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Infant Mortality of Zygotic Twins and Influencing Factors in Japan, 1995 – 2008

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Abstract

Objective: We aimed to determine the infant mortality rates (IMRs) for monozygotic (MZ) and dizygotic (DZ) twins along with risk factors associated with these IMRs.

Study design: IMRs of zygotic twins were estimated using vital statistics from Japan between 1995 and 2008.

Results: In 1995, IMRs were 21.7 for MZ twins and 15.6 for DZ twins per 1000 deliveries, and they significantly decreased to 9.8 and 5.8, respectively, in 2008. During the study period, IMRs were the lowest at maternal ages (MAs) of 35–39 years for MZ (14.4) twins and 30–34 years for DZ twins (8.2). The highest IMRs were for MZ (23.6) and DZ (24.9) twins at MAs of <20 years. At MAs of 20–24 and 35–39 years, IMRs were significantly higher for MZ than DZ twins. IMRs were also the lowest at gestational ages (GAs) of 37 weeks for MZ (3.0) twins and 39 weeks for DZ twins (1.9). At GAs of <29 weeks and 33–34 weeks, IMRs were significantly higher for MZ than DZ twins.

Conclusion: IMR was significantly higher for MZ than DZ twins, although these rates significantly decreased each year. For both MZ and DZ twins, mortality risk factors were MAs of <20 years and GAs of up to 35 weeks.

Keywords: Infant mortality rate; Twins; Zygosity; Maternal age; Gestational age; Vital statistics

Introduction

Although stillbirth and perinatal mortality rates for twins have been reported by many authors, infant mortality data are scarce, particularly for zygotic twins. Infant mortality rates (IMRs) for twins have decreased in Japan since 1974 [1-3]. Recognized risk factors for twin mortality include the sex and birth order of twins [1-4], zygosity [1,4], maternal age (MA) [1,3,4], gestational age (GA), birth weight (BW) [1,3,4], race [5-7], mother's health condition, and monthly household expenditure [8].

The present study estimated IMRs for monozygotic (MZ) and dizygotic (DZ) twins in Japan between 1995 and 2008 and identified risk factors associated with these IMRs.

Materials and Methods

Data sources

Data on twin live births (LBs) between 1995 and 2008 were obtained from national statistical records. The Statistics and Information Department, Ministry of Health, Labour and Welfare (Tokyo, Japan) maintains records covering the entire Japanese population. LB certificates include details about the nationality, sex, birth date, address, GA, BW, parental birth dates and ages, single or multiple births, and birth order in multiple births. Infant death (D) certificates contain the same information as LB certificates (excluding paternal age) as well as the date and cause of death.

Describing twin data

Infant death data were obtained for twin pairs with both LBs (Ds), one LB (D), and one LB (D)–one fetal death (FD). We estimated the number of MZ and DZ twins using the Weinberg method [9]. MA and GA were not always the same for twin pairs because each twin could be born on a different date; therefore, in some cases, the number of like- or unlike-sexed twin pairs included odd numbers of twins.

To calculate IMRs for MZ and DZ twins, denominators (total live twin pairs at birth: both LBs at birth and one LB–one FD) were obtained from (Tables 1-3) of the study by Imaizumi and Hayakawa [10]. For the purpose of our study, LB twin pairs [both LBs plus (one LB–one FD)/2] were used as the denominator. The numerators used were twin pairs of both LBs–Ds plus [one LB (S)–one LB (D)]/2 plus [one LB (D)–one FD]/2. IMRs for MZ and DZ twins are presented as 1000 twin pairs of infant deaths divided by LB twin pairs.

Results

Annual changes in IMRs for zygotic twins

Table 1 and Figure 1 show the annual changes in IMRs for MZ and DZ twins between 1995 and 2008. IMRs for both MZ and DZ twins decreased year by year. The linear regression coefficients of IMRs for MZ and DZ twins on the year were –0.82 and –0.49, respectively. These values are significant at the 0.1% level. By 2008, IMRs had declined to approximately 1/2 of the 1995 value for MZ twins and 1/3 for DZ twins.

