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Sudden Infant Death Syndrome in Twins and Singletons in Japan, 1995-2008

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Abstract

Objective: To compare the infant mortality rate (IMR) due to sudden infant death syndrome (SIDS) in twins and singletons and consider the risk factors of SIDS.

Materials and methods: The IMR due to SIDS was analyzed among twins and singletons from 1995 to 2008 using the Japanese Vital Statistics.

Results and discussion: The IMR for both twins and singletons decreased (1/3-1/4) significantly during 1995-2008 and was significantly higher among twins than in singletons during 1995-2000 and 2003-2004. The relative risks of SIDS for maternal age groups between <25 years and 30–34 years were 9-fold for twins and 3-fold for singletons. The IMR increased with parity for both 1st- and 2nd-twin born. Seasonal variations were observed in IMRs for twins and singletons. The time of death from 4 a.m. to 7 a.m. was a risk factor for SIDS in twins and singletons.

Conclusion: The relative risks for SIDS in twins and singletons decreased after 2005. The SIDS IMR was lower in Japan than in the US, the UK, and Canada which related to lower percentage of prone and facedown sleeps position in Japan. The concordance rate of SIDS was uncommon in twins. Younger maternal age is a risk factor for both twins and singletons.

Keywords: Sudden infant death syndrome; Twins; Singletons; Risk factors

Introduction

According to vital statistics in Japan, congenital malformations (37.4% among total number of infant deaths) was the first leading cause of deaths in 2010, the second was respiratory and cardiovascular disorders (13.9%), and third was sudden infant death syndrome (SIDS) (5.7%). The former two causes of death consists of a set of many detailed lists of codes in the International Classification of Diseases, 10th Revision (ICD-10th) [1], but SIDS has only one code (R95, ICD-10th). The proportion of SIDS deaths among the total number of infant deaths was 10.4% in 1995, which decreased to 5.5% in 2008. In the US, the IMR due to SIDS decreased from 1.2 per 1000 live births in 1992 to 0.56 in 2001, but the IMR has remained constant from 2001 to 2006 [2]. Much of the decrease in IMR due to SIDS was because of the change in sleeping position for both twins and singletons in England and Wales from 1993 to 2003 [3].

Risk factors for death due to SIDS are race, sleeping position [4], tobacco [5], seasonality [6], twins [7], zygosity [3], maternal education level [8], and birth weight (BW) [9]. A primary cardiac channelopathy was estimated to cause 5%-15% of SIDS cases [2].

The purpose of this study was to compare the IMRs in twins and singletons and consider the risk factors of SIDS.

Materials and Methods

Data on live births and infant deaths were obtained from the vital statistics of Japan for the duration of 1995-2008 (Health and Welfare Statistics and Information Department, Ministry of Health, Labour and Welfare, Japan); these data cover the entire population of Japan. Death certificate records provide information concerning nationality, sex, dates, BW, Gestational Age (GA), parental age, single or multiple births, birth order of multiple births, cause of death, and other details. ICD-10 for 1995-2008 assigned SIDS with the code R95. Birth certificate records contain this same information, except for data related to death. In Japan, Early Neonatal Death (END) refers to cause of death of a live-born infant occurring <7 completed days from the time of birth and Neonatal Mortality Rate (NMR) refers to the number of children <28 days of age who die per 1000 live births. Post-Neonatal Mortality (28 days-1 year of age) Rate (PNMR) and IMR refer to the number of these deaths (after birth upto 1 year of age) per 1000 live births.

Expectation values were computed by multiplying the total number of SIDS deaths by a proportion of total number of days in each season to test the seasonality of the IMRs. The number of SIDS deaths of twins in each hour was small. Then number of deaths was divided into four continuous hours to compute the χ^2-test. Expectation values were obtained by multiplying the total number of deaths by 1/6 (e.g., 25 for twins and 666.8 for singletons).

