Journal of Neonatal Biology
ISSN: 2167-0897

Imaizumi and Hayakawa, J Neonatal Biol 2015, 4:3
DOI: 10.4172/2167-0897.1000188

Research Article Open Access

Perinatal Mortality Rates and Risk Factors for Mortality among Zygotic Twins and Singletons in Japan, 1995-2008

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Abstract

Objective: We aimed to determine the perinatal mortality rates (PMRs) for monozygotic (MZ) twins, dizygotic (DZ) twins, and singletons, together with the associated risk factors for these PMRs.

Study design: PMRs of zygotic twins and singletons were estimated using Japanese vital statistics from 1995 to 2008.

Results: Declines were seen in fetal death rates [FDRs; defined as deaths after a gestational age of (GA) 22 weeks], early neonatal death rates (ENDRs), and PMRs from 1995 to 2008 to approximately 1/4–1/3 for DZ twins and to 1/2 for both MZ twins and singletons. ENDRs and PMRs were the lowest at maternal ages (MAs) of 30–34 years for MZ and DZ twins and at 25–29 years for singletons. Each mortality rate in singletons was significantly lower at 25–29 years compared with those at other MAs. PMRs were significantly higher for MZ and DZ twins than for singletons in each MA group, except when MA was ≥40 years for DZ twins. PMR was the lowest at GA of 37 weeks for both MZ (6.6) and DZ (3.0) twins but was the lowest at GA of ≥40 weeks in singletons (1.1). PMRs were higher for both MZ and DZ twins than for singletons, except for GA of <36 weeks. PMR was significantly higher for MZ twins than for DZ twins for all GAs, except when GA was ≥39 weeks. The recent increase in preterm birth (i.e., GA of <37 weeks, excluding fetuses delivered at GA of <22 weeks) was associated with a reduction in PMRs for both MZ and DZ twins.

Conclusion: In this Japanese population, PMRs decreased for zygotic twins and singletons between 1995 and 2008. The most marked decline was for DZ twins.

Keywords: Perinatal mortality rate; Zygotic twins; Singletons; Maternal age; Gestational age; Preterm birth

Introduction

Research has shown that perinatal mortality rates (PMRs) have decreased for both singletons and twins [1-4]. Moreover, studies have demonstrated that maternal age (MA) [3], gestational age (GA) [2-5], birth weight (BW) [2-3], BW discordance (BWD) [6-8], zygosity [9], and chorionicity [5, 10-13] are important risk factors that affect PMR.

In Japan, the fetal death rate (FDR; defined as death after GA of ≥22 weeks) decreased significantly between 1980/81 and 1998 [3]. During this period, FDRs for monozygotic (MZ) and dizygotic (DZ) twins decreased from 73 to 32 per 1000 twin deliveries and from 33 to 10 per 1000 twin deliveries, respectively [3]. However, there is no information on early neonatal deaths (ENDs) and PMRs for zygotic twins and singletons in Japan.

This study aimed to estimate PMRs for MZ twins, DZ twins, and singletons between 1995 and 2008 and to identify risk factors associated with perinatal mortality.

Materials and Methods

Data sources

Data on live births (LBs), fetal deaths (FDs), and ENDs for twins were obtained from statistical records between 1995 and 2008. We used the records maintained by the Statistics and Information Department, Ministry of Health, Labour and Welfare (Tokyo, Japan) that covered the entire Japanese population. LB certificates included details about the nationality, sex, date of birth, BW, and GA, as well as the ages and dates of birth of parents and dates of birth, whether the birth was single or multiple, and the birth order in multiple births. FD certificates were provided for deaths occurring at ≥12 completed gestational weeks and mostly contained the same information, including the date, but excluding the dates of parents' births. ENDs refer to deaths of live-born babies before the first week of life. Infant death certificates contained the same information as the LB and FD certificates; however, they excluded paternal age. PMR included all FDRs from 22 completed weeks of gestation and over (i.e., FDR for GA of ≥22 weeks) and all ENDs. Data for singleton births (males and females) were obtained using the vital statistics records [14].

Describing twin data

Twin pairs at delivery were described as LB–LB (2LB), FD–FD (2FD), and LB–FD. The 2LB and 2FD cases were obtained from the LB and FD records, respectively, while the LB–FD cases were obtained from the LB and FD records that excluded 2LB and 2FD twin pairs. We identified 99.99% of the 166,690 twin pairs (including unknown sexes) during the study period.

Data for ENDs were obtained from twin pairs of 2LBs (2LB–2END or 2LB–END) and LB–FD (LB–END). The number of MZ and DZ twins was estimated using the Weinberg method [15]. MA and GA were 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 included odd numbers of twins in some cases. All rates are presented

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Received July 22, 2015; **Accepted** August 19, 2015; **Published** August 26, 2015

Citation: Imaizumi Y, Hayakawa K (2015) Perinatal Mortality Rates and Risk Factors for Mortality among Zygotic Twins and Singletons in Japan, 1995-2008. J Neonatal Biol 4: 188. doi:10.4172/2167-0897.1000188

as those per 1000 deliveries or LBs, as appropriate. Statistical analyses were performed with SPSS software (Version 22; SPSS, Chicago, IL).

