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Research Article

Increase in BMI from 1.5 to 3 Years of Age is a Risk for Cardiometabolic Disease

Osamu Arisaka, MD, PhD[1], Go Ichikawa, MD, PhD[1], Satomi Koyama, MD, PhD[1], Toshimi Sairenchi, PhD[2]

[1]*Department of Pediatrics, Dokkyo Medical University, Mibu, Tochigi-ken, 321-0293 Japan*

[2]*Public Health, Dokkyo Medical University, Mibu, Tochigi-ken, 321-0293 Japan*

**Corresponding author: Dr. Osamu Arisaka, MD, PhD, Department of Pediatrics, Dokkyo Medical Universuty, Mibu, Tochigi-ken, 321-0293 Japan. Tel: +81282861111; Fax: +81282867521; Email: arisaka@dokkyomed.ac.jp*

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Abstract

Background

Changes of body composition related to excessive weight gain during infancy may play a pivotal role in the development of future cardiometabolic risk. Therefore, we elucidated whether overweight/obesity related cardiometabolic risk factors at 12 years of age could be estimated based on changes of body mass index (BMI) at 1.5 to 3 years of age, because 1.5 years and 3 years health check of infants were routinely conducted in Japan.

Methods

A total of 217 children in the birth cohort were enrolled in the study. We used Fisher's exact test to evaluate whether increases in BMI from 1.5 to 3 years of age were associated with the increased risk of higher atherogenic index (≥ 2.5) or elevated blood pressure (≥125 or 70 mmHg) at 12 years of age.

Results

The proportion of elevated blood pressure in the increased BMI infants was higher than the decreased BMI male subjects (16.7% vs 2.4%, p<0.05). On the other hand, among females the proportion of high atherogenic index in the increased BMI subjects was higher than in the decreased BMI subjects (13.4% vs 0, p<0.05).

Conclusions

It was clarified that an increase of BMI from 1.5 to 3 years of age increased cardiometabolic risk at 12 years of age. These at-risk children should be given appropriate instructions to improve their lifestyle to avoid further increases of their BMI.

Keywords: Adiposity Rebound; Obesity/Overweight; Cardiometabolic Risk Factor; Infancy

Introduction

Excessive weight gain in early childhood has been considered to lead to adult obesity- related morbidity and mortality [1-3]. The age of adiposity rebound (AR) is defined as the time at which the BMI (body mass index) starts to increase after infancy and is thought to be an indicator of later obesity [4]. In a birth cohort, we recently demonstrated that children with an earlier AR (< 4 years of age) were associated with a lipoprotein phenotype representative of insulin resistance and increased blood pressure [5].

The age of AR onset is estimated retrospectively, by identifying the age with the lowest BMI after repeated measurements of BMI over the course of early childhood. Due to the complexity of this method, some have suggested that it is not practical to use AR in the estimation of future obesity-related risk. We elucidated whether the cardiometabolic risk factors at 12 years of age could be estimated based on changes of BMI in children at 1.5 to 3 years of age. We examined children at 1.5 to 3 years of age because the BMI data for these children could be obtained during the health check of infants conducted by the Ministry of Health, Labour and Welfare in Japan.

Methods

All 217 children born in F town in Tochigi prefecture in Japan between 1995 and 1996 were enrolled prospectively in the study. The population of this town is 18 000, with one-half of the people working as farmers and 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 up with 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. At 12 years of age, all the high school children underwent a blood examination. The formula for BMI is weight in kilograms divided by height in meters squared.

When we evaluated the physical constitution of our subjects aged 1.5 years based on the standard value of Japanese children, it was found that 6 (5%) out of the 113 male child subjects exhibited BMI of the 95^{th} percentile or higher, and 10 subjects (9%) exhibited BMI of the 85^{th} - 95^{th} percentile. Furthermore, 5 (5%) out of 102 female child subjects exhibited BMI of the 95^{th} percentile or higher, and 8 subjects (8%) exhibited BMI of the 85^{th} - 95^{th} percentile. Thus, the proportion of our 1.5-year-old subjects who exhibited obesity and were overweight was average for Japanese children [6].