The MZ twinning rate (per 1000 births) during 1995-2008 was presumed on the basis of the considerations given below (rates per 1000 births). The MZ twinning rate remained nearly constant between 1975 (3.7) [10] and 1998 (4.3) [11]. In the present study, the MZ twinning rate was assumed to be 4.35 per 1000 births during1995-2008 [12]. To compute IMRs due to SIDS among like- and unlike-sexed twins, denominators for both types of twin pairs were estimated on the basis of the considerations given below. The total twinning rate was computed as the number of live birth twins divided by 2 and multiplied by 1000 and divided by the total number of total live births in each year. Then, the DZ twinning rate was estimated by the total twining rate minus the MZ rate (4.35 per 1000 live births) in each year. Weinberg's method [13] was used to estimate the total number of like- and unlike-sexed twins, which is shown in table 2. As for numerators, we analyzed the data from the Japan-linked birth and death certificate tapes from 1995 to 2008 to find the co-twin of SIDS twins. We used odds ratio (OR) to test the difference between IMRs for males and females, for twins and singletons, and between maternal age groups as well as GA and BW.

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Results

Trend in infant mortality

Table 1 shows the number of SIDS infant deaths and IMRs for singletons and twins from 1995-1996 through 2007-2008. The proportion of SIDS infant deaths among total infant deaths was 3.8% for twins and 9.3% for singletons during the period 1995-2008. IMRs for both twins and singletons significantly decreased during the period. The overall IMR was 0.49 per 1000 live births in twins and 0.26 in singletons; it was significantly higher in the former than in the latter [OR, 1.9; 95%CI, 1.6-2.2]. SIDS IMR was significantly higher in males than in females during the periods 1995-1996 and 1999-2000 for twins and during each two-year period for singletons. IMRs were computed using overall information for number of deaths, including unknown maternal age (Table 1). Distribution of maternal age at birth has changed for the last decade. Next, age-adjusted IMR was computed for the period 1999-2008. Crude IMRs excluding deaths due to SIDS in unknown maternal age groups were computed, but the crude and age-adjusted IMRs were similar during each two-year period for twins and singletons. However, the maximum difference between the two types of IMR was 0.03 per 1000 live births during 2003-2004 for twins and 0.01 during 2005-2008 for singletons. Namely, decreased IMR was not related to the changed maternal age during the period (Table 1) and also shows the NMR and PNMR due to SIDS and these proportions among infant deaths during 1995-2008. The proportion of infant deaths was 8% for twins and singletons. The NMR was not significantly different between twins and singletons, but the PNMR was 1.92-fold significantly higher in twins than that in singletons.

Infant mortality according to risk factors

Table 2 shows the IMRs due to SIDS according to maternal age, BW, and GA in twins and singletons. The highest IMR was 1.30 per 1000 live births for twins and 0.38 for singletons among mothers aged <25 years, whereas the lowest rate was 0.15 for twins and 0.13 for singletons among mothers age 30-34 years. The twin-singleton relative risk (3.4-fold) was statistically significant at the 5% level for mothers aged <25 and 25-29 years. The highest IMR in twins was 1.37 per 1000 live births for those with BWs <1500 g and decreased to 0.30 for infants with BWs ≥ 2500 g. The corresponding rates in singletons were 1.23 and 0.20, respectively. The relative risk between both BWs was 4.6-fold for twins and 6.1-fold for singletons. The IMR was similar for both twins and singletons with BWs <2500 g. In contrast, the relative risk (1.5-fold) was significantly higher in twins than that in singletons with BWs ≥ 2500 g. The IMR was only significantly higher in twins (0.30) than that in singletons (0.15) for those with GA of ≥ 38 weeks. Proportion of unknown BW was 0% (0/152) in twins during 1995-2008 and the percentage of unknown GA was 2.3% (2/88) in singletons during 1999-2008. In contrast, the corresponding values in singletons were 11.1% (447/4009) and 12.3% (273/2217), respectively. From table 2, the IMR due to SIDS was similar for the first-born (0.46) and second-born twin (0.48) during 1995-2008. Table 2 also shows the IMR due to SIDS according to like- and unlike-sexed twin deliveries from 1995 to 2008. The IMR was 0.43 for like-sexed twins and 0.33 for unlike-sexed twins, which was not significantly different. The concordance rate of SIDS was 1/151 pairs of twins. Table 3 shows the IMR due to SIDS according to order of twins, parity, and maternal age in twin births during 1999-2008. The IMR increased with parity for both 1st- and 2nd-twin born. As for maternal age, IMRs decreased significantly with maternal age