In every year except 2007, the IMR was higher in MZ than DZ twins, and was significant at the 5% level.

IMRs in zygotic twins by MA

Table 2 shows IMRs for zygotic twins by MA during the study period. IMRs were the lowest at MAs of 35–39 years for MZ twins and

Year	Both LB (D)	One LB (S) , one LB (D)	One LB (D), One FD	Twin pairs of Ds	Both LB	One LB, one FD	Twin pairs of LBs	IMR	Odds ratio [95% CI] MZ vs. DZ twins
Monozygotic twins									
1995	38.0	105.0	29.0	105.0	4749	165	4831.5	21.7	1.41* [1.04-1.89]
1996	39.0	102.0	24.0	102.0	4869	179	4958.5	20.6	1.97* [1.42-2.73]
1997	31.0	94.0	22.0	89.0	4885	157	4963.5	17.9	1.67* [1.20-2.34]
1998	31.0	86.0	26.0	87.0	4793	147	4866.5	17.9	1.54* [1.11-2.12]
1999	30.0	99.0	31.0	95.0	4723	136	4791.0	19.8	2.25* [1.61-3.16]
2000	32.0	112.0	10.0	93.0	4683	100	4733.0	19.6	1.86* [1.36-2.55]
2001	15.0	83.0	13.0	63.0	4536	98	4585.0	13.7	1.53* [1.07-2.19]
2002	26.0	79.0	18.0	74.5	4630	130	4695.0	15.9	1.78* [1.27-2.49]
2003	13.0	102.0	20.0	74.0	4550	121	4610.5	16.1	1.67* [1.20-2.32]
2004	22.0	77.0	18.0	69.5	4359	93	4405.5	15.8	1.97* [1.40-2.79]
2005	21.0	75.0	13.0	65.0	4374	92	4420.0	14.7	2.00* [1.39-2.87]
2006	18.0	56.0	7.0	49.5	4267	100	4317.0	11.5	1.64* [1.11-2.43]
2007	14.0	58.0	7.0	46.5	4395	103	4446.5	10.5	1.26 [0.86-1.86]
2008	13.0	54.0	6.0	43.0	4322	89	4366.5	9.8	1.70* [1.10-2.68]
Dizygotic twins									
1995	28.0	88.0	8.0	76.0	4832	102	4883	15.6	
1996	8.0	88.0	8.0	56.0	5266	62	5297	10.6	
1997	8.0	98.0	2.0	58.0	5338	74	5375	10.8	
1998	20.0	88.0	4.0	66.0	5602	74	5639	11.7	
1999	12.0	76.0	6.0	53.0	5914	88	5958	8.9	
2000	14.0	102.0	10.0	70.0	6528	102	6579	10.6	
2001	22.0	70.0	4.0	59.0	6518	82	6559	9.0	
2002	12.0	96.0	8.0	64.0	7080	80	7120	9.0	
2003	28.0	84.0	2.0	71.0	7306	80	7346	9.7	
2004	10.0	98.0	6.0	62.0	7650	98	7699	8.1	
2005	8.0	90.0	2.0	54.0	7240	72	7276	7.4	
2006	10.0	84.0	2.0	53.0	7528	78	7567	7.0	
2007	20.0	80.0	0	60.0	7196	66	7229	8.3	
2008	8.0	56.0	4.0	38.0	6492	62	6523	5.8	

Linear regression coefficient (p-value) of IMR on the year; MZ twins -0.82(<0.001); DZ twins -0.49 (<0.001)
LB: Live birth; (D): Infant death; (S): Survived; FD: Fetal death (12 weeks of gestation and over);
IMR: Infant mortality rate per 1000 twin pairs of LBs; CI: Confidence interval

Table 1: Infant mortality rate in zygotic twins, 1995-2008.

