Journal of Neonatal Biology
ISSN: 2167-0897

Imaizumi and Hayakawa, J Neonatal Biol 2014, 3:5
DOI: 10.4172/2167-0897.1000164

Research Article Open Access

Stillbirth Rates and Risk Factors for Stillbirths among Zygotic Twins in Japan, 1995-2008

Yoko Imaizumi* and Kazuo Hayakawa

Department of Health Sciences, Graduate School of Medicine, Osaka University, Suita City, Osaka, Japan

Abstract

We aimed to determine the Stillbirth Rates (SRs) for monozygotic (MZ) and dizygotic (DZ) twins, with the risk factors for stillbirth. SRs were estimated using Japanese vital statistics from 1995 to 2008. The SRs of zygotic twins significantly decreased during the period. The SR was the lowest at maternal age (MA) of 30-34 years for MZ (66) and DZ twins (18) and significantly higher at MA <20 years than the other MA groups for both zygosities. The SR was the lowest at Gestational Age (GA) of 37 weeks for MZ (5.7) and DZ twins (1.8). The SR was significantly higher for MZ than for DZ twins at each GA group except for those born at GA 39 and GA ≥ 40 weeks. The SR significantly decreased from 1995-1998 to 2004-2008 except GA ≥ 40 for both zygotic twins and 32-35 weeks for DZ twins. Incidences of preterm delivery increased from 1995 (43% for MZ and 38% for DZ twins) to 2008 (62% and 55%, respectively). The SRs were significantly higher in like-sexed twins than in unlike-sexed twins in every birth weight (BW) group. The SR was similar between BW 2000–2499 g and ≥ 2500 g in each twin group. The SR increased progressively when the percentage of BW discordance exceeds 10% for MZ twins and exceeds 20% for DZ twins. The SR due to twin–twin transfusion syndrome was 14% among spontaneous stillbirths in MZ twins. In conclusion, declining SR attributed to medical care during twin pregnancies less than 40 weeks for MZ and DZ twins. Excess BW discordance of 10% for MZ twins lead to higher SRs compared with those in DZ twins. The increased premature rate in twins might bring severe problems such as cardiovascular risk in their future life.

Keywords: Stillbirth rate; Zygotic twins; Gestational age; Preterm birth; Birth weight; Intra-pair birth weight discordance

Introduction

The Stillbirth Rate (SR) is higher in monozygotic (MZ) than in dizygotic (DZ) twins [1-6]. It is well known that Maternal Age (MA), Gestational Age (GA), Birth Weight (BW) are risk factors for the SR of twins. BW discordance (BWD) is also a risk factor for fetal deaths in like- and unlike-sexed twins [7-9].

The stillbirth rate in Japan significantly decreased from 1960 (270 per 1000 twin deliveries) to 1994 (81) for monozygotic (MZ) twins, and the corresponding rates in dizygotic (DZ) twins were 224 and 28, respectively [2,3].

This study aimed to estimate the SRs for MZ and DZ twins during the period 1995–2008 and to identify the risk factors associated with stillbirth.

Materials and Methods

Data sources

Data on Live Births (LBs) and Fetal Deaths (FDs) were obtained from vital statistic records maintained by the Statistics and Information Department, Ministry of Health, Labour and Welfare (Tokyo, Japan) for the years 1995-2008. These data cover the entire Japanese population. LB certificates contain information on nationality, sex, date of birth, BW, GA, parental dates of birth and age, single or multiple birth, and birth order in multiple births, as well as other details. FD certificates (at 12 completed weeks of gestation and over) contain the same information, including the date, spontaneous or induced termination of pregnancy and cause of spontaneous FD, but excluding the parental dates of birth.

All cause of spontaneous FDs were classified into five categories according to the ICD 10th revision [9]: P05–P08 (disorders related to length of gestation and fetal growth), P50.3 (twin–twin transfusion syndrome, TTTS), P95 (fetal death of unspecified cause), Q00–Q99 (birth defects), and others. Cause–specific SRs were computed according to the above five categories.

Describing twin data

Twin pairs were estimated using three record pairings: LB–LB (2LB), FD–FD (2FD), and LB–FD. Cases recorded as 2LB and 2FD were obtained from the LB and FD certification records, respectively. The LB–FD cases were obtained from LB and FD certification records that excluded 2LB and 2FD twin pairs. We identified 99.99% of 166,690 twin pairs (including unknown sexes) during the period 1995-2008.

The number of MZ and DZ twins was estimated using the Weinberg method [10]. MA and/or GA are not always the same between twin pairs because each twin could be born on different dates; thus, the number of like- or unlike-sexed twin pairs consisted of both odd and even numbers of twin pairs.

The SR related to BW was calculated based on the individual weights of like- and unlike-sexed twins. Intra-pair BWD was computed by subtracting the BW of the smaller twin from that of the larger, dividing the difference by the heavier BW and multiplying by 100 [8]. BWD was categorized into six groups: less than 5%, 5%–9%, 10%–19%, 20%–29%, 30%-39%, and ≥ 40%.