Year	No. of SIDS			IMR due to SIDS			Odds ratio [95% CI]	No. of live births			Age-adjusted
	Males	Females	Total	Males	Females	Total	Twins vs. Singletons	Males	Females	Total	IMR
Twins											
1995-1996	20	9	29	1.00*	0.45	0.72		20060	19997	40057	
1997-1998	18	17	35	0.85	0.82	0.84		21156	20635	41791	
1999-2000	27	11	38	1.21*	0.50	0.86		22319	21917	44236	0.86
2001-2002	7	9	16	0.30	0.39	0.35		23206	22847	46053	0.35
2003-2004	10	8	18	0.41	0.34	0.37		24454	23829	48283	0.44
2005-2006	3	4	7	0.13	0.17	0.15		23953	23371	47324	0.16
2007-2008	8	1	9	0.35	0.04	0.20		22667	22634	45301	0.18
Total	93	59	152	0.59*	0.38	0.49		157815	155230	313045	-
Neonatal deaths			12(8%)			0.038					
Postneonatal deaths			140(92%)			0.447					
Singletons											
1995–1996	582	389	971	0.48*	0.34	0.41	1.8 [1.2-2.5]*	1207282	1144366	2351648	-
1997–1998	464	357	821	0.39*	0.31	0.35	2.4 [1.7-3.4]*	1206219	1144919	2351138	-
1999–2000	395	249	644	0.33*	0.22	0.28	3.1 [2.2-4.3]*	1193613	1128444	2322057	0.24
2001–2002	330	196	526	0.28*	0.18	0.23	1.5 [0.9-2.5]	1169665	1107081	2276746	0.21
2003–2004	237	175	412	0.21*	0.17	0.19	2.0 [1.2-3.2]*	1120974	1063390	2184364	0.17
2005–2006	215	129	344	0.20*	0.13	0.16	0.9 [0.4-1.9]	1080873	1025662	2106535	0.15
2007–2008	175	116	291	0.16*	0.11	0.14	1.5 [0.8-2.8]	1096162	1038372	2134534	0.13
Total	2398	1611	4009	0.30*	0.21	0.26	1.9 [1.6-2.2]*	8074788	7652234	15727022	-
Neonatal deaths			340(8%)			0.022	1.770 [0.997-3.150]				
Postneonatal deaths			3669(92%)			0.233	1.917 [1.620-2.270]*				
Overall total number of infant deaths (Proportion of deaths due to SIDS)											
Twins			4035(3.8%)								
Singletons			43340(9.3%)								

Note: IMR, infant mortality rate per 1000 live births; *significant at the 5% level (Males vs. Females & Twins vs. Singletons)

Table 1: Trends of infant mortality due to SIDS and number of live births by sex in twins and singletons, 1995-2008.