Maternal age	Both LB (D)	One LB (S), one LB (D)	One LB (D), one FD	Pairs of Ds	Both LB	One LB, one FD	Pairs of LBs	IMR	Odds ratio [95% CI]	Odds ratio [95% CI]: MZ vs. DZ twins
Monozygotic twins										
<20	8	22	6	22.0	920.0	22.0	931.0	23.6	1.66* [1.05-2.63]	0.95 [0.43-2.08]
20-24	62	202	35	180.5	8276.0	219.5	8385.8	21.5	1.51* [1.19-1.90]	2.38* [1.73-3.28]
25-29	128	432	83	385.5	23161.0	633.5	23477.8	16.4	1.14 [0.93-1.41]	1.64* [1.40-1.92]
30-34	103	373	83	331.0	22590.5	591.5	22886.3	14.5	1.01 [0.81-1.24]	1.79* [1.53-2.08]
35-39	38	129	32	118.5	8129.5	206.5	8232.8	14.4	1.00: Reference	1.47* [1.16-1.85]
≥40	4	22	4	17.0	1058.0	37.0	1076.5	15.8	1.10 [0.66-1.83]	1.71 [0.88-3.30]
Dizygotic twins										
<20	4	10	0	9.0	359.0	4.0	361.0	24.9	3.11* [1.61-6.14]	
20-24	16	64	0	48.0	5210.0	62.0	5241.0	9.2	1.12 [0.83-1.53]	
25-29	76	348	22	261.0	25667.0	317.0	25825.5	10.1	1.24* [1.05-1.46]	
30-34	76	456	30	319.0	38905.0	445.0	39127.5	8.2	1.00: Reference	
35-39	32	288	12	182.0	18324.0	260.0	18454.0	9.9	1.21* [1.01-1.45]	
≥40	4	28	2	19.0	2025.0	32.0	2041.0	9.3	1.14 [0.72-1.82]	

LB: Live birth; (D): Infant death; (S): Survived; FD: Fetal death (12 weeks of gestation and over); IMR: Infant mortality rate per 1000 twins pairs of LBs; CI: Confidence interval

Table 2: Infant mortality rate in zygotic twins by maternal age, 1995-2008.