***Corresponding author:** Yoko Imaizumi, Department of Health Sciences, Graduate School of Medicine, Osaka University, Suita City, Osaka, Japan, Tel: +81-78-928-6027; E-mail: yoko1234go@m5.gyao.ne.jp

Received June 18, 2014; **Accepted** November 21, 2014; **Published** November 23, 2014

Citation: Imaizumi Y, Hayakawa K (2014) Stillbirth Rates and Risk Factors for Stillbirths among Zygotic Twins in Japan, 1995-2008. J Neonatal Biol 3: 164. doi:10.4172/2167-0897.1000164

Statistical analysis

All SR data were described as the rate per 1000 twin deliveries. The linear regression coefficient of the SR on the year was used to test changes in the SR. Odds Ratio (OR) and 95% confidence interval (CI) were used to test the differences between the SRs for two categories. Statistical significance was accepted at the 5% level ($p<0.05$).

Results

Yearly change in the SR for zygotic twins

Table 1 and Figure 1 show the yearly change in SRs for MZ and DZ twins from 1995 to 2008. The SR of MZ twins was 75 per 1000 twin deliveries in 1995 and decreased to 60 in 2008. Similarly, the corresponding SR of DZ twins was 38 and 15, respectively. The linear regression coefficients of the SRs for MZ and DZ twins on the year showed significantly decreased from 1995 to 2008. The SR was significantly higher in MZ twins than in DZ twins in each year.

SRs for MZ and DZ twins by MA

Table 2 and Figure 2 show the SRs for MZ and DZ twins according to MA during the period 1995–2008. The highest SR was 192 in MZ and 95 in DZ twins for the youngest MA group. The lowest SR was 66 in MZ and 18 in DZ twins for the MA of 30–34 years. In MZ twins, SRs were similar between 25-29 and 35-39 years. On the contrary, the SRs for DZ twins were similar for the MA of 30-34 years and MA ≥ 40. The SR under 20 years was significantly higher than the rates for the other age groups for MZ and DZ twins. The SR was also significantly higher in MZ than in DZ twins for each MA group.

SRs for zygotic twins by GA and incidence of preterm delivery

Table 3 shows the SRs for MZ and DZ twins according to GA during the period 1995–2008. The SR of MZ twins rapidly decreased from GA <24 weeks (956) to GA 30 weeks (72) and reached the lowest at GA 37 weeks (5.7) and increased thereafter. The corresponding SRs of DZ twins were 836, 34, and 1.8, respectively. For MZ twins, the SRs were similar for GA 36–39 weeks (5.7–8.4) and the SR at GA 37 weeks was significantly lower than for those born at GA <36 and GA ≥40 weeks. On the contrary, the SR of DZ twin at GA 37 weeks was significantly lower than for those at the other GA categories. For both zygotic twins, the SR was significantly higher at GA <24 than GA 24 weeks (O R, 32.9, [95% CI, 25.3-42.8] for MZ twins; 28.2, [20.1-39.6] for DZ

Year	MZ twin deliveries					DZ twin deliveries					MZ vs. DZ twins
	2LB[1]	LB-FD	2FD[2]	Total	SR[3]	2LB	LB-FD	2FD	Total	SR	Odds ratio [95% CI]
1995	4749	165	310	5224	75.1	4832	102	144	5078	38.4	2.0 [1.7–2.4]
1996	4869	179	357	5405	82.6	5266	62	120	5448	27.7	3.2 [2.6–3.8]
1997	4885	157	298	5340	70.5	5338	74	92	5504	23.4	3.2 [2.6–3.9]
1998	4793	147	351	5291	80.2	5602	74	96	5772	23.0	3.7 [3.0–4.5]
1999	4723	136	341	5200	78.7	5914	88	128	6130	28.1	1.8 [1.6–2.0]
2000	4683	100	334	5117	75.0	6528	102	90	6720	21.0	3.8 [3.3–4.4]
2001	4536	98	323	4957	75.1	6518	82	96	6696	20.5	3.9 [3.4–4.5]
2002	4630	130	290	5050	70.3	7080	80	142	7302	24.9	3.0 [2.6–3.4]
2003	4550	121	273	4944	67.5	7306	80	128	7514	22.4	3.2 [2.8–3.6]
2004	4359	93	273	4725	67.6	7650	98	122	7870	21.7	3.3 [2.9–3.7]
2005	4374	92	288	4754	70.3	7240	72	108	7420	19.4	3.8 [3.1–4.7]
2006	4267	100	285	4652	72.0	7528	78	84	7690	16.0	4.8 [4.1–5.5]
2007	4395	103	259	4757	65.3	7196	66	92	7354	17.0	4.0 [3.5–4.7]
2008	4322	89	236	4647	60.4	6492	62	68	6622	15.0	4.2 [3.6–5.0]
Linear regression coefficient (p–value) of SR on the year											
–1.15 (0.0008)						–1.18(0.0002)					
[1]LB: Live birth, [2]FD: Fetal death, [3]SR per 1000 twin deliveries, CI: Confidence interval											

Table 1: Monozygotic (MZ) and dizygotic (DZ) twin deliveries by survival states of twins and stillbirth rates (SR), 1995–2008.