Results

Yearly changes in PMRs for zygotic twins and singletons

Table 1 shows the yearly change in FDR, ENDR, and PMR for MZ and DZ twins between 1995 and 2008. For MZ and DZ twins, each death rate significantly decreased every year during the study period. By 2008, each mortality rate declined to approximately half of the 1995 value for MZ twins, but this decrease was to a third or a quarter of the initial value for DZ twins. FDRs and PMRs were also significantly higher for MZ twins than DZ twins in each year. However, ENDRs were only significantly higher for MZ twins than for DZ twins in eight years (1995, 1996, 1999, 2000, 2003, 2005, 2007, and 2008).

Table 2 shows the yearly changes in FDR, ENDR, and PMR for singletons during the study period. Each mortality rate significantly decreased every year during this period. By 2008, each mortality rate declined to approximately half of the 1995 value. Each year, the mortality rates were significantly higher for MZ twins and DZ twins than for singletons, and all mortality rates decreased every year.

PMRs in zygotic twins and singletons by MA

Table 3 shows FDRs, ENDRs, and PMRs for zygotic twins by MA group during the study period. FDR for MZ twins was the highest for MA of ≥ 40 years, followed by MA of <20 years and was lowest for MA of 35–39 years where the rate was significantly lower than MA of 20–24 years. The highest FDR for DZ twins was at MA of <20 years and the lowest was at MA 30–34 years where the rate was significantly lower than the rates for MAs of 20–24 years, 25–29 years, and 35–39 years. FDR was significantly higher for MZ twins than for DZ twins in each MA group, except when MA was <20 years. As for ENDRs, the highest rates were the youngest MA groups for both zygotic twins. The lowest rates occurred at MA of 30–34 years for MZ twins and the oldest MA groups for DZ twins. ENDR was significantly higher for MZ twins than for DZ twins in each MA group except MA of <20 years and MA of

Year	Twin pairs of FDs	FDR	Twin pairs of ENDs	ENDR	Twin pairs of PDs	PMR	Twin pairs of LBs	Twin pairs of LBs & FDs	Odds ratio [95% CI] : MZ vs. DZ twins		
Monozygotic twins									FDR	ENDR	PMR
1995	167.5	33.5	60.5	12.5	228.0	45.6	4831.5	4999.0	2.13* [1.63-2.79]	1.50* [1.01-2.22]	1.92* [1.53-2.40]
1996	161.8	31.6	58.5	11.8	220.3	43.0	4958.5	5120.3	2.47* [1.86-3.28]	1.96* [1.27-3.03]	2.32* [1.83-2.94]
1997	152.5	29.8	41.5	8.4	194.0	37.9	4963.5	5116.0	3.21* [2.33-4.41]	1.25 [0.80-1.96]	2.40* [1.86-3.10]
1998	161.8	32.2	45.5	9.3	207.3	41.2	4866.5	5028.3	3.12* [2.32-4.21]	1.43 [0.92-2.21]	2.48* [1.94-3.17]
1999	136.5	27.7	49.5	10.3	186.0	37.7	4791.0	4927.5	2.25* [1.69-2.99]	2.48* [1.53-4.01]	2.32* [1.81-2.96]
2000	105.3	21.8	49.0	10.4	154.3	31.9	4733.0	4838.3	1.89* [1.40-2.54]	2.54* [1.58-4.07]	2.06* [1.61-2.65]
2001	110.5	23.5	30.0	6.5	140.5	29.9	4585.0	4695.5	2.75* [1.99-3.79]	1.48 [0.89-2.47]	2.33* [1.78-3.05]
2002	118.0	24.5	34.0	7.2	152.0	31.6	4695.0	4813.0	3.34* [2.42-4.63]	1.23 [0.78-1.94]	2.42* [1.87-3.13]
2003	107.5	22.8	37.5	8.1	145.0	30.7	4610.5	4718.0	3.06* [2.21-4.23]	2.00* [1.24-3.24]	2.70* [2.06-3.53]
2004	86.8	19.3	27.0	6.1	113.8	25.3	4405.5	4492.3	2.45* [1.76-3.39]	1.35 [0.82-2.23]	2.05* [1.56-2.70]
2005	92.3	20.4	42.5	9.6	134.8	29.9	4420.0	4512.3	3.49* [2.43-5.02]	3.52* [2.07-6.00]	3.52* [2.60-4.75]
2006	93.8	21.3	19.0	4.4	112.8	25.6	4317.0	4410.8	3.50* [2.46-4.97]	1.07 [0.61-1.90]	2.53* [1.89-3.39]
2007	95.8	21.1	27.5	6.2	123.3	27.1	4446.5	4542.3	4.04* [2.78-5.89]	1.72* [1.01-2.95]	3.11* [2.30-4.22]
2008	82.5	18.5	22.0	5.0	104.5	23.5	4366.5	4449.0	3.52* [2.37-5.24]	2.20* [1.14-4.24]	3.13* [2.23-4.40]
Dizygotic twins											
1995	79.5	16.0	43.0	8.8	122.5	24.7	4883	4962.5			
1996	70.0	13.0	32.0	6.0	102.0	19.0	5297	5367.0			
1997	51.5	9.5	36.0	6.7	87.5	16.1	5375	5426.5			
1998	60.0	10.5	37.0	7.4	97.0	17.0	5639	5699.0			
1999	75.5	12.5	25.0	4.2	100.5	16.7	5958	6033.5			
2000	77.5	11.6	27.0	4.1	104.5	15.7	6579	6656.5			
2001	57.5	8.7	29.0	4.4	86.5	13.1	6559	6616.5			
2002	53.5	7.5	42.0	5.9	95.5	13.3	7120	7173.5			
2003	56.0	7.6	30.0	4.1	86.0	11.6	7346	7402.0			
2004	62.0	8.1	35.0	4.5	97.0	12.5	7699	7761.0			
2005	43.5	6.0	20.0	2.7	63.5	8.7	7276	7319.5			
2006	47.0	6.2	31.0	4.1	78.0	10.2	7567	7614.0			
2007	38.5	5.3	26.0	3.6	64.5	8.9	7229	7267.5			
2008	35.0	5.4	15.0	2.3	50.0	7.6	6523	6558.0			

