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Original article

Early Infantile Growth and Cardiovascular Risks in Adolescent Japanese Women

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Abstract

Objective: Early life events connected with the risk of later disease can occur not only *in utero*, but also in infancy. In study of the developmental origins of health and disease, the relationship between infantile growth patterns and adolescent body mass index and blood pressure is one of the most important issues to verify.

Materials and Methods: We analyzed the correlation of current body mass index and systolic blood pressure of 168 female college students with their growth patterns *in utero* and in infancy.

Results: Body mass index and systolic blood pressure in adolescence showed positive correlations with changes in weight-for-age z scores between 1 and 18 months but not with those between 18 and 36 months. Stepwise multiple regression analysis showed that both change in weight-for-age z scores from 1 to 18 months and body mass index at 1 month were significantly and independently associated with systolic blood pressure in adolescence. Body mass index at 36 months was positively correlated with body mass index in adolescence, while body mass index at birth was negatively correlated with body mass index in adolescence.

Conclusion: Our findings shows that restricted growth *in utero* and accelerated weight gain in early infancy are associated with the cardiovascular risk factors of high systolic blood pressure and high body mass index in adolescence. In Japan, an increasing proportion of low birth weight infants and accelerated catch-up growth after birth have been observed in recent decades. This might be an alarming harbinger of an increase in diseases related to the developmental origins of health and disease in Japan.

Key words: body mass index, systolic brood pressure, developmental origins of health and disease, early infantile growth

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Introduction

In the 1990s, Barker proposed that the origins of many adult diseases could be found *in utero*[1]. This *fetal origins hypothesis* has grown into the concept of developmental origins of health and disease (DOHaD) by pulling together a wide range of research results showing that the early life events that determine, in part, the risk of later disease occur not only in the fetal period specifically but also throughout the entire plastic phase of development[2]. Stettler *et al*. studied in detail the relationship between infantile growth patterns and body mass index (BMI) in adulthood and clarified that weight gain in the first week of life was strongly associated with obesity in adulthood in formula-fed European-American subjects[3]. That study, however, did not address blood pressure (BP), which is one of the most important cardiovascular risk factors. It is important to clarify the relationship between infantile growth patterns and cardiovascular risk factors, including BP and obesity, in a variety of ethnic and social environments. In Japan, previous research addressing this issue is lacking[4–6].

Detailed growth data from infantile medical check-ups (held at municipal health centers) are recorded in individual maternal and child health handbooks given to all pregnant women in Japan. More than 90% of infants nationwide receive these check-ups at regular intervals. (http://www.mhlw.go.jp/toukei/saikin/hw/c-hoken/07/c1.html: accessed September 19, 2012). In this study, we analyzed the relationship between detailed growth records and current BMI and BP as measured by medical check-ups at college admission of adolescent Japanese females.

Table 1 Characteristics of subjects in adolescence and infancy

		Available data n	Mean	SD	Min	Max
In adolescence	Age, years old	168	18.1	0.4	18	20
	BMI, kg/m^2	168	21.2	2.6	16.2	29.9
	Systolic BP, mmHg	167	114.9	11.7	90	148
	Diastolic BP, mmHg	167	70.9	9.2	49	92
At birth	Maternal age at pregnancy, years old	122	27.3	3.9	18	42
	Birth order First	69				
	Second or later	65				
	Unknown	34				
	Gestational age, days	133	276.1	8.8	244	297
	Weight, kg	168	3.094	0.366	1.83	3.814
	BMI	167	12.9	1.2	7	15.1
	WAZ (weight-for-age Z score), SD	168	0.3	0.9	–3	2.1
At 1 month old	Weight, kg	153	4.223	0.467	2.95	6.46
	BMI	153	14.7	1.1	12	17.5
	WAZ	152	0.4	1	–2.1	5.4
	Change in WAZ from birth to 1 month, SD	153	0.1	0.8	–2.2	5
At 18 months old	Weight, kg	144	10.4	1.1	8.1	14.4
	BMI	142	16.1	1.2	13.5	19.7
	WAZ, SD	144	0.3	1	–2.2	3.8
	Change in WAZ from 1 to 18 months old, SD	143	–0.1	1.2	–4.7	3.3
At 36 months old	Weight, kg	138	14	1.7	11	19.6
	BMI	138	15.8	1.2	12.6	21.5
	WAZ, SD	138	0.2	1	–1.9	3.4
	Change in WAZ from 18 to 36 months old, SD	133	–0.1	0.6	–1.7	1.8

BMI, body mass index; BP, blood pressure; WAZ, weight-for-age z score.