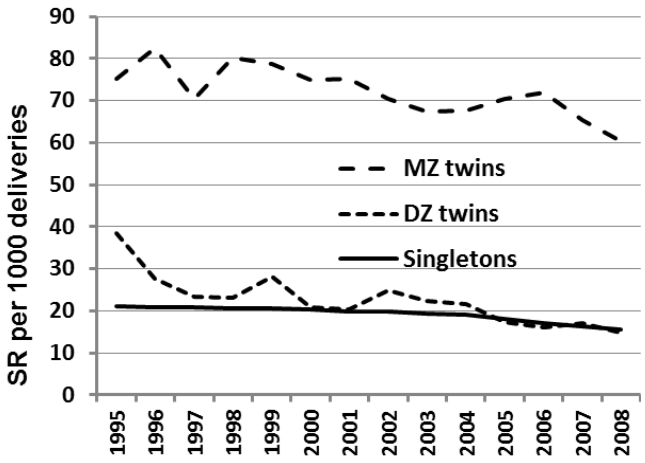

Figure 1: Yearly change of stillbirth rate per 1000 deliveries for MZ twins, DZ twins, and singletons, 1995 2008.

Maternal	MZ twin deliveries					DZ twin deliveries				
age	2LB[1]	LB–FD	2FD[2]	Total	SR[3]	2LB	LB–FD	2FD	Total	SR
<20	920.0	22.0	210.0	1152.0	191.8	359.0	4.0	36.0	399.0	95.2
20–24	8276.0	219.5	726.0	9221.5	90.6	5210.0	62.0	166.0	5438.0	36.2
25–29	23161.0	633.5	1351.0	25145.5	66.3	25667.0	317.0	476.0	26460.0	24.0
30–34	22590.5	591.5	1320.0	24502.0	65.9	38905.0	445.0	496.0	39846.0	18.0
35–39	8129.5	206.5	493.0	8829.0	67.5	18324.0	260.0	308.0	18892.0	23.2
≥40	1058.0	37.0	118.0	1213.0	112.5	2025.0	32.0	28.0	2085.0	21.1
Odds ratio [95% CI]										
	MZ twins			DZ twins			MZ vs. DZ twins			
<20	3.36 [2.88–3.93]		1.00 Reference	5.73 [4.07–8.07]		1.00 Reference	2.26 [1.57–3.25]			
20–24	1.41 [1.29–1.54]		0.42 [0.36–0.49]	2.05 [1.74–2.40]		0.36 [0.25–0.51]	2.65 [2.26–3.11]			
25–29	1.01 [0.94–1.08]		0.30 [0.26–0.35]	1.34 [1.20–1.49]		0.23[0.17–0.33]	2.89 [2.63–3.17]			
30–34	1.00 Reference		0.30 [0.25–0.35]	1.00 Reference		0.17[0.12–0.25]	3.84 [3.52–4.20]			
35–39	1.03 [0.93–1.13]		0.31 [0.26–0.36]	1.29 [1.15–1.46]		0.23 [0.16–0.32]	3.05 [2.69–3.46]			
≥40	1.80 [1.49–2.16]		0.53 [0.42–0.67]	1.17 [0.86–1.60]		0.20 [0.13–0.32]	5.88 [4.15–8.33]			

[1]LB: Live birth, [2]FD: Fetal death, [3]SR per 1000 twin deliveries, CI: Confidence interval

Table 2: Stillbirth rates (SRs) for monozygotic (MZ) and dizygotic (DZ) twins according to maternal age, 1995–2008.

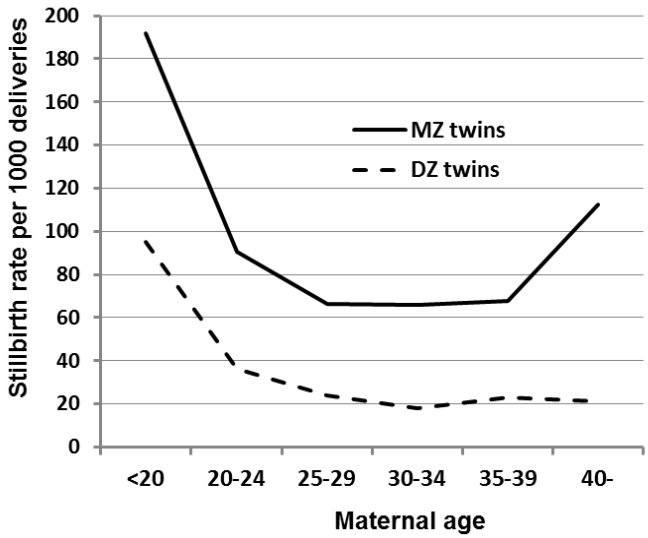

Figure 2: Stillbirth rate per 1000 deliveries by maternal age, 1995–2008.

twins). With two exceptions for those born at GA 39 and GA ≥40 weeks, the SR was significantly higher for MZ twins than for DZ twins.

