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## Multiple Births and Congenital Anomalies in Tokyo Metropolitan Hospitals, 1979-1990

K. Kato<sup>1</sup>, K. Fujiki<sup>2</sup>

<sup>1</sup>Department of Neurology, Tokyo Metropolitan Institute for Neuroscience; <sup>2</sup>Department of Ophthalmology, Juntendo University School of Medicine, Tokyo, Japan.

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**Abstract.** The rate of multiple births and the incidence of congenital anomalies in Tokyo Metropolitan Hospitals were studied during the period 1979-1990. The number of twins was 968 pairs (8.23 per 1,000 deliveries) and of triplets 18 sets (15.3 per 100,000 deliveries) among 117,672 deliveries including 1,587 stillbirths after 16 weeks gestation. Multiple birth rates increased yearly. Stillbirth rates in twins and triplets were 5.5% and 16.7% respectively, which were both significantly higher than that in singletons (1.3%). The number of congenital anomalies was 42 in 1,936 twins (2.17%), 2 in 54 triplets (3.7%) and 1721 in 116,686 singletons (1.47%). The most common defects in twins were those of the cardiovascular system (0.72% in twins vs 0.52% in singletons) and of the musculoskeletal system (0.72% in twins vs 0.50% in singletons), followed by upper respiratory tract and/or mouth conditions (0.67% in twins vs 0.35% in singletons), all of which had no significant difference in frequency between twins and singletons. Though some anomalies had a significantly higher frequency in twins than in singletons, the concordance rate in the like-sexed twins was very low.

**Key words:** Multiple birth, Congenital anomaly, Birth defect monitoring, Hospital base

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### INTRODUCTION

The study of twins is helpful in separating genetic factors from environmental influences in the etiology of birth defects, because each pair of twins has a similar intrauterine environment, and monozygotic twins (MZ) are also genetically identical, but dizygotic twins (DZ) are siblings.

We have monitored all deliveries in Tokyo Metropolitan Hospitals (TMH) since April, 1978. The present study is a report of the rate of multiple births and the incidence of congenital anomalies in TMH during the period 1979-1990.

## MATERIALS AND METHODS

Data on 968 twin pairs and 18 sets of triplets were obtained from among 117,672 deliveries (including 1,587 stillbirths) after 16 weeks gestation at TMH during the 12 year period, 1979-1990. In order to collect the data, one of the authors (Kato) visited the hospitals at intervals of one or two month(s). Gestational age (weeks), order of birth, birth-weight, maternal age, congenital anomalies of new-born babies and other relative data were carefully registered by the author. The definition of congenital anomaly and criteria for selection was the presence of a gross physical or anatomic developmental anomaly at birth or detected during the first week of life. Kato et al [5] reported details of the monitoring system employed at TMH.

## RESULTS

Table 1 shows secular changes in the rate of multiple births from 1979 to 1990, where the total number of twins was 968 pairs (8.23 per 1,000 deliveries) and triplets, 18 sets (15.29 per 100,000 deliveries). The twinning rates gradually increased from 6.70 per

**Table 1 - Secular changes of twin and triplet birth rates at Tokyo Metropolitan Hospitals, 1979-1990.**

Year	Total deliveries	N. Twins					Twinning rate			Triplets	
		MM	FF	MF	UK	Total	MZ per 1,000	DZ	Total	sets	/100,000
1979	12383	28	33	22	-	83	3.15	3.55	6.70	1	8.07
1980	11186	31	36	24	-	91	3.84	4.29	8.14	3	26.81
1981	10884	39	35	23	1	98	4.69	4.23	9.00	1	9.18
1982	10561	30	25	12	1	68	4.07	2.27	6.44	0	-
1983	10213	39	29	7	1	76	5.97	1.37	7.44	1	9.79
1984	10431	40	29	13	-	82	5.37	2.49	7.86	1	9.58
1985	10467	39	37	14	-	90	5.92	2.68	8.60	1	9.55
1986	10078	30	31	15	2	78	4.56	2.98	7.74	2	19.84
1987	9242	29	30	19	-	78	4.33	4.11	8.44	3	32.46
1988	8435	29	29	19	3	80	4.62	4.51	9.48	2	23.71
1989	7104	28	30	12	-	70	6.48	3.38	9.85	1	14.07
1990	6688	22	34	16	2	74	5.98	4.78	11.06	2	29.90
<b>Total</b>	<b>117672</b>	<b>384</b>	<b>378</b>	<b>196</b>	<b>10</b>	<b>968</b>	<b>4.81</b>	<b>3.33</b>	<b>8.23</b>	<b>18</b>	<b>15.29</b>

1,000 deliveries in 1979 to 11.06 in 1990. The twinning rates by zygosity were estimated by Weinberg's differential method, resulting in MZ and DZ twinning rates of 4.8 and 3.3 per 1,000 deliveries, respectively.

