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Research article

Reference birthweight range for multiple birth neonates in Japan

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Abstract

Background: A reference range for the birthweight of multiple births neonates is necessary for the assessment for intrauterine growth.

Methods: Pairs of multiple births were identified by birthplace, the ages of the parents, gestational age, and the year and month of birth. We studied a total of 32,232 livebirth-livebirth pairs of twins, 1894 triplet live births, and 206 quadruplet live births.

Results: The median birthweight of males, taking gestational age into account, was ca. 0.05 kg–0.1 kg heavier than that of females. Compared to singleton neonates, the median birthweight of twins was ca. 0.15 kg smaller at the gestational age of 34 weeks, increasing to ca. 0.5 kg at 42 weeks of gestation. As for birth order, the mean birthweight of the first-born twin was heavier than that of the second-born. The standard deviation of birthweight was larger for second-born twins. The birthweight of twins from multiparous mothers was greater than those from primiparous mothers. The median birthweight according to gestational age was found to be the greatest in twins, lower in triplets and the lowest in quadruplets. In triplets, the 50th percentile was 0.08 kg heavier in boys than for girls.

Conclusion: Our results can be used for assessment of birthweight of multiple births in Japan.

Background

Since the introduction of assisted reproductive technology, the rate of multiple births has been increasing rapidly in Japan [1]. A reference range for the birthweight of multiple births neonates is necessary for the assessment for intrauterine growth. Studies on the birthweight of twins have been conducted in many countries [2-5], and some of these studies have used hospital birth records [6].

The aim of this research is to present a methdologic approach to constructing birthweight reference ranges for multiples based on Japanese birth certificates, and also to clarify how the population-based data are useful for creation of birthweight reference for multiple births. Results of the research would be helpful to perinatologists for evaluating intrauterine growth of multiples, and for evaluating twin percentile rank at birth.

Methods

In Japan, birth, death, and stillbirth certificates are currently stored in data files on magnetic tapes. These certificates are filed in the city health department and changed into computerized files in Ministry of Health, Labour and Welfare of Japan. This database contains sex, birthweight, gestational age, parity, ages of father and mother. The database is limited because twins are not linked to each other and information about mode of conception ie. spontaneous or iatrogenic is not available from database.

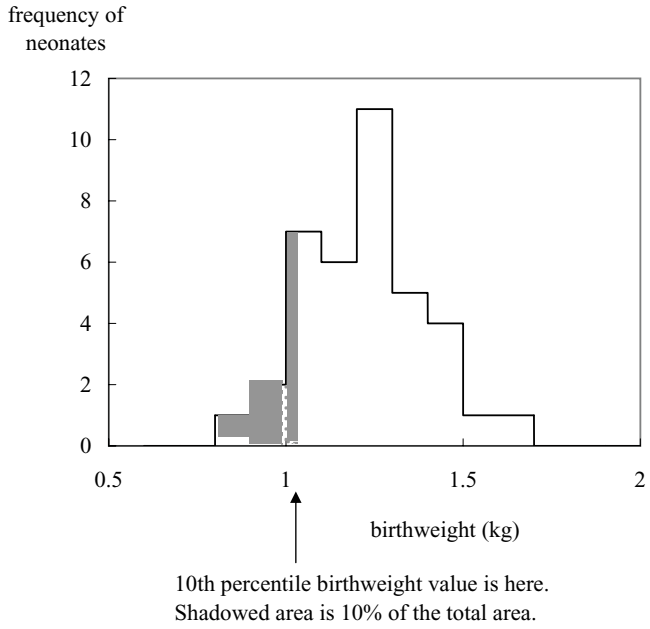

Figure 1
Calculation of 10th birthweight percentile value from histogram of birthweight from male triplets with gestation of 29 weeks

From these tapes, we identified 66,005 twins, 1,894 triplets and 206 quadruplets who were born in Japan between 1988 and 1991. Because mean birthweight of Japanese neonates is declining year by year [7], comparison of birthweight between multiple births and singletons[8] should be done between the birth of the same period, which is around the year 1990.

Unlikely combinations of birthweight and gestational age were defined within each stratum of multiplicity, gender and gestational age as recorded with birthweight more than 3SD from the mean.