Linear regression coefficient (p-value) of FDR, ENDR, and PMR on the year:			
	FDR	ENDR	PMR
MZ twins	–1.11 (<0.001)	–0.49 (<0.001)	–1.58 (P<0.001)
DZ twins	–0.72 (<0.001)	–0.36 (P<0.001)	–1.04 (P<0.001)

FD: Fetal deaths (22 weeks of gestation and over); FDR: Fetal death rate per 1000 births;
ENDR: Early neonatal death rate per 1000 live births (LBs);
PMR: Perinatal mortality rate (PMR) per 1000 births

Table 1: Fetal deaths rate (≥ 22 weeks of gestation), early neonatal death rate, and perinatal mortality rate in zygotic twins, 1995-2008.

Year	Singletons								Odds ratio [95% CI] for PMR	
	No. of FDs	No. of ENDs	No. of PDs	FDR	ENDR	PMR	LBs	LBs&FDs	MZ twins vs. Singletons	DZ twins vs. Singletons
1995	5992	1586	7578	5.11	1.36	6.46	1166596	1172588	7.40* [6.47–8.40]	3.86* [3.22–4.63]
1996	5789	1521	7310	4.86	1.28	6.14	1185052	1190841	7.28* [6.35–8.35]	3.14* [2.58–3.82]
1997	5502	1412	6914	4.68	1.21	5.88	1170040	1175542	6.66* [5.76–7.70]	2.77* [2.24–3.43]
1998	5291	1427	6718	4.46	1.21	5.66	1181098	1186389	7.55* [6.56–8.69]	3.04* [2.48–3.72]
1999	5069	1323	6392	4.37	1.15	5.51	1155131	1160200	7.08* [6.10–8.22]	3.06* [2.51–3.73]
2000	4905	1308	6213	4.19	1.12	5.30	1166926	1171831	6.18* [5.25–7.27]	2.99* [2.46–3.64]
2001	4698	1174	5872	4.08	1.02	5.10	1147496	1152194	6.02* [5.08–7.14]	2.59* [2.09–3.20]
2002	4541	1195	5736	4.01	1.06	5.06	1129250	1133791	6.41* [5.46–7.55]	2.65* [2.16–3.25]
2003	4221	1114	5335	3.83	1.01	4.84	1098800	1103021	6.52* [5.52–7.71]	2.42* [1.95–3.00]
2004	3980	1017	4997	3.65	0.94	4.59	1085564	1089544	5.64* [4.67–6.80]	2.75* [2.24–3.36]
2005	3707	936	4643	3.56	0.90	4.46	1038400	1042107	6.88* [5.78–8.18]	1.96* [1.52–2.51]
2006	3668	917	4585	3.42	0.86	4.28	1068135	1071803	6.11* [5.05–7.38]	2.41* [1.92–3.02]
2007	3499	920	4419	3.27	0.86	4.13	1065737	1069236	6.72* [5.61–8.06]	2.16* [1.69–2.76]
2008	3447	849	4296	3.21	0.79	4.01	1068797	1072244	5.98* [4.91–7.28]	1.91* [1.44–2.53]
Linear regression coefficients (p-value) of FDR, ENDR, and PMR on the year:										
	FDR		ENDR		PMR					
	–0.14 (<0.001)		–0.04 (P<0.001)		–0.18 (P<0.001)					

FDs: Fetal deaths (22 weeks of gestation and over); FDR: Fetal death rate per 1000 births (LBs and FDs);
ENDR: Early neonatal death rate per 1000 live births (LBs); PMR: Perinatal mortality rate per 1000 births

Table 2: Fetal death rate (≥22 weeks of gestation), early neonatal death rate, and perinatal mortality rates in singletons, 1995-2008.

