, 2, 4, 6, 12, 18, 24, 36, 52, and 60 months (11 occasions). Only 25% of the children had 3–6 measurements; the rest had ≥ 7 . At each time point, we calculated BMI (weight/height²; kg/m²), z-score of BMI (BMI Z), height-for age z-score, prevalence

of overweight ($1 < \text{BMI Z} \leq 2$), and obesity ($\text{BMI Z} > 2$) by gender, using as a reference for each of these, the World Health Organization 2006 growth standards 0–5 years (12) and the World Health Organization 2007 growth reference 5–19 years (13). Less than 1% of the measurements were excluded from the analyses after being flagged as outliers (weight-for age z-score < -6 or > 5 ; height-for age z-score < -6 or > 6 ; BMI Z < -5 or > 5); z-scores standard deviations were within the valid range accepted by World Health Organization.

We classified the children into three groups according to their nutritional status at 5 years: OB, OW, and a third group that we named N. Only 19 children had BMI Z < -1 ; these were included in the normal category because their mean BMI Z was very close to the lower limit of the normal group. We plotted the cumulative frequency of obesity at each time point for the OB 5-year-old group (Figure 2). We also plotted the BMI (Figure 3) and BMI Z trajectories (Figure 4) from birth to 5 years (adjusting by gender and exact age at the 5-year measurement) and determined whether there were significant differences among groups using general linear model and Tukey test. Based on the BMI curves, we visually estimated the timing of adiposity rebound (AR) (defined as the age in which BMI increases following its nadir) (14).

In order to explore the influence of the prenatal period on the differences observed in BMI Z from birth until 5 years, between OB and N 5-year-old children, the basic model adjusted by age and gender (model 1) was subsequently adjusted by birth weight (model 2) and additionally by pre-pregnancy BMI and prenatal variables (weight gain and smoking during pregnancy and presence of gestational diabetes and preeclampsia (model 3). Information about the variables included in model 3 was not available for the total sample, thus, sample size for this analysis was restricted to those with complete information ($n = 754$ –441, depending on the age). At each age, differences and its 95% confidence interval were estimated using general linear model.

At all time points, BMI and BMI Z differences among the three groups were similar by gender (P -for-interaction ≥ 0.05); thus, these are not presented stratified by gender. All analyses were conducted using Stata 10.1 statistical package (15).

RESULTS

Anthropometric measures at each time point by gender are shown in Table 1. Mean birth weight (s.d.) was 3.44 (0.43) kg. Children were born with normal mean BMI Z (slightly higher

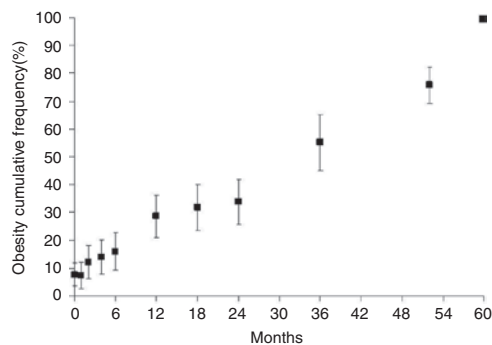


Figure 2 Prevalence of obesity from birth to 5 years in obese 5-year-old Chilean children.

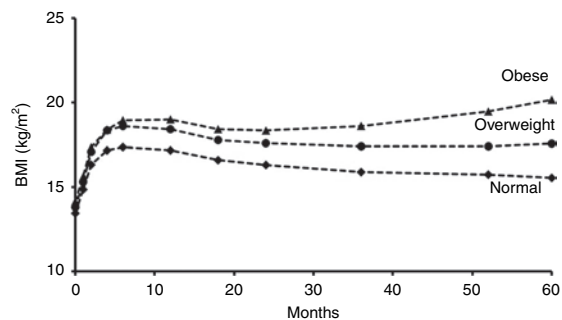


Figure 3 Evolution of BMI from birth to 5 years in normal, overweight, and obese 5-year-old Chilean children.