Because the database was limited and twins were not linked to each other, these twins were arranged into pairs in order to determine twin pairs are like-sexed or unlike-sexed. Both pairs were born in the same municipality, within 10 days of each other to parents of the same age. By this method, 32,232 livebirth-livebirth pairs of twins were selected for analysis in this study. According to Weinberg's formula [9], the estimated values of monozygotic and dyzygotic pairs were 18,830 and 13,402 respectively.

To calculate the mean birthweight and the standard deviation, 50 grams were added to the recorded birth weight because birth weight is recorded every 100 grams, which does not exceed actual birthweight value. To calculate the mean gestational age and the standard deviation, 3.5 days were added to the recorded gestational age because gestational age is recorded at full weeks which do no exceed actual gestational age.

Significance of differences in mean values of gestational age and birthweight was statistically analyzed using student t-test for 2 groups and ANOVA for 3 groups and more. Significance of differences in median values was not statistically tested.

Figure 1 illustrates the 10th birthweight percentile value calculated from a histogram of birthweights from 38 cases of male triplets with gestation of 29 weeks. The number of the cases was smaller than that of twins in each gestational week. Shadowed area corresponds to lower 10% of relative cumulative frequency. The right side of the shadowed area corresponds to 10th percentile value of male triplets with gestation of 29 weeks. 50th and 90th percentile birthweight values were determined in the same way. The number of subjects used to calculate these values is shown on Table 1. Gestational age of 42 weeks is certainly too long for twins, but they are not supposed to be caused by errors in filing data but are considered to be clinically rare cases.

The percentiles obtained for twins were smoothed using the cubic spline function [10], while those of triplets and quadruplets were smoothed using quadratic or cubic polynomial functions with the smaller sum of the square residuals.

Results

The mean gestational age and birthweight were analyzed according to gender, birth order, parity, and gender combination within the pair (Table 2). Female, multiparous, and unlike-sexed pairs were found to exhibit the longer gestational age. Male, multiparous, 1st born and unlike-sexed pairs were found to have heavier birthweights. Differences by parity were twice as large as sex difference. Males of unlike-sexed pairs exhibited the heaviest birthweight, followed by males of unlike-sexed pairs, females of unlike-sexed pairs, females of like-sexed pairs. Differences of mean values between/among groups stated above were all statistically significant.

Birthweight according to the gestational age of twins as calculated in our study are shown in Figures 2 and 3. Males were heavier than females, and average difference through overall gestational ages was 70 grams for primipara and 90 grams for multipara (Table 3).

Median birthweight curves of multiple births were compared with that of singletons as reported by Ogawa [8]. At

Table 1: Number of subjects analyzed from each gestational week

gestational age (weeks)	Twins		triplets		quadruplets	
	male	female	male	female	male	female
24	76	64	14	14	3	1
25	121	111	11	7	5	6
26	105	116	7	11		
27	176	145	14	25	3	7
28	208	196	26	35	13	11
29	211	204	38	40	17	11
30	309	287	33	27	15	12
31	427	325	51	52	13	15
32	673	549	59	54	10	8
33	906	844	109	108	10	7
34	1366	1356	115	123	12	11
35	2306	2122	141	131	3	5
36	4257	4132	143	154	2	2
37	7276	7128	89	96		
38	6963	7343	41	66		
39	4358	4632	16	21		
40	1924	2135		1		
41	456	470				
42	39	39				

Table 2: gestational age and birthweight of twins according to variables

gestational age	no. of cases	mean (weeks)	standard deviation (weeks)	significance of difference
total	64464	37.2	2.7	
male	32211	37.2	2.6	***
female	32253	37.3	2.6	
primipara	29106	37.1	2.8	***
multipara	35358	37.3	2.6	
like-sexed male	25510	37.1	2.7	***
like-sexed female	25552	37.3	2.7	
unlike-sexed	13402	37.4	2.6	
birthweight	no. of cases	mean (kg)	standard deviation (kg)	
total	64447	2.39	0.51	
male	32202	2.43	0.51	***
female	32245	2.36	0.50	
primipara	29098	2.31	0.50	***
multipara	35349	2.46	0.50	
1st twins	32156	2.42	0.50	***
2nd twins	32153	2.36	0.51	
like-sexed male	25501	2.41	0.52	***
like-sexed female	25545	2.35	0.50	
unlike-sexed male	6701	2.49	0.50	
unlike-sexed female	6700	2.39	0.48	