Maternal age	2FD	LB-FD	Pairs of FD	2LB-2END	2LB-END	LB-END	Pairs of ENDs	Pairs of PM	2LB	LB-FD*	FDR	ENDR	PMR
	Monozygotic twins												
<20	17.0	22.0	28.0	4.5	10.0	3.0	11.0	39.0	920.0	22.0	29.2	11.8	40.7
20-24	140.0	218.0	249.0	28.5	92.0	24.0	86.5	335.5	8276.0	219.5	28.8	10.3	38.9
25-29	295.5	625.5	608.3	70.5	195.0	57.0	196.5	804.8	23161.0	633.5	25.3	8.4	33.4
30-34	267.5	583.0	559.0	61.0	160.0	58.0	170.0	729.0	22590.5	591.5	23.8	7.4	31.1
35-39	93.0	205.5	195.8	26.0	64.0	23.0	69.5	265.3	8129.5	206.5	23.2	8.4	31.5
≥40	15.5	36.0	33.5	2.0	13.0	4.0	10.5	44.0	1058.0	37.0	30.2	9.8	39.6
	Dizygotic twins												
<20	4.0	4.0	6.0	2.0	2.0	0	3.0	9.0	359.0	4.0	16.3	8.3	24.5
20-24	36.0	61.0	66.5	12.0	34.0	0	29.0	95.5	5210.0	62.0	12.5	5.5	18.0
25-29	92.0	309.0	246.5	50.0	172.0	12.0	142.0	388.5	25667.0	317.0	9.5	5.5	14.9
30-34	84.0	432.0	300.0	35.0	232.0	12.0	157.0	457.0	38905.0	445.0	7.6	4.0	11.6
35-39	46.0	250.0	171.0	17.0	136.0	6.0	88.0	259.0	18324.0	260.0	9.2	4.8	13.9
≥40	3.0	31.0	18.5	2.0	12.0	0	8.0	26.5	2025.0	32.0	9.0	3.9	12.9

	Monozygotic twins: Odds ratio [95% CI]			Dizygotic twins: Odds ratio [95% CI]			Odds ratio [95% CI]:MZ vs. DZ twins		
	FDR	ENDR	PMR	FDR	ENDR	PMR	FDR	ENDR	PMR
<20	1.09 [0.85-1.89]	1.60 [0.87-2.96]	1.32 [0.95-1.84]	2.17 [0.96-4.90]	2.08 [0.66-6.55]	2.14* [1.10-4.18]	1.81 [0.74-4.41]	1.43 [0.40-5.14]	1.69 [0.81-3.51]
20-24	1.25* [1.03-1.51]	1.39* [1.07-1.81]	1.26*[1.10-1.44]	1.65* [1.27-2.16]	1.38 [0.93-2.05]	1.56* [1.25-1.95]	2.34* [1.78-3.07]	1.87* [1.23-2.86]	2.21* [1.75-2.78]
25-29	1.09 [0.93-1.28]	1.13 [0.92-1.39]	1.08 [0.97-1.19]	1.24* [1.05-1.47]	1.37* [1.09-1.72]	1.29* [1.13-1.48]	2.71* [2.34-3.15]	1.53* [1.23-1.90]	2.29* [2.02-2.58]
30-34	1.03 [0.87-1.21]	1.00 : Reference	1.00 : Reference	1.00 : Reference	1.00 : Reference	1.00 : Reference	3.19* [2.77-3.67]	1.86* [1.49-2.31]	2.74* [2.43-3.08]
35-39	1.00 : Reference	1.14 [0.86-1.51]	1.01 [0.88-1.17]	1.21* [1.001-1.46]	1.19 [0.92-1.54]	1.20* [1.03-1.40]	2.57* [2.09-3.16]	1.78* [1.30-2.44]	2.30* [1.94-2.74]
≥40	1.31 [0.90-1.90]	1.32 [0.70-2.46]	1.29 [0.94-1.75]	1.18 [0.74-1.89]	0.98 [0.48-1.99]	1.11 [0.75-1.65]	3.43* [1.94-6.09]	2.50 [0.99-6.30]	3.17* [1.94-5.16]

FD: Fetal deaths (22 weeks of gestation and over); FD*: Fetal deaths (12 weeks of gestation and over); LB: Livebirths; FDR: Fetal deaths rate per 1000 births
ENDR; Early neonatal death rate per 1000 live births (LBs); PMR: Perinatal mortality rate per 1000 births

Table 3: Fetal death rate (≥22 weeks of gestation), early neonatal death rate, and perinatal mortality rate in zygotic twins by maternal age, 1995-2008.

≥ 40 years. The highest PMRs were the youngest MA groups, and the lowest rates were at MA of 30–34 years for both zygotic twins. PMR was significantly higher for MZ twins than for DZ twins in each MA group, except for the MA group of <20 years.

Table 4 shows FDRs, ENDRs, and PMRs for singletons according to MA during the study period. Each mortality rate was the highest at MA of ≥ 40 years and was the lowest at MA of 25–29 years; each mortality rate was significantly lower at MA of 25–29 years compared with those at other MAs.

Figure 1 shows PMR by MA for MZ twins, DZ twins, and singletons during the study period. With one exception, PMR was significantly higher for MZ and DZ twins than for singletons in each MA group. At MA of ≥ 40 years in the DZ twin cohort, PMRs were similar between DZ twins and singletons [odds ratio, 1.1 (95% confidence interval: 0.7–1.6)].

