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Fetal Deaths with Birth Defects Among Japanese Multiples, 1974

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Abstract. Source of data is “Survey on Socio-Economic Aspects of Vital Events – Plural Births in 1975”, including 12,392 twin pairs, 124 triplet sets, 7 quadruplet sets and 1 quintuplet set. Fetal deaths were 3,285 for twins, 141 for triplets, 17 for quadruplets, and 5 for quintuplets, among which the numbers of birth defects were 78, 3, 0, and 0, respectively. Concordant twin pairs with the same category of birth defect were 20 among 56 pairs (0.36). As for the remaining 36 pairs, 2 pairs had different category of birth defects, 27 pairs had liveborn cotwins, and 7 pairs were both fetal deaths among which a twin had birth defect. The second-born twins had birth defects more frequently than the first-born twins among fetal deaths (28 vs 6).

Key words: Birth defects, Fetal deaths, Twins, Triplets

INTRODUCTION

It is well known that the incidence of birth defects is about 1% at birth. The rate is higher in twins than single births [15], either live birth [14], or fetal death [9,15]. However, if twins and nontwins share a common etiology of birth defects, twin studies may shed light on the genetic contribution in the etiology of birth defects, and in fact twin concordance rates have been reported for several birth defects [1,3-5,15].

The present study deals with the incidence of birth defects among fetal deaths in twins and higher multiples. It also deals with the twin concordance rate of birth defects.

MATERIALS AND METHODS

Source of data is the “Survey on Socio-Economic Aspects of Vital Events – Plural Births in 1975 ” [13]. This consists of two surveys, A and B. In the present study, only Survey A was used, which includes data on 12,392 twin pairs, 124 sets of triplets, 7 sets of quadruplets, and 1 set of quintuplets, derived from certificate records of live births and fetal deaths (after the beginning of the fourth month of fetal life) for all of Japan in 1974. Items included in Survey A and analysed are sex, survival states, type of plural births and classified causes of fetal death. Details of the survey have been reported elsewhere [2,10].

RESULTS

Fetal Deaths with Birth Defects in Twins

As for the survival states of twins at birth there are four types: both live birth, first-born live birth and second-born fetal death, first-born fetal death and second-born live birth, and both fetal death. The corresponding numbers of twin pairs in 1974 were 10,418, 515, 148, and 1,311, respectively [2]. Then, among 24,784 twin births, 3,285 were fetal deaths, 1,459 first-born and 1,826 second-born. Table 1 shows concordance and dis-

Table 1 - Twin concordance and discordance for fetal death with birth defects, Japan 1974

1st-born P list ^a	2nd-born									p67	LB ^b	Total
	p69	p71	p72	p73	p74	p75	p77	p79	p80			
p69	4											4
p71		3								1	1	5
p72											1	1
p73				1							1	2
p74							1				1	2
p75												0
p77							1					1
p79								3	1			
p80										8	1	9
p38										1		1
p40	1											1
p66										1		1
p68	1							1	1			3
LB ^b	6	8		1		1		1	5			22
Total	12	11	0	2	0	1	2	5	17	1	5	56

^a For P list numbers, see Appendix.

^b LB: Live birth.

Table 2 - Classification of twin pairs by birth defects and sex, 1974

P list number	Concordant				Discordant								Total	Pairwise concordant rate
	MM	FF	MF	??	MM*	M*M	FF*	F*F	M*F	F*M	??*	?*?		
p69	2	2	0	0	0	5	0	2	1	0	0	0	12	0.33
p71	2	1	0	0	1	3	1	4	0	1	0	0	13	0.23
p72	0	0	0	0	0	0	1	0	0	0	0	0	1	0
p73	0	1	0	0	1	0	0	1	0	0	0	0	3	0.33
p74	0	0	0	0	1	0	0	0	0	0	1 ^a	0	2	0
p75	0	0	0	0	0	0	0	1	0	0	0	0	1	0
p77	1	0	0	0	0	0	0	0	0	0	0	1 ^a	2	0.50
p79	2	1	0	0	0	1	0	0	0	0	1 ^b	1	6	0.50
p80	2	3	1	2	0	2	1	3	0	0	0	4 ^b	18	0.44

M*: unaffected male; F*: unaffected female; ?*: unaffected unknown sex.

^a One twin pair has p74 and p77.

