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Height Growth of Triplets from Birth to 12 Years of Age in Japan

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We analyzed the characteristics associated with the growth in height of Japanese triplets from birth to 12 years of age. The study included 376 mothers and their 1,128 triplet children, who were born between 1978 and 2006. Data were collected through a mailed questionnaire sent to the mothers asking for information recorded in medical records. For these births, data on triplets' length and height growth, gestational age, sex, parity, maternal age at delivery, and maternal height were obtained from records in the Maternal and Child Health Handbooks and records in the school which children receive health check-ups. The height deficit of the triplets compared to the general population of Japan remained between 2% and 5% until 12 years of age. Moreover, at 12 years of age, the differences of height between the general population and triplets were approximately -3.6 cm for male and -4.4 cm for female. Maternal height showed the strongest contribution to height of triplets from 6 to 12 years of age. In conclusion, triplets remain shorter than singletons until 12 years of age.

■ **Keywords:** triplet, height, growth, very low birthweight, maternal height, sex

It is well known that the growth patterns of twins and triplets during pregnancy, especially in the third trimester, are very different than those of singletons. Studies conducted in many countries have shown that twins and triplets have lower birth weight and length than singletons (Arbuckle et al., 1993; Buckler & Green, 1994; Glinianaia et al., 2000; Min et al., 2000; Min et al., 2004; Kato & Uchiyama, 2005). However, there are few previous studies on the postnatal growth of triplets in the world, while a number of studies on the postnatal growth of twins have been conducted (Akerman & Fischbein, 1992; Alfieri et al., 1987; Luke et al., 1995; Ooki & Yokoyama 2004; Philip 1981; Silventoinen et al., 2008; Wilson 1974; 1976; 1979).

Triplets are typically born prematurely, and 40–50% of them weigh less than 1500 g at birth (Ziadeh, 2000; Kato, 2004). Meanwhile, it is indicated that subjects who demonstrate catch-up growth are at greatest risk for alteration in metabolism, hormonal output, and distribution of cardiac output, which may result in obesity, type 2 diabetes, and cardiovascular disease in middle age (Ciandarani et al., 1999; Fall, 1995; Forsen et al., 1999; Law, 2001). Studies on the long-term growth of low birthweight infants, including triplets, the majority of whom experience intrauterine and/or neonatal growth failure, may yield important information in this regard (Bukowski et al., 2001; Ehrenkranz et al., 1999; Hack, 1982).

Triplets have been found to be behind singletons even in mid-childhood, in spite of the rapid catch-up growth during the first year of life (Luke et al., 2006; Yokoyama et al., 2008; 2009). However, there have been no reports of physical growth of triplets after 6 years of age. The purpose of this study was to analyze the characteristics of growth in height of Japanese triplets until 12 years of age using an extension in time and number of participants of an existing cohort of triplets for whom growth to age 6 years has been previously reported (Yokoyama et al., 2008).

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TABLE 1

Number of Triplet Individuals According to Sex and Age

Age		Number of subjects with available height data	
		Male	Female
Birth	0–1 months	508	503
1 year	0–6	182	164
2 years	0–6	247	239
3 years	0–6	272	269
4 years	0–6	195	190
5 years	0–6	185	192
6 years	0–6	201	190
7 years	0–6	134	124
8 years	0–6	120	106
9 years	0–6	107	114
10 years	0–6	94	89
11 years	0–6	64	60
12 years	0–6	45	41

Subjects and Methods

The subjects of this study were recruited from the Osaka City University Higher Order Multiple Births Registry (Yokoyama et al., 1995; Yokoyama, 2002; Yokoyama et al., 2005), which consisted of 578 mothers with triplets who were born between 1978 and 2006. Mothers and their triplet children were enrolled also from several other sources, such as various Japanese Mother's Organizations for Higher Order Multiple Births and referrals from public health nurses. The response rate was 67.0%. We had 1,164 triplet individuals having information on growth, but 36 triplets with unrecorded sex were excluded from the analyses. Ultimately, the subjects of this study were 376 mothers and their 1,128 triplet children. The mothers gave written informed consent to participate in the present study.

Data were collected through a mailed questionnaire sent to the mothers asking for information recorded in medical records. For these births, data on triplets' birthweight, height growth data, gestational age, sex, parity, maternal age at delivery and maternal height were obtained from records in the Maternal and Child Health Handbooks. This handbook was established by the Maternal and Child Health Law in Japan and is provided to the expecting mother by the authorities after a report of pregnancy. The purpose of this handbook is the maintenance of maternal and child health, and it includes information on health check-ups during pregnancy, the condition of the newborn, the progress of infant growth, periodic medical check-ups for the infant and vaccinations recorded by obstetricians or pediatricians. In addition, information on infertility treatment was obtained.