	FDs	ENDs	PDs	FDR	ENDR	PMR	LBs	LBs & FDs	Odds ratio [95% CI]		
MA									**FDR**	**ENDR**	PMR
<20	1774	352	2126	7.19	1.44	8.61	245082	246856	2.00* [1.91-2.10]	1.54* {1.39-1.72]	1.91* [1.83-2.00]
20–24	8713	2129	10842	4.05	0.99	5.04	2140676	2149389	1.13* [1.10–1.16]	1.07* [1.02–1.12]	1.11* [1.09–1.14]
25–29	20920	5389	26309	3.60	0.93	4.53	5789957	5810877	1.00: Reference	1.00: Reference	1.00: Reference
30–34	20774	5588	26362	3.81	1.03	4.83	5436770	5457544	1.06* [1.04–1.08]	1.10* [1.06–1.15]	1.07* [1.05–1.09]
35–39	9835	2596	12431	5.22	1.39	6.60	1873647	1883482	1.45* [1.42–1.49]	1.49* [1.42–1.56]	1.46* [1.43–1.49]
≥40	2281	591	2872	9.39	2.46	11.82	240697	242978	2.62* [2.51–2.74]	2.64* [2.43–2.88]	2.63* [2.53–2.73]
GA											
<24	12470	1770	14240	735.22	421.13	839.57	4203	16961	4113* [3929–4306]	1803* [1676–1939]	4851* [4625–5088]
24–27	14590	2291	16881	365.50	91.21	422.89	25118	39918	534* [517–551]	249* [235–264]	679* [658–701]
28–31	9674	1778	11452	145.47	31.32	172.21	56771	66502	252* [243–262]	80* [75–85]	193* [187–199]
32–35	9992	2789	12781	37.46	10.87	47.92	256691	266708	58* [56–60]	27* [26–29]	47* [45–48]
36–39	12872	5298	18170	1.38	0.57	1.95	9306743	9319643	2.05* [1.98–2.12]	1.41* [1.35–1.48]	1.81* [1.76–1.86]
≥40	4098	2449	6547	0.67	0.40	1.08	6070945	6075048	1.00: Reference	1.00: Reference	1.00: Reference

Singletons (males and females); FDs: Fetal deaths (22 weeks of gestation and over); FDR: Fetal death rate per 1000 births; ENDR: Early neonatal death rate per 1000 live births (LBs); PMR: Perinatal mortality (PM) rate per 1000 births

Table 4: Fetal death rate (≥22 weeks of gestation), early neonatal death rate, and perinatal mortality rate in singletons according to maternal age (MA) and gestational age (GA), 1995-2008 period.

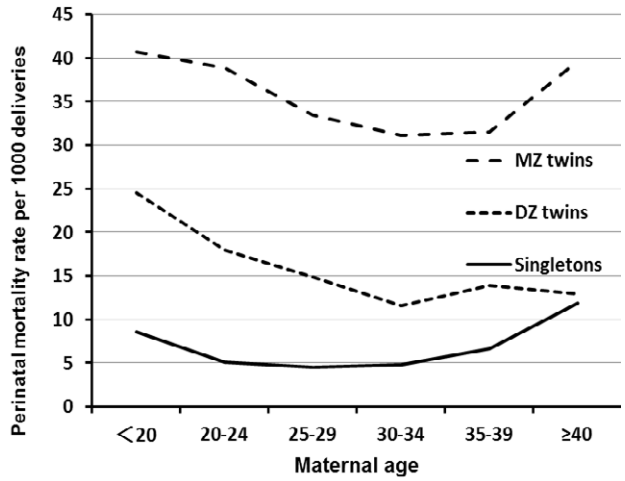

Figure 1: Perinatal mortality rate per 1000 deliveries in MZ twins, DZ twins, and singletons by maternal age, 1995–2008. Odds ratio (95%CI) for DZ twins vs. singletons is 1.1 (0.7–1.6) at maternal age ≥40 years.

PMRs for zygotic twins and singletons by GA

Table 5 shows FDRs, ENDRs, and PMRs for zygotic twins by GA during the study period. FDR for MZ twins was 665 per 1000 twin deliveries at GA of <24 weeks but decreased with increasing GA to 37 weeks (5.7). However, FDR at 37 weeks' GA was significantly lower than that at <36 weeks and ≥ 40 weeks. FDR for DZ twins was 419 at GA of <24 weeks and decreased with increasing GA to 37 weeks (1.7), when FDR was significantly lower than that for other GA groups. ENDR for MZ twins was 581 for GA of <24 weeks and decreased with increasing GA to 37 weeks (0.8) and was significantly lower at 37 weeks than at either <36 weeks or at 38-39 weeks. In DZ twins, ENDR was 333 at GA of <24 weeks and decreased with increasing GA up to 39 weeks (0.7) before increasing by ≥ 40 weeks (4.3). ENDR at 39 weeks' GA was significantly lower than at either <36 weeks or ≥ 40 weeks. PMR for MZ twins was 859 at GA of <24 weeks and decreased with increasing GA to 37 weeks (6.6). The rate for DZ twins was 612 for GA of <24 weeks and decreased with increasing GA to 37 weeks (3.0). PMR for DZ twins was significantly lower at GA of 37 weeks than in the other GA groups but was significantly higher for MZ twins than for DZ twins per GA group, except for GA of ≥ 39 weeks.

Table 4 also shows FDRs, ENDRs, and PMRs for singletons according to GA group during the study period. All rates were significantly lower at GA of ≥ 40 weeks compared with those at other GAs.