Table 1 Evolution of anthropometric characteristics from birth to 5 years of age of the sample, by gender

	Birth	1 month	2 months	4 months	6 months	12 months	18 months	24 months	36 months	52 months	60 months
Boys											
N	538	384	386	365	347	441	391	426	302	538	539
Weight (kg)	3.4 (0.4)	4.4 (0.6)	5.6 (0.7)	7.2 (0.8)	8.1 (1.0)	10.1 (1.1)	11.5 (1.3)	12.9 (1.5)	15.5 (1.9)	18.3 (2.7)	20.3 (3.4)
Height (cm)	50.1 (1.7)	53.9 (1.9)	57.3 (2.1)	63.3 (2.2)	66.9 (2.2)	75 (2.6)	81.4 (2.9)	86.8 (3.3)	95.3 (3.6)	104.6 (4.4)	109.7 (4.9)
BMI	13.7 (1.3)	15.2 (1.5)	16.9 (1.5)	17.9 (1.6)	18.1 (1.8)	18.0 (1.5)	17.3 (1.4)	17.1 (1.4)	16.7 (1.6)	16.7 (1.6)	16.8 (1.9)
BMI Z	0.14 (0.9)	0.11 (1.0)	0.30 (1.0)	0.46 (1.0)	0.50 (1.0)	0.80 (1.0)	0.83 (0.9)	0.80 (1.0)	0.80 (1.1)	0.97 (1.1)	0.99 (1.2)
% OW	12.9	14.1	19.1	21.8	23.3	28.8	28.3	30	24	28.6	25.8
% OB	3.9	3.8	5.5	7.1	7.2	11.9	12.5	10.3	16.5	16.3	18.6
Girls											
N	545	397	381	367	366	452	420	429	350	549	550
Weight (kg)	3.4 (0.4)	4.3 (0.5)	5.3 (0.6)	6.7 (0.7)	7.6 (0.9)	9.6 (1.1)	11 (1.2)	12.5 (1.5)	14.9 (1.9)	18.1 (2.7)	19.9 (3.2)
Height (cm)	49.7 (1.7)	53.3 (1.8)	56.6 (1.9)	61.8 (1.3)	65.7 (1.9)	73.7 (2.4)	80.3 (2.8)	85.9 (3.2)	94.4 (3.5)	103.8 (4.3)	108.9 (4.6)
BMI	13.6 (1.3)	15.0 (1.4)	16.5 (1.4)	17.4 (1.6)	17.7 (1.7)	17.6 (1.5)	17.0 (1.4)	16.9 (1.6)	16.7 (1.6)	16.8 (1.7)	16.8 (1.9)
BMI Z	0.20 (1.0)	0.20 (1.0)	0.40 (0.9)	0.40 (1.0)	0.47 (1.0)	0.77 (0.9)	0.87 (0.9)	0.80 (1.0)	0.85 (1.0)	0.90 (1.0)	0.85 (1.0)
% OW	17.5	19.2	23.3	20.9	22.8	29.6	34.9	30.2	31.4	29.2	25.5
% OB	3.6	1.7	3.0	5.5	6.8	8.1	8.3	10.3	10.4	12.5	12.6

for girls); the prevalence of overweight was 12.9 and 17.5% for boys and girls, respectively, although obesity rates were <4%. BMI increased till ~12 months in both genders, declining slightly thereafter; BMI Z increased continuously after 1 month, especially between 6 and 12 months and from 3 to 4 years. In boys, the prevalence of overweight increased continuously until 2 years of age, reaching 30% at that age and declining slightly thereafter. In girls, the trend was similar, but less pronounced, peaking at 18 months. The prevalence of obesity in boys increased continuously after birth till 5 years, except for a small drop at 2 years. At age 5, the prevalence of obesity in boys was 18.6%; in girls, the prevalence declined from birth to 1 month increasing continuously thereafter, reaching 12.6% at 5 years.

Figure 2 shows the cumulative obesity prevalence from birth to 5 years for the OB at age 5 ($N = 169$). The prevalence of

obesity for this group rose from 7.7 to almost 30% from birth until 12 months, remained relatively stable during the first year of life and then rose significantly until 5 years.

