



Acta Genet Med Gemellol 41: 197-203 (1992)
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Seventh International Congress
on Twin Studies

Perinatal Mortality and Prevalence of Major Congenital Malformations of Twins in Taipei City

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Abstract. In order to examine perinatal mortality and prevalence of major congenital malformations in twins, deliveries in four teaching hospitals in Taipei City were studied. Among a total of 73,264 deliveries from October 1985 to June 1989, there were 844 pairs of twins. The zygosity of the twin pairs was determined by sex, placentation and 12 red blood cell antigens. There were 482 MZ and 252 DZ twin pairs identified, but the zygosity of a further 110 twin pairs was indeterminable due to lack of information on placentation and/or blood types. A total of 4,573 singletons delivered in one study hospital from July 1986 to June 1987 were also studied as controls. The perinatal mortality rate was 7.5% for MZ twins, 1.4% for DZ twins, and 0.7% for singletons. The concordance rate of perinatal death was significantly higher in MZ (60%) than in DZ (0%) twins. The prevalence of major congenital malformations was 2.7% for MZ twins, 1.0% for DZ twins, and 0.6% for singletons. The concordance rate of major congenital malformations was 18% for MZ twins, but no DZ pair was concordant in any major congenital malformation. The concordance rate of facial clefts was 29% for MZ twins. There were 2 sets of conjoined twins giving a prevalence rate of 2.7 per 100,000 deliveries. These findings showing the prevalence of perinatal mortality and major congenital malformation to be highest in MZ twins, intermediate in DZ twins and lowest in singletons, suggest the importance of intrauterine environments in the determination of perinatal mortality and congenital malformations.

Key words: Perinatal mortality, Congenital malformation, Conjoined twins, Chinese.

INTRODUCTION

Despite continuing improvements in both prenatal and neonatal care twin fetuses and neonates still have a higher mortality rate than singletons. The main contributor to this

elevated death rate is prematurity and its complications. Although there have been several studies on the perinatal mortality of Caucasian, African and Japanese twins [1-3,6,11,13,20,24,25,27,28,30], until now data were not available for Chinese twins in Taiwan.

Although the prevalence and concordance rate of congenital malformations in twins vary greatly between studies, twin births are known to have a higher prevalence of anomalies than singleton births [17]. MZ twins have a higher prevalence and concordance of congenital malformations than DZ twins [5,8,21-23,29]. In a previous study in Taiwan, twins were reported to have a higher prevalence of congenital malformations (2.3%) than singletons (1.3%) [12]. This prevalence was not further analyzed for MZ and DZ twins separately, nor was the concordance between cotwins studied.

The present study was carried out to examine the perinatal mortality and prevalence of major congenital malformations among MZ and DZ twins and singletons, and to compare the concordance rate of perinatal deaths and major congenital malformations between MZ and DZ twins.

MATERIALS AND METHODS

Twin subjects were recruited from four teaching hospitals in Taipei City including the National Taiwan University Hospital, McKay Memorial Hospital, Taipei Municipal Maternal and Child Hospital, and the National Nursing School Hospital between October 1985 and June 1989. During this study period, a total of 73,264 deliveries including 844 twin births took place. The zygosity of the twin pairs was determined by sex, placentation and red blood cell antigens including A,B,C,D,E, c,e,M,N, Le^a, Le^b, and P₁. Monochorionic twin pairs as well as dichorionic same-sexed twin pairs with concordant red blood cell antigens were regarded as MZ. Different-sexed twin pairs and dichorionic same-sexed twin pairs with one or more discordant blood types were classified as DZ. Among the 844 twin pairs studied there were 482 MZ and 252 DZ pairs thus classified. The zygosity of the remaining 110 twin pairs was indeterminable due to lack of information on placentation, red blood types, or both.