*** $p < 0.001$

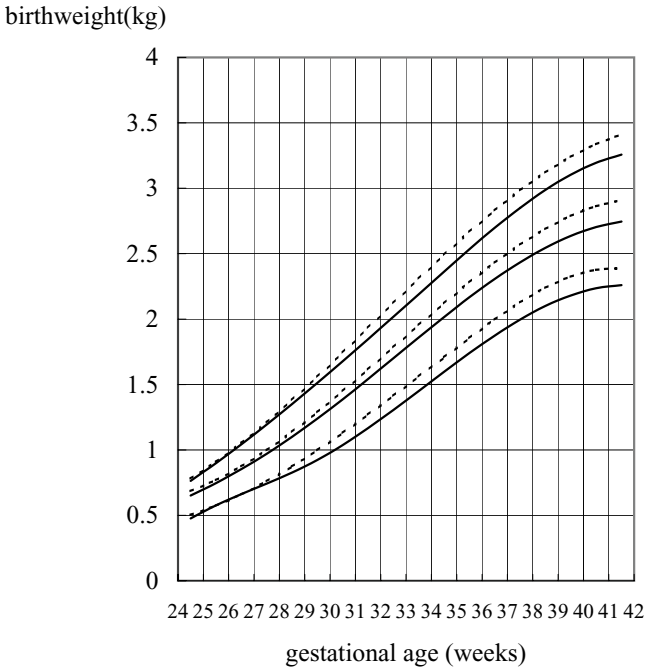

Figure 2
Birthweight percentile curves of twins (male) dotted lines: multipara solid lines: primipara The 3 lines of each category correspond to the 10th, 50th and 90th percentiles

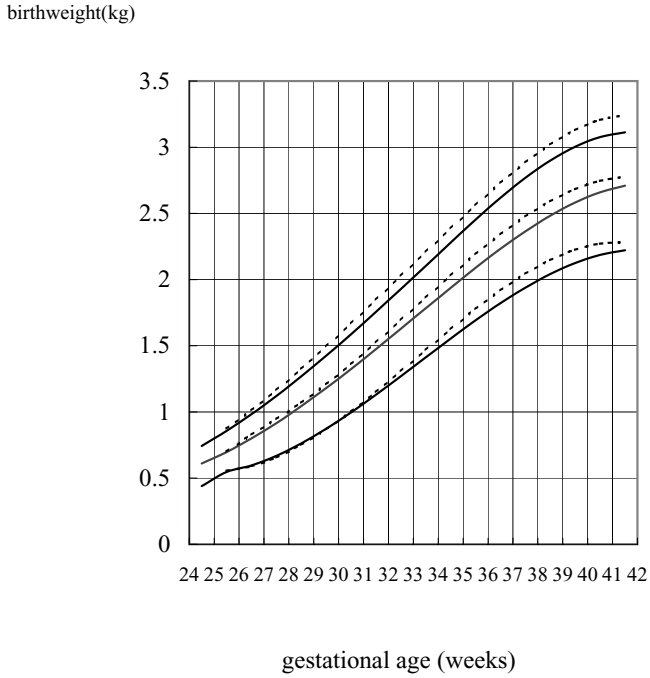

Figure 3
Birthweight percentile curves of twins (female) dotted lines: multipara solid lines: primipara The 3 lines of each category correspond to the 10th, 50th and 90th percentiles

gestational ages of less than 34 weeks, the mean birthweight of twins was 150 grams lighter than that of singletons. This difference increased to 500 grams at 40 weeks of gestation.

In multiple birth neonates, the median birthweight according to gestational age was found to be the greatest in twins, followed by triplets and quadruplets (Figures 4 and 5).