In Japan, the health check-up system after birth differs according to life stage. Until six years of age, children participate in health check-ups administered by the Ministry of Health, Labor and Welfare based on age, which is counted as actual weeks, months, or years after the birth. The length/height data of children based on health check-ups are routinely recorded in the Handbook. After six years of age, Japanese children receive health check-ups administered by the Ministry of Education, Culture, Sports, Science and Technology under the School Health Law. The height measures from these school-based health check-ups are routinely recorded in the school records and made available to each family. Mothers have access to the school records from every grade and can check them directly. Mothers participating in this study were advised to refer to these records when completing the questionnaire. The height growth data were assigned to the appropriate age groups on the basis of time (in days) since birth, which was calculated as the date at the check-up minus the child's birthday.

TABLE 2

Major Characteristics of the Triplet Individuals

Characteristics	Number
Gestational age (weeks)	
≤ 28	69 (6.1%)
29–32	309 (27.4%)
33–36	639 (56.6%)
37 ≤	96 (8.5%)
Unknown	15 (1.3%)
Mean ± standard deviation	33.1±2.64
Range	25–38
Birth weight (g)	
< 1000	76 (6.7%)
1000 ≤ a <1500	270 (23.9%)
1500 ≤ a <2000	510 (45.2%)
2000 ≤ a <2500	227 (20.1%)
2500 ≤	32 (2.8%)
Unknown	13 (1.2%)
Mean ± standard deviation	1695.0±428.0
Range	574–3078
Sex	
Male	574 (50.9%)
Female	554 (49.1%)
Parity of mother	
0	855 (75.8%)
≥ 1	246 (21.8%)
Unknown	27 (2.4%)
Infertility treatment by mother	
Not used	201 (17.8%)
Used	891 (79.0%)
Unknown	36 (3.2%)
Maternal age of delivery (years)	
< 25	24 (2.1%)
25–29	373 (33.1%)
30–34	528 (46.8%)
35 ≤	182 (16.1%)
Unknown	21 (1.9%)
Mean ± standard deviation	31.0±3.58
Range	20–42
Maternal height (cm)	
< 155	177 (15.7%)
155–159	286 (25.4%)
160–164	221 (19.6%)
165 ≤	87 (7.71%)
Unknown	357 (31.6%)

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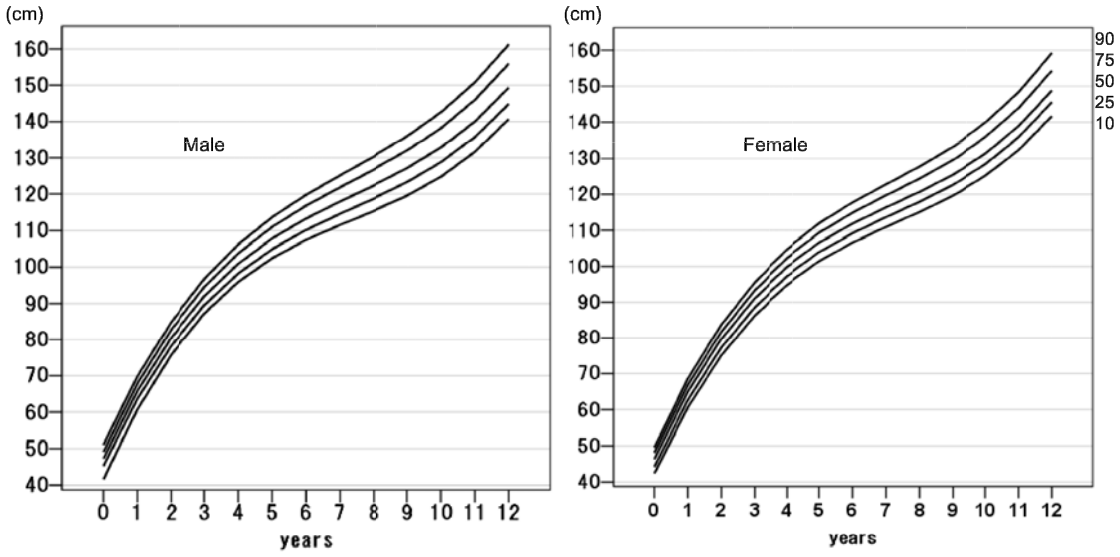

FIGURE 1
Body height of triplets according to age percentiles from birth to 12 years of age.