^b One twin pair has p79 and p80.

cordance according to the category of birth defects which is indicated by P list numbers. There were a total of 56 twin pairs with birth defects. Twenty-two pairs had both birth defects. Among them, two pairs had different categories of birth defects, one pair p74 (congenital anomalies of respiratory system) and p77 (congenital anomalies of musculoskeletal system), and the other pair p79 (other congenital syndromes affecting multiple systems) and p80 (other and unspecified congenital anomalies). Among discordant pairs, 6 first-born and 28 second-born twins had birth defects. Therefore, the second-born twins were indicated to have birth defects more frequently than the first-born twins. The overall incidence of birth defects was 2.4% (78/3,285) among twin fetal deaths, where the rate was 2.0% (34/1,663) for males, 2.4% (32/1,356) for females and 4.5% (12/266) for sex unknown. The difference between sexes is not significant.

Table 2 shows the category of birth defects and sex of twins. The sex of twins was ascertained for 48 of the 56 pairs. The number of like-sexed pairs was 45 and that of unlike-sexed pairs 3. Twenty of the 56 pairs (36%) were concordant and had the same category of birth defects, where the concordance rates were 38% (17/45) in like-sexed twins, 33% (1/3) in unlike-sexed twins, and 25% (2/8) in unknown-sexed twins. As to neural tube defects, the concordance rates were 33% (4/12) for anencephalus (p69) and 23% (3/13) for congenital hydrocephalus (p71). These defects accounted for 41% (32/78) of total fetal deaths with birth defects. Rates of anencephalus and congenital hydrocephalus were both 0.49% (16/3,285) among twin fetal deaths.

Fetal Deaths with Birth Defect in Triplets and Higher Multiples

Table 3 shows data on two sets of triplets. In case 1, two triplet girls were fetal deaths and had the same category of birth defect (P79: other congenital syndromes affecting multiple systems), whereas a triplet girl was live birth and no information was available

Table 3 - Survival states, sex and cause of death in two cases of triplets, 1974

Triplets	Case 1			Case 2		
	1st-born	2nd-born	3rd-born	1st-born	2nd-born	3rd-born
Survival states	LB	FD	FD	FD	FD	FD
Sex	F	F	F	US	US	US
P list number	-	p79	p79	p69	p67	p67

LB: Live birth; FD: Fetal death; US: Sex unknown.

as to the presence or absence of birth defect. In case 2, all triplets were sex unknown, one being anencephalus and the other two fetal deaths with P67 (maceration). The incidence of birth defects was 2.1% (3/141) among triplet fetal deaths. Corresponding rates were zero in quadruplets (0/17) and zero in quintuplets (0/5).

DISCUSSION

In 1974, the overall proportion of unlike-sexed twin births was 16% (1,974/12,250) in Japan [10], and the value in the present study was 6.3% (3/48). The difference between the two values is statistically significant at the 0.1% level. The frequency of birth defects was significantly higher in monozygotic (MZ) than in dizygotic (DZ) twins [1,15]. Since like-sexed pairs include both MZ and DZ twins, the deficiency of unlike-sexed twins in the present study may be attributed to the higher incidence of birth defects in MZ twins.

In the present study, the incidence of birth defects was similar in twins (2.4%) and in triplets (2.1%), whereas the rate was zero in quadruplets and in quintuplets. On the other hand, according to the annual volume, "Vital Statistics of Japan in 1974" [12], the overall incidence of birth defects was 2.3% (2,507/107,816) among total fetal deaths attended by physicians, being similar to the rates in twins and triplets.

According to Imaizumi [6,8], the concordance rates of twins were 8.3% (9/109) for anencephalus and 15% (16/107) for congenital hydrocephalus. In the present study, the sample size was small, and the corresponding rates were 33% and 23%, respectively, higher than the previous study. Overall rates were 0.84% (921/109,738) for anencephalus [11] and 0.27% (293/109,738) for congenital hydrocephalus [7] among fetal deaths in 1974. In the present study, corresponding rates in twin fetal deaths were both 0.49%. Among fetal deaths, the rate of anencephalus was significantly higher in the general population than in twins, whereas the opposite appeared for the rate of congenital hydrocephalus.

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Appendix

P List Numbers and International Classification of Diseases (ICD) Codes^a

P list	Causes of death	ICD codes
p69	Anencephalus	740
p71	Congenital hydrocephalus	742
p72	Other congenital anomalies of central nervous system and eye	743,744
p73	Congenital anomalies of circulatory system	746,747
p74	Congenital anomalies of respiratory system	748
p75	Congenital anomalies of digestive system	749-751
p77	Congenital anomalies of musculoskeletal system	754-756
p79	Other congenital syndromes affecting multiple systems	759.0-759.2 759.4-759.9
p80	Other and unspecified congenital anomalies	745,757,758
p38	Hydramnions	769.2
p40	Multiple pregnancy	769.4
p66	Other conditions of fetus	778.9
p67	Maceration	779.0
p68	Other fetal death of unknown cause	779.9

^a Included in cause of death in this study.