To compare the perinatal mortality and prevalence of major congenital malformations between twins and singletons, 4,573 singletons delivered in Taipei Municipal Maternal and Child Hospital between July 1986 and June 1987 were also studied. Congenital malformations of twin and singleton neonates were diagnosed by well trained neonatologists according to a structured check list. Both major and minor malformations were examined, but only major malformations were analyzed. These major malformations included anencephaly, meningocele, congenital hydrocephaly, crumples auricle, depressed nasal bridge, cleft lip, cleft palate, cleft lip with cleft palate, congenital heart disease, imperforated anus, hypospadias, polydactyly, syndactyly, club foot, Down's syndrome, ambiguous external genitalia, and conjoined twins.

Information on perinatal deaths was extracted from medical records or obtained through telephone and home-visit interviews. Perinatal mortality was calculated by dividing the sum of stillbirths (gestational age greater than 28 weeks) and neonatal deaths which occurred within 7 days after birth by the number of total livebirths as defined by the World Health Organization.

RESULTS

The perinatal mortality rates of twins and singletons are shown in Table 1. The rates were 7.5%, 1.4% and 0.7%, respectively, for MZ twins, DZ twins and singletons. Compared with singletons, MZ and DZ twins had a much higher perinatal mortality rate with a relative risk factor of 10.0 and 1.9, respectively. There were 45 MZ and 7 DZ twin pairs where at least one cotwin had died perinatally. The concordance rate of perinatal death was 60% (27/45) for MZ twins and 0% (0/7) for DZ twins.

Table 1 - Perinatal mortality rate and relative risk of MZ and DZ twins and singletons

	Total	Deaths	Mortality	
			Rate	Relative risk
MZ twins	964	72	7.5%	10.0
DZ twins	504	7	1.4%	1.9
Singletons	4573	34	0.7%	1.0

The prevalence of major congenital malformations in twins and singletons is shown in Table 2. The prevalence was 2.7%, 1.0% and 0.6%, for MZ twins, DZ twins and singletons respectively. Compared to singletons, MZ and DZ twins had a much higher prevalence of major congenital malformations with a relative risk factor of 4.6 and 1.7, respectively. Twenty-two MZ and 5 DZ twin pairs had at least one cotwin affected with major congenital malformations. The concordance rate for major congenital malformations was 18% (4/22) for MZ twins and 0% (0/5) for DZ twins. The prevalence of selected major malformations in twins is shown in Table 3. The prevalence of anencephaly, meningocele and congenital hydrocephaly was 69.7, 69.7 and 139.5 per 100,000 twins, respectively. For cleft lip, cleft palate, and cleft lip with cleft palate the prevalence was 69.7, 348.7 and 209.2 per 100,000 twins, respectively. Seven MZ twin pairs had at least one cotwin affected with facial clefts, while none of DZ twins were affected with the diseases. The concordance rate of facial clefts was 29% (2/7) for MZ twins. Of the 73,264 deliveries in the four study teaching hospitals, there were 2 sets of conjoined twins. This gave a prevalence rate of 2.7 per 100,000 deliveries.

Table 2 - Prevalence of major congenital malformations and relative risk of MZ and DZ twins and singletons

	Total	Deaths	Major malformations	
			Prevalence	Relative risk
MZ twins	964	26	2.7%	4.6
DZ twins	504	5	1.0%	1.7
Singletons	4573	27	0.6%	1.0

Table 3 - Prevalence (per 100,000 deliveries) of selected malformations in twins

Selected malformations	Prevalence
<i>Head and central nervous system</i>	
Anencephaly	69.7
Menigocele	69.7
Congenital hydrocephaly	139.5
<i>Facial clefts</i>	
Cleft lip	69.7
Cleft palate	348.7
Cleft lip and cleft palate	209.2

DISCUSSION

It has been reported that twins have a perinatal mortality rate at least three times higher than that of singletons. In the UK, 2% of births and 9% of perinatal deaths were twins [3], the perinatal mortality rate was higher in MZ than in DZ twins and higher in males than in females [28]. A similar difference in perinatal mortality between twins and singletons was also observed in other countries, eg. three times greater in twins than singletons in the USA [11], four times in Nigeria [24] and nearly six times in Scotland [27]. In this study, perinatal mortality was about eight times higher in twin (5.4%) than in singleton (0.7%) births. Here the higher twin-singleton difference in perinatal mortality may be attributable to the higher MZ/DZ ratio of twin births.

