



Motor Development of Triplets: A Japanese Prospective Cohort Study

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We analyzed whether motor development in early life is different between singletons and triplets in Japan. The motor development was reported by mothers by postal questionnaire for 1,121 triplet children and in regular health check-ups for 13,906 singleton children. Children who were suspected of having neurological abnormality or disability were excluded from the analysis. The ages of milestone achievements were significantly higher in triplets for each outcome compared to singletons. Further, after adjustment for gestational age, birthweight, and birth length, the differences were significant for maintaining head, sitting alone and standing holding on. In children with birthweight of 2 kg or more, the ages of milestone achievements were significantly higher in triplets for each outcome compared to singletons, except walking holding on. Moreover, after adjustment for the confounding factors, the differences were significant for sitting alone and walking independently. On the contrary, singletons attained motor development facilitating crawling, walking holding on, and walking independently slower than triplets among those children with birthweight of 2 kg or less after adjustment for gestational age. In conclusion, triplets are overall at higher risk for the delay of gross motor milestones as compared to singletons independently of birth-related factors. In contrast, among children with a birthweight of less than 2 kg, singletons showed slower motor development than triplets after adjusting for gestational age. There is an obvious need to apply developmental standards that consider at least both multiple birth status (singleton, twin or triplet) and birthweight.

■ **Keywords:** triplet, singleton, motor development, birthweight

Multiple birth rates have increased in all industrialized countries since the 1980s because of the increased use of infertility treatment, whereas the birth rates in general are decreasing. Especially the triplet rate has rapidly increased: for example, in Japan, there was a 4.2-fold increase from 1974 to 2001 (Imaizumi, 2003). The infant mortality rate of triplets is higher than that of singletons (Imaizumi, 2001), and birth defects associated with multiple births are an important problem for the children, their families and the whole public health sector.

The attainment of gross motor milestones is a significant indicator of motor development in early life, which is further like to play an important role in the long-term neurodevelopment (Peter et al., 1999). Neurodevelopment can be impaired by a number of conditions (Bhargava, 2000; Gross, 1991; Hediger et al., 2002; Koepfen-

Schemerus et al., 2000; Petterson et al., 1993; Sherriff et al., 2001), but premature infants, especially those born with very low birthweights, are at the highest risk for neurologic impairments and cognitive delay (Anderson et al., 2003; De Kleine et al., 2003; Feldman et al., 1998; Hack et al., 2000; Taylor et al., 2004; Wolke, 1998) and have long-term risks of metabolic diseases (Kajantie et al., 2005).

Twins are prone to developmental delay due to prematurity and low birthweight (Myianthopoulos et al., 1976).

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Studies in Gambia (Goetghebuer et al., 2003) and Japan (Yokoyama et al., 2007) have also reported that twinning is an independent risk factor for developmental delay in early life after adjusting for confounding factors.

Triplets are typically born prematurely, and 40–50% of them weigh less than 1500 g at birth (Angel, 1999; Kato, 2004; Ziadeh, 2000). Feldman and Eidelman (2005) reported cognitive development of triplets compared to singletons in the first two years of life and demonstrated that triplets appeared to be at higher risk for cognitive delays. However, little research has been done on the motor development of triplets, and there has been no study evaluating whether motor development in early life is different between singletons and triplets in Japan. This present study was therefore performed to analyze whether motor development in early life is different between singletons and triplets. For better comparison and investigation, we conducted the analyses in three groups: the entire sample, a group with a birthweight of 2 kg or greater, and a group with a birthweight of less than 2 kg. This value of low birthweight (< 2 kg) was used because the number of singletons with a birthweight of less than 1.5 kg was very small.

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 65.9%. The mothers gave written informed consent to participate in the present study. After excluding 22 children who were suspected of having neurological abnormality or disability, the study sample included 374 mothers and their 1,121 triplet children.

