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Short Communication

Insufficient weight gain under 3 years of age correlates with short stature in school-aged children

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Highlights

- Poor weight gain under 3 yr of age correlates with short stature in adolescence.
- Birth weight does not affect the height in adolescence.
- Poor weight gain in infancy may indicate reduced adult height.

Key words: infancy-childhood-puberty (ICP) model, insufficient weight gain, short stature, constitutional delay of growth and maturation

Introduction

Karlberg developed the infancy-childhood-puberty (ICP) growth model, which describes human growth from the latter half of intrauterine life to adolescence (1). The components of infancy, childhood, and puberty periods depend on nutrition, GH, and the synergism between sex steroids and GH, respectively. The periods of infancy and childhood are defined as the durations from the latter half of intrauterine life to approximately 3 yr of age and from approximately 1.5 yr of age to adolescence, respectively. Some children show insufficient weight gain at approximately 1 yr of age, just after weaning. If such children show inadequate weight gain because of poor dietary intake, their growth velocity will also decrease, especially in those younger than 3 yr.

We hypothesized that insufficient weight gain in infants and toddlers may not only lead to underweight but also to short stature during childhood, and that this trend will follow through adolescence. This hypothesis has not previously been validated. Therefore, we investigated the relationship between height and incremental weight gain in children under 3 yr of age and in children with ages ranging from 3 yr to pubertal age. The data presented below represent the initial auxological findings regarding the relationship between weight gain and stature in children.

Materials and Methods

We enrolled 271 healthy children (147 boys and 124 girls) born in Tochigi Prefecture, Japan, between 1995 and 1996. Length or height and weight were measured at the following ages: birth (weight only), 1.6, 3, and 7 yr in both boys and girls, 10 yr in girls, and 12 yr in boys, of which, the final two values coincide with the onset of puberty in girls and boys in Japan. Pearson correlation coefficients were calculated to determine the relationships of the increment in weight gain under 3 yr with height and weight at 3 yr, 7 yr, and pubertal

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age, 10 yr in girls, and 12 yr in boys. We examined the incremental weight gain in the two groups by age. The first group included children from birth to 1.6 yr, which corresponds to Karlberg's infancy period and is affected by nutrition. The second group included children from 1.6 to 3 yr. Pearson correlation coefficients were also calculated to determine the relationships of birth weight with height and weight at 3 yr, 7 yr, and pubertal age. Furthermore, logistic regression analysis was performed to determine whether birth weight affected the relationship between insufficient weight gain in infancy and height at puberty.

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).

Results

The Pearson correlation coefficients describing the strength of the relationship between weight gain from birth to 1.6 yr of age and weight at 3 yr, 7 yr, and pubertal age were 0.76, 0.51, and 0.34 in boys, and 0.76, 0.49, and 0.47 in girls, respectively. Pearson's r values describing the relationship between weight gain from birth to 1.6 yr of age and height at 3 yr, 7 yr, and pubertal age were 0.58, 0.46, and 0.34 in boys, and 0.62, 0.56, and 0.65 in girls, respectively. The data are presented in **Table 1a**. In the second age group, the Pearson correlation coefficients between weight gain from 1.6 to 3 yr of age and weight at 3 yr, 7 yr, and pubertal age were 0.84, 0.66, and 0.37 in boys, and 0.74, 0.50, and 0.48 in girls, respectively. The Pearson correlation coefficients between weight gain from 1.6 yr to 3 yr of age and height at 3 yr, 7 yr, and pubertal age were 0.59, 0.48, and 0.24 in boys, and 0.49, 0.37, and 0.40 in girls, respectively. These data are presented in **Table 1b**. All correlations, except for the relationship between weight gain from 1.6 yr to 3 yr of age and height at 12 yr of age in boys ($P < 0.1$), were significant ($P < 0.05$).

The correlations between weight gain in both age groups and pubertal weight were almost identical for both boys and girls. However, a stronger correlation between height at puberty and weight gain from birth to 1.6 yr was observed compared to that with weight gain from 1.6 to 3 yr. While this was observed in both boys and girls, the correlation was stronger in girls than in boys at the pubertal age. The strongest correlation was observed between weight gain from birth to 1.6 yr and height achieved during puberty in girls (r = 0.65; **Fig. 1**).

