Original Article
PEDIATRIC OBESITY

Obesity

The Effects of Pre-Pregnancy BMI and Maternal Factors on the Timing of Adiposity Rebound in Offspring

Jeannette Linares[1], Camila Corvalán[2], Bárbara Galleguillos[2], Juliana Kain[2], Laura González[2], Ricardo Uauy[2], María Luisa Garmendia[2], and Verónica Mericq[1]

Objective: To assess the effect of pre-pregnancy body mass index (BMI), gestational weight gain (GWG), and other maternal factors on the timing of adiposity rebound (AR).
Methods: In this study, 594 mothers (mothers who do not have diabetes and not underweight) from the longitudinal Growth and Obesity Chilean Cohort Study self-reported their weights at the beginning and end of their pregnancies, and their heights were measured. Pre-pregnancy BMI was categorized as normal weight, overweight, or obesity, and GWG was assessed according to Institute of Medicine guidelines. For children, weight and height measurements from 0 to 3 years were retrieved from records, and they were measured from age 4 to 7 years. BMI curves from 0 to 7 years were used to estimate the age at AR, which was categorized as early (<5 years), intermediate (5-7 years), or late (>7 years). The associations between pre-pregnancy BMI and GWG and early AR were tested using logistic regression models.
Results: In total, 33% of the mothers had excess pre-pregnancy weight, 31.2% exceeded Institute of Medicine recommendations, and 45% of children had early AR. The pre-pregnancy BMI and parity were associated with earlier AR (OR = 1.07, 95% CI = 1.02-1.11; OR = 0.86; 95% CI = 0.74-0.99, respectively), but GWG was unrelated.
Conclusions: These results suggest that preventive strategies for promoting normal pre-pregnancy BMI, especially in women's first pregnancies, could delay the timing of AR, with protective metabolic effects on offspring.

Obesity (2016) **24**, 1313-1319. doi:10.1002/oby.21490

Introduction

Today, there is great interest in the concept of critical windows for health and disease. Critical windows correspond to specific periods in early life in which environmental exposures can induce permanent anatomical and functional changes that can, in turn, lead to long-term health risks (1). One of the periods proposed as a critical window corresponds to the age at adiposity rebound (AR): the age at which body mass index (BMI) increases after reaching a nadir, that is approximately 6 years (2). The concept of AR was introduced by Rolland-Cachera et al. in 1984. Performing a prospective study of 151 children, the authors observed that subjects who had early AR (<5.5 years) had more severe obesity at an age of 16 years than the late rebounders. They hypothesized that during AR, the size and number of adipocytes increased (3).

Longitudinal follow-up studies conducted later in other countries (2,4,5) have shown a clear association between earlier AR and a higher risk of obesity and diabetes in adulthood (2,3,5). AR has also been linked to developmental outcomes such as bone maturation (3,6) and pubertal tempo (6,7).

Few reports have established the determinants of AR. Recent evidence shows that parental genetic variants associated with adult BMI can have an effect on early childhood growth (8). There is also increasing evidence that susceptibility to disease is influenced by environmental exposures that occur *in utero* and during early postnatal life (9). In the case of AR, there is controversial evidence on the role of infant protein intake (10,11) and breastfeeding (12) and more consistent evidence of a relationship between higher circulating concentrations of insulin growth factor-1 (13) during infancy and earlier AR. A variety of gestational exposures, particularly pre-pregnancy BMI and gestational weight gain (GWG), have been associated with childhood obesity and metabolic and cardiovascular risk factors (14,15). In this regard, parental BMI has been

[1] IDIMI, Institute of Maternal and Child Research, University of Chile, Santiago, Chile. Correspondence: Verónica Mericq (vmericq@med.uchile.cl)
[2] INTA, Institute of Nutrition and Food Technology, University of Chile, Santiago, Chile.

Funding agencies: This work was supported by FONDECYT grant 1090252 and 1120326 and the Wellcome Trust Fellowship.
Disclosure: The authors declared no conflict of interest.
Author contributions: Linares, Corvalán, Uauy, and Mericq: designed the study; Corvalán: planned analyses; González, Galleguillos, and Garmendia: conducted the analyses; Linares: wrote the original draft of the article; and Corvalán, Garmendia, Mericq, Kain, and Linares: helped edit the drafts.
Received: 25 June 2015; **Accepted:** 6 January 2016; **Published online 18 April 2016. doi:10.1002/oby.21490**

associated with early AR (7,11), but other maternal variables have not been studied.