Figure 2 shows PMR by GA for MZ twins, DZ twins, and singletons during the study period. PMRs were higher for singletons than for either the MZ or DZ twin cohorts between GA of <24 weeks and 32–35 weeks, but these PMRs were reversed at GA of 36–39 weeks and at GA of ≥ 40 weeks.

Rate of preterm birth

Table 6 shows the preterm birth rates for MZ twins, DZ twins, and singletons during the study period. The preterm birth rate included all births with GA of <37 weeks and were calculated after excluding fetuses that had been delivered at GA of <22 weeks. For MZ twins, the rate was 44% in 1995 and gradually increased to 62% in 2008. For DZ twins, the corresponding rates were 39% and 55%. The rates for singletons were 4.6% in 1999 and 4.9% in 2008. The recent increase in preterm birth was associated with reduced PMRs for MZ and DZ twins.

Among the perinatal deaths during the study period, the preterm birth rate was 89% (1968.1/2216.2) for MZ twins and 83% (1020.5/1233) for DZ twins (data in Table 5).

Discussion

PMR was 6-fold higher for twins than for singletons in Japan between 1980 and 1991 [16]. In the present study, we showed that the relative risk of PMR for MZ twins versus singletons was 7-fold (45.6/6.46) higher than that of singletons in 1995 and that this risk decreased to 5.9-fold (23.5/4.01) in 2008; these relative risks were 3.8-fold (24.7/6.46) and 1.9-fold (7.6/4.01) for DZ twins versus singletons in 1995 and 2008, respectively. The relative risk of PMR increased 2- to 3-fold between MZ and DZ twins during the study period. PMR was markedly improved for DZ twins than for MZ twins and singletons. As for FDRs, declines to approximately 1/4–1/3 for DZ twins and to 1/2 for both MZ twins and singletons were seen during the study period. Imaizumi [3] estimated FDRs for zygotic twins from 1980–1981 to 1998. However, ENDRs and PMRs for zygotic twins were estimated for the first time in the present study.