Figures 3 and **4** depict BMI and BMI Z trajectories from birth to 5 years, according to the BMI category at 5 years, adjusting for gender and age. **Figure 3** shows that at birth, BMI values were 13.5, 13.8, and 14.1 for N, OW, and OB, respectively; these values were significantly different for all group combinations. As expected, BMI increased with age, peaking in the three groups at 6 months of age (17.2, 18.4, and 19, respectively). After 6 months, it declined continuously in the N group reaching 15.5 at 5 years, no AR was observed in this group; for the OW, the nadir was observed at ~52 months, after which a slight upward rebound was noted. Finally for the OB, the nadir was observed at ~24 months of age, followed by a brisk rebound.

Table 2 Differences in BMI z-scores from 0 to 5 years between normal and obese 5-year-old Chilean children.

Age		N in model	BMI Z Diff OB-N	(95% CI) ^a
Birth	Model 1	1,086	0.51	(0.31 to 0.71)
	Model 2	1,086	0.12	(0.01 to 0.24)
	Model 3	754	0.15	(0.01 to 0.30)
1 month	Model 1	771	0.54	(0.30 to 0.78)
	Model 2	771	0.34	(0.12 to 0.56)
	Model 3	555	0.21	(-0.06 to 0.48)
2 months	Model 1	764	0.68	(0.46 to 0.90)
	Model 2	763	0.60	(0.38 to 0.82)
	Model 3	545	0.42	(0.16 to 0.68)
4 months	Model 1	727	0.77	(0.54 to 1.00)
	Model 2	726	0.72	(0.49 to 0.95)
	Model 3	515	0.50	(0.21 to 0.79)
6 months	Model 1	708	0.97	(0.73 to 1.20)
	Model 2	707	0.87	(0.64 to 1.10)
	Model 3	492	0.76	(0.46 to 1.05)
12 months	Model 1	886	1.15	(0.96 to 1.34)
	Model 2	885	1.08	(0.89 to 1.13)
	Model 3	617	0.98	(0.73 to 1.24)
18 months	Model 1	801	1.17	(0.98 to 1.35)
	Model 2	800	1.11	(0.92 to 1.30)
	Model 3	551	0.91	(0.66 to 1.15)
24 months	Model 1	847	1.33	(1.14 to 1.52)
	Model 2	846	1.26	(1.07 to 1.45)
	Model 3	586	1.16	(0.91 to 1.41)
36 months	Model 1	622	1.79	(1.57 to 2.00)
	Model 2	622	1.77	(1.55 to 1.99)
	Model 3	441	1.77	(1.49 to 2.05)
52 months	Model 1	1,087	2.25	(2.12 to 2.38)
	Model 2	1,080	2.20	(2.08 to 2.34)
	Model 3	752	2.13	(1.97 to 2.29)
60 months	Model 1	1,089	2.25	(2.12 to 2.38)
	Model 2	1,088	2.50	(2.48 to 2.70)
	Model 3	754	2.53	(2.40 to 2.67)

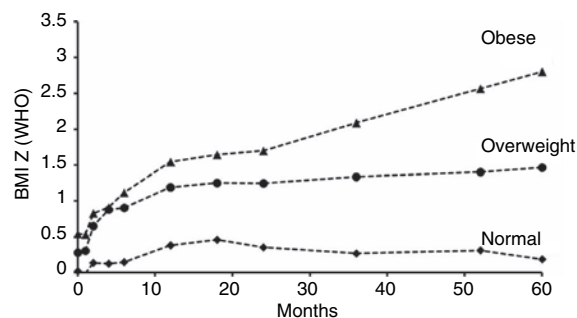
Model 1 adjusted by exact age and gender. Model 2 adjusted by exact age, gender, and birth weight. Model 3 adjusted by exact age, gender, birth weight, pre-pregnancy BMI, weight gain during pregnancy, presence of gestational diabetes and preeclampsia, and smoking during pregnancy.

CI, confidence interval; N, normal weight; OB, obese.

^aAll differences are significant, except for model 3 at month 1.