Therefore, the aim of this research was to evaluate the effects of pre-pregnancy BMI and GWG during pregnancy and the interactions between these two variables and other maternal variables (age, height, education, parity, and smoking) on the timing of AR using data from the Growth and Obesity Chilean Cohort Study (GOCS). We hypothesize that pre-pregnancy obesity and increased GWG would be independently associated with earlier AR.

Methods

The study sample was drawn from children who were enrolled in the GOCS cohort, which assesses the association between early growth and development of adiposity and metabolic risk in low- to middle-income Chilean children (1). Children were eligible for the study if they were 3.0 to 4.9 years of age and attending Junta Nacional de Jardines Infantiles nursery schools from the south area of Santiago, Chile, in September 2006; were singletons; had a gestational age between 37 and 42 weeks; had a birth weight >2,500 g and <4,500 g (data retrieved from medical registries); and had no physical or psychological conditions that could severely affect growth. Nearly 85% of the total eligible population agreed to participate ($n = 1,196$), and no significant differences in age, sex, birth, or anthropometric measures were observed at age 4 between participants and nonparticipants ($P > 0.05$). Thereafter (from 3 to 4 years of age), anthropometrical annual evaluations have been carried out (ongoing study). The study protocol was approved by the Institutional Review Board of the Institute of Nutrition and Food Technology of the University of Chile (FONDECYT grant: 1090252 and 1120236, Wellcome Trust Fellowship). Informed consent was obtained from all parents or guardians of the children.

The inclusion criteria for our subsample were all GOCS children with information available concerning the following parameters: pre-pregnancy nutritional status and GWG of their mothers and complete data to estimate time of AR. We excluded children of mothers who were underweight before their pregnancies because there were few women in this category. Children of mothers with gestational diabetes were also excluded because this condition could disturb the relationship between GWG and early AR.

As part of the original GOCS, when the children were age 4, we interviewed the mothers who had self-reported their weights at the beginning and the end of pregnancy, and height was measured by trained dietitians. From the complete GOCS survey, we extracted the following variables: maternal education, parity (including this offspring), child order, maternal smoking, and breastfeeding. Pre-pregnancy BMI was categorized as normal weight (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2), or obesity (≥30 kg/m^2) according to WHO recommendations (16). GWG, defined as the difference between the mothers' self-reported weights, was classified as less than, equal to, or greater than Institute of Medicine (IOM) guidelines: 11.5 to 16 kg for normal weight, 7 to 11.5 kg for overweight, and 5 to 9 kg for obesity (17).

In all children, weight and height measurements from the ages of 0 to 3 years were obtained from health records and measured by trained dietitians from the ages of 4 to 7 years. Weight was measured with a portable electronic scale (Seca 770; Seca, Hamburg, Germany) with a precision of 0.1 kg; height was measured with a portable stadiometer (Harpenden 603; Holtain LTD, Crosswell, UK) with 0.1 cm accuracy. The validity of the data obtained from the health records was confirmed against other anthropometric data from open registries (1). BMI curves were built from the ages of 0 to 7 years. From these curves, we estimated age and timing of AR using a computational process that was visually validated using 10% of the cases (18).

TABLE 1 Anthropometric characteristics between mother–child pairs included and excluded from the Growth and Obesity Chilean Cohort Study (GOCS)

	Included, mean (SD)	Excluded, mean (SD)	*P*
Sample, *n* (%)	594 (49.7)	602 (50.3)	
Girls, *n* (%)	291 (48.9)	312 (51.1)	0.326
Birth weight (kg)	3.4 (0.4)	3.4 (0.4)	0.319
Birth length (cm)	49.9 (1.67)	50.0 (1.8)	0.347
Weight at 2 yr of age (kg)	12.6 (1.45)	12.9 (1.62)	0.003
Weight at 2 yr of age (*Z*-score)	0.45 (0.04)	0.63 (1.00)	0.005
Length at 2 yr of age (cm)	86.1 (3.3)	86.7 (3.2)	0.012
Length at 2 yr of age (*Z*-score)	−0.33 (1.05)	−0.16(1.0)	0.014
BMI at 2 yr of age (kg/m^2)	17.0 (1.37)	17.2 (1.6)	0.023
BMI at 2 yr of age (*Z*-score)	0.91 (0.92)	1.04 (1.05)	0.055
Weight at 3 yr of age (kg)	14.9 (1.8)	15.4 (2.0)	0.002
Weight at 3 yr of age (*Z*-score)	0.37 (0.92)	0.6 (1.01)	0.003
Height at 3 yr of age (cm)	94.5 (3.6)	95.2 (3.6)	0.015
Height at 3 yr of age (*Z*-score)	−0.28 (0.94)	−0.10 (0.93)	0.017
BMI at 3 yr of age (kg/m^2)	16.61 (1.5)	16.80 (1.65)	0.113
BMI at 3 yr of age (*Z*-score)	0.77 (1.05)	0.89 (1.12)	0.146

Z-score based on WHO standards (16).