The means and standard deviations of height from birth to 12 years of age for triplets were calculated according to gestational age, very low birth weight (< 1500g), sex, parity, birth order, maternal age at triplet delivery and maternal height. The significance of differences between mean values of factors was tested using linear mixed model where adjustment for familial clustering (i.e., sets of triplets) is achieved by including a familial random effect and other factors are included as fixed effects. Separate analysis of the association between body height (response) and fixed effect factors were performed at 6, 8, 10 or 12 years of age. The explanatory variables fixed effect variables were very low birthweight, gestational age, sex, and maternal height.

The selected percentiles (10th, 25th, 50th, 75th, and 90th) of height were calculated according to age and sex. Smoothing of growth curves was performed by cubic polynominal functions. The height deficit of the triplets was calculated as the percentage difference between the value of the general population and that of the triplets divided by the value of the general population; the standard error of the triplet means was used to compute the confidence interval for the height deficit. The height deficits were calculated using mean values of the growth standards presented by the Ministry of Health, Labor and Welfare (Kato et al., 2001) and the Ministry of Education, Culture, Sports, Science and Technology (2009). The SPSS statistical package (PASW), version 18.0 for Windows (2009) was used for the statistical analysis.

Results

Table 1 presents the number of subjects according to sex and age for which height data were available. Table 2 summarizes the characteristics of the subjects. Gestational age at birth did not differ by maternal height and was 33.1±2.57 weeks in women whose height is less than 155 cm, 32.9±2.84 weeks in women whose height is 155–160 cm, 33.1±2.67 weeks in women whose height is 160–165 cm and 33.5±2.44 weeks in women whose height is more than 165 cm. The 10th, 25th, 50th, 75th, and 90th percentiles of height from birth to 12 years of age are presented in Figure 1.

Table 3 shows the mean length/height at birth and at 6, 8, 10 and 12 years of age analyzed according to gestational age, very low birthweight, sex, parity, birth order, maternal age at triplet delivery and maternal height. Females and triplets whose gestational age was earlier had a shorter birth length and shorter height at 6, 8, and 10 years of age; these differences were statistically significant, except for the sex difference for height at 10 years of age. Very low birthweight infants had a shorter birth length and shorter height at 6, 8, 10, and 12 years of age. Triplets born to shorter mothers had a shorter height at 6, 8 and 10 years of age than triplet children born to taller mothers.

Table 4 shows the results of linear mixed effects multiple regression analysis of height at 6, 8, 10 or 12 years of age. Maternal height had the strongest contribution to height from 6 to 12 years of age, but also very low birthweight and sex affected height at 6 and 8 years of age.

The length/height deficit of triplets was approximately 15% at birth, related to the growth standards of the general Japanese population (male, -7.34 cm; female, -7.10 cm). The deficit decreased rapidly within the first year of age, but fluctuated between 2% and 5% until 12 years of age (male, -3.62 cm; female, -4.43 cm) (Table 5).

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TABLE 3

Birth Length and Height at Six, Eight, Ten and Twelve Years of Age According to Maternal and Own Characteristics Among Japanese Triplets