Data were collected through a mailed questionnaire sent to the mothers asking for information recorded in medical records. For these births, data on the ages of attainment of a set of gross-motor milestones, birthweight, birth length, head circumference at delivery, gestational age, sex, parity, mode of delivery, and maternal age at delivery 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 pregnant mothers 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 pediatri-

TABLE 1
Motor Milestones and Their Definitions

Milestones	Definitions
Maintain head	Assessed by pulling the baby's arms.
Roll over	Assessed if the child was able to roll over completely from prone to supine or supine to prone.
Sit without support	Defined as sitting up and maintaining the head position without rear support.
Crawl	Assessed if the child was able to move forwards or backwards either on the stomach or on hands and knees.
Sit up	Assessed if the baby was able to move from a lying to a sitting position independently.
Stand holding on	Defined as maintaining a standing position by holding on to ones hand.
Walk holding on	Defined as walking a few steps by holding on to ones hand.
Stand independently	Assessed if the child was able to stand independently.
Walk independently	Assessed if the child was able to walk independently.

cians. The Denver Development Screening Test milestones used in this study are defined in Table 1 (Frankenburg & Dodds, 1967).

In order to compare with age of milestone achievement of triplets, we used the database of health check-ups for 13,906 singleton children aged 3 years. They received health check-ups at 4 months, 1.5 years, and 3 years of age. These data, except personal information, are transcribed into computerized files between April 2001 and July 2004 in Nishinomiya City. Nishinomiya is a residential area with a population of approximately 460,000, and the number of births per year is about 4,700. These health check-ups are given to almost 95% of children in Japan. Children who were suspected of having neurological abnormality or disability were referred to specialists and excluded from the database.

Categorical variables were analyzed using chi-square test and continuous variables using *t* test. Furthermore, a general factor of motor development was calculated using factor analysis (one factor unrotated solution). Age at developmental outcome as the dependent variable was compared for triplets and singletons using multiple linear regressions, adjusting for gestational age, birthweight, and birth length. The SPSS statistical package version 18.0 for Windows (2009) was used for the statistical analyses.

Results

Overall, 13,776 children were singletons of birthweight of 2 kg or greater, 263 children were triplets of a birthweight of 2 kg or greater, while 130 singleton children were of birthweight less than 2 kg, and 858 triplet children were of birthweight less than 2 kg.

Table 2 summarizes the characteristics of the subjects overall as well as in each group. There was a significantly higher rate of infants who underwent cesarean section among triplets than among singletons in entire sample

TABLE 2
Major Characteristics of Subjects in Each Group

	Entire sample		Group with birthweight ≥ 2 kg		Group with birthweight < 2 kg	
	Singleton (N = 13,906) N (%)	Triples (N = 1,121) N (%)	Singleton (N = 13,776) N (%)	Triples (N = 263) N (%)	Singleton (N = 130) N (%)	Triples (N = 858) N (%)
Sex						
Male	7125 (51.2)	549 (50.5)	7052 (51.2)	147 (57.4)	73 (56.2)	402 (48.3)
Female	6781 (48.8)	539 (49.5)	6724 (48.8)	109 (42.6)	57 (43.8)	430 (51.7)
Parity						
Primipara	7786 (56.0)	873 (78.3)***	7715 (56.0)	183 (69.6)	71 (54.6)	690 (81.0)***
Multipara	6118 (44.0)	242 (21.7)	6059 (44.0)	80 (30.4)	59 (45.4)	162 (19.0)
Mode of delivery						
Vaginal delivery	12,181 (87.6)	115 (10.3)***	12,130 (88.1)	40 (15.2)***	51 (39.2)	75 (8.8)***
Cesarean section	1725 (12.4)	1000 (89.7)	1646 (11.9)	223 (84.8)	79 (60.8)	777 (91.2)
Maternal age at delivery (years)						
Mean ± SD	29.6 ± 3.93	0.9 ± 3.64***	29.6 ± 3.92	30.6 ± 3.34***	29.8 ± 4.41	31.0 ± 3.7.2**
Range	16–47	20–42	16–47	23–39	18–40	20–42

Note: Excluding persons with unknown sex, parity, and mode of delivery.
* $p < .05$, *** $p < .001$

TABLE 3
Gestational Age and Body Size Parameters at Birth of Subjects in Entire sample, Group with Birthweight ≥ 2 kg and Group with Birthweight < 2 kg