From the original cohort ($n = 1,196$), 554 mothers had incomplete BMI and/or GWG data; from the 642 remaining mother and child pairs, we excluded 48 mothers (33 with gestational diabetes and 15 who were underweight), and thus, 594 mother and child pairs were included as the study sample. Anthropometry at birth was not significantly different between the included and excluded children. At the ages of 2 and 3 years, weight, length, and height, were significantly higher in excluded children; however, the BMI *z*-scores remained unchanged at the same ages (Table 1).

The age at AR was defined as the average age between the age of the lowest BMI after 18 months and a subsequent BMI 0.3 kg/m^2 greater than the lowest BMI. This ensured that the slope was positive; the value of 0.3 kg/m^2 corresponded to twice the largest BMI measurement error obtained by GOCS dietitians. If the difference was less than the criterion value, the differences between subsequent BMIs were verified. The age at AR was considered to be above 7 years of age if the lowest BMI corresponded to the measurement at 7 years of age.

Timing of AR was as follows: the age at AR was categorized using cutoff points described elsewhere (2), in short, as early (<5 years), intermediate (5-7 years), and late (>7 years).

TABLE 2 Maternal variables and timing of AR in mother–child dyads of participants in the Growth and Obesity Chilean Cohort Study (GOCS)

	Total, mean (SD)	Boys, mean (SD)	Girls, mean (SD)	*P*
N **(%)**	594 (100.0)	291 (49.0)	303 (51.0)	
Pregestational BMI (kg/m^2)	24.0 (4.2)	24.2 (4.2)	23.8 (4.2)	0.285
Pregestational BMI				
18.5–24.9 kg/m^2, *N* (%)	387 (66.7)	190 (49.1)	197 (50.9)	0.307
25–29.9 kg/m^2, *N* (%)	145 (25.0)	82 (56.6)	63 (43.5)	
≥30 kg/m^2, *N* (%)	48 (8.3)	25 (52.1)	23 (47.9)	
Gestational weight gain (kg)	12.3 (4.7)	12.2 (4.9)	12.3 (4.6)	0.742
Gestational weight gain according to IOM				0.791
Less than, *N* (%)	190 (32.8)	101 (53.2)	89 (46.8)	
Equal to, *N* (%)	209 (36.0)	106 (50.7)	103 (49.3)	
Greater than, *N* (%)	181 (31.2)	90 (49.7)	91 (50.3)	
Time of AR	5.3 (1.8)	5.4 (1.7)	5.2 (1.8)	0.155
<5 yr, *N* (%)	265 (44.6)	130 (49.1)	135 (50.9)	0.630
5–7 yr, *N* (%)	192 (32.3)	99(51.6)	93 (48.4)	
>7 yr, *N* (%)	137 (23.1)	74(54.0)	63 (46.0)	
Mother height (cm)	156.5 (5.4)	156.1 (5.4)	156.9 (5.4)	0.080
Maternal age at birth (yr)	27.3 (7.0)	26.9 (6.9)	27.7 (7.1)	0.260
Maternal education (full high school), *N* (%)	405 (68.8)	204 (50.4)	201 (49.6)	0.872
Maternal smoking during pregnancy (yes), *N* (%)	57 (9.7)	31 (54.4)	26 (45.6)	0.574
Parity, no. children	2.1 (1.1)	2.0 (1.1)	2.2 (1.2)	0.011
Order of the child	1.9 (1.1)	1.8 (1.1)	2.0 (1.1)	0.031
Breastfeeding, *N* (%)	551 (93.1)	277 (50.3)	274 (49.7)	0.186

We present the data as either mean and SD for continuous variables or frequencies for categorical variables; non-normal distributions were log-transformed. The relationships among pre-pregnancy BMI, GWG, and early AR (yes/no) were tested using logistic regression models adjusted for sex, child order, breastfeeding, and maternal variables (age, height, education, parity, and smoking). To assess whether the associations were independent of adiposity status, we ran a model for further adjustment using the *Z*-scores for birth weight and the weight at age 2 (prior to AR). Interactions by sex were all nonsignificant, and thus, models are presented for both sexes combined. We fitted separate multiple logistic regression models for each exposure and generated interaction terms to evaluate moderating effects between pre-pregnancy BMI and GWG on early AR.