Fasting blood sampling and measurement of blood pressure were performed at school. In order to obtain blood samples after an overnight fast, students were allowed to bring a packet box breakfast, which they took after undergoing the health examination at the school-room. Blood pressure was measured in the sitting position after a 5 min resting period by trained observers with an electronic sphygmomanometer (H- 55,TERUMO, Japan) using a cuff that was appropriate to the size of the child's upper right arm. Levels of total cholesterol (TC) (Cholestest CHO, Daiichi Pure Chemicals Co. Ltd., Tokyo, Japan) were determined using enzymatic methods. High- density lipoprotein (HDL-C) was measured by precipitation of other lipoproteins with the direct method (Cholestest NHD, Daiichi Pure Chemicals Co. Ltd.). Atherogenic index (AI) was calculated according to the following formula: [TC-HDL-C]/ HDL-C.

We previously confirmed that AI correlated with low-density lipoprotein particle size (r= -0.40, p<0.01, n=314), which reflected insulin resistance [7]. Therefore, AI was used as a metabolic indicator of insulin resistance. An AI of 2.5 (mean at 12 years of age + 2 standard deviations) or greater was considered high. Diastolic pressure ≥70 mmHg or systolic blood pressure ≥125 mmHg were considered high, based upon the Japanese diagnostic criteria for metabolic syndrome in childhood [8].

Although there are no clear sex differences in blood concentrations of sex hormone and leptin before puberty [9], sex differences were confirmed regarding the relationship with the risk factors for arteriosclerosis at the age of AR and at 12 years of age in our previous study [5]. Therefore, we analyzed the data by sex in the current study.

We used Fisher's exact test to evaluate whether increases in BMI from 1.5 to 3 years of age were associated with the increased risk of higher AI or elevated blood pressure at 12 years of age.

Written informed consent was obtained from the guardian for the physical examination. The study was approved by the ethics committee of Dokkyo Medical University.

Results

The results are shown in Table 1. The mean BMI at 12 years of age was higher in the female subjects with increased BMI (p<0.05). Likewise, the mean BMI at 12 years of age was higher in the increased BMI male infants but this was not statistically significant (p=0.09). The proportion of elevated blood pressure (≥125 or 70 mmHg) in the increased BMI infants was higher than the decreased BMI male subjects (16.7% vs 2.4%, p<0.05). On the other hand, among females the proportion of high AI (≥ 2.5) in the increased BMI subjects was higher than in the decreased BMI subjects (13.4% vs 0, p<0.05).

Table 1. Relationship between decreases or increases in BMI between 1.5 years and 3 years and BMI, atherogenic index, and blood pressure at 12 years of age

Comparison of BMI between 1.5 years and 3 years	Mean BMI at 12 years of age Mean (SD)	Atherogenic index ≥ 2.5 N (%)	Blood prresure ≥ 125/ or 70 mmHg N (%)
Male 3y BMI <1.5y BMI (n=83)	19.4 (3.3)	3 (3.6)	2 (2.4)
Male 3y BMI >1.5y BMI (n=30)	21.1 (5.0) †	2 (6.7)	5 (16.7) *
Female 3y BMI < 1.5y BMI (n=65)	19.4 (2.4)	0 (0.0)	9/65 (13.8)
Female 3y BMI > 1.5y BMI (n=37)	21.2 (4.8) ‡	5 (13.5) *	3/37 (8.1)

*p<0.05 by Fisher's exact test; †p=0.09 by unpaired t-test; ‡p<0.05 by unpaired t-test

Discussion

In this study, it appeared that, when BMI at 3 years of age was increased, compared with those children at 1.5 years of age, the proportions of higher blood pressure in male children and higher AI levels in female children at 12 years of age were increased. These findings suggest that increased BMI from 1.5 to 3 years of age is associated with an increased frequency of cardiometabolic risk factors at 12 years of age.

Although the mechanisms underlying the observed sexually dimorphic differences cannot be interpreted easily [5, 10, 11], changes of body composition related to excessive weight gain during this period may play a pivotal role in the development of future insulin resistance [1, 3, 5]. It was recently suggested that the acquisition of leptin resistance before 3 years of age, due to excessive weight gain during this period, might be related to the subsequent development of insulin resistance [12,13]. Furthermore we recently reported that a rapid increase of weight in early childhood, not in infancy, contributes to increased adiposity at 12 years of age [14].

While an increase of BMI from age 1.5 to 3 years does not necessarily indicate AR, and indeed, there have been cases in which BMI decreased again after 3 years of age, in the present study it was clarified that an increase of BMI from 1.5 to 3 years of age increased cardiometabolic risk at 12 years of age. These at-risk children should be given appropriate instructions to improve their lifestyle to avoid further increases of their BMI, and to prevent the early AR that contributes to increased risk of obesity-related complications in the future.

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