Gestational age	Both LB (D)	One LB (S), one LB (D)	One LB(D), one FD	Twin pairs of Ds	Both LB	One LB, One FD	Twin pairs of LBs	IMR	Odds ratio [95% CI]	Odds ratio [95% CI]: MZ vs. DZ twins
Monozygotic twins										
<24	92.0	31	22	118.5	142.0	56.5	170.3	696.0	751.2* [493.4-1143.7]	1.58* [1.06-2.36]
24	56.0	62	27	100.5	179.0	64.5	211.3	475.7	297.7* [204.0-434.5]	1.82* [1.25-2.65]
25	46.5	106	28	114.0	274.0	57.0	302.5	376.9	198.4* [139.5-282.2]	2.58* [1.79-3.72]
26	38.0	111	26	106.5	369.0	73.0	405.5	262.6	116.9* [82.8-165.0]	2.35* [1.61-3.43]
27	34.5	86	34	94.5	507.0	82.5	548.3	171.5	68.3* [48.4-96.5]	2.26* [1.51-3.36]
28	23.0	112	31	94.5	658.0	105.5	710.8	131.6	49.7* [35.3-70.0]	3.45* [2.19-5.44]
29	7.5	64	14	46.5	684.5	107.0	738.0	63.0	22.1* [14.8-32.8]	1.48* [0.93-2.38]
30	6.0	50	10	36.0	845.5	106.0	898.5	40.1	13.7* [9.0-21.0]	1.26* [0.76-2.08]
31	6.0	54	7	36.5	1194.5	102.5	1245.8	29.3	9.9* [6.5-15.1]	1.30* [0.79-2.14]
32	5.5	61	7	39.5	1777.0	113.5	1833.8	21.5	7.2* [4.8-10.9]	1.65* [0.97-2.78]
33	4.0	54	7	34.5	2379.5	97.5	2428.3	14.2	4.7* [3.1-7.3]	1.80* [1.04-3.13]
34	3.0	77	2	42.5	3886.5	96.0	3934.5	10.8	3.6* [2.4-5.4]	1.84* [1.13-2.98]
35	7.0	60	9	41.5	6806.5	143.0	6878.0	6.0	2.0* [1.3-3.0]	1.07 [0.71-1.62]
36	3.0	77	7	45.0	14193.5	171.0	14279.0	3.2	1.04 [0.7-1.5]	0.84 [0.58-1.21]
37	5.0	93	7	55.0	18014.0	167.5	18097.8	3.0	1.00 :Reference	1.16 [0.82-1.63]
38	3.0	45	5	28.0	7733.5	88.0	7777.5	3.6	1.2 [0.8-1.9]	1.23 [0.74-2.03]
39	0.0	25	1	13.0	3206.0	47.0	3229.5	4.0	1.3 [0.7-2.4]	2.17 [0.90-5.25]
≥40	1.0	14	0	8.0	1269.0	31.5	1284.8	6.2	2.1 [0.98-4.3]	1.29 [0.50-3.36]
Dizygotic twins										
<24	118	70	36	171	242	97.0	290.5	588.6	780* [375-1622]	
24	28	98	14	84	239	27.0	252.5	332.7	267.9* [127.6-562.3]	
25	20	72	6	59	295	31.0	310.5	190.0	126.1* [59.6-266.7]	
26	10	72	2	47	337	41.0	357.5	131.5	81.3* [38.1-173.7]	
27	9	56	2	38	428	43.0	449.5	84.5	49.6* [23.0-107.1]	
28	0	50	0	25	570	35.0	587.5	42.6	23.9* [10.7-53.2]	
29	7	50	0	32	669	46.0	692.0	46.2	26.1* [12.0-56.8]	
30	2	50	2	28	842	61.0	872.5	32.1	17.8* [8.1-39.2]	
31	6	42	2	28	1207	58.0	1236.0	22.7	12.5* [5.7—27.4]	
32	0	44	0	22	1637	59.0	1666.5	13.2	7.2* [3.2-16.2]	
33	0	40	0	20	2498	45.0	2520.5	7.9	4.3* [1.9-9.8]	
34	0	54	0	27	4525	87.0	4568.5	5.9	3.2* [1.5-7.0]	
35	0	98	0	49	8641	81.0	8681.5	5.6	3.1* [1.4-6.5]	
36	4	150	0	79	21015	112.0	21071.0	3.7	2.0 [0.98-4.2]	
37	2	152	2	79	30036	102.0	30087.0	2.6	1.4 [0.7-2.9]-	
38	2	64	0	34	11180	94.0	11227.0	3.0	1.6 [0.8-3.5]	
39	0	16	0	8	4281	52.0	4307.0	1.9	1.00 :Reference	
≥40	0	18	0	9	1840	49.0	1864.5	4.8	2.6* [1.01-6.8]	
LB: Live birth; D: Infant death; FD: Fetal death (12 weeks of gestation and over); IMR: Infant mortality rate per 1000 twins pairs of LBs; CI: Confidence interval										

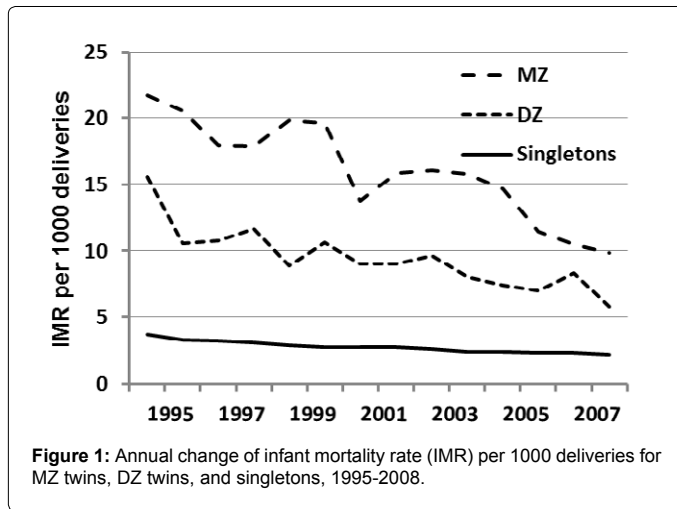**Table 3:** Infant mortality rate in zygotic twins by gestational age, 1995-2008.