Many studies have shown a higher perinatal mortality rate among MZ than DZ twins [2,11,13,28,30] and among same-sexed rather than different-sexed twins [6,28]. In this study, MZ twins had a perinatal mortality of (7.5%) ie. about 5 times that of DZ twins (1.4%). The difference between MZ and DZ twins may be because MZ twins have a less advantageous intrauterine environment than DZ twins, especially in the case of monochorionic MZ twins. Our previous study also showed MZ twin neonates to have a lower birth weight than DZ ones [7]. The concordance in perinatal deaths was also higher in MZ than in DZ twins.

Several methodological issues must be taken into consideration in the study of congenital malformations. The definitions of congenital malformations and methods of their ascertainment may vary from one study to another and consequently affect the validity of the comparison between twins and singletons of different studies. In the present study, congenital malformations of both the twins and singletons were actively examined by qualified neonatologists in four teaching hospitals according to a precisely formulated check list rather than just passively abstracting notes from medical records without any standardization of diagnosis. The comparability of congenital malformation ascertainment is considered more enlightening than in some previous studies. Furthermore, major congenital malformations only were compared thus avoiding any dilution of difference resulting from minor anomalies.

Most, but not all, studies have shown a higher prevalence of congenital malformations in twins than in singletons [17]. In recent studies where zygosity has been deter-

mined by a more direct method rather than by Weinberg's rule, it resulted than MZ twins had a higher prevalence of congenital malformations than DZ twins [5,8,21-23,29]. In our study, twin births were found to have a prevalence of major congenital malformations of (2.1%) ie. about 4 times that of singletons (0.6%). The MZ twins also had a much higher prevalence of major congenital malformations (2.7%) than the DZ twins (1.0%). These results, consistent with those of many previous studies, suggest the adverse effects of the intrauterine environment in twin pregnancy on the development of congenital malformations. In addition, it has also been documented that MZ twins have a higher concordance than DZ twins for all malformations [4]. This study showed MZ twins had a higher concordance rate for major congenital malformations (18%) than DZ twins (0%). Several previous studies have shown a higher concordance rate of cleft palate in MZ than in DZ twins [9,14,17,18]. The concordance rate for facial clefts in this study, was found to be 29% in MZ twins. No DZ twin was affected with the disease. Therefore the comparison of concordance for facial clefts between MZ and DZ twins could not be ascertained. However, the low concordance of facial clefts found among MZ twins suggests the relatively more important role of intrauterine environment in the development of facial clefts rather than genetic involvement.

Conjoined twins are considered tragic malformations of MZ twinning and result from the imperfect division of the embryo after the formation of two embryonic discs [26,32]. Given its rarity the prevalence rate of conjoined twins varies greatly from one study to another. In our study of Chinese in Taipei City a prevalence rate of 2.7 per 100,000 deliveries was observed. This was much lower than in Uganda [31] or India [19] but higher than the figure for European countries, Australia, New Zealand, South Africa [12], the USA [10], and Japan [16] as shown in Table 4. Factors contributing to these racial variations deserve further investigation.

Table 4 - Prevalence (per 100,000 deliveries) of conjoined twins in selected countries

Country [Reference]	Prevalence
Sweden [15]	0.5
New Zealand [15]	0.6
England and Wales [15]	0.7
Norway [15]	0.8
France [15]	0.4-0.8
USA [10]	1.0
Spain [15]	1.1
Australia [15]	1.3
South Africa [15]	1.3
Hungary [15]	1.4
Italy [15]	1.4
Czechoslovakia [15]	1.3-1.4
Japan [16]	2.0
Taiwan	2.7
India [19]	16.0
Uganda [31]	23.6

Acknowledgements: This study was supported by grants (75-0412-B002-23, 76-0412-B002-42, 77-0412-B002-18, 78-0412-B002-117) from the National Science Council, Executive Yuan, Republic of China.

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