To evaluate the associations between other maternal factors (maternal age, height, education, parity, smoking during pregnancy) and early AR, we fitted univariate and multivariate logistic regression models by adjusting pre-pregnancy BMI, GWG, breastfeeding, birth weight, weight at 2 years of age and other maternal variables.

The associations were considered significant if $P < 0.05$. The analyses were conducted using Stata 11.0 (StataCorp LP, TX).

Results

The maternal variables and timing of the ARs of the 594 mother-child pairs are presented in Table 2. One out of three women had excess weight before pregnancy (25% overweight, 8.3% obesity). The mean GWG was 12.3 kg, and 31.2% of the women exceeded IOM recommendations based on their pre-pregnancy nutritional status. On average, the AR occurred at approximately 5 years of age, and thus, nearly half of the children had early AR (44.7%). The percentages of children with early AR (<5 years of age) by pre-pregnancy BMI category were 41%, 50%, and 56% for mothers with normal weight, overweight, and obesity, respectively, and 43%, 45%, and 46% for the IOM GWG categories; neither analysis reached a statistically significant difference, although the results suggest that the risk of early AR increases as pre-pregnancy BMI and GWG increase.

Pre-pregnancy BMI and GWG

The associations of pre-pregnancy BMI and GWG, both analyzed as continuous and categorical variables with AR before 5 years of age, are shown in Tables 3 and 4, respectively. Higher pre-pregnancy BMI was directly associated with early AR (OR = 1.07, 95% CI = 1.02-1.12, $P < 0.002$), and a similar trend was observed when the analysis was performed using a categorical variable (i.e., pre-pregnancy nutritional status); however, the results did not reach statistical significance ($P > 0.05$). GWG was unrelated to earlier AR as either a continuous or a categorical variable (i.e., compliance with IOM recommendations).

No moderating effect was found for GWG on the association between pre-pregnancy BMI, GWG, and the timing of AR.

TABLE 3 Association between continuous pre-pregnancy BMI and gestational weight gain and early AR (before 5 years of age) in mother–child dyads of participants in the Growth and Obesity Chilean Cohort Study (GOCS)

	Univariate (unadjusted)			Multivariate (adjusted[a])		
	OR	95% CI	*P*	OR	95% CI	*P*
Pre-pregnancy BMI (kg/m^2)	1.07	1.02–1.11	0.002	1.07	1.02–1.13	0.006
Gestational weight gain (kg)	1.01	0.97–1.04	0.680	1.00	0.96–1.04	0.994

[a]Adjusted for maternal age, maternal height, maternal education, smoking during pregnancy, parity, child order, and breastfeeding.

Potential intermediate role of adiposity

All analyses were repeated after adjusting for birth weight and weight at 2 years of age; the results remained roughly the same in magnitude and direction for both pre-pregnancy BMI and GWG (Table 5).

Other maternal and child variables associated with earlier AR

Other maternal variables by timing of AR (categorical variable: early/not early) are shown in Table 6. In adjusted logistic regression models, an older maternal age at birth and less parity were associated with earlier AR ($P < 0.05$). Regarding the child variables, we found that being the first born was associated with earlier AR (OR = 0.43 95% CI: 0.26-0.7, $P < 0.001$).

Discussion

Our main findings are the positive association between maternal factors, such as pre-pregnancy BMI, maternal age, less parity and child order (offspring variable), and the risk of early AR.

In this Chilean cohort of full-term, normal-birth weight children, we found that AR occurred on average at approximately 5 years of age. In addition, we found early AR in nearly half of our cohort (46.4% girls; 42.9% boys), greater percentages than those found in previous cohorts (2,3,11). In 1984, Rolland-Cachera et al. reported that 32% of girls and 29% of boys from a French sample of children born in 1953 presented with early AR (defined as <5.5 years) (3). In the UK Avon Longitudinal Study of Parents and Children (ALSPAC) cohort, which began in 1991, 27% of children had early AR (<5 years). These differences can be explained by the high obesity prevalence reported in recent GOCS findings for age 7 (13.4% in girls and 21.8% in boys) (18) and by a secular trend toward an earlier maturational tempo, at least in occidental societies. In this regard, the age of AR decreased from 6.2 years in 1955 to 5.6 years in 1985 (2,3,11), and the Chilean GOCS cohort is the most contemporary, with children born in 2002.