Characteristic	Twins			Singletons			OR [95%CI] Twins vs. Singletons
	Deaths	IMR[3)]	OR [95%CI]	Deaths	IMR[3)]	OR [95%CI]	
Maternal age[1)], y							
<25	26	1.30	8.76 [4.57-16.78]*	601	0.38	2.97 [2.64-3.35]	3.42 [2.45-4.76]
25-29	37	0.55	3.71 [2.00-6.86]*	614	0.16	1.26 [1.12-1.41]	3.42 [2.45-4.76]
30-34	14	0.15	1.00 Reference	504	0.13	1.00 Reference	1.16 [0.68-2.17]
≥ 35	8	0.16	1.09 [0.46-2.59]	240	0.15	1.15 [0.98-1.34]	1.10 [0.55-2.23]
Birthweight[2)], g							
<1500	32	1.37	4.59 [2.78-7.59]*	103	1.23	6.12 [5.03-7.45]	1.11 [0.75-1.65]
1500-2499	91	0.47	1.58 [1.04-2.40]*	524	0.48	2.38 [2.17-2.61]	0.99 [0.79-1.23]
≥ 2500	29	0.30	1.00 Reference	2935	0.20	1.00 Reference	1.48 [1.03-2.14]
Gestational age[1)], w							
<32	17	1.08	3.85 [2.20-6.76]*	68	1.09	7.17 [5.62-9.13]	0.99 [0.58-1.69]
32-34	15	0.59	2.09 [1.16-3.75]*	57	0.63	4.13 [3.17-5.39]	0.93 [0.53-1.64]
35-37	43	0.28	2.09 [1.16-3.75]*	362	0.28	1.82 [1.62-2.04]	1.01 [0.74-1.39]
≥ 38	11	0.30	1.07 [0.55-2.08]	1457	0.15	1.00 Reference	1.97 [1.09-3.57]
Sex combination of twins[2)]							
Like-sex	97[4)]	0.43	1.27 [0.84-1.91]*				
Unlike-sex	30	0.35	1.00 Reference				
Total	152[5)]	0.49					

Note: [1)]Reported period, 1999-2008; [2)]Reported period, 1995-2008; [3)]IMR per 1000 live births; [4)]Including one case of SIDS-SIDS; [5)]Including unknown sex of co-twin; *significant at the 5% level

Table 2: Infant mortality rate due to SIDS of selected characteristics for twins and singletons.

Parity	Maternal Age	1st-born			2nd-born		
		SIDS	IMR[1)]	OR [95%CI]	SIDS	IMR[1)]	OR [95%CI]
0		17	0.25	1.00 Reference	15	0.22	1.00 Reference
1		15	0.42	1.72 [0.86-3.45]	9	0.26	1.18 [0.52-2.69]
≥ 2		8	0.71	2.92 [1.26-6.76]*	14	1.27	5.83 [2.81-12.07]*
0	<25	5	0.67	8.89 [2.12-37.21]*	4	0.54	7.12 [1.59-31.84]*
	25-29	9	0.41	5.40 [1.46-19.96]*	8	0.36	4.84 [1.27-18.12]*
	≥ 30	3	0.08	1.00 Reference	3	0.08	1.00 Reference
≥1	<25	7	2.69	14.54 [4.88-43.31]*	7	2.73	14.58 [4.89-43.40]*
	25-29	10	0.85	4.61 [1.67-12.68]*	8	0.69	3.68 [1.28-10.62]*
	≥ 30	6	0.19	1.00 Reference	6	0.19	1.00 Reference
Total[2)]		73	0.46		75	0.48	

Note: [1)]IMR per 1000 live births; [2)]Reported period, 1995-2008; *significant at the 5% level

Table 3: Infant mortality rate due to SIDS according to parity and maternal age in twins, 1999-2008.

groups for both parities 0 and ≥ 1. The risk of the IMR due to SIDS was more related to the maternal age than parity.

Time of death in SIDS

Table 4 shows the number of deaths due to SIDS according to the time of death and place of death for twins and singletons during 1995-2008. The SIDS deaths were grouped into 4-h blocks. The percentage of deaths was higher from 4 a.m. to 7 a.m. than in other time periods for both twins and singletons. The risk of death due to SIDS was significantly lower between 8 p.m. and 11 p.m. for twins and between 4 p.m. and 11 p.m. for singletons. In contrast, the risk of death due to SIDS was significantly higher between 4 a.m. and 11 a.m. for singletons. The number of SIDS deaths was 2.8-fold (34/12) for twins and 2.5-fold (907/360) for singletons higher in the time period from 4 a.m. to 7 a.m. than from 8 p.m. to 11 p.m. Remarkable differences in the numbers of deaths for time of death were observed in both twins and singletons.