Table 4 shows the comparisons of SRs for MZ and DZ twins according to GA during two periods: 1995–1998 and 2004–2008. The SR of MZ twins significantly decreased during these periods except GA where the SR increased the recent period. As for DZ twins, the SR significantly decreased for three GA groups for GA<32 weeks and 36–39 weeks. On the contrary, the SRs for GA ≥40 weeks remained similar values for both periods.

Figure 3 shows the SR at a GA <37 weeks and the incidence of preterm delivery (i.e. infant born at a GA <37 weeks) for MZ and DZ twins from 1995 to 2008. The SRs decreased from 153 for MZ twins and 87 for DZ twins in 1995 to 92 and 25 in 2008, respectively. The regression coefficients of the SR on the year show significant at the 1% level for MZ and DZ twins. On the contrary, the incidences of preterm delivery increased from 43% for MZ and 38% for DZ twins in 1995 to 62% and 55% in 2008, respectively. The incidences significantly higher in MZ twins than DZ twins (OR, 1.22; 95% CI, 1.12–1.32) in 1995 and (1.34; 1.24–1.45) in 2008, respectively. The regression coefficients of the incidence on the year show significant at the 1% level for MZ and DZ twins.

SRs for like-sexed and unlike-sexed twins by BW

Table 5 shows the SRs for like- and unlike-sexed twins according to BW during the period 1995–2008. The SR decreased with BW in each sex combination of twin pairs. However, the SRs between BW 2000-2499 g and ≥ 2500 g were similar at the 5% level in each sex combination of twin pairs. The SRs were significantly higher in male–male and female–female twins than in male–female twins for each BW group. The SR was also significantly higher in male–male than in female–female twins for BW<1000 g and 1500-1999 g.

Figure 4 shows the SRs for twins (MM, FF, and MF) according to BW during the period 1995–2008. The SRs decreased significantly year by year in each BW group. The regression coefficients (standard error) on the year were –11.07 (0.15) for BW <1000 g, –3.14 (0.58) for 1000–1499 g, –1.20 (0.16) for 1500–1999 g, –0.32 (0.05) for 2000–2499 g, and –0.21 (0.03) for ≥ 2500 g. These coefficients were significant at the 0.1% level.

GA	MZ twin deliveries							DZ twin deliveries							Odds ratio [95% CI]
(weeks)	2LB[1]	LB-FD	2FD[2]	Total	SR[3]	Odds ratio [95% CI]		2LB	LB-FD	2FD	Total	SR	Odds ratio [95% CI]		MZ vs. DZ twins
<24	142.0	56.5	3701.0	3899.5	956.3	3858	[3013–4941]	242	97	1427	1766	835.5	2883	[2142–3882]	4.3 [3.5–5.3]
24	179.0	64.5	108.5	352.0	399.9	117.4	[88.0–156.6]	239	27	32	298	152.7	102.3	[67.6–154.9]	3.7 [2.5–5.4]
25	274.0	57.0	80.5	411.5	264.9	63.5	[47.4–85.0]	295	31	23	349	110.3	70.4	[45.8–108.2]	2.9 [2.0–4.3]
26	369.0	73.0	57.0	499.0	187.4	40.6	[30.2–54.7]	337	41	5	383	66.6	40.5	[25.0–65.7]	3.2 [2.0–5.1]
27	507.0	82.5	45.0	634.5	135.9	27.7	[20.6–37.4]	428	43	5	476	55.7	33.5	[20.8–53.8]	2.7 [1.7–4.2]
28	658.0	105.5	24.0	787.5	97.5	19.0	[14.0–25.8]	570	35	6	611	38.5	22.7	[13.9–37.2]	2.7 [1.7–4.3]
29	684.5	107.0	28.0	819.5	99.5	19.5	[14.4–26.3]	669	46	2	717	34.9	20.5	[12.7–33.2]	3.1 [1.9–4.8]
30	845.5	106.0	17.0	968.5	72.3	13.7	[10.1–18.7]	842	61	0	903	33.8	19.8	[12.7–31.1]	2.2 [1.4–3.4]
31	1194.5	102.5	27.0	1324.0	59.1	11.1	[8.2–14.9]	1207	58	0	1265	22.9	13.3	[8.4–21.0]	2.7 [1.7–4.1]
32	1777.0	113.5	22.0	1912.5	41.2	7.6	[5.6–10.2]	1637	59	0	1696	17.4	10.1	[6.4–15.8]	2.4 [1.6–3.7]
33	2379.5	97.5	20.5	2497.5	27.7	5.0	[3.7–6.8]	2498	45	1	2544	9.2	5.3	[3.3–8.6]	3.1 [1.9–4.9]
34	3886.5	96.0	11.0	3993.5	14.8	2.6	[1.9–3.6]	4525	87	2	4614	9.9	5.7	[3.8–8.4]	1.5 [1.0–2.2]
35	6806.5	143.0	18.0	6967.5	12.9	2.3	[1.7–3.1]	8641	81	0	8722	4.6	2.7	[1.8–4.0]	2.8 [1.9–4.1]
36	14193.5	171.0	15.5	14380.0	7.0	1.25	[0.95–1.64]	21015	112	3	21130	2.8	1.6	[1.1–2.3]	2.5 [1.8–3.5]
37	18014.0	167.5	19.0	18200.5	5.7	1.00 Reference		30036	102	2	30140	1.8	1.00 Reference		3.2 [2.3–4.5]
38	7733.5	88.0	16.0	7837.5	7.7	1.36	[0.99–1.87]	11180	94	0	11274	4.2	2.4	[1.6–3.5]	1.8 [1.3–2.7]
39	3206.0	47.0	4.0	3257.0	8.4	1.50	[0.98–2.29]	4281	52	0	4333	6.0	3.4	[2.1–5.5]	1.4 [0.8–2.4]
≥40	1269.0	31.5	4.0	1304.5	15.1	2.7	[1.7–4.4]	1840	49	2	1891	14.0	8.1	[5.1–12.9]	1.1 [0.6–2.0]