30–34 years for DZ twins. IMRs for MZ twins at MAs of 35–39 years were significantly lower than those at MAs of <20 and 20–24 years. For DZ twins, IMR at MAs of 30–34 years was significantly lower than that of other MAs, with the exception at MAs of 20–24 and ≥40 years. IMRs were also significantly higher in MZ than DZ twins for MAs between 20–24 and 35–39 years.

IMRs for zygotic twins by GA

Table 3 shows IMRs for zygotic twins by GA during the study period. IMR for MZ twins was 696 at GA of <24 weeks and decreased as GA increased beyond 37 weeks (3.0). IMRs for MZ twins were similar at GA of ≥ 36 weeks (3.0–6.2). For DZ twins, IMR was 589 at GA of <24 weeks and continued to decrease as GA increased beyond 39 weeks (1.9) (except for at 38 weeks). At GAs of <29 weeks and 33–34 weeks, IMRs for MZ twins were significantly higher than those for DZ twins.

Discussion

To provide context for the present study, we used data from the study by Imaizumi et al (Table 2) [1] to recalculate IMRs for MZ and DZ twins in 1974, finding IMRs of 47.51 (116 × 1000/2441.5) for MZ twins and 45.23 (64 × 1000/1415) for DZ twins. These IMRs were similar for MZ and DZ twins [odds ratio (OR) 1.05, 95% confidence interval (CI): 0.77–1.44] and were significantly higher than those in 1995 (MZ twins: OR 2.22, 95% CI: 1.70–2.91; DZ twins: OR 3.00, 95% CI: 2.14–4.20). In the 21 years from 1974 to 1995, the corresponding IMRs for MZ and DZ twins dramatically decreased to 21.7 and 15.6, respectively. By 2008, these rates had again markedly decreased by 1/2 and 1/3 respectively. The improved medical care may explain the declining IMRs for MZ and DZ twins in the last 34 years. From (Figure 1), the ratio of IMRs for DZ twins and singletons was 4.2 in 1995 and decreased to 2.6 in 2008 where IMR was significantly higher in DZ

Figure 1: Annual change of infant mortality rate (IMR) per 1000 deliveries for MZ twins, DZ twins, and singletons, 1995-2008.

twins than singletons in each year. Our results also indicated that risk factors such as MA and GA influence IMRs for MZ and DZ twins.

We found that IMRs were significantly higher for MZ than DZ twins in every year except 2007. During 1995–2008, the overall IMRs were 16.3 (1056 × 1000/64990) for MZ twins and 9.1 (840 × 1000/91857) for DZ twins (Table 1). The study by Imaizumi and Hayakawa [11] reported that there were 352 infant deaths due to twin-to-twin transfusion syndrome (TTTS) during 1995–2008. However, overall, there were 1056 infant MZ twin pair deaths during the same period (Table 1). This indicates that 16.7% (176/1056) of IMRs for MZ twins was explained by TTTS.

There may be some errors in the estimated infant deaths for MZ and DZ twins resulting from the available data. For example, we found that the data contained cases where there were different addresses for twin pairs due to migration between birth and death. Twenty five twin pairs with one LB (D)–one FD (unknown sex) were eliminated due to unknown MZ and DZ twins. Data from Imaizumi (Table 3) [2] and Imaizumi and Hayakawa (Table 2) [3] indicate that the total number of infant deaths (males and females) was 1365 for 1995–1998 and 2670 for

1999–2008. However, we found that there were 3792 infant deaths for individual MZ and DZ twins (Table 1), giving an estimated proportion of 94.6% [3792/(4035-25)] infant deaths for zygotic twins. Another minor underestimation might be present for 2008 as some infants surviving in 2008 may have died in 2009. As far as vital statistics is used to estimate IMRs for zygotic twins, it seems not possible to avoid an error of about 5%.

Acknowledgements

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