Gestational age	2FD	LB-FD	Pairs of FDs	2LB-2END	2LB-END	LB-END	Pairs of ENDs	Pairs of PM	2LB	LB-FD*	FDR	ENDR	PMR	Odds ratio [95% CI]							
														FDR		ENDR		PMR		MZ vs. DZ (PMR)	
Monozygotic twins																					
<24	311.5	36.5	329.8	71	24.0	27.0	96.5	426.3	138	56.5	664.8	580.5	859.4	345*	[263-451]	1646*	[910-2977]	926*	[678-1264]	3.87*	[2.84-5.27]
24	108.5	64.5	140.8	30.0	22.0	18.0	50.0	190.8	174	64.5	405.6	242.4	549.7	119*	[89-158]	381*	[209-692]	185*	[140-244]	3.25*	[2.34-4.52]
25	80.5	57.0	109.0	21.5	48.0	17.0	54.0	163.0	271	57.0	266.8	180.3	399.0	63*	[47-85]	262*	[146-470]	101*	[77-132]	2.96*	[2.12-4.14]
26	57.0	73.0	93.5	14.0	47.0	19.0	47.0	140.5	369	72.0	187.8	116.2	282.1	40*	[30-54]	156*	[87-282]	50*	[46-78]	2.78*	[1.94-3.99]
27	45.0	82.5	86.3	18.5	33.0	21.0	45.5	131.8	497	82.5	138.1	84.5	211.0	28*	[21-38]	110*	[61-198]	41*	[31-53]	2.47*	[1.74-3.52]
28	24.0	105.5	76.8	10.5	52.0	15.0	44.0	120.8	650	105.5	98.5	62.6	154.9	19*	[14-26]	79*	[44-144]	28*	[21-36]	2.69*	[1.85-3.92]
29	28.0	107.0	81.5	5.0	33.0	8.0	25.5	107.0	650	107.0	103.9	36.3	136.4	20*	[15-27]	45*	[24-85]	24*	[18-31]	2.89*	[1.97-4.23]
30	17.0	106.0	70.0	4.0	26.0	5.0	19.5	89.5	840	106.0	72.7	21.8	93.0	14*	[10-19]	27*	[14-52]	16*	[12-21]	1.86*	[1.29-2.68]
31	27.0	102.5	78.3	2.0	33.0	4.0	20.5	98.8	1166	102.5	60.4	16.8	76.3	11*	[8-15]	20*	[10-40]	13*	[10-17]	2.66*	[1.82-3.88]
32	22.0	113.5	78.8	1.5	30.0	4.0	18.5	97.3	1757	113.5	41.6	10.2	51.4	8*	[6-10]	12*	[6-24]	8*	[6-11]	2.19*	[1.51-3.16]
33	20.5	97.5	69.3	3.0	25.0	5.0	18.0	87.3	2337	97.5	28.2	7.5	35.5	5*	[4-7]	9*	[5-18]	6*	[4-7]	2.58*	[1.74-3.81]
34	11.0	96.0	59.0	0.0	38.0	2.0	20.0	79.0	3829	96.0	15.0	5.2	20.1	2.7*	[1.9-3.7]	6*	[3-12]	3.1*	[2.3-4.1]	1.64*	[1.17-2.32]
35	18.0	143.0	89.5	4.0	31.0	8.0	23.5	113.0	6692	143.0	13.1	3.5	16.5	2.3*	[1.7-3.1]	4*	[2-8]	2.5*	[2.0-3.3]	2.18*	[1.61-2.95]
36	15.5	171.0	101.0	3.0	33.0	5.0	22.0	123.0	13981	171.0	7.1	1.6	8.7	1.25	[0.95-1.64]	1.86	[0.97-3.59]	1.33*	[1.03-1.71]	1.86*	[1.43-2.42]
37	19.0	167.5	102.8	0.5	24.0	5.0	15.0	117.8	17775	167.5	5.7	0.8	6.6	1.00	:Reference	1.00	:Reference	1.00	:Reference	2.22*	[1.69-2.92]
38	16.0	88.0	60.0	2.0	19.0	5.0	14.0	74.0	7697	88.0	7.7	1.8	9.5	1.35	[0.98-1.85]	2.16*	[1.04-4.47]	1.45*	[1.08-1.94]	1.83*	[1.30-2.57]
39	3.0	47.0	26.5	0.0	13.0	1.0	7.0	33.5	3176	47.0	8.2	2.2	10.4	1.44	[0.94-2.21]	2.61*	[1.06-6.40]	1.59*	[1.08-2.34]	1.57	[0.95-2.58]
≥40	4.0	31.5	19.8	1.0	4.0	0.0	3.0	22.8	1262	31.5	15.2	2.3	17.5	2.7*	[1.7-4.4]	2.80	[0.81-9.68]	2.7*	[1.7-4.3]	0.96	[0.57-1.64]
Dizygotic twins																					
<24	182.0	61.0	212.5	77.0	28.0	14.0	98.0	310.5	246	97.0	419.1	332.8	612.4	413*	[299-570]	721*	[226-2293]	532*	[405-699]		
24	32.0	27.0	45.5	14.0	40.0	6.0	37.0	82.5	243	27.0	150.7	144.2	273.2	102*	[67-154]	244*	[75-796]	126*	[91-175]		
25	23.0	31.0	38.5	6.0	36.0	4.0	26.0	64.5	298	31.0	109.4	82.9	183.2	70*	[46-108]	131*	[39-434]	76*	[54-106]		
26	5.0	41.0	25.5	6.0	32.0	0.0	22.0	47.5	338	41.0	66.4	61.4	123.7	41*	[25-66]	94*	[28-317]	48*	[33-69]		
27	5.0	43.0	26.5	6.0	28.0	2.0	21.0	47.5	438	43.0	54.5	45.7	97.7	33*	[21-54]	69*	[21-233]	36*	[25-52]		
28	6.0	35.0	23.5	0.0	32.0	0.0	16.0	39.5	578	35.0	38.0	26.9	63.8	23*	[14-37]	40*	[12-137]	23*	[16-34]		
29	2.0	46.0	25.0	2.0	24.0	0.0	14.0	39.0	704	46.0	33.2	19.3	51.9	20*	[12-32]	28*	[8-99]	18*	[13-27]		
30	0.0	61.0	30.5	2.0	28.0	2.0	17.0	47.5	848	61.0	33.6	19.4	52.3	20*	[13-31]	29*	[8-97]	19*	[13-27]		
31	0.0	58.0	29.0	2.0	16.0	0.0	10.0	39.0	1236	58.0	22.4	7.9	30.1	13*	[8-21]	12*	[3-42]	10*	[7-15]		
32	0.0	59.0	29.5	0.0	24.0	0.0	12.0	41.5	1657	59.0	17.2	7.1	24.2	10*	[6-16]	10*	[3-37]	8*	[6-12]		
33	1.0	45.0	23.5	0.0	26.0	0.0	13.0	36.5	2541	45.0	9.1	5.1	14.1	5.3*	[3.2-8.5]	7*	[2-26]	5*	[3-7]		
34	2.0	87.0	45.5	0.0	24.0	0.0	12.0	57.5	4583	87.0	9.7	2.6	12.3	5.6*	[3.8-8.4]	3.8*	[1.1-13.3]	4*	[3-6]		
35	0.0	81.0	40.5	0.0	54.0	0.0	27.0	67.5	8756	81.0	4.6	3.1	7.6	2.6*	[1.8-4.0]	4.5*	[1.4-14.7]	3*	[2-4]		
36	3.0	112.0	59.0	0.0	82.0	0.0	41.0	100.0	21228	112.0	2.8	1.9	4.7	1.6*	[1.1-2.3]	2.8	[0.9-9.0]	1.6*	[1.2-2.1]		
37	2.0	102.0	53.0	1.0	70.0	2.0	37.0	90.0	30275	102.0	1.7	1.2	3.0	1.00	:Reference	1.8	[0.5-5.7]	1.00	:Reference		
38	0.0	94.0	47.0	0.0	24.0	0.0	12.0	59.0	11217	94.0	4.2	1.1	5.2	2.4*	[1.6-3.5]	1.5	[0.4-5.5]	1.8*	[1.3-2.5]		
39	0.0	52.0	26.0	0.0	6.0	0.0	3.0	29.0	4311	52.0	6.0	0.7	6.6	3.4*	[2.1-5.5]	1.00	:Reference	2.3*	[1.5-3.4]		
≥40	2.0	49.0	26.5	2.0	12.0	0.0	8.0	34.5	1847	49.0	14.0	4.3	18.2	8.1*	[5.1-13.0]	6.2*	[1.6-23.4]	6.2*	[4.2-9.3]		

FD: Fetal death (22 weeks of gestation and over); FD*: Fetal deaths (12 weeks of gestation and over); LB: Livebirth; FDR: Fetal death rate per 1000 births ENDR; Early neonatal death rate per 1000 live births (LBs); PMR: Perinatal mortality rate per 1000 births

Table 5: Fetal deaths rate at 22 weeks of gestation and over, early perinatal death rate, and perinatal mortality rate in zygotic twins by gestational age, 1995-2008.