Table 3: Comparison of stillbirth rates (SRs) of monozygotic (MZ) and dizygotic (DZ) twins according to gestational age (GA), 1995–2008.

GA	1995–1998					2004–2008					Odds ratio [95% CI]
(weeks)	2LB[1]	LB-FD	2FD[2]	Total	SR[3]	2LB	LB–FD	2FD	Total	SR	1995–1998 vs. 2004–2008
	MZ twin deliveries										
<24	32.0	10.0	1106.0	1148.0	967.8	58.0	17.0	1222.5	1297.5	948.7	1.62 [1.08–2.44]
24–27	341.0	104.0	115.0	560.0	298.2	537.5	86.5	65.5	689.5	157.7	2.27 [1.73–2.98]
28–31	850.5	160.5	36.0	1047.0	111.0	1311.0	116.5	25.0	1452.5	57.3	2.05 [1.53–2.76]
32–35	4004.0	177.0	31.5	4212.5	28.5	5503.5	107.0	18.0	5628.5	12.7	2.28 [1.70–3.06]
36–39	13348.0	182.5	24.5	13555.0	8.5	14165.0	136.0	10.0	14311.0	5.5	1.57 [1.18–2.10]
≥40	714.5	13.5	3.0	731.0	13.3	143.0	14.0	0.0	157.0	44.6	0.29 [0.11–0.78]
	DZ twin deliveries										
<24	55.0	28.0	410.0	493.0	860.0	110.0	36.0	471.0	617.0	792.5	1.61 [1.17–2.22]
24–27	272.0	35.0	28.0	335.0	135.8	498.0	40.0	3.0	541.0	42.5	3.54 [2.10–5.96]
28–31	688.0	54.0	8.0	750.0	46.7	1312.0	60.0	0.0	1372.0	21.9	2.19 [1.33–3.60]
32–35	3709.0	76.0	1.0	3786.0	10.3	7229.0	103.0	0.0	7332.0	7.0	1.47 [0.97–2.23]
36–39	15475.0	102.0	3.0	15580.0	3.5	26623.0	129.0	0.0	26752.0	2.4	1.44 [1.00–2.07]
≥40	839.0	17.0	2.0	858.0	12.2	328.0	8.0	0.0	336.0	11.9	1.03 [0.32–3.28

[1]LB: Live birth, [2]FD: Fetal death, [3]SR per 1000 twin deliveries, CI: Confidence interval

Table 4: Comparison of stillbirth rates (SRs) for monozygotic (MZ) and dizygotic (DZ) twins for 1995–1998 and 2004–2008 according to gestational age (GA).

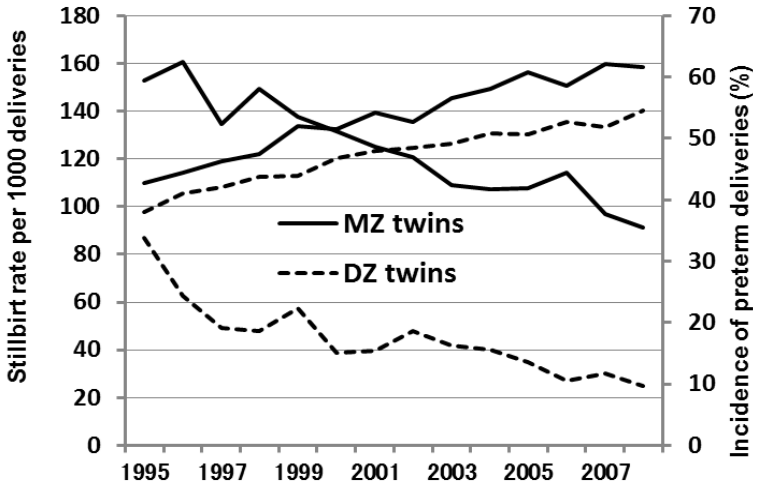

Figure 3: Stillbirth rate at gestational age <37 weeks and incidence of preterm delivery for MZ and DZ twins, 1995–2008.