In the context of maternal variables that could influence the timing of AR, it is important to highlight the fact that in our cohort, the prevalence of mothers with excess weight (33%) was high. This finding is in agreement with the advanced stage of nutrition transition that our country presents. Indeed, a recent report on the GOCS cohort found alarming weight gain at follow-up. Mothers with normal nutritional status at the beginning gained more weight than did those who initially had obesity, showing that pregnancy and parity were the main risk factors for maternal obesity in adulthood (19).

Our results showed that higher pre-pregnancy BMI (used as a continuous variable) was an independent risk factor for early AR, regardless of the child's nutritional status, and this was also a novel finding. Indeed, Koyama et al. assessed whether weight gain in early infancy (<12 months) was related to the timing of AR in a contemporary prospective cohort of 271 Japanese children, although they observed no such association. The authors hypothesized that infantile weight gain was not related to offspring obesity through AR (20).

TABLE 4 Association between categorical pre-pregnancy BMI and gestational weight gain and early AR (before 5 years of age) in mother–child dyads of participants in the Growth and Obesity Chilean Cohort Study (GOCS)

	Univariate (unadjusted)			Multivariate (adjusted[a])		
	OR	95% CI	*P*	OR	95% CI	*P*
Pre-pregnancy BMI (%)						
Normal weight, 18.5–24.9 kg/m^2	REF	REF	REF	REF	REF	REF
Overweight/obesity, ≥25 kg/m^2	1.49	1.06–2.11	0.023	1.48	0.96–2.29	0.076
Gestational weight gain according to IOM (%)						
Less than	0.89	0.60–1.32	0.571	0.98	0.63–1.55	0.947
Equal to	REF	REF	REF	REF	REF	REF
Greater than	1.02	0.68–1.52	0.937	1.00	0.63–1.55	0.988

[a]Adjusted for maternal age, maternal height, maternal education, smoking during pregnancy, parity, child order, and breastfeeding.

TABLE 5 Association between pre-pregnancy BMI and early AR (before 5 years) adjusted by birth weight and weight at 2 years in mother–child dyads of participants in the Growth and Obesity Chilean Cohort Study (GOCS)

	OR	95% CI	*P*
Pre-pregnancy BMI (kg/m^2) (model 1)[a]	1.07	1.02–1.13	0.006
Model 1 + birth weight	1.07	1.02–1.13	0.008
Model 1 + weight at 2 yr	1.07	1.01–1.13	0.018
Model 1 + birth weight + weight at 2 yr	1.07	1.01–1.13	0.020

[a]Model 1: Adjusted for maternal age, maternal height, maternal education, smoking during pregnancy, parity, child order, breastfeeding.

Indeed, the concept that Rolland-Cachera introduced suggests that early AR is an indicator of accelerated maturation rather than adiposity (6,7). Thus, we could hypothesize that maternal nutritional status programs offspring's maturation tempos. In this context, GOCS cohort data showed advancement in bone age in the group with early AR (18), and these results are in line with reports from other countries that show consistent evidence of associations between maternal pre-pregnancy BMI, GWG, and daughter's age at menarche (21).

The fact that pre-pregnancy BMI can affect AR timing means that the early period of fetal nutrition may serve as a critical window for offspring AR. There is evidence that a number of prenatal factors such as maternal diet (total energy intake, macronutrient, and micronutrient composition), maternal obesity, microbiome, and environment can affect fetal epigenomic regulation through altered gene and protein expression, leading to a higher risk of the offspring acquiring metabolic-syndrome-related diseases (22,23). Furthermore, there is growing evidence in animal and human models of how epigenetic programming through maternal embryonic growth modulator genes, specifically genes that affect DNA damage and telomere shortening associated with accelerated cellular aging (24), maybe associated with growth trajectories in infancy. In this vein, hypomethylation of the insulin growth factor-2 differentially methylated regions (DMR) has been found to be associated with early weight gain in infancy (25). Soubry et al., in the Newborn Epigenetics Study, examined DNA from umbilical cord blood and from parents who have obesity reported an increase in DNA methylation in H19 DMRs among newborns from mothers with obesity (26).

