Association between Timing of Adiposity Rebound and Body Weight Gain during Infancy

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Objective To investigate whether increments of weight gain in early infancy are related to the timing of adiposity rebound (AR).

Study design A total of 271 children (147 boys and 124 girls) in 1 community were enrolled in the study. Serial measurements of body mass index were carried out at the ages of 4, 8, and 12 months and 1.5, 2, 3, 4, 5, 6, 7, 8, 9, and 10 years, based on which the age of AR was determined. We also calculated body weight increments in 3 separate periods: birth to 4 months, 4-8 months, and 8-12 months.

Results There was no significant relationship between weight gain in any period of infancy and the age of AR. Weight gain between birth and 4 months was positively correlated only with body mass index at 7 years of age.

Conclusions We could not find an association between body weight gain during infancy and the timing of AR. This suggests that infantile weight gain is not related to childhood obesity through AR. *(J Pediatr 2015;166:309-12)*.

A rapid increase in body mass index (BMI) generally occurs during the first year of life. BMI subsequently declines and reaches a nadir at around 6 years of age and then increases again throughout childhood. This second rise in BMI following the last minimum BMI (nadir) is referred to as the adiposity rebound (AR).[1] The timing of the rebound is thought to have predictive value for obesity in adulthood.[2-5] Children with an earlier AR have higher BMI in boys and girls and a greater atherogenic metabolic status in boys at 12 years of age.[6] Low BMI in early childhood followed by early AR and an accelerated increase in BMI until adulthood have been associated with an increased risk of developing type 2 diabetes.[7-9] Higher BMI during childhood and BMI at 7-13 years of age for boys and 10-13 years of age for girls have been associated with an increased risk of coronary heart disease in adulthood.[10] Early AR and a higher BMI during childhood are also associated with an increased risk of developing type 2 diabetes and coronary heart disease in adulthood.[7-10] Stunted fetal growth or early infant weight gain may also be a predisposition for development of type 2 diabetes mellitus, hypertension, and coronary heart disease in later life.[11,12] These findings imply that children who exhibit high weight gain in early life are at significantly higher risk for development of metabolic syndrome and subsequent diabetes or cardiovascular disease in adulthood.

Three systematic reviews have shown that children who grow rapidly during infancy are at increased risk of subsequent obesity.[13-15] Rapid weight gain during infancy has been associated with later obesity and the risk of future metabolic syndrome in children born preterm[16] and at term.[17-19] Rapid postnatal weight gain has consistently been associated with a risk of insulin resistance and greater adiposity in children and young adults, but the critical period for the association between weight gain and later risk is uncertain. Insulin resistance has been related to changes in early infancy (0-6 months) or between 2 and 11 years old.[7,20,21] On the other hand, obese children under 3 years of age have been suggested to be at low risk for obesity in adulthood.[22] Other studies have suggested that there may be no association between infant growth and later obesity.[23-25] In this study, we investigated whether increments of weight gain in early infancy are related to the timing of AR. If early infantile obesity is related to later obesity and health risks, rapid weight gain during infancy should be associated with early AR.

Methods

All 296 children (157 boys and 139 girls) born in the town of Fujioka in Tochigi prefecture in Japan between 1995 and 1996 were enrolled in the study. The population of this town is 18 000, with one-half of the people working as farmers and the other one-half commuting to nearby large cities. The town has 4 elementary schools and 2 junior high schools. All of the children in the study were followed in infant health checks at a health center during the preschool period, and data were stored at a regional health center. During the school age period, children underwent an annual physical examination at school, and the resulting data were also kept at the regional health center. We excluded

AR	Adiposity rebound
BMI	Body mass index

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25 children (10 boys and 15 girls) from the study because of missing BMI data from 1-8 years of age that prevented determination of the age of AR. These data were missing because some children did not attend all health checks and physical examinations. This left a total of 271 children (147 boys and 124 girls) in the analysis. We also excluded some of these subjects in each analysis because of missing weight data at birth or at 4, 8, or 12 months, or missing BMI data at 7 or 10 years old. Of the 147 boys, 104 had weight data at birth and 4 months old, and 97 had data at 4 and 8 months and at 8 and 12 months. Of the 124 girls, 93 had weight data at birth and 4 months and at 8 and 12 months, and 88 had data at 4 and 8 months. Only 2 boys had no BMI data at 7 years old, and 82 boys and 62 girls had BMI data at 10 years old.

Written informed consent for physical examinations was obtained from parents or guardians. The study was approved by the ethics committee of Dokkyo Medical University (approval number 23020).