Additional correlations were performed to further explore the relationship of birth weight with height and weight at different ages. The Pearson correlation coefficients describing the strength of the relationship between birth weight and weight at 3 yr, 7 yr, and pubertal age were 0.41, 0.24, and 0.25 in boys and 0.41, 0.26, and –0.03 in girls, respectively. The Pearson coefficients of the relationship between birth weight and height at 3 ys, 7 yr, and pubertal age were 0.37, 0.29, and 0.15 in boys and 0.20, 0.18, and –0.11 in girls, respectively. The results are summarized in **Table 2**. Birth weight correlated positively with weight at each age, except for that with the pubertal age in girls. In boys, birth weight correlated positively with height at 3 and 7 yr but not at pubertal age. In girls, a weak correlation was observed between birth weight and height at 3 yr but not at 7 yr of age or pubertal age. These results suggest that birth weight does not affect height during adolescence. The results also show that birth weight does not affect the correlation between insufficient weight gain in infancy and height at pubertal age, as determined via a multivariate analysis using logistic regression analysis ($P = 0.280$).

Table 1. Pearson correlation coefficients between weight gain under 3 yr of age and height or weight at 3 yr, 7 yr, and pubertal age in boys and girls

a. Weight gain from birth to 1.6 yr of age

	3 yr		7 yr		10 yr		12 yr	
	Ht	Wt	Ht	Wt	Ht	Wt	Ht	Wt
boys	0.58***	0.76***	0.46***	0.51***			0.34*	0.34*
girls	0.62***	0.76***	0.56***	0.49***	0.65***	0.47**		

Ht, height; Wt, weight. *** $P < 0.0001$, ** $P = 0.001$, * $P < 0.01$.

b. Weight gain from 1.6 to 3 yr of age

	3 yr		7 yr		10 yr		12 yr	
	Ht	Wt	Ht	Wt	Ht	Wt	Ht	Wt
boys	0.59***	0.84***	0.48***	0.66***			0.24 ($P < 0.1$)	0.37*
girls	0.49***	0.74***	0.37***	0.50***	0.40*	0.48**		

Ht, height; Wt, weight. *** $P < 0.0001$, ** $P = 0.001$, * $P \leq 0.005$.

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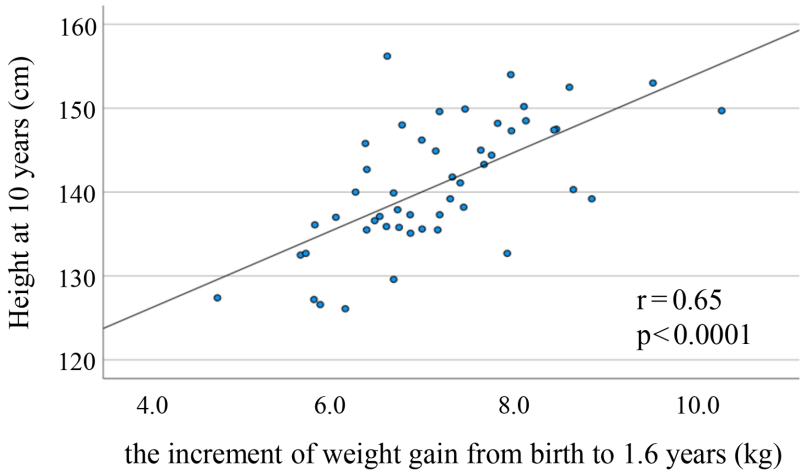

Fig. 1. Pearson correlation coefficients between weight gain from birth to 1.6 yr and height at 10 yr in girls.

Table 2. Pearson correlation coefficients between birth weight and height or weight at 3 yr, 7 yr, and pubertal age in boys and girls

	3 yr		7 yr		10 yr		12 yr	
	Ht	Wt	Ht	Wt	Ht	Wt	Ht	Wt
boys	0.37***	0.41***	0.29***	0.24**			0.15	0.25*
girls	0.20*	0.41***	0.18	0.26**	–0.11	–0.03		

Ht, height; Wt, weight. *** $P < 0.001$, ** $P < 0.01$, * $P < 0.05$.