In triplets, the 50th percentile of birthweight was 0.08 kg heavier in boys than in girls (Figure 6, Table 4). In quadruplets, only a small difference was observed between boys and girls, except for 27 weeks of gestation (Figure 7 and Table 4). For triplets and quadruplets, sample size was too small for calculation of birthweight percentile values by parity and also by gestational age less than 27 weeks.

Discussion

Population-based data are used in the analysis in many countries. Reference birthweight is calculated from population-based data in Canada [2]. Data were obtained from vital statistics of health department birth registrations. Birth weight percentile values were calculated with each stratum of multiplicity, gender, and gestational age. The population-based reference birthweight was also created in Norway[4] from Medical Birth Registry. Percentile value for each gestational week was smoothed assuming a normal distribution. These studies clarified that population-based data are useful for production of reference birthweight.

We found that the birthweight of twins born after 34 weeks of gestation was greater than that calculated by Fukuda [6]. This discrepancy is thought to be because Fukuda obtained data from a hospital specializing in high risk pregnancy, which are not suitable for creating reference which IUGR of multiple birth is diagnosed. Population-based data is with large sample size and with less bias as high risk pregnancy, while quality of data such as gestational age is higher in hospital-based data.

Gestational age is thought to be influenced by gender, placentation, zygosity and parity. Preterm delivery of boys is thought to be related to the production of androgenic hormones, which disturbs the endocrine balance that controls the initiation of labor[12]. According to Bleker [11], dichorial twins exhibited a longer gestational age