Standard anthropometric measurements of length or height and weight using strict protocols were conducted by a small group of trained staff at the ages of 4, 8, and 12 months, and 1.5, 2, 3, 4, 5, 6, 7, 8, 9, and 10 years. Anthropometric data at age ≤5 years are more accurate than those after age 6 years because the assessment was performed close to the child's birthday under 5 years, but performed at school on 1 date each year for all children. Thus, for example, data at 6 years of age were collected between 6 and 6.9 years of age.

Most of the subjects underwent 11 measurements between 4 months and 8 years old, and about 53% of the subjects underwent measurements at 9 and 10 years old. Length or height was measured to the nearest 0.1 cm using a digital baby table (M-5000K; Nakamura Medical Industry Co, Ltd, Tokyo, Japan) at birth and at follow-up under 2 years of age, and thereafter using a digital height and weight scale (AD-6224A; A and D Company, Ltd, Tokyo, Japan). Weight was assessed to the nearest 100 g, using the digital baby table at birth and under 2 years of age, and the Yamato digital weight scale (DP-7100W; Yamato Weighing and Information Technology, Hyogo, Japan) thereafter. At each follow-up, BMI was calculated from the measured height and weight using the formula: weight (kg)/height $(m)^2$. Under 2 years of age, a proxy for BMI was used: weight (kg)/length $(m)^2$.[26,27]

The age of AR was defined as the age between 1 and 10 years at which the lowest BMI occurred before the second BMI rise. When the BMI curve had repeating minor increases and decreases or a plateau, the age of AR was defined as that at which the lowest BMI occurred. Body weight increments were calculated in the 3 periods (birth to 4 months, 4-8 months, and 8-12 months) to investigate if the weight increment in each period in infancy is associated with the timing of AR and with BMI at 7 and 10 years old.

Spearman correlation coefficients were calculated for the relationships of weight gain in infancy with age of AR, and for BMI at ages 7 and 10 years with age of AR and weight gain. All statistical analyses were conducted with SAS v 9.3 (SAS Institute, Inc, Cary, North Carolina).

Results

The mean age of AR was 4.8 ± 1.4 (mean ± 2 SD) years in boys and 4.7 ± 1.5 years in girls. Geometric means of birth weight and weight gain between birth and 4 months, 4 and 8 months, and 8 and 12 months, and BMI at AR and at 7 and 10 years of age in boys and girls are shown in Table I. Correlations between weight gain in the 3 periods of early infancy and the age of AR in boys and girls are shown in Table II. The data showed no association between weight gain in any period of infancy and the age of AR, suggesting that obesity in infants is not related to childhood obesity.

Correlations of BMI at 7 and 10 years old with the age of AR and increments of weight gain during early infancy are shown in Table III. BMI at 7 and 10 years old was negatively correlated with the age of AR. Weight gain between birth and 4 months was positively correlated only with BMI at 7 years of age. Weight gain in other periods was not correlated with BMI at 7 or 10 years of age.

Discussion

Three systematic reviews have shown that children who grow rapidly during infancy are at increased risk of subsequent obesity.[13-15] Rapid weight gain during infancy has been associated with later obesity and the risk of future metabolic syndrome in children born preterm[16] and at term.[17-19] All subjects in our cohort were born at term, but only weight gain between birth and 4 months, and not that between 4 and 8 months or 8 and 12 months, was associated with BMI at 7 years old. Weight gain in all periods showed no association with BMI at 10 years old in boys and girls. In previous studies, Stettler et al showed that a pattern of rapid weight gain during the first 4 months of life is associated with an increased risk of an overweight status at age 7 years, independent of birth weight and weight attained at age 1 year.[28] Reilly et al found that high rates of weight gain in the first 12 months were

Table I. Geometric means (SD in parentheses) of birth weight; weight gain between birth and 4 months, 4 and 8 months, and 8 and 12 months; and BMI at AR, and 7 and 10 years of age in boys and girls

	Boys	Girls
Birth weight (g)	3068 (1.2) n = 147	3041 (1.2) n = 124
Weight gain between birth and 4 mo (g)	4280 (1.2) n = 104	3745 (1.2) n = 93
Weight gain between 4 and 8 mo (g)	1448 (1.4) n = 97	1377 (1.4) n = 88
Weight gain between 8 and 12 mo (g)	761 (1.5) n = 97	634 (2.0) n = 93
BMI at AR (kg/m^2)	15.40 (1.1) n = 139	15.29 (1.1) n = 121
BMI at 7 y (kg/m^2)	16.62 (1.2) n = 145	16.57 (1.1) n = 124
BMI at 10 y (kg/m^2)	18.62 (1.2) n = 82	18.78 (1.2) n = 62

The number of subjects is shown for each analysis.