Discussion

Our key finding is that insufficient weight gain from birth to 1.6 yr of age and from 1.6 yr to 3 yr of age is not only associated with underweight children but also with short stature at 3 yr of age. Furthermore, this effect continued until the age of 7 yr and at the onset of puberty. The adult height and weight may also be affected.

Growth failure reportedly starts in early infancy in children with short stature, detected at the age of 6 yr. These children are poor bottle feeders and poor eaters after weaning (2).

Moreover, the change in height standard deviation score from birth to 3 yr of age also reportedly shows a strong positive correlation with the change in weight from birth to 3 yr of age (3). The fact that height had the strongest correlation with weight gain in infancy supports our hypothesis that weight gain during infancy is important in determining adolescent stature. Moreover, protein intake in early life programs the body composition and height growth later in life, perhaps mediated by insulin-like growth factor 1 (IGF-1) (4). This relationship indicates another mechanism by which insufficient weight gain in infancy influences height during adolescence. Furthermore, in both boys and girls, a stronger correlation was observed between height at pubertal age and weight gain from birth to 1.6 yr than that from 1.6 to 3 yr. This indicates that the components of the infancy period in the ICP model depend on nutrition.

Most children with constitutional delay of growth and maturation (CDGM) begin to deviate from the normal growth curve before age 2 yr, subsequently grow at a relatively normal rate, and then have a delayed pubertal growth spurt (5). This growth pattern is similar to that observed in malnourished children, suggesting that CDGM may lie on the spectrum of nutritional dwarfing. Furthermore, Albanese *et al.* reported that only 0.7% of patients with CDGM attained a final height above the mid-parental corrected height (6). We also showed that insufficient weight gain under 3 yr of age is associated with a short stature and underweight during adolescence.

Several mechanisms may explain how nutrient deprivation leads to stunted growth. Stunted growth related to environmental enteric dysfunction (EED) is commonly defined as an acquired subclinical disorder of the small intestine and is characterized by villous atrophy and crypt hyperplasia, especially in children in developing countries (7). Nutrient deprivation increases GH and decreases insulin levels, promoting lipolysis and depleting white adipose fat stores, thereby reducing adipocyte-derived leptin levels. Hypoleptinemia downregulates the hypothalamic-pituitary-thyroid axis and inhibits the conversion of thyroxine to its active form, triiodothyronine (8). Decreased triiodothyronine levels impair chondrocyte maturation and growth (9). The

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stress of acute malnutrition activates the hypothalamic-pituitary-adrenal axis and stimulates an increase in cortisol and IGF-binding protein 1, which in combination inhibit IGF-1 action and induce chondrocyte apoptosis (9). Furthermore, fibroblast growth factor 21 (FGF21) inhibits bone growth by antagonizing the effects of GH on chondrocyte proliferation and differentiation (10). Increased FGF21 levels during nutrient deprivation may contribute to growth failure by directly inhibiting chondrogenesis in patients with EED (10).

A sex difference was identified in the association between body weight gain during early infancy and height at puberty. We were unable to identify the factors that caused these sex differences. However, since girls were examined two years earlier than boys at the age of onset of puberty, this might have resulted in a more significant difference. We did not confirm whether the participant entered puberty at 10 yr in girls and 12 yr in boys in this study. Although this could be a limitation, we do not consider it a major limitation. Future studies may use pubertal age or Tanner stage to verify the pubertal state, which may help confirm our results.

The present study had some limitations. For example, we did not assess the dietary intake throughout childhood for each participant, and we did not have information on the parents' heights. In addition, the design of our exploratory study limits our ability to make overarching conclusions; therefore, we cannot confirm whether insufficient weight gain in infancy indeed affects the achievement of the target height. However, the results of our study show that these variables are related. In addition, we did not measure the levels of GH, IGF-1, or other related variables. Future studies should include these measures to better elucidate the impact of weight gain during infancy on stature.

Further research is needed to determine whether insufficient weight gain in children under 3 yr of age, especially under 1.5 yr of age, leads to short stature in adults, and if it correlates with hormonal dysregulation. Overall, poor weight gain in children under 3 yr of age is likely associated with a short stature in adolescence and will likely continue into adulthood.

Conflict of interests: The authors have no conflicts of interest to disclose.

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