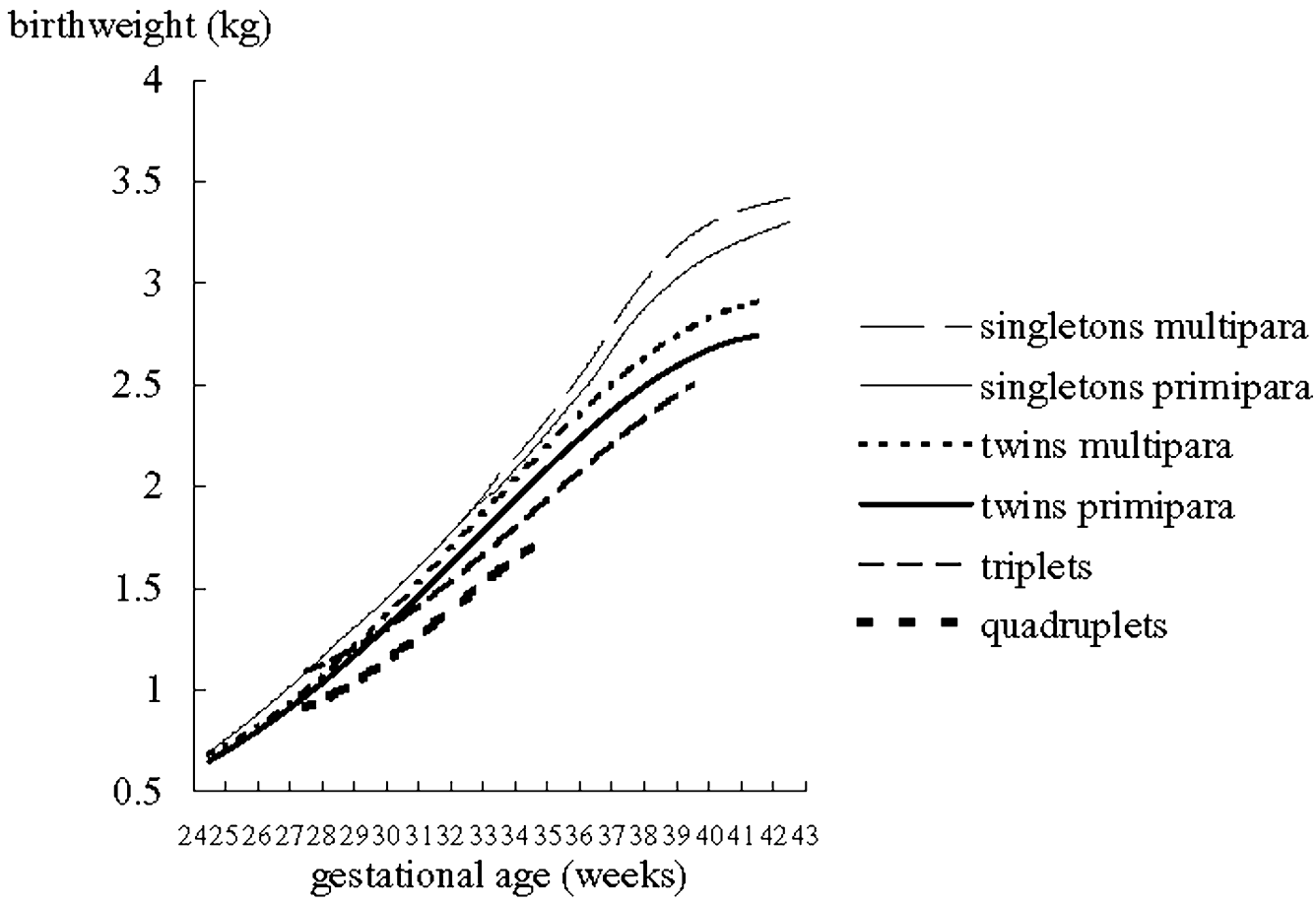

Figure 4
Median birthweight of neonates of multiple births (male)

than monochorial twins, and multiparous twins exhibited longer gestational ages than primiparous twins.

MacGillivray [12] found that the gestational age of MZ is shorter than that of DZ, and that the gestational ages of males is shorter than that of females. These results are consistent with those of our study. With zygosity, preterm delivery of MZ often accompanies preterm membrane rupture due to either acute hydroamnios or weakness in the membranes [12]. More than half of MZ twins are with monochorionic membranes and monochorionic membranes are weak because they are shared by both twins, thus shortening the gestational ages of MZ twins [12].

Our study shows that gestational age of like-sexed twins is shorter than that of unlike-sexed, and that of males is shorter than females. In our data, unlike-sexed twins are all DZ, and 73.7% of like-sexed twins are MZ calculated from Weinberg's formula [9]. Average gestational age of like-sexed twins is more similar to MZ in our study than to DZ.

With parity, the amount of distention tolerated by the uterus at a given time during pregnancy is greater in multiparae than in primiparae whose gestational ages are shorter [11].

Median birthweight values of Japanese twins were compared with those of singletons derived from database in which birthweights were rounded to 10 g.

According to the report by Karn [13], twins exhibited greater weight deficit than singletons after 30 weeks gestation. According to the report in Naeye [14], after 33 weeks gestation, the mean weight of twins is markedly less than that of singletons. Blecker et al [11] reported that the difference in weight between twins and singletons at 39 to 40 weeks is about 600 grams.