Materials and Methods

Participants were first-year female students in the Department of Early Childhood Education, Nayoro City University Junior College. They were asked to provide records from their maternal and child health handbooks. The data included maternal age at pregnancy, birth order, gestational age, and the child's weight and height at birth and 1, 18 and 36 months. To adjust weight during infancy for physiological growth and birth order, the weight-for-age z score (WAZ) in SD units was calculated at each measurement point with a reference population of Japanese children[7] according to the procedure of a previous study[3]. The students' BMIs and blood pressures in adolescence were obtained by medical check-up at college entry. BP was measured using an automated sphygmomanometer (OMRON HEM-1000). Informed consent for use of personal records was obtained from each student. The protocol of this study was approved by the Ethics Committee of Nayoro City University.

Correlations between BMI and BP in adolescence and growth *in utero* and infancy were analyzed by calculating Pearson's product-moment correlation coefficients between the respective records. To estimate the contribution of an individual variable to adolescent SBP and BMI, stepwise multiple regression analysis was performed. Systolic BP or BMI, in separate models, was used as the dependent variable, while the independent variables included BMI in adolescence, BMI and WAZ at birth and 1, 18, 36 months, change in WAZ from birth to 1 month, from 1 to 18 months and from 18 to 36 months, gestational age, birth order (first, second or later) and maternal age at pregnancy. Statistical analysis was performed using the Dr. SPSS 2 for Windows 11.0.1J statistical package.

Results

In the 5 years from 2005 to 2009, we obtained the approval of 168 out of a total of 198 first-year female students to use the records in their maternal and child health handbooks. All subjects were born singly and were nonsmokers (Table 1).

Diastolic BP in adolescence showed a negative correlation with gestational age (Table 2). Significant correlations were shown between BMI in adolescence and BMI at 18 and

Table 2 Correlation of body mass index and blood pressure in adolescence with growth *in utero* and in infancy

			In adolescence		
			BMI	Systolic BP	Diastolic BP
At birth	Gestational age	γ	0.098	–0.122	–0.202
		P	0.259	0.164	0.020
	Weight	γ	0.013	–0.049	–0.139
		P	0.864	0.528	0.074
	BMI	γ	–0.087	–0.096	–0.169
		P	0.255	0.219	0.030
	WAZ	γ	0.011	–0.053	–0.143
		P	0.889	0.497	0.066
At 1 month	BMI	γ	0.110	0.101	0.011
		P	0.172	0.215	0.890
	WAZ	γ	0.130	–0.010	–0.041
		P	0.105	0.903	0.612
	Change in WAZ from birth to 1 month	γ	0.204	0.034	0.096
		P	0.011	0.673	0.239
At 18 months	BMI	γ	0.330	0.131	0.042
		P	<0.001	0.120	0.618
	WAZ	γ	0.348	0.225	0.193
		P	<0.001	0.007	0.021
	Change in WAZ from 1 to 18 months	γ	0.241	0.243	0.222
		P	0.003	0.004	0.008
At 36 months	BMI	γ	0.470	0.164	0.125
		P	<0.001	0.056	0.146
	WAZ	γ	0.409	0.215	0.177
		P	<0.001	0.011	0.038
	Change in WAZ from 18 to 36 months	γ	0.073	–0.017	–0.065
		P	0.397	0.844	0.459

BMI, body mass index; BP, blood pressure; WAZ, weight-for-age z score; γ, Pearson's product-moment correlation coefficient; *P*, *P* value for correlation.

36 months of age, WAZ at 18 and 36 months and changes in WAZ from 1 to 18 months. In the same way, systolic BP in adolescence showed significant positive correlations with WAZ at 18 and 36 months and changes in WAZ from 1 to 18 months. However, no significant correlation was shown between BMI and BP in adolescence or changes in WAZ from 18 to 36 months of age. Diastolic BP in adolescence showed a positive correlation with changes in WAZ from 1 to 18 months. Table 3 shows the correlation between growth *in utero* and in infancy. Subjects with low weight, BMI and WAZ at birth tended to demonstrate a greater increase in WAZ from birth to 1 month and from 1 to 18 months but not from 18 to 36 months of age.

Stepwise multiple regression analysis showed that both change in WAZ from 1 to 18 months and BMI at 1 month were significantly and independently associated with systolic BP in adolescence (Table 4). BMI at 36 months was positively correlated with BMI in adolescence, while BMI at birth was negatively correlated with BMI in adolescence.