	Birth length (cm)			Six years of age (cm)			Eight years of age (cm)			Ten years of age (cm)			Twelve years of age (cm)		
	N	Mean	*SD*	*N*	Mean	*SD*	*N*	Mean	*SD*	*N*	Mean	*SD*	*N*	Mean	*SD*
Gestational age															
≤ 28	59	34.04	2.09***	19	108.41	4.84*	6	120.80	4.58*	12	127.41	6.32***	3	147.17	0.38
29–32	263	39.01	2.81	108	110.61	4.41	57	120.80	5.74	44	131.22	5.87	18	146.04	9.50
33–36	577	42.71	2.43	208	111.78	4.48	132	124.27	5.06	111	135.89	5.30	50	149.57	7.17
37 ≤	80	45.05	2.52	42	110.93	4.74	25	122.13	4.41	14	133.21	4.57	15	147.03	5.15
Very low birthweight infant															
Yes	308	37.54	3.03***	130	109.72	4.47***	60	120.38	5.36***	50	130.43	6.41***	22	144.85	8.44*
No	700	43.09	2.36	258	111.93	4.43	166	124.05	5.10	131	135.34	5.31	64	149.49	6.64
Sex															
Male	508	41.66	3.78***	201	111.58	4.58*	120	124.23	5.70***	92	134.64	6.15	45	148.88	7.94
Female	503	41.13	3.47	190	110.83	4.51	106	121.77	4.75	89	133.31	5.87	41	147.67	6.74
Parity of mother															
Multipara	214	42.03	3.60	76	110.56	4.67	40	121.42	5.20	35	133.74	4.80	15	145.89	3.99
Primipara	771	41.23	3.64	298	111.36	4.55	180	123.39	5.35	137	134.04	6.33	68	149.04	7.91
Birth order															
First-born	337	41.57	3.47*	130	111.37	4.39	78	123.20	5.60	62	134.09	5.96	29	149.08	7.64
Second-born	338	41.47	3.62	130	111.53	4.15	74	123.46	5.00	59	134.28	5.37	29	149.09	7.08
Third-born	336	41.13	3.80	131	110.74	5.08	74	122.57	5.62	60	133.58	6.76	28	146.69	7.39
Maternal age at triplet delivery															
< 25	16	39.04	3.91	9	113.18	6.31	3	125.5	3.12	6	130.68	3.50	3	142.50	0.92**
25–29	320	41.57	3.71	93	111.53	3.86	63	122.18	5.31	66	133.71	5.89	25	146.40	7.92
30–34	490	41.35	3.63	211	111.33	4.66	117	123.56	4.94	87	134.26	6.10	42	148.33	7.04
35 ≤	165	41.38	3.53	64	109.88	4.76	37	122.65	6.69	16	134.15	6.79	13	154.28	5.34
Maternal height															
< 155	158	40.72	3.25	77	108.22	3.76***	47	120.73	4.19*	41	131.65	4.96*	24	145.00	4.18
155–159	255	41.52	3.65	121	110.50	4.54	74	122.47	4.89	69	133.59	5.33	26	147.66	5.84
160–164	192	41.32	4.04	92	112.95	3.93	56	124.65	5.88	35	135.21	7.58	21	152.04	10.56
165 ≤	84	42.43	3.42	37	114.58	3.38	17	126.08	3.92	12	138.78	4.53	6	152.12	5.520

Note: *SD*: standard deviation; All variables included in the model; * $p < .05$, ** $p < .01$, *** $p < .001$

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TABLE 4

Result of Linear Mixed Effects Multiple Regression Analysis of Factors Associated with Body Height

Dependent variable	Independent variable	Beta	95% CI	*p*
Height at 6 years	Very low birthweight			
	No	1.783	0.746–2.819	*P* < .001
	Yes	0		
	Sex			
	Male	0.780	0.031–1.530	*P*=0.041
	Female	0		
	Maternal height	0.392	0.273 – 0.510	*P* < .001
	Gestational age	0.028	-0.223 – 0.278	*P* = .829
Height at 8 year	Very low birthweight			
	No	3.597	1.867–5.326	*P* < .001
	Yes	0		
	Sex			
	Male	1.193	0.116–2.270	*P* = .030
	Female	0		
	Maternal height	0.309	0.133–0.484	*P* = .001
	Gestational age	-0.118	-0.533–0.296	*P* = .572
Height at 10 years	Very low birthweight			
	No	2.285	-0.098 – 4.669	*P* = .060
	Yes	0		
	Sex			
	Male	-0.237	-1.780–1.305	*P* = .762
	Female	0		
	Maternal height	0.356	0.136–0.576	*P* = .002
	Gestational age	0.521	0.019–1.023	*P* = .042
Height at 12 years	Very low birthweight			
	No	1.244	-2.536–5.024	*P* = .513
	Yes	0		
	Sex			
	Male	-1.406	-3.790–0.978	*P* = .243
	Female	0		
	Maternal height	0.573	0.085–1.061	*P* = .023
	Gestational age	0.316	-0.715–1.348	*P* = .537

Discussion

Compared to the general population of Japan, the height deficit of Japanese twins is largest at birth but decreased dramatically during the first 6 to 12 months, reaching as little as approximately 2%, around 1 cm for height, by 6 years of age (Ooki & Yokoyama, 2004). These trends were consistent with those reported by Bucker and Green (1994). Meanwhile, the height deficit of the triplets compared to the general population was greatest at birth: approximately 15%. These deficits decreased within the first year of age, but were found to remain between 2% and 5% for height until 6 years of age (Yokoyama et al., 2009).

In the present study, the height deficit of triplets compared to the general population of Japan remained between 2% and 5% until 12 years of age. Moreover, at 12 years of age, the differences of height between the general population and triplets were approximately -3.6 cm for male and -4.4 cm for female. There are no physical growth charts of triplet children after 6 years of age in the world. However, these results are similar to that reported by Powls et al. (1996) who found that very low birthweight children in a Caucasian population were significantly shorter than their normal birthweight peers at 12 years of age, with a deficit of -3.8 cm for male and -4.4 cm for female. In addition, Hack et al. (2003) indicated that catch-up growth in height occurred between 8 and 20 years among very low birthweight females but not among very low birthweight males who remained significantly smaller than their controls at 20 years of age. Further follow-up is needed to investigate whether triplets achieve normal height later in life, as our follow-up ends at the start of puberty and the associated growth spurt.