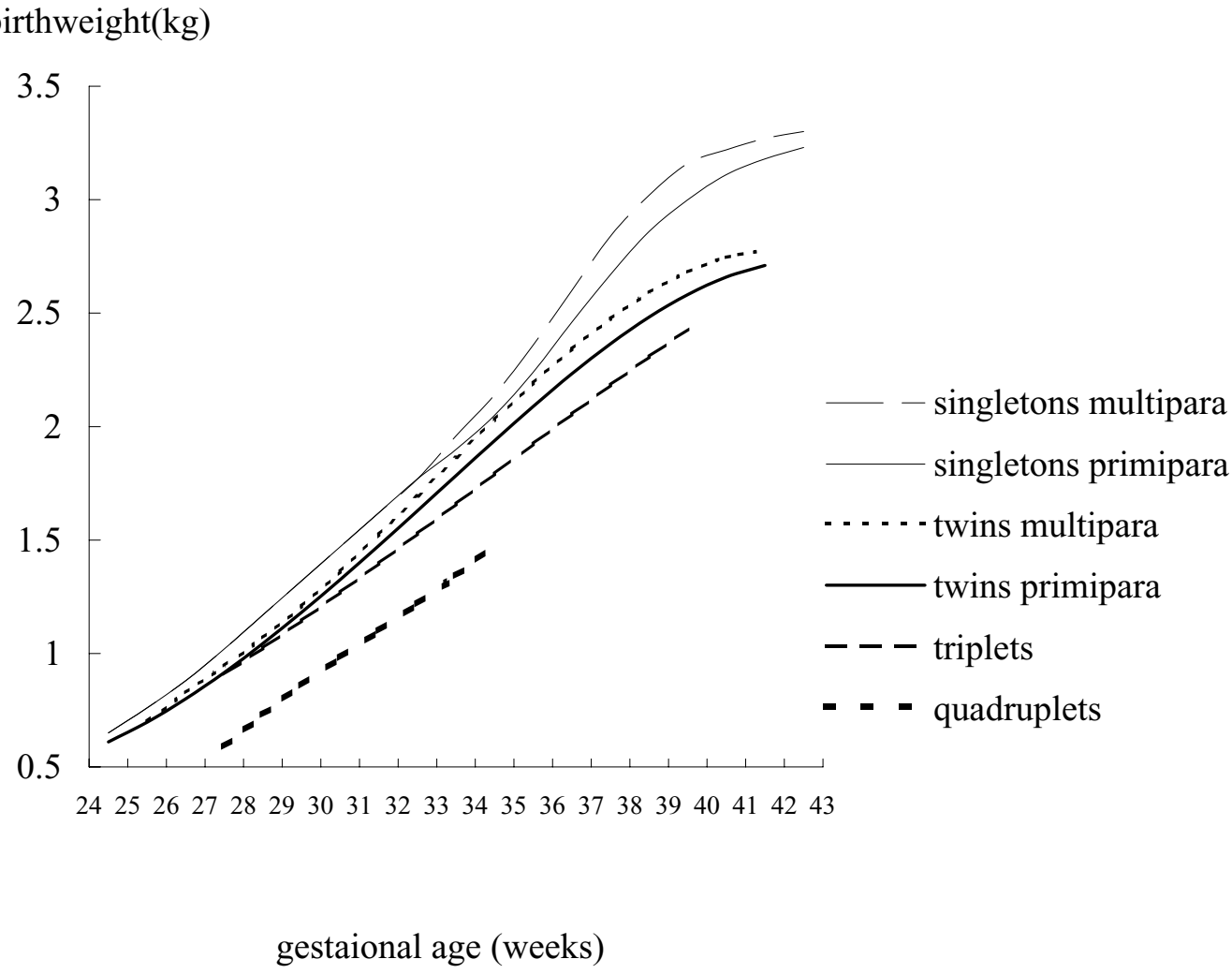

Figure 5
Median birthweight of neonates of multiple births (female)

The median birthweight curves of the subjects in this study, which are similar to those of McKewn et al [15], suggest that growth limitation within the uterus becomes more marked with increasing numbers of fetuses. Besides, median birthweight curves created by McKewn et al are not population-based and do not contain iatrogenic multiples.

According to the report by Naeye et al [14], the mean birthweight of males is approximately 80 grams heavier than that of that of females at 24–26 weeks of gestation, increasing to 150 heavier at 40 weeks of gestational age. The difference of birthweight between males and females was found to differ less in twins than in singletons [11]. Our study found that this sex difference was almost the same within twins and singletons (Figures 2 and 3).

The birthweight of twins differs according to sex composition. Unlike-sexed twins were found to be 63 g to 141 g heavier than like-sexed twins [13,16,17].

The influence of sex on birthweight is less significant than the influence of sex combination, as reported by Corney et al [17]. Corney et al also found that monochorial twins are lighter than dichorial twins [17], and that monochorial twins use their placenta less effectively. The low birthweight of MZ is attributed to the placenta itself [18].