Table 2 shows the stillbirth rates according to sex. The stillbirth rate was 5.5% in twins, 16.7% in triplets and 1.30% in singletons, showing a significant difference between multiple births and single births.

**Table 2 - Stillbirth rate in singleton, twin and triplet births.**

	Sex	No. births	Livebirths	Stillbirths	Stillbirth rate (%)	
Singleton	Male	59795	59016	779	1.30	**
	Female	56721	56199	522	0.92	
	Unknown	170	—	170	—	
	Total	116686	115215	1471	1.26	
Twins	Male	967	910	57	5.89	ns
	Female	954	919	35	3.67	
	Unknown	15	—	15	—	
	Total	1936	1829	107	5.53	**
Triplets	Male	29	23	6	20.69	ns
	Female	25	22	3	12.00	
	Unknown	—	—	—	—	
	Total	54	45	9	16.67	**
Total	Male	60791	59949	842	1.39	**
	Female	57700	57140	560	0.97	
	Unknown	185	—	185	—	
	Total	118676	117089	1587	1.34	

\*\* : p < 0.01  
 ns: not significant

Table 3 shows the incidence of congenital anomalies as 1.47% in 116,686 singletons, 2.17% in 1,936 twins and 3.70% in 54 triplets. While the incidence of anomaly was significantly higher in twins than in singletons, there were no significant differences between the twins and triplets, or between the singletons and triplets.

Table 4 shows the incidence of each anomaly in twins and triplets. As for singletons, only those anomalies observed also in multiple births were shown.

**Table 3 - Incidence of congenital anomalies in singleton, twin and triplet births.**

	Sex	No. births	No. anomalies	Incidence %		No. symptoms	Incidence per 1000 births
Singleton	Male	59795	946	1.58	*]	1270	21.2
	Female	56721	769	1.36		1053	18.6
	Unknown	170	6	3.53	20	117.6	
	Total	116686	1721	1.47	2343	20.1	
Twins	Male	967	21	2.17	ns]	27	27.9
	Female	954	20	2.10		33	34.6
	Unknown	15	1	6.67	1	66.7	
	Total	1936	42	2.17	61	31.5	
Triplets	Male	29	2	6.90	ns]	7	241.4
	Female	25	—	—		—	—
	Unknown	—	—	—	—	—	
	Total	54	2	3.70	7	129.6	

\*:p&lt;0.05

ns: not significant

Table 5 shows the concordance of anomalies in like-sexed and unlike-sexed multiple births. The rate of concordance of anomalies was very low, 9.1% in like-sexed twins, 0% in unlike-sexed twins and 0% in triplets.

## DISCUSSION

Multiple birth rates in Tokyo have gradually increased year by year as shown in Table 1. This tendency is similar to that recorded for overall rates in Japan [2-4]. The twinning rate was 8.23 per thousand and the triplet rate 152.9 per million deliveries. These values were higher than those of the 1990 nationwide survey in Japan [3, 4] where the twinning rate was 7.00 per 1,000 deliveries and the triplet rate was 121.4 per million births. These facts would seem to bias data because it could be that pregnant women diagnosed prenatally as multiple births would choose such a public hospital as TMH.

As regards anomalies, the most common defects found in twins were in the cardiovascular and musculoskeletal systems, followed by those of the digestive system, which were the same as those in the singletons. Integumentary system defects were 20.7 per 1,000 deliveries in twins, which was significantly higher than that in singletons. Hay and Wehrung [1] in a survey of approximately 2,000 twins among 96,000 livebirths reported a substantially higher incidence of anencephaly, hydrocephaly and congenital heart disease in like-sexed twin pairs compared to unlike-sexed pairs or singletons. Given the relatively high incidence yet low concordance of anencephaly, hydrocephaly, and congenital

Table 4 - Congenital anomalies among multiple births.