Birthweight	No. of FD twin pairs			SR per 1000 twin deliveries			Odds ratio [95% CI]		
(g)	MM	FF	MF	MM	FF	MF	MM vs. MF	FF vs. MF	MM vs. FF
<1000	3685.5	1695.5	924.0	700.9	523.2	493.6	2.41 [2.16–2.68]	1.13 [1.01–1.26]	2.14 [1.95–2.34]
1000–1499	122.5	114.0	38.0	41.5	38.0	20.3	2.09 [1.44–3.02]	1.91 [1.31–2.76]	1.10 [0.85–1.42]
1500–1999	117.5	101.0	38.0	13.7	10.3	5.5	2.50 [1.73–3.62]	1.87 [1.29–2.72]	1.34 [1.03–1.75]
2000–2499	90.0	73.0	22.0	3.7	2.8	1.0	3.56 [2.23–5.68]	2.69 [1.67–4.33]	1.33 [0.97–1.81]
≥ 2500	60.0	38.5	12.0	3.2	2.7	0.8	3.93 [2.11–7.31]	3.30 [1.73–6.32]	1.19 [0.79–1.79]
	Odds ratio [95% CI]								
	MM			FF			MF		
<1000	739.2 [569.8–958.9]			412[298.1–569.5]			1208.5 [681.2–2143.8]		
1000–1499	13.7 [10.0–18.7]			14.8[10.3–21.4]			25.7[13.4–48.3]		
1500–1999	4.4 [3.2–6.0]			3.9[2.7–5.7]			6.9[3.6–13.2]		
2000–2499	1.2[0.9–1.6]			1.1[0.7–1.6]			1.3[0.6–6.9]		
≥ 2500	1.0 Reference			1.0 Reference			1.00 Reference		
CI: Confidence interval									

Table 5: Comparisons of stillbirth rates (SRs) for like-sexed and unlike-sexed twins according to birthweight, 1995–2008.

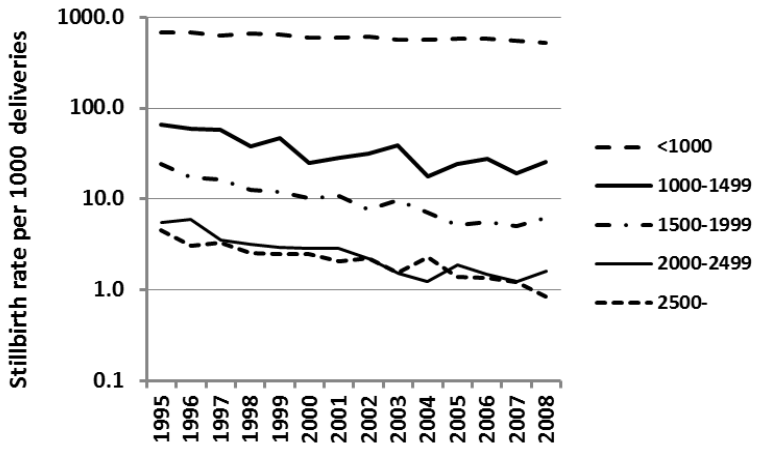

Figure 4: Stillbirth rate of twins (MM, FF, and MF) by birth weight, 1995–2008.

SRs for zygotic twins by intra-pair BWD

Table 6 shows the SRs for the MZ and DZ twins according to intra-pair BWD during the period 1995–2008. Among MZ twins, the proportions of BWD categories for the lowest to the highest were 28%, 24%, 28%, 11%, 5%, and 4%, respectively. The corresponding values among DZ twins were 23%, 24%, 33%, 13%, 4%, and 3%, respectively. The SR for MZ twins was the lowest at BWD 5-9% (40) and increased up to the largest BWD ≥40% (382). The SR of MZ twins was significantly lower in BWD 5-9% than the other BWD categories. On the contrary, the SR was significantly higher at the largest BWD ≥ 40% than at BWD 30-39% (OR, 0.39; 95% CI, 0.35–0.44) and also at the other BWD categories. As for DZ twins, the SRs were similar between BWD <5% and BWD10–19% (16.6-17.6) and significantly increased to BWD 20–29% (20.0) and suddenly increased at the largest BWD category (170). The SR in DZ twins was significantly higher in the largest BWD category than at BWD 30–39% (OR, 0.16; 95% CI, 0.13–0.20) and also at the other BWD categories. The SR was significantly higher in the MZ twins than in the DZ twins at each BWD category.

Cause-specific SR

Table 7 shows cause–specific SRs for MZ and DZ twins during the period 1995–2008. Cause–specific FDs were only limited to spontaneous stillbirth. TTTS only occurs in MZ twins, and the SR was 6.9 which value was 14% among spontaneous still births in MZ twins. The SRs for birth defects were 1.9 for MZ twins and 0.5 for DZ twins, with the rate being significantly higher in the MZ twins. The corresponding SRs for fetal death of unspecified cause (P95) were 24.9 and 8.7, respectively, with the rate also being significantly higher in the MZ twins. The proportions of cause-specific FDs among total FDs in the MZ twins were as follows: 2% were attributable to disorders related to length of gestation and fetal growth (P05–P08), 14% to TTTS, 52% to P95, 4% to birth defects, and 27% for other cause of FDs. The corresponding proportions for DZ twins were 3%, 0%, 59%, 3%, and 35%, respectively.