	Entire sample		Group with a birthweight ≥ 2 kg		Group with a birthweight < 2 kg	
	Singleton (N = 13,906) N (%)	Triples (N = 1,121) N (%)	Singleton (N = 13,776) N (%)	Triples (N = 263) N (%)	Singleton (N = 130) N (%)	Triples (N = 858) N (%)
Gestational age (weeks)						
≥ 37	13,366 (96.2)	253 (22.7)***	13,345 (96.9)	64 (24.9)***	16 (12.3)	36 (4.2)***
32–36	487 (3.5)	759 (68.1)	419 (3.0)	192 (74.7)	68 (52.3)	561 (66.1)
< 32	48 (0.3)	103 (9.2)	2 (0.0)	1 (0.4)	46 (35.4)	252 (29.7)
Mean ± SD	39.0 ± 1.48	33.2 ± 2.62***	39.1 ± 1.32	35.5 ± 1.35***	32.9 ± 3.42	32.5 ± 2.51
Birthweight(g)						
Mean ± SD	3064.0 ± 400.9	1700.4 ± 425.8***	3077.9 ± 374.6	2248.0 ± 206.5***	1587.7 ± 356.9	1532.6 ± 322.0
Range	718–5090	574–3078	2000–5090	2000–3078	718–1996	574–1998
Birth length (cm)						
Mean ± SD	48.9 ± 2.09	41.5 ± 3.59***	49.0 ± 1.92	45.2 ± 1.98***	40.6 ± 3.51	40.3 ± 3.19
Range	30–60	28–51	33–60	39–51	30–47	28–49
Head circumference(cm)						
Mean ± SD	33.1 ± 1.43	28.6 ± 3.22***	33.2 ± 1.36	31.1 ± 2.14***	29.0 ± 2.34	27.8 ± 3.10***
Range	23–45	15–37	23–45	26–37	23–33	15–35

Note: Excluding persons with unknown gestational age.
 $p < .05$, *** $p < .001$

($p < .001$), a group with a birthweight of 2 kg or greater ($p < .001$) and a group with a birthweight of less than 2 kg ($p < .001$).

As shown in Table 3, gestational age was significantly higher among singletons than among triplets in entire sample ($p < .001$), a group with a birthweight of 2 kg or greater ($p < .001$) and a group with a birthweight of less than 2 kg ($p < .001$). In entire sample and a group with a birthweight of 2 kg or greater, triplets had lower birthweight and shorter birth length than singletons.

Table 4 shows ages of milestone achievements in triplets and singletons in entire sample. The ages of mile-

stone achievements were significantly higher in triplets for each outcome compared to singletons. Moreover, after adjustment for gestational age, birthweight, and birth length, in which there were differences between triplets and singletons in entire sample, the differences were significant for maintaining head ($p < .001$), sitting alone ($p < .001$) and standing holding on ($p = .004$).

Table 5 shows ages of milestone achievements in triplets and singletons with a birthweight of 2 kg or more. The ages of milestone achievements were significantly higher in triplets for each outcome compared to singletons, except walking holding on. Further, after adjustment

TABLE 4

Age of Milestone Achievement in Triplets and Singletons of Entire Sample

	Singletons N = 13,906 Mean (95%CI)	Triplets N = 1,121 Mean (95%CI)	p value	Adjusted p value
Maintain head (months)	3.25 ± 0.72 (3.23–3.26) (n = 13,076)	4.11 ± 1.12 (4.04–4.19) (n = 831)	< .001	< .001
Roll over (months)	5.02 ± 1.28 (4.99–5.04) (n = 10,579)	6.27 ± 1.46 (6.17–6.37) (n = 802)	< .001	.113
Sit (alone) (months)	6.66 ± 1.03 (6.64–6.68) (n = 12,922)	7.94 ± 1.56 (7.83–8.05) (n = 760)	< .001	< .001
Crawl (months)	7.77 ± 1.46 (7.74–7.80) (n = 10,593)	8.79 ± 1.59 (8.68–8.90) (n = 792)	< .001	.228
Stand holding on (months)	8.59 ± 1.53 (8.56–8.62) (n = 10,778)	10.02 ± 2.03 (9.88–10.16) (n = 818)	< .001	.004
Walk holding on (months)	9.74 ± 1.69 (9.71–9.77) (n = 10,477)	10.84 ± 1.76 (10.61–11.06) (n = 243)	< .001	.892
Walk independently (months)	12.37 ± 2.01 (12.33–12.40) (n = 13,114)	13.76 ± 2.54 (13.59–13.92) (n = 929)	< .001	.098
General factor of motor development	-0.02 ± 0.99 (-3.33–8.62) (n = 9634)	0.97 ± 1.09 (-1.75–5.07) (n = 173)	< .001	.351

Note: Adjustment was made for gestational age, birthweight, and birth length.

for gestational age, birthweight, and birth length, in which there were differences between triplets and singletons, the differences were significant for sitting alone ($p < .001$) and walking independently ($p = .029$).