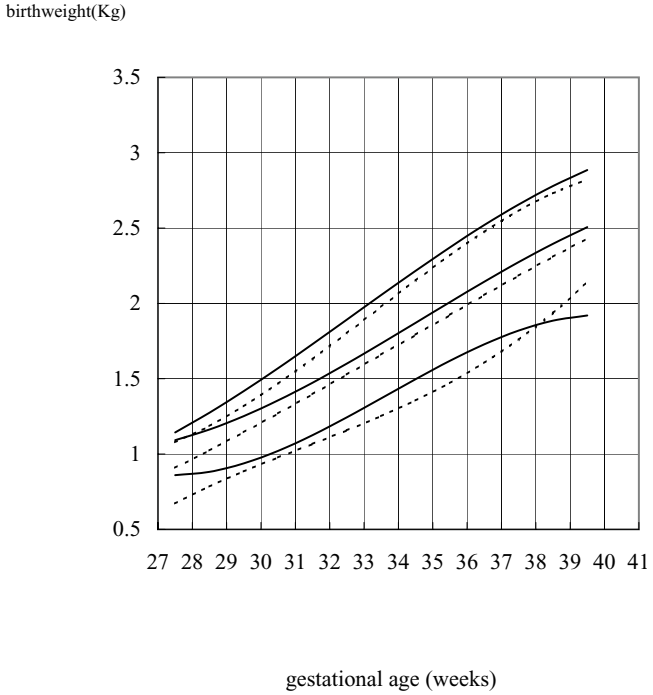

Figure 6
Birthweight percentile curves of triplets dotted lines: multipara solid lines: primipara The 3 lines of each category correspond to the 10th, 50th and 90th percentiles

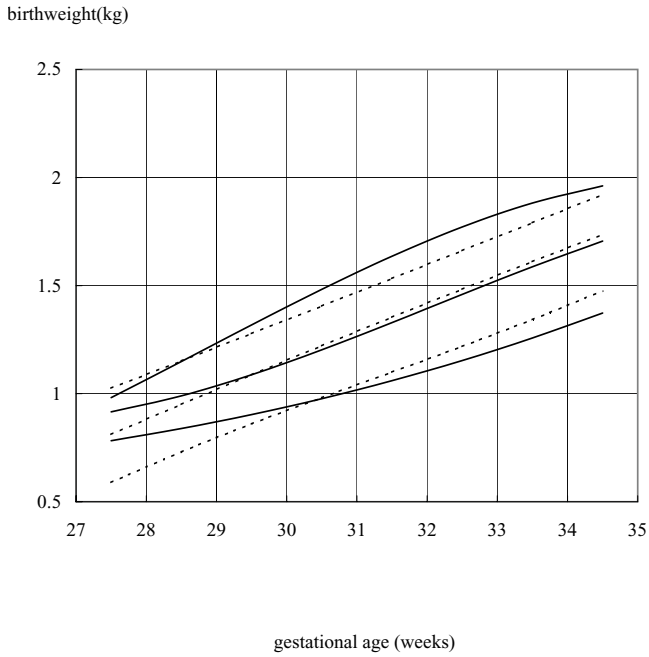

Figure 7
Birthweight percentile curves of quadruplets dotted lines: multipara solid lines: primipara The 3 lines of each category correspond to the 10th, 50th and 90th percentiles

Bleker [11] reported that the influence of parity to birthweight is grater than that of gender. They found that multiparous neonates were heavier at birth because of increased ability of the uterus to distend that subsequently permits more intrauterine growth. According to the report by Asaka [19], the mean birthweight of first-born twins is 52 g larger than that of second-born twins, a result consistent with our findings.

According to the concept of "total fetal mass", in which all the fetuses are included, it is actually greater in twins and higher order multiples. In this point of view, Multiples as total fetal mass are actually growth promoted. Smaller size is considered to reflect fetal adaptation to the inability of the uterus to nurture the larger fetal mass [20].

The fetus is affected by the limitation of uterine expansion in the later gestational weeks, but any growth retardation is recovered after birth [21]. Intrauterine growth standards are referred to in the assessment of birthweight according to gestational age. If birthweight reference for singletons are used for the assessment of intrauterine growth of multiple births, considerable part of them are misclassified as IUGR even if they are with adequate intrauterine growth as multiples. This report showed a birthweight reference range for exclusive use in the assessment of multiple births. This study considers only live-born twins. Analysis of the birthweight of twins who die in utero is in progress.

Conclusions

Birthweight reference curves for multiple births can be developed using population-based data better than using other kind of data sources. Results of the present study can be used for assessment of multiple births whether they are really growth retarded or with appropriate intrauterine growth as mutiples. These results are helpful to clinicians to provide adequate care for the multiples.

Competing interests

None declared.