Loos et al. [10] reported that the stillbirth rate was significantly higher for MZ monochorionic (MC) twins than for DZ twins in Belgium. Unfortunately, the data available to us did not include details of twin chorionicity, which precludes direct comparison. Glinianaia et al. [13] also reported that MC twins have higher stillbirth rates compared with MZ dichorionic (DC) twins in England for the period between 1998 and 2007.

The increased risk of stillbirth in MC twins than DC twins has been primarily attributed to twin–twin transfusion syndrome (TTTS) [11-13, 17,18]. In addition, Morikawa et al. [19] reported that Japanese women with MC, diamniotic twins were 2.2-fold more likely to experience stillbirth than those who had DC, diamniotic twins between 2005 and 2008. Imaizumi and Hayakawa [20] also reported that 14% of stillbirths in MZ twins were attributed to TTTS and that 4% of stillbirths were due to birth defects, whereas the corresponding vales in DZ twins were 0% and 3%, respectively, between 1995 and 2008. In the present study, PMRs for MZ and DZ twins significantly decreased between 1995 and 2008, and the rate was significantly higher for MZ twins than for DZ twins every year. The higher PMR for MZ twins than DZ twins could be attributed to the higher rates of TTTS and birth defects.

In a comprehensive literature review, Mercuro et al. [21] reported that preterm birth and low BW contributed to an increase in cardiovascular risk in later life. Although preterm birth rates increased by 18% for MZ twins and by 16% for DZ twins from 1995 to 2008, PMR decreased for both MZ and DZ twins. As for singletons, preterm birth rates increased by only 0.3% from 1999 to 2008. It is therefore plausible that the higher rate of prematurity in twins increases the risk of late-life complications, such as cardiovascular risk, in this group than in singletons.

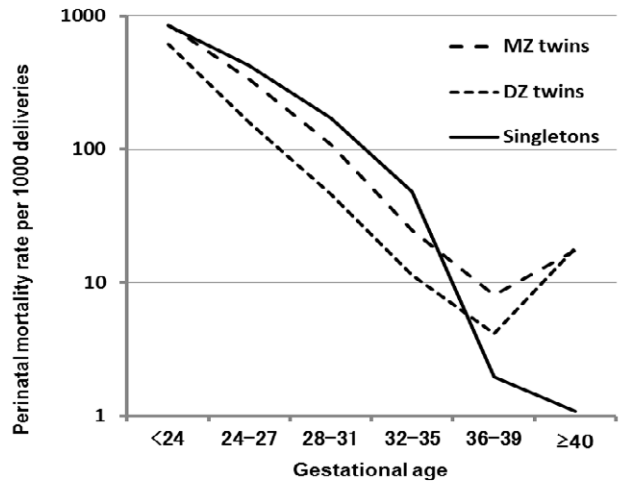

Figure 2: Perinatal mortality rate per 1000 deliveries in MZ twins, DZ twins and singletons by gestational age, 1995–2008.

Year	Twin pairs or singletons of LBs and FDs (<37 weeks)			Rates of preterm birth (%)		
	MZ twins	DZ twins	Singletons	MZ twins	DZ twins	Singletons
1995	2210.0	1914.5	–	44.2	38.6	–
1996	2339.3	2241.0	–	45.7	41.8	–
1997	2431.0	2303.5	–	47.5	42.5	–
1998	2453.5	2522.0	–	48.8	44.3	–
1999	2611.0	2680.5	53653	53.0	44.4	4.6
2000	2528.8	3132.5	55955	52.3	47.1	4.8
2001	2581.0	3192.5	53897	55.0	48.3	4.7
2002	2571.0	3497.5	53081	53.5	49.8	4.7
2003	2702.5	3658.0	52166	57.3	49.4	4.7
2004	2634.3	3973.0	52210	58.7	51.2	4.8
2005	2768.3	3714.5	49842	61.3	50.8	4.8
2006	2612.8	4020.0	51443	59.2	52.8	4.8
2007	2841.8	3780.5	52169	62.6	52.0	4.9
2008	*2762.5*	*3581.0*	*52499*	*62.1*	*54.6*	*4.9*
Linear regression coefficients (p-value) of preterm birth rates for MZ twins, DZ twins and singletons on the year:						
MZ twins		*DZ twins*		*singletons*		
1.43 (<0.001)		*0.49 (<0.001)*		*0.026 (0.006)*		

LBs: Live births, FDs: Fetal deaths (≥ 22 weeks of gestation),
Rates of preterm birth (< 37 weeks): Nos. of preterm births divided by nos. of LBs and FDs.

Table 6. Rates of preterm birth in zygotic twins and singletons, 1995–2008.

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