Table 6 shows ages of milestone achievements in triplets and singletons of a birthweight of less than 2 kg. The age of milestone achievement was higher in singletons for walking holding on compared to triplets. Moreover, after adjustment for gestational age, in which there were differences between triplets and singletons in this group, the differences were significant for crawling ($p = .009$), walking holding on ($p = .015$), and walking independently ($p = .028$).

Discussion

Despite the recent rapid increase in multiple births, including triplets, and subsequently the augmenting need to provide appropriate information to their parents, there are few previous studies on the motor development of triplets. Furthermore, ethnic differences in motor development were reported by Iløje et al. (1991), who showed that black children attained gross motor milestones earlier than white children. There has been no study evaluating whether motor development in early life is different between singletons and triplets in Japan. The present data

TABLE 5

Age of Milestone Achievement in Triplets and Singletons of Birthweight < 2kg

	Singletons (N = 13,776) Mean (95%CI)	Triplets (N = 263) Mean (95%CI)	p value	Adjusted p value
Maintain head (months)	3.24 ± 0.71 (3.22–3.25) (n = 12,953)	3.52 ± 0.73 (3.42–3.62) (n = 203)	< .001	.887
Roll over (months)	5.00 ± 1.27 (4.98–5.03) (n = 10,485)	5.55 ± 1.40 (5.35–5.74) (n = 198)	< .001	.942
Sit (alone) (months)	6.65 ± 1.01 (6.63–6.66) (n = 12,801)	7.31 ± 1.26 (7.13–7.49) (n = 189)	< .001	< .001
Crawl (months)	7.76 ± 1.46 (7.73–7.78) (n = 10,496)	8.13 ± 1.59 (7.91–8.35) (n = 196)	< .001	.093
Stand holding on (months)	8.57 ± 1.52 (8.54–8.60) (n = 10,679)	9.32 ± 1.86 (9.05–9.58) (n = 191)	< .001	.271
Walk holding on (months)	9.72 ± 1.68 (9.69–9.75) (n = 10,378)	10.00 ± 1.49 (9.57–10.43) (n = 48)	0.252	.064
Walk independently (months)	12.35 ± 1.99 (12.31–12.38) (n = 12,989)	12.83 ± 2.18 (12.54–13.12) (n = 222)	< .001	.029
General factor of motor development	-0.3 ± 0.98 (-3.33–8.62) (n = 9558)	0.42 ± 0.89 (-1.53–2.19) (n = 38)	0.005	.379

Note: Adjustment was made for gestational age, birthweight, and birth length.

are also the largest triplet sample in the world to provide ages of gross motor milestone achievements of triplets.

The present study showed that the age of milestone achievements were significantly higher in triplets for each outcome compared to singletons. Moreover, the differences were significant for maintaining head, sitting alone and standing holding on after adjusting gestational age, birthweight, and birth length. In addition, our study identified different tendencies among those with a birthweight of 2 kg or greater and those with a birthweight of less than 2 kg. The results in those with a birthweight of 2 kg or greater indicated that the ages of milestone achievements were significantly higher in triplets for each outcome compared to singletons, except walking holding on. Further, the differences were significant for sitting alone and walking independently after adjusting for gestational age, birthweight, and birth length. These results suggest that being a triplet with a birthweight of 2 kg or greater is an independent risk factor for the delay of gross motor milestones.

Studies on twins with a birthweight of 2.5 kg or greater indicated that twinning was an independent risk factor for the delay of gross motor milestones in early life (Goetghebuer et al., 2003; Yokoyama et al., 2007). A Finnish longitudinal follow-up study reported that twins attained motor development facilitating walking independently later than singletons (Moilanen & Rantakallio,