Meanwhile, our data showed that when adjusting for very low birthweight and other confounding factors, maternal height had the strongest contribution to the height of triplets from 6 to 12 years of age. Blickstein et al. (2003) and Blumenfeld et al. (2006) indicated that taller women are more likely to deliver heavier triplets and are at lower risk of delivering very low birthweight triplets. Moreover, Buckler and Green (2008) reported that parental heights accounted for the difference in height of twins. In addition, adult height of very low birthweight infants was found to be predicted by maternal height (Hack et al., 2003). These results suggest that maternal height has a significant effect not only on birth length/height but also on height during childhood and later life, demonstrating the pervasiveness of genetic effects even in triplets whose growth may be otherwise compromised by

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TABLE 5

Height Deficit of Triplets as to the Mean Compared with the General Population from Birth to 12 Years of Age

		Male		Female	
		(%)	95%CI	(%)	95%CI
Birth		14.98	14.31–15.65	15.03	14.39–15.65
1 year	0–1 mo	5.18	4.33–6.03	3.82	3.30–4.34
2 years	0–6 mo	4.00	3.36–4.65	4.01	3.55–4.48
3 years	0–6 mo	2.80	2.31–3.29	3.42	3.01–3.84
4 years	0–6 mo	3.07	2.46–3.68	3.62	3.40–3.84
5 years	0–6 mo	3.08	2.47–3.68	3.02	2.44–3.60
6 years	0–6 mo	4.31	3.76–4.85	4.30	3.74–4.85
7 years	0–6 mo	3.57	2.86–4.28	4.15	3.54–4.76
8 years	0–6 mo	3.09	2.30–3.89	4.42	3.71–5.13
9 years	0–6 mo	3.58	2.68–4.48	4.74	4.04–5.44
10 years	0–6 mo	4.45	3.55–5.36	4.91	4.04–5.78
11 years	0–6 mo	2.86	1.73–3.99	4.28	3.19–5.37
12 years	0–6 mo	2.37	0.85–3.90	2.91	1.56–4.27

Note: The height deficit of the triplets was calculated as the percentage difference between the triplets' observed mean height (95% CI) and the mean value of the general population.

prenatal environmental constraints. To some degree this can also be because of prenatal environmental factors, as tall women are larger and can accommodate even three growing fetuses better than short women.

Further, very low birthweight was a significant factor affecting height at six and eight years of age. It is indicated that deficient growth in twins between the age of 2 and 9 years was most evident in those babies light at birth (Buckler & Green, 2008). Moreover, Powls et al. (1996) indicated that very low birth weight children had a higher risk of short stature later in life. It is probable that very low birth weight affects also growth of height in triplets. Infants with very low birth weight may need careful and extensive longitudinal follow-up.

Regarding other factors associated with height of triplets, sex was a significant factor affecting height at 6 and 8 years of age. Male triplets had taller pre-pubertal height than females. This result is in accordance with previous reports on twins (Buckler & Green, 2004; Ooki & Asaka, 1993) and singletons (Karlberg, 2002). Data on zygosity, maternal smoking, maternal previous obstetric outcome, maternal weight gain during pregnancy, and breast-feeding are lacking in this study, and it has been suggested that these factors are associated with height growth (Luke et al., 2002; Martin et al., 2002; Ooki & Yokoyama, 2003; Vogazianos et al., 2005).

The limitation of the present study was that these data were semi-longitudinal. Specifically, data on the same individual were used according to the recorded times. Some of our subjects provided most of longitudinal data. On the other hand, others provided data from birth to 6 years of age. Additionally, the number of subjects in each age group varied considerably as some children were younger than 12 years at the time of the survey. Consequently, the range of measurements in each group becomes small, especially at 12 years of age. However, since the mothers reported the growth of their children retrospectively based on records, there is no age-related drop-out in our data. The clinical use of 10th percentiles and 90th percentiles of this growth charts as indicators of growth retardation might not be necessarily appropriate.

In conclusion, triplets have shorter height than singletons and the height deficit of the triplets compared to the general population of Japan remained between 2% and 5% until 12 years of age. Maternal height had the strongest contribution to height of triplets from 6 to 12 years of age. Further follow-up of the triplets should reveal whether their growth catches up with singletons before adulthood.

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