Interestingly, we did not find an association between AR timing and GWG analyzed either in categories or as a continuous variable or in our analyses of their interactions with pre-pregnancy BMI. It is known that pre-pregnancy BMI is stronger than GWG as a determinant of childhood obesity and metabolic outcomes and adult offspring cardiometabolic risk factors (27). Some studies also show that mothers with higher pre-pregnancy BMI gain more weight than women with normal pre-pregnancy BMI, making it difficult to differentiate the effects of pre-pregnancy BMI and GWG; these findings suggest that GWG according to the IOM recommendations could attenuate the effects of increased pre-pregnancy BMI on metabolic and maturational programming (28). In our cohort, we did not confirm this observation; our mothers who have obesity and overweight did not show higher GWG. However, these effects are proven predictors for offspring metabolic risk, not biologic maturation, and early AR is an accelerated maturation indicator rather than obesity or adiposity, as explained above.

Regarding other maternal factors, our results showed that maternal age as a continuous variable was an independent risk factor for early AR. Advanced maternal age has been linked to adverse perinatal outcomes such as perinatal mortality, intrauterine fetal death, and neonatal death (29). Moreover, advanced maternal age is positively associated with macrosomia, being extremely large or small for gestational age and gestational diabetes in offspring, and all are risks factors for obesity and metabolic syndrome (30); however, our results were adjusted for birth weight. Several lines of evidence suggest that the life spans of offspring are affected by the ages of the parents at conception; one hypothesis is that progressive degeneration of the respiratory capacity of mitochondria in the oocytes of women of advanced age affects developing embryos, with consequences such as reduced potential life spans, through the inheritance of mitochondria DNA from the mother (31). It is possible that reduced lifespan is linked with early maturation. Our findings contribute to the list of possible determinants of the timing of AR.

Another interesting finding was the association of less parity with early AR. Maternal parity may be considered a proxy for birth order. First-born newborns tend to be smaller and of lower birth weight than do later-born siblings (32,33), and the association

TABLE 6 Association between other maternal variables and timing of AR (early[a] or not early) in mother–child dyads of participants in the Growth and Obesity Chilean Cohort Study (GOCS)

	Univariate (unadjusted)			Multivariate (adjusted[b])		
	OR	95% CI	*P*	OR	95% CI	*P*
Maternal smoking during pregnancy (yes)	0.87	0.51–1.49	0.613	1.38	0.63–3.02	0.423
Maternal age at birth (yr)	1.02	0.99–1.04	0.144	1.05	1.01–1.07	0.009
Maternal education (% full high school)	1.31	0.93–1.84	0.122	1.04	0.67–1.63	0.860
Mother height (cm)	0.97	0.94–0.99	0.040	0.98	0.95–1.02	0.425
Parity (no. children)	0.86	0.74–0.99	0.003	0.63	0.49–0.81	<0.001

[a]Early AR: before 5 years of age.
[b]Adjusted by pre-pregnancy BMI, gestational weight gain, breastfeeding, birth weight, weight at 2 years, and the other maternal variables included in the table.

between smaller birth size and greater cardiovascular risk has been well documented (34,35). However, these studies come from low- and middle-income countries (32,33,36), but studies in higher-income countries have more mixed findings (37-39). Chile is a post-transitional country, and we did not find precedents that linked the order of the child at birth and the timing of AR. Because our results were adjusted by birth weight, we do not have a plausible explanation for this finding.

Our study has limitations as well. The child data were extracted from health records for the first 3 years, but these data had high correlations with other clinical measurements (pediatric consults in a subsample). Serial measurements of weight and height were made annually, and AR may have occurred mid-year. However, to reduce misclassification, AR age was used in categories, and the results were subjected to various sensitivity tests, which gave confidence and validity. AR was estimated using an automatic mathematic model procedure and was visually validated (18). Therefore, we feel confident about the method that we used to estimate AR timing. The mothers' data were self-reported and retrospective, but had high correlations with data from obstetric medical records in a subsample of our mothers (~80%). The only misclassification was found in the group of women who have obesity, making the association even stronger.

Our main strengths are that we had a large cohort of mother-child pairs that included full-term, normal-weight children, and that this is the first study to assess maternal factors such as pre-pregnancy BMI, maternal age, and less parity as determinants of early AR in a contemporary cohort.

Conclusion

In conclusion, we found that high pre-pregnancy BMI, high maternal age, and less parity were associated with earlier AR, and AR is a sensitive period for programming lifetime metabolic risk. Thus, it could be used as an early marker of higher-risk children to focus efforts at both individual and population levels. A modifiable maternal factor such as pre-pregnancy BMI could be modulated to delay the timing of AR and to multiply this protective effect in terms of metabolic risk and early maturation. Targeted pre- and interconception weight management efforts should be particularly encouraged in older mothers, especially those in their first pregnancies. O

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