Significant differences were found between all 5-year BMI categories after 6 months of age; at younger ages, BMI of N was lower than those observed in the OW and OB categories; the latter groups were similar for the first 6 months of life.

BMI Z for the three groups was already different at birth (shown in **Figure 4**), 0.02, 0.28, and 0.54 for the N, OW, and OB, respectively. For the N group, BMI Z increased till 18 months,

**Figure 4** Evolution of BMI z-score from birth to 5 years in normal, overweight, and obese 5-year-old Chilean children.

reaching a value of +0.46 and remaining stable thereafter. In the OW category, BMI Z also increased till 18 months (at a significantly faster rate) leveling off thereafter; while for the OB, BMI Z increased continuously from birth to 5 years. Gains were greatest between 6 and 12 months and from 3 to 4 years of age. Significant differences were found between BMI Z of N and OW or OB groups throughout the first 12 months of age. After 12 months, differences in BMI Z were significant across all groups. The mean BMI Z of 3-year olds was greater than +2 and continued to increase, reaching 2.1, 2.6, and 2.8 at 36, 52, and 60 months, respectively. Half of those obese at 5 years were already obese at 2 years.

The modeling of BMI Z differences between the OB and N categories (**Table 2**) demonstrates that after adjusting by birth weight, differences between the categories tend to decline for the first 6 months; after 12 months there is minimal or no effect. In fact at 5 years, there is a slight gain in the difference. Additional adjustment by pre-pregnancy BMI and prenatal variables (weight gain, smoking, and presence of diabetes and preeclampsia) further decreased the BMI Z differences for the first 24 months with virtually no effect after this age.

DISCUSSION

The results of this study show that in preschool (5 years old) children from middle-low and low socioeconomic levels in Chile, the prevalence of obesity is very high, significantly more so in boys. In fact, this rate doubles the mean prevalence of preschool children from Latin American countries (16) and is similar to the obesity prevalence found in developed countries (17).

In our study cohort selected to have a birth weight of 2,500–4,500 g, mean BMI Z was only slightly >0 from birth till 1 month for boys and 2 months for girls; it then increased continuously in both genders until 5 years of age. Obesity rates followed this same general pattern, but it is worthwhile noting that in our sample, small changes in mean BMI Z scores are related to important changes in the upper tail of the distribution (OB children). In terms of overweight, the prevalence was high at birth, increasing progressively, and reaching its highest values at 18 months for girls (35%) and 24 months for boys (30%).

In our sample of 5-year olds, obesity risk increased with age. Irigoyen *et al.* (18) assessed the prevalence of obesity among a large sample of 1- to 5-year olds from New York estimating risk

by age and gender. The authors found that the highest increases in obesity occurred between ages 1 and 3 years and that boys were more likely to be obese than girls. Our results from Chile, a country that has undergone a very rapid epidemiologic transition (from nutritional deficit to excess) and economic transformation, show that although the rise in obesity takes place very early in life (almost 30% of the 5-year-old OB children were already obese at 12 months), it is more evident after 2 years of age. Other studies (19–21) have also shown that the obesity epidemic can be traced to very early in life. Dubois and Girard (22) examined in a population-based cohort of children from Quebec followed from birth to 4.5 years ($n = 1,550$), factors that might contribute to childhood overweight. The analyses indicated that the greatest proportion of OW children were born of normal weight at birth, but showed more rapid weight gain from birth to 5 months.

When comparing the trajectories of BMI from birth to 5 years, we visually are able to observe major differences in the approximate mean age of AR. For those in the normal categories of BMI at 5 years of age, it is beyond 5 years, while for the overweight it is between 4 and 5 years and for the obese, by 2–3 years of age. Our data as well as other studies support the original findings by Rolland-Cachera (14); however, our current observations analyzed with the newly defined World Health Organization growth standards are even more striking, as the approximate mean age of the AR for the obese occurred earlier than previously reported. Several studies have investigated the association between age at AR and adult obesity (23,24). Rolland-Cachera in a French sample showed that the earlier the AR, the higher the BMI or subscapular skinfold at 21 years (25). Studies have shown that an early AR is mainly caused by a faster accumulation of body fat rather than lean body mass, which is not only associated with cardiovascular disease in adults (26) but also predicts higher blood pressure at a very young age, as shown in the US cohort study, Project Viva (27).