Discussion

Vital statistics data do not have twin chorionicity. Loos et al. [11] reported that the SR was significantly higher in MZ Mono Chorionic (MC) twins than in DZ twins in Belgium. Glinianaia et al. [12] also reported that MC twins have higher SRs compared with MZ Di Chorionic (DC) twins in England during the period 1998-2007. Increased stillbirth risk in MC compared with DC twins are mainly attributed to twin–twin transfusion syndrome (TTTS) [13-16]. According to Morikawa et al. [17], Japanese women with MC diamniotic twins were 2.2-fold more likely to experience stillbirth than women with DC diamniotic twins during the period 2005–2008.In the present study, 14% of FDs in MZ twins were attributable to TTTS. Sago reported that after laser surgery for TTTS, the fetal survival rate was 81.5% (295/362) [18]. The widespread application of laser surgery for TTTS will reduce the SR among MZ twins.

BWD	MZ twin deliveries						DZ twin deliveries						OR [95% CI]
(%)	2LB[1]	LB-FD	2FD[2]	Total (%)	SR[3]	OR [95% CI]	2LB	LB-FD	2FD	Total (%)	SR	OR [95% CI]	MZ vs. DZ twins
<5	18712	130	840	19682(28)	46.0	1.17 [1.05–1.29]	21252	80	320	21652(23)	16.6	1.00 Reference	2.9 [2.5–3.2]
5–9	16186	129	608	16923(24)	39.7	1.00 Reference	22538	54	378	22970(24)	17.6	1.06 [0.92–1.22]	2.3 [2.0–2.6]
10–19	17954	285	938	19177(28)	56.3	1.44 [1.31–1.59]	30448	112	468	31028(33)	16.9	1.02 [0.89–1.16]	3.5 [3.1–3.9]
20–29	6751	228	691	7670 (11)	105.0	2.83 [2.55–3.15]	11812	128	178	12118(13)	20.0	1.21 [1.02–1.42]	5.8 [5.0–6.7]
30–39	2443	187	521	3151 (5)	195.0	5.85 [5.21–6.58]	3576	114	62	3752 (4)	31.7	1.94 [1.57–2.39]	7.4 [6.0–9.1]
≥40	1222	748	613	2583 (4)	382.1	14.94[13.38–16.69]	1726	630	104	2460 (3)	170.3	12.14[10.47–14.08]	3.0 [2.6–3.4]
[1]LB: Live birth, [2]FD: Fetal death, [3]SR per 1000 twin deliveries, OR: Odds ratio, CI: Confidence interval													

Table 6: Stillbirth rates (SRs) of monozygotic (MZ) and dizygotic (DZ) twins according to intrapairbirthweight discordance (BWD), 1995–2008.

Cause of spontaneous	MZ twin deliveries				DZ twin deliveries				Odds ratio [95% CI]
fetal death (ICD–10th code)	2LB[1]	LB–FD	2FD[2]	SR[3] (%)	2LB	LB–FD	2FD	SR (%)	MZ vs. DZ twins
Disorders related to length of gestation and fetal growth(P05–P08)	–	20.0	56.5	0.98 (2)	–	22.0	30.0	0.44 (3)	2.21 [1.49 –3.26]
Twin–twin transfusion syndrome (TTTS: P50.3)	–	154.5	387.0	6.85 (14)	–	0.0	0.0	0.00 (0)	–
Fetal death of unspecified cause (P95)	–	368.5	1504.0	24.90 (52)	–	330.0	637.0	8.70 (59)	2.91 [2.67 –3.17]
Birth defects (Q00–Q99)	–	80.5	87.5	1.88 (4)	–	62.0	11.0	0.46 (3)	4.14 [2.92 –5.87]
Others	–	228.5	766.5	12.99 (27)	–	143.0	410.0	5.23 (35)	2.51 [2.24 –2.80]
Total	64135.0	852.0	2801.5	47.61 (99)	90490.0	557.0	1088.0	14.83 (100)	3.32 [3.11 –3.54]
[1]LB: Live birth, [2]FD: Fetal death, [3]SR per 1000 twin deliveries, CI: Confidence interval									

Table 7: Cause–specific stillbirth rate (SR) in monozygotic (MZ) and dizygotic (DZ) twins, 1995–2008.

In the present study, the SRs for MZ and DZ twins decreased significantly from 1995 to 2008 where the odds ratios [95% CI] of SRs for MZ vs. DZ twins increased from 2.0 [1.7– 2.4] in 1995 to 4.2 [3.6–5.0] in 2008. Higher SR for MZ than DZ twins was attributable to TTTS and birth defects. BWD as a risk factor contributed to remarkably higher SR in MZ twins than in DZ twins.