According to Japanese vital statistics, 99% (15863154/16051673) live births took place in a hospital or a clinic between 1995 and 2008. Table 4 shows that ENDs due to SIDS occurred at these places: 100% (10/10) in twins and 95.6% (152/159) in singletons. ENDs due to SIDS occurred between 12 a.m. and 11 a.m. (50%) and between 12 p.m. and 11 p.m. (50%) in twins, whereas the corresponding values in singletons were 70% and 30%, respectively. The relative risk ratio of ENDs in the morning to these in the afternoon was 1 for twins and 2.3-fold for singletons. In contrast, the percentage of infant deaths due to SIDS in hospitals or clinics was 72.8% (110/151) for twins and 64.5% (2580/4001) for singletons. The percentage of infant deaths due to SIDS occurring at home was 25.8% for twins and 31.8% for singletons. The relative risk ratio of infant deaths in the morning to those in the afternoon was 1 (55/55) for twins and 1.3-fold (1468/1112) for singletons in hospitals and clinics, whereas the corresponding relative risk ratio of deaths at home was 2.9-fold (29/10) and 2.7-fold (926/347), respectively. Therefore, a higher relative risk of infant deaths due to SIDS in the morning occurred at home compared at hospitals or clinics.

Seasonality of SIDS

Table 4 also shows number of deaths due to SIDS according to four seasons for twins and singletons during 1995-2008. The proportion of deaths was significantly higher in winter (December-February) for twins and singletons and higher in spring for singletons compared with the expected proportion of deaths (25%). In contrast, the proportion of deaths in summer and autumn were significantly lower than the

	Twins						Singletons					
	Hospital	Clinic	Home	Others	Total	χ^2	Hospital	Clinic	Home	Others	Total	χ^2
Time of death: Infant deaths												
12-3 a.m.	7	0	11	0	18 (11.9)	2.02	290	20	362	36	708 (17.7)	2.5
4-7 a.m.	22	1	11	0	34 (22.5)	3.10	479	32	370	26	907 (22.7)	86.5**
8-11 a.m	25	0	7	1	33 (21.9)	2.44	623	24	194	29	870 (21.7)	61.9**
0-3 p.m	25	2	3	0	30 (19.9)	0.93	456	19	148	29	652 (16.3)	0.3
4-7 p.m.	19	0	4	1	24 15.9)	0.05	362	9	116	17	504 (12.6)	39.8**
8-11 p.m.	9	0	3	0	12 (7.9)	6.89*	257	9	83	11	360 (9.0)	141.2**
Total	107	3	39	2	151	15.45**	2467	113	1273	148	4001	332.2**
Time of death: Early neonatal deaths												
12-11 a.m.	4	1	0	0	5 (50.0)		55	51	3	2	111 (69.8)	
0-11 p.m.	5	0	0	0	5 (50.0)		33	13	1	1	48 (30.2)	
Total	9	1	0	0	10		88	64	4	3	159	

Season of death	No. of deaths	Exp.	χ^2	No. of deaths	Exp.	χ^2
Winter (Dec.-Feb.)	54 (35.5)	38	7.20**	1217 (30.4)	991	51.75**
Spring (March-May)	34 (22.4)	38	0.48	1129 (28.2)	1010	14.07**
Summer (June-Aug.)	32 (21.1)	38	1.03	823 (20.5)	1010	34.55**
Autumn (Sept.-Nov.)	32 (21.1)	38	0.91	840 (21.0)	999	25.25**
Total	152		9.62*	4009 (100.1)	4010	125.63**

Note: Figures in parentheses indicate the percentage of deaths due to SIDS.; Obs., Number of deaths due to SIDS; Exp., Expectation values; *Significant at the 5% level; **Significant at the 1% level. To compute χ^2-value, the expectation value was 25 for twins and 666.8 for singletons in each time at death categories.