Several studies have concluded that specific periods during early life are more important than others in defining later obesity risk; some of the critical windows correspond to the first few weeks of life (28), 0–6 month period (20,29); 0–24 months (30,31), although others report after 24 months (32). Other authors argue that obesity is a consequence of gradual accrual of weight over the pre- and postnatal periods, instead there being certain critical windows (33,34). Lack of consistency in these findings are probably due to the differences in the nutritional background of the study population and/or methodological issues related to the analyses of the data, specifically on the approach used to run the regression modeling of the effects of growth on later obesity. Within the context of this study, we clearly observe age intervals where BMI gain is greatly accelerated relative to the expected; this is well illustrated in **Figures 3** and **4**. The time from 0 to 12 months, especially the first 6 months of life shows clear evidence of BMI Z gains; later on, after 2 years, we can clearly recognize that the obese gain progressively BMI Z with advancing age. Nonetheless, these results could vary when using prospective analyses and/or mean BMI as the outcome. On the long term, the only valid

definition of critical periods for tackling obesity should be based on results of preventive initiatives implemented at specific times of early life.

Kinra *et al.* investigated the extent to which growth in the prenatal, early postnatal (birth to 6 weeks), and late postnatal (6 weeks to 18 months) periods predict future risk of childhood obesity in English children born at term (35). The results of their study showed that weight gain occurring in any of these periods, contributed equally to the variation in BMI at age 7 years. In our sample, it is evident (**Table 2**) that the postnatal weight gain, especially after 2 years of age, contributes more importantly to obesity in 5-year-old children than birth weight, pre-pregnancy BMI, and prenatal variables. As numerous studies have found (22,36), we also observed that significantly more OB mothers have OB children; in our sample 26.4% OB mothers had OB children, compared to 11.7% mothers of normal weight.

Despite the rapid improvement in nutritional status in every nutritionally deficient population group, maternal height in low-income women remains low; for this cohort the mean value is 1.57 m; this is ~6 cm below the normal (13). Our results present the dilemma of whether we should expect similar growth in children from mothers who are of less than normal height. The possibility that the rapid rise in BMI during the first 6 months of life might be linked not only to rapid weight gain but insufficient linear growth needs to be explored; BMI gain later in life may be more related to increased weight gain than insufficient linear growth. The association among pre- and postnatal growth and adiposity acquisition during early life might be associated to hormonal responses in glucose/insulin or in pituitary growth hormone/insulin-like growth factor mediated effects (37,38). Additional research to characterize these responses is clearly needed in order to interpret growth patterns, which translate in the observed differences in age of AR.

Limitations of this study include the fact that initial anthropometry was collected at the health clinics under a standardized procedure, but less stringent than the one used by our research team. The assessment of within group variability and outliers reveals no significant discontinuity. The maternal data used in the analysis (i.e., pre-pregnancy weight and prenatal variables) are self-reported, which might introduce systematic reporting bias; however, mean and prevalence of these variables are consistent with Chilean data (9,39–41). In this study, we have analyzed BMI growth trajectories only until 5 years of age. Although a longer follow-up of this cohort would allow us to test the consistency of our results, recent studies in which children have been followed until 9 and 13 years of age have shown that most excess weight of those that were overweight at those ages was gained before 5 years of age (42,43). Thus, we believe that these results will not vary significantly in a longer follow-up of this cohort.

In conclusion, this longitudinal data set confirms our previous observations from cross-sectional data that indicate that in children from a post-transitional country, the rise in obesity prevalence is occurring at progressively younger ages and much earlier than the AR. The influence of prenatal factors on

adiposity acquisition may extend at most until 2 years of life, although BMI gains thereafter are more related to postnatal variables. Therefore, potential interventions for tackling the obesity epidemic need to be designed with a life-course approach.

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DISCLOSURE

The authors declared no conflict of interest.

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