TABLE 6

Age of Milestone Achievement in Triplets and Singletons of Birthweight < 2 kg

	Singletons (N = 130) Mean (95%CI)	Triples (N = 858) Mean (95%CI)	p value	Adjusted p value
Maintain head	4.40 ± 1.11 (4.20–4.61) (n = 113)	4.31 ± 1.16 (4.22–4.40) (n = 625)	.426	.077
Roll over	6.45 ± 1.54 (6.12–6.78) (n = 86)	6.51 ± 1.41 (6.40–6.62) (n = 601)	.705	.889
Sit (alone)	7.99 ± 1.54 (7.70–8.28) (n = 111)	8.14 ± 1.59 (8.01–8.27) (n = 568)	.359	.689
Crawl	9.34 ± 1.67 (8.98–9.69) (n = 88)	9.00 ± 1.52 (8.88–9.12) (n = 593)	.057	.009
Stand holding on	10.21 ± 1.83 (9.82–10.59) (n = 90)	10.23 ± 2.02 (10.09–10.39) (n = 624)	.925	.669
Walk holding on	11.52 ± 1.94 (11.11–11.92) (n = 90)	11.00 ± 1.70 (10.76–11.24) (n = 192)	.024	.015
Walk independently	14.48 ± 2.50 (14.01–14.94) (n = 113)	14.05 ± 2.58 (13.86–14.24) (n = 705)	.102	.028
General factor of motor development	1.49 ± 1.30 (-0.86–5.28) (n = 76)	1.25 ± 1.09 (-1.75–5.07) (n = 135)	.040	.148

Note: Adjustment was made for gestational age.

1989). These reports of twins were consistent with the results of triplets in the present study.

Moreover, Feldman and Eidelman (2005) compared the cognitive development of triplets with twins and singletons matched for gestational age and fetal growth parameters and demonstrated that the triplet's situation itself constitutes a separate risk condition for cognitive development independent of the effects of other known medical risks to infant development. Our results were correspondent to this study. In general, our findings emphasize the professional attention that must be paid to the development of triplets.

Meanwhile, results for those with a birthweight of less than 2 kg showed different tendency from those with a birthweight of 2 kg or greater. After adjusting for gestational age, singletons attained motor development facilitating crawling, walking holding on, and walking independently slower than triplets with a birthweight of less than 2 kg. Our population-based study on comparison of motor development between twins and singletons (Yokoyama et al., 2007) identified that after adjusting for gestational age, singletons with a birthweight of less than 2.5 kg attained motor development facilitating walking independently slower than twins with a birthweight of less than 2.5 kg. This study of twins was consistent with the present results for triplets. There is a likelihood that singletons with a birthweight of less than 2 kg might be

disadvantaged in their developmental status, especially concerning crawling and walking in early life, compared to multiple births. However, a birthweight of less than 2 kg was much rare in singletons than in triplets.

We also observed that all motor milestones were attained at slower age by triplets with a birthweight of less than 2 kg compared to twins with a birthweight of less than 2.5 kg, whereas there were no differences in development between triplets with a birthweight of greater than 2 kg and twins with a birthweights of greater than 2.5 kg (Yokoyama et al., 2007). Most notable, the mean age of attaining an ability to walk independently was 14.05 months and 12.98 months in Japanese triplets and Japanese twins, respectively, with differences being almost one month.

The delay observed in triplets could be due to prenatal factors that do not affect gestational age, birthweight, and length, such as a reduced space in the uterus or limitation of uterine capacity including nutrition. Although the uterus has a remarkable ability to expand and adapt (Dwight et al., 1993; Steingrimsdottir et al., 1995; Yokoyama, 2002), the potential to increase its volume and nutritional capacity is limited. In most cases of triplets, the total triplet birthweights exceed 6 kg. Malinowska et al. (1998) showed that the shortening of twin pregnancy duration was caused by the total fetal body mass attaining 5.5 kg, and this point may indicate the main limitation of uterine capacity. In the meanwhile, triplet births represent a greater child care burden to the parents (Yokoyama et al., 2004; Yokoyama & Ooki, 2004), which may result in less stimulation of the infants, and therefore less opportunity for gross and fine motor experiences in early life. The reason for the delay observed in triplets should be investigated in the future.

Data on weight at one year of age, feeding methods, discordant triplets and maternal behavior were lacking in this study, and it has been suggested that these factors are associated with developmental status (Angelsen et al., 2001; Feldman and Eidelman, 2009; Goetghebuer et al., 2003; Ostfeld, 2000). These factors will be investigated in the future.

In conclusion, triplets with a birthweight of 2 kg or greater were an independent risk factor for the delay of gross motor milestones. Meanwhile, after adjusting for gestational age, singletons with a birthweight of less than 2 kg attained motor development facilitating crawling, walking holding on, and walking independently slower than triplets with a birthweight of less than 2 kg. There is a likelihood that singletons with a birthweight of less than 2 kg might be disadvantaged in their developmental status compared to multiple births. Thus, there is a need to consider both multiple birth status and birthweight when evaluating the development of infants and small children.

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