Discussion

Our findings that restricted growth *in utero* and accelerated weight gain in early infancy are associated with the cardiovascular risk factors of high systolic BP and high BMI in adolescence corresponds with previous studies[1–6]. According to the concept of DOHaD, early life events that partly determine the risk of later disease occur not only in the fetal period but also throughout the plastic phase of development[1–3]. So, what period actually corresponds to the plastic phase? Stettler *et al.* showed that the critical period for the development of obesity in adulthood was the first 8 days in formula-fed European-Americans[3]. Although the exact plastic phase was not shown accurately, our results demonstrated that the extremely early period after birth was included in the plastic phase relating to cardiovascular risk factors in adolescence. Low weight, BMI and WAZ at birth were, however, associated with a greater increase in weight from 1 to 18 months of age, which correlated significantly

Table 3 Correlation between growth *in utero* and in infancy

At birth		Change in WAZ		
		From birth to 1 month	From 1 to 18 months	From 18 to 36 months
Gestational age	γ	–0.094	–0.152	–0.093
	P	0.305	0.107	0.345
Weight	γ	–0.344	–0.314	–0.033
	P	<0.001	<0.001	0.704
Height	γ	–0.108	–0.075	–0.041
	P	0.182	0.372	0.634
BMI	γ	–0.296	–0.345	–0.002
	P	<0.001	<0.001	0.984
WAZ	γ	–0.347	–0.314	–0.027
	P	<0.001	<0.001	0.754

BMI, body mass index; BP, blood pressure; WAZ, weight-for-age z score; γ, Pearson's product-moment correlation coefficient; *P*, *P* value for correlation.

Table 4 Factors associated with systolic blood pressure and body mass index in adolescence by stepwise multiple regression analysis

Independent variable	Systolic BP (mmHg)			
	β	95% confidence interval of β	Standardized β	*P*
Change in WAZ from 1 to 18 months	3.393	1.163, 5.624	0.323	0.003
BMI at 1 month	2.841	0.413, 5.269	0.248	0.022
Independent variable	BMI (kg/m^2)			
	β	95% confidence interval of β	Standardized β	*P*
BMI at 36 months	0.991	0.650, 1.332	0.516	<0.001
BMI at birth	–0.389	–0.769, –0.008	–0.181	0.045

BMI, body mass index; BP, blood pressure; WAZ, weight-for-age z score; β, partial regression coefficient; *P*, significance level.

with BMI and BP in adolescence. These results might show that restricted growth *in utero* is also associated with cardiovascular risks in adolescence. We could not also show that these independent variables were related to both systolic BP and BMI. One possible explanation for this may be the low statistical power of the small sample size. Unfortunately, it was difficult for us to increase the number of participants due to the need for informed consent and the manpower required for reliable data collection.

Though adolescent BMI and BP may not have strong correlations with growth *in utero* and infancy, pairwise correlation coefficients and β coefficients in our study were, however, comparable with those of previous studies[3, 5, 6, 8]. With regard to cardiovascular risk factors, i.e., BMI and BP, criteria have been established. Therefore, statistical comparison of growth *in utero* and infancy should be performed among groups classified according to the established criteria. Within our subject age group, almost all participants were classified into the low-risk group. Dependable statistical comparison among groups was difficult because of the very small sample size of moderate or high risk groups. Therefore, we performed statistical analysis in the same fashion as previous studies[3, 5, 6].

In previous studies, we reported an increase, since the 1970s in the proportion of low birth weight infants, and a simultaneous reduction in the ratio of male/female births in Japan[9, 10]. Based on detailed analyses of vital statistics in Japan, we suggested that these phenomena might be consequences of a progressive deterioration in the uterine environment, in which the more vulnerable male fetuses were lost at an early stage of gestation and the relatively less vulnerable female fetuses survived but were not able to grow sufficiently.

On the other hand, both the weight and height of Japanese infants have been increasing in recent decades[11, 12]. Considering the increase in the proportion of low birth weight infants and the concurrent increase in weight and height during infancy, we can surmise that catch-up growth after birth has become more accelerated during this period, which fits well with the Japanese saying "Bear them small, raise them up big!"

According to the concept of DOHaD, restricted growth

due to a deteriorated environment *in utero* and subsequent accelerated weight gain in early infancy are correlated with risks for several diseases in adulthood, including cardiovascular diseases and diabetes. In the future, morbidity and mortality due to DOHaD-related diseases may increase strikingly in Japan. The monitoring of factors relating to DOHaD should be continued.

Conclusion

We analyzed the correlation of current body mass index and systolic blood pressure of 168 female college students with their growth patterns *in utero* and in infancy. Restricted growth *in utero* and accelerated weight gain in early infancy are associated with the cardiovascular risk factors of high systolic blood pressure and high body mass index in adolescence.

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