Figure 1 shows the SRs for DZ twins and singletons from 1995 to 2008. Data on singletons were obtained from vital statistics in each year from 1995 to 2008 and data on multiple births were obtained from mentioned at the section 'Materials and Methods'. Namely, data on singletons were obtained using two different data sources. The SRs were significantly higher in DZ twins than singletons in 1995 (OR, 1.8, [95% CI, 1.6–2.1]), 1996 (1.3, 1.1–1.6), 1999 (1.4, 1.2–1.6), and 2002 (1.3, 1.1–1.5). The SRs indicated similar values between DZ twins and singleton after 2002. Then the former's medical care may be improved recently in Japan.

The incidence of preterm delivery in industrialized countries has remained 5-10% over the last 30 years [19]. Mercuro et al. reported by a comprehensive literature review that preterm birth and low birth weight contribute towards an increased cardiovascular risk [19]. In the present study, the incidence of preterm delivery in twins was very high for both zygotic twins. Although the incidence increased during the period 1995-2008, the SR decreased for both zygotic twins. Then the higher premature rate in twins might bring severe problems such as cardiovascular risk in the future life in Japanese population.

Acknowledgements

We are grateful to the staff of Statistics and Information Department, Ministry of Health, Labour and Welfare in Japan.

References

1. Barr A, Stevenson Ac (1961) Stillbirths and infant mortality in twins. Ann Hum Genet 25: 131-140.
2. Imaizumi Y, Asaka A, Inouye E (1980) Analysis of multiple birth rates in Japan. II. Secular trend and effect of birth order, maternal age, and gestational age in still birth rate of twins. Acta Geneticae Medicae et Gemellologiae 29: 223-231.
3. Imaizumi Y, Nonaka K (1998) Yearly changes in stillbirth rates of zygotic twins in Japan, 1975-1994. Acta Genet Med Gemellol (Roma) 47: 19-30.
4. Derom C, Derom R (2005) The East Flanders prospective twin survey. In: Multiple Pregnancy, 2nd ed, Editors: Blickstein I, Keith LG. London and New York: Taylor and Francis 39-47.
5. Fellman J, Eriksson AW (2006) Stillbirths in multiple births: test of independence. Twin Res Hum Genet 9: 677-684.
6. Fellman J, Eriksson AW (2007) Estimation of the stillbirth rate in twin pairs according to zygosity. Twin Res Hum Genet 10: 508-513.
7. Hollier LM, McIntire DD, Leveno KJ (1999) Outcome of twin pregnancies according to intrapair birth weight differences. Obstet Gynecol 94: 1006-1010.
8. Demissie K, Ananth CV, Martin J, Hanley ML, MacDorman MF, et al. (2002) Fetal and neonatal mortality among twin gestations in the United States: the role of intrapair birth weight discordance. Obstet Gynecol 100: 474-480.
9. Weinberg W (1901) Beiträge zur Physiologie und Pathologie der Mehrlinggeburten beim Menschen. Pflügers Archive fur die gesamte physiologie de Menschen und der Tiere 88: 346-430.
10. http://apps.who.int/classifications/icd10/browse/2015/en
11. Loos R, Derom C, Vlietinck R, Derom R (1998) The East Flanders Prospective Twin Survey (Belgium): a population-based register. Twin Res 1: 167-175.
12. Glinianaia SV, Obeysekera MA, Sturgiss S, Bell R (2011) Stillbirth and neonatal mortality in monochorionic and dichorionic twins: a population-based study. Hum Reprod 26: 2549-2557.
13. Minakami H, Honma Y, Matsubara S, Uchida A, Shiraishi H, et al. (1999) Effects of placental chorionicity on outcome in twin pregnancies. A cohort study. J Reprod Med 44: 595-600.
14. Acosta-Rojas R, Becker J, Munoz-Abellana B, Ruiz C, Carreras E, et al. (2007) Twin chorionicity and the risk of adverse perinatal outcome. Int J Gynaecol Obstet 96: 98-102.
15. Hack KE, Derks JB, Elias SG, Franx A, Roos EJ, et al. (2008) Increased perinatal mortality andmorbidity in monochorionic versus dichorionic twin pregnancies:clinical implications of a large Dutch cohort study. BJOG 115: 58 – 67.
16. Ortibus E, Lopriore E, Deprest J, Vandenbussche FP, Walther FJ, et al. (2009) The pregnancy and long-term neurodevelopmental outcome of monochorionic diamniotic twin gestations: a multicenter prospective cohort study from the first trimester onward. Am J Obstet Gynecol 200: 494.
17. Morikawa M, Yamada T, Yamada T, Sato S, Cho K, et al. (2012) Prospective risk of stillbirth: monochorionic diamniotic twins vs. dichorionic twins. J Perinat Med 40: 245-249.
18. Sago H (2008) Fetoscopic laser photocoagulation for TTTS. Ninsanpushi 60:282–287.(In Japanede)
19. Mercuro G, Bassareo PP, Flore G, Fanos V, Dentamaro I, et al. (2013) Prematurity and low weight at birth as new conditions predisposing to an increased cardiovascular risk. Eur J Prev Cardiol 20: 357-367.