Table 4: Number of deaths due to SIDS according to time of death and season in twins and singletons, 1995-2008

value of expected deaths for singletons. Remarkable differences in the number of deaths among four seasons were obtained for both twins and singletons.

Discussion

In singletons, percentages of higher risk factors for SIDS from 1999-2003 to 2004-2008 decreased slightly for mothers aged <30 years (from 62.9% to 60.5%), for GA of <35 weeks (6.7% to 6.0%), for proportion of males (61.5% to 60.2%), and for proportion of infant deaths in winter (30.6% to 28.7%). In contrast, corresponding values were increased for BW<2500 g (17.5% to 19.3%) and for time of death from 4 a.m. to 7 a.m. (23.9% to 27.3%), respectively. It seems that these risk factors for SIDS were very little effect to reduce the IMR from 1999-2003 to 2004-2008 in singletons.

The IMR of SIDS in the US was 1.3 per 1000 live births for twins and 0.7 for singletons during 1995-1998 [14]. On the other hand, the corresponding IMR was 0.63 and 0.58, respectively in the US during 1995-2000 where these data only included full-term (≥ 37 weeks) and non-low BW (>2500 g) infants [7]. Then, the IMRs due to SIDS for both twins and singletons were lower in Japan than those in the U.S. A prone and facedown sleep position is a risk factor of SIDS [4]; however, the percentage of SIDS occurring while the child was in this position was extremely low in Japan (4.2% in 1996 and 2.0% in 1998) [15] compared with the U.S. (30.1%) [16]. In Japan, the declining IMR due to SIDS was not related to the decreased percentage of prone and facedown sleep position [15]. In the US, 90% SIDS cases occur before an infant reaches 6 months of age [17]. In the present study, the percentage was 60% (91/152) for twins and 75% (3,000/4,009) for singletons. In England during 1993–1996, 51% of SIDS infants died in the morning (5 a.m. to 9 a.m.) [18]. In Japan, the percentage was 31% (47/151) for twins and 29% (1149/4001) for singletons. The IMR due to SIDS in England and Wales was 0.91 for twins and 0.46 in singletons during 1993-2003 [3], where the corresponding rates were 0.49 and 0.26, respectively in Japan. Then lower IMRs for both singletons and twins may be related to lower percentage of prone and facedown sleep position in Japan.

In the U.S. in 1991, IMRs due to SIDS in twins were 3.6 (per 1000 live births) for mothers aged <19 years and 1.7 for >35 years [8]. The corresponding rates in singletons were 1.3 and 0.6, respectively. The relative risk for SIDS in maternal age groups of <19 and >35 years was 2.1-fold for twins and 2.2-fold for singletons. In Canada, IMRs due to SIDS in singletons were 0.70 for mothers aged <30 years and 0.28 for mothers aged ≥ 30 years during 1991-2005 (recomputed from table 3 of [19]). In the present study, the corresponding rates in singletons were 0.22 and 0.13, respectively, during 1999-2008. The relative risk for SIDS in maternal age groups of <30 and ≥ 30 years was 2.5 (2.2–2.8) in Canada and 1.5 (1.3-1.6) in Japan. Then younger maternal age is a risk factor for both twins and singletons.

According to Malloy and Freeman [8], the concordance of SIDS is uncommon (7/760=0.9%). A similar result was obtained in the present study (1/151=0.7%).

Limitation of the present study was lack of information concerning BW and GA in singletons. Percentage of missing values for SIDS infants was 11.1% for BW and 12.3% for GA in singletons, whereas the corresponding value in twins was 0% and 2.3%, respectively. Another limitation was to find the co-twin of a SIDS twin. Sixteen percent of co-twin with a SIDS twin could not be determined because of a changed address between at birth and death.

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