Organ/system Anomalies	ICD-code	Twins No.	(per 10000)	Triplets No.	(per 10000)	Singletons No.	(per 10000)
Nervous system		4	(20.7)			174 <sup>+</sup>	(14.9)
Anencephaly	740.0	3	(15.5)			86	(7.4)
Congenital hydrocephaly	742.3	1	(5.2)			21	(1.8)
Ear, face and neck		7	(36.2)			216 <sup>+</sup>	(18.5)
Malformed or lowset ear	744.2	5	(25.8)**			32	(2.7)
Auricular fistula	744	2	(10.3)			72	(6.2)
Cardiovascular system		14	(72.3)			611 <sup>+</sup>	(52.4)
Tetralogy of fallot	745.2	1	(5.2)			16	(1.4)
Ventricular septum defect	745.4	4	(20.7)			211	(18.1)
Pulmonary stenosis	747.3	1	(5.2)			18	(1.5)
Congenital heart disease	—	8	(41.3)			252	(21.6)
Digestive system		13	(67.1)			402 <sup>+</sup>	(34.5)
Cleft palate	749.0	2	(10.3)			73	(6.3)
Cleft lip	749.1	1	(5.2)			60	(5.1)
Cleft palate with cleft lip	749.2	3	(15.5)			89	(7.6)
Tracheo-esophageal fistula	750.3a	1	(5.2)*			8	(0.7)
Esophageal atresia	750.3a	2	(10.3)**			16	(1.4)
Atresia ani	751.2c	3	(15.5)*	1	(185.2)	56	(4.8)
Fistula recto-labialis	751.5	1	(5.2)*			2	(0.2)
Genital system		1	(5.2)			96 <sup>+</sup>	(8.2)
Retentio testis ★	752.5	1	(5.2)			6	(0.5)
Musculoskeletal system		14	(72.3)			587 <sup>+</sup>	(50.3)
Scoliosis	754.2	1	(5.2)**			1	(0.1)
Polydactyly	755.0	2	(10.3)			107	(9.2)
Syndactyly	755.1	2	(10.3)			45	(3.9)
Hypodactyly	755.2	1	(5.2)			29	(2.5)
Clavicula defect	755.5	2	(10.3)**			3	(0.3)
Cleft hand	755.5	1	(5.2)**			5	(0.4)
Campodactyly	755.5	1	(5.2)*			7	(0.6)
Supernumerary vertebra	756.1	1	(5.2)**			1	(0.1)
Exomphalos or gastroschisis	756.7	3	(15.4)**			35	(3.0)
Integumentary system		4	(20.7)**			67 <sup>+</sup>	(5.7)
Epidermal nevus	757.3	1	(5.2)			16	(1.4)
Congenital alopecia	757.4	2	(10.3)**			1	(0.1)
Others	757.8	1	(5.2)**			1	(0.1)
Other and unspecified		3	(15.5)			93 <sup>+</sup>	(8.0)
Acardius acephalus	759.8	1	(5.2)			—	
Micrognathia	524.0	2	(10.3)**			25	(2.1)
<b>Total anomalies</b>		<b>61</b>	<b>(315.1)</b>			<b>2343</b>	<b>(200.8)</b>
Syndrome							
Down syndrome	758.0	1	(5.2)			125	(10.7)
Epidermal nevus syndrome	759.6	1	(5.2)			6	(0.5)
Goltz syndrome	759.8	2	(10.3)			—	
Multiple anomalies	759.7	8	(41.3)	1	(185.2)	224	(19.2)
<b>Total syndrome</b>		<b>12</b>	<b>(62.0)</b>	<b>1</b>	<b>(185.2)</b>	<b>460</b>	<b>(39.4)</b>

★: Per 10,000 male births

\*: P&lt;0.05, \*\*: P&lt;0.01 (significance level between twins and singletons)

†: Total number of anomalies in singletons including those not listed in this table.

Table 5 - Concordance of congenital anomalies in multiple births.

	Sex	Pairs or Sets	Concordant	Discordant	Total
Twins	Like-sexed	762	3*(9.1%)	30 (90.9%)	33
	Unlike-sexed	196	—	8 (100%)	8
	Unknown	10	—	1	1
	Total	968	3 (7.1%)	39 (92.9%)	42
Triplets	Like-sexed	11	—	1 (100%)	1
	Unlike-sexed	7	—	1	1
	Total	18	— (0%)	2 (100%)	2

- \* 1) M and M, Micrognathia, malformed ear, low-set ear.  
 2) F, Cleft palate.  
 F, Cleft palate, VSD, atresia ani, anorectal anomalies, supernumerary vertebra.  
 3) F, Goltz syndrome (congenital alopecia, clavicular defect).  
 F, Goltz syndrome (congenital alopecia, clavicular defect, polydactyly, cleft hand, single umbilical artery).

heart disease in like-sexed twins, they concluded that placental conditions may play an important role in the occurrence of these anomalies. Myrianthopoulos [7] showed also that among 53,257 singletons and 1,195 twin individuals, the frequency of cardiovascular, alimentary tract, liver and spleen anomalies was significantly higher in twins than in singletons. From a population survey, Layde et al [6] reported the overall rate of malformed infants, as well as the incidence of several specific defects, to be higher for twins than for singletons. In the present study, the rate of anomalies in like-sexed and unlike-sexed twins was 4.3% (33/762) and 4.1% (8/196), respectively, and 9.1% (1/11) in like-sexed and 14.3% (1/7) in unlike-sexed triplets. The concordance rate was 9.1% in like-sexed and 0% in unlike-sexed twins and 0% in triplets. Although the sample size is too small to offer conclusions, these facts may indicate that environmental factors are more important than genetic components to the etiology of congenital anomalies.

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**Correspondence:** Keiko Fujiki, Ph.D. Department of Ophthalmology, Juntendo University School of Medicine, 3-1-3 Hongo, Bunkyo-ku, Tokyo 113, Japan.