Author's contributions

NK conceived of the study, provided study design, conducted analysis and prepared the manuscripts.

Table 3: Birthweight percentiles of twins (kg)

gestational age (week)	male						female					
	primipara			multipara			primipara			multipara		
	10th	50th	90th	10th	50th	90th	10th	50th	90th	10th	50th	90th
24	0.476	0.651	0.763	0.504	0.686	0.782	0.440	0.610	0.743			
25	0.576	0.746	0.899	0.574	0.770	0.909	0.547	0.697	0.857	0.556	0.701	0.874
26	0.662	0.853	1.043	0.660	0.875	1.053	0.596	0.800	0.983	0.590	0.828	1.013
27	0.743	0.971	1.194	0.761	0.999	1.212	0.669	0.916	1.121	0.656	0.946	1.165
28	0.827	1.100	1.350	0.874	1.138	1.382	0.762	1.044	1.269	0.751	1.070	1.326
29	0.923	1.239	1.512	0.999	1.289	1.560	0.873	1.181	1.425	0.868	1.209	1.495
30	1.037	1.387	1.678	1.131	1.450	1.745	0.997	1.325	1.588	1.003	1.362	1.669
31	1.166	1.542	1.846	1.271	1.616	1.934	1.130	1.475	1.756	1.151	1.525	1.848
32	1.305	1.701	2.018	1.415	1.786	2.123	1.270	1.629	1.929	1.308	1.694	2.028
33	1.450	1.860	2.190	1.562	1.955	2.310	1.413	1.784	2.104	1.468	1.864	2.209
34	1.597	2.016	2.363	1.709	2.121	2.492	1.555	1.938	2.280	1.626	2.031	2.387
35	1.740	2.167	2.534	1.855	2.281	2.667	1.692	2.089	2.453	1.778	2.192	2.562
36	1.874	2.307	2.698	1.997	2.432	2.832	1.822	2.233	2.618	1.919	2.342	2.730
37	1.996	2.434	2.850	2.127	2.569	2.985	1.939	2.365	2.769	2.044	2.476	2.885
38	2.100	2.545	2.987	2.239	2.689	3.121	2.042	2.483	2.899	2.147	2.591	3.020
39	2.180	2.636	3.103	2.324	2.788	3.240	2.125	2.582	3.004	2.225	2.682	3.129
40	2.236	2.704	3.195	2.377	2.863	3.337	2.187	2.659	3.077	2.271	2.746	3.206
41	2.260	2.745	3.257	2.389	2.909	3.411	2.222	2.710	3.113	2.282	2.777	3.243

Table 4: Birthweight percentiles of supertwins (kg)

gestational age (weeks)	triplets						quadruplets					
	male			female			male			female		
	10th	50th	90th	10th	50th	90th	10th	50th	90th	10th	50th	90th
27	0.860	1.092	1.143	0.672	0.909	1.079	0.782	0.916	0.982	0.589	0.812	1.025
28	0.882	1.163	1.274	0.784	1.024	1.186	0.839	0.990	1.149	0.730	0.950	1.151
29	0.938	1.252	1.418	0.884	1.145	1.317	0.903	1.088	1.318	0.860	1.087	1.278
30	1.021	1.357	1.571	0.977	1.270	1.467	0.977	1.203	1.483	0.981	1.221	1.405
31	1.125	1.474	1.730	1.067	1.398	1.630	1.060	1.329	1.636	1.100	1.353	1.533
32	1.244	1.601	1.892	1.157	1.528	1.802	1.153	1.459	1.771	1.219	1.483	1.662
33	1.370	1.734	2.056	1.252	1.660	1.977	1.258	1.587	1.882	1.342	1.611	1.791
34	1.497	1.871	2.216	1.355	1.792	2.151	1.373	1.706	1.961	1.475	1.736	1.921
35	1.619	2.008	2.372	1.471	1.924	2.318						
36	1.729	2.144	2.520	1.604	2.055	2.474						
37	1.820	2.274	2.656	1.758	2.183	2.613						
38	1.886	2.396	2.779	1.937	2.309	2.730						
39	1.920	2.506	2.885	2.144	2.430	2.821						

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