Acta Genet Med Gemellol 32:31–35 (1983)
The Mendel Institute/Alan R. Liss, Inc.

Congenital Anomalies in Twins in Aberdeen and Northeast Scotland

G. Corney[1], I. MacGillivray[2], D.M. Campbell[2], B. Thompson[3], and J. Little[3]
[1]M.R.C. Human Biochemical Genetics Unit, The Galton Laboratory, University College, London, England; [2]Department of Obstetrics and Gynecology, University of Aberdeen, Aberdeen, Scotland; and [3]M.R.C. Medical Sociology Unit, Institute of Medical Sociology, Aberdeen, Scotland

Data with regard to the proportion of congenital malformations found at birth are presented from a survey of 657 pairs of twins of known zygosity and placentation delivered in Aberdeen and Northeast Scotland between 1968 and 1979. There was an excess of malformed individuals from monozygotic (MZ) pairs, but this did not reach statistical significance. The possible effect of monochorionic placentation in the causation of malformations in MZ twins in general is discussed. It seems that this type of placentation may be of less causative importance than has been previously suggested.

Key words: Congenital malformations, Twins, Monozygotic pairs, Monochorionic placentation

INTRODUCTION

The evidence on the etiology of malformation is confusing. In attempts to partition genetic and environmental influences twin study methods have been used. However, if the etiology of malformations differs between twins and singletons or between monozygotic (MZ) and dizygotic (DZ) twins, the results of these methods cannot be extrapolated to the general population.

In most studies, malformations have been found to be commoner in twins than in singletons [8,9,10,13,17,18,20] but others have reported no such difference [3,15,22].

In multiple pregnancy, the probabilities of the conceptuses developing anomalies may depend not only on the zygosity but also on the type of placentation. In most studies, zygosity has been considered only indirectly by classifying twin pairs as of like or unlike sex. The reports show that the highest prevalence rates at birth are observed for "all malformations" in twin pairs of the same sex. This observation has also been made for certain specific anomalies; for example, anencephalus [9], hydrocephalus [9,15], and encephalocele [13]; and for certain groups of anomalies, namely those of the cardiovascular [9,13–15] and gastrointestinal [13] systems. A general problem has been the small numbers of affected twins. In some literature reviews, data from several studies have been discussed in relation to specific malformations in an attempt to solve this problem. These have given support to the higher prevalence of cardiovascular anomalies in like-

From the proceedings of a workshop on twin pregnancies held in Paris on April 29 and 30, 1982.

sex twins [1]. However, the position for neural tube defects is less clear. One review suggests that the prevalence rate at birth of anencephalus is highest in twin pairs of like sex [12], but no such excess was found for anencephalus and spina bifida in a wider review of the literature [6].

The specific association between prevalence of malformation in twin births and zygosity has been considered only in the National Collaborative Perinatal Project (NCPP) for the United States [16–18]. As had been suggested by most of the indirect studies based on the sex distribution of twin pairs, there was an excess of malformation among MZ twin pairs compared with DZ twin pairs and singletons. This excess was accounted for by anomalies of the ear, of the cardiovascular system, and of the gastrointestinal system.

It has been suggested that monochorionic placentation is of importance in the etiology of structural malformations among MZ (twin) conceptions [4]. Placentation has been considered in only one previous study, again the NCPP [16–18]. No significant excess of malformations among MZ pairs with monochorionic placentae was found.

In view of the general biological importance of twin study methods, the interrelationship between malformation, zygosity, and placentation was investigated in Northeast Scotland.

METHODS

The present study is based on a survey of multiple births in Aberdeen between August 1968 and December 1979. Zygosity was determined from the type of placentation together with investigation of a variety of genetic markers in blood and placental tissue [5]. Malformations were ascertained retrospectively by reviewing records of routine neonatal examinations, and classified according to the European Congenital Malformations and Twins Project (EUROCAT) revision of the International Classification of Disease [23,24]. Comparisons of prevalence rates at birth between MZ and DZ twin pairs and, again, between monochorionic pairs and dichorionic pairs within the MZ group were effected by the χ^2 test for heterogeneity.

As the number of twin pairs from the NCPP study [18] is about the same as from the Aberdeen study, data from the two studies were compared.

RESULTS

Details of sex, zygosity, and placentation for the total Aberdeen series of 657 twin pairs are presented in Table 1. It was not possible to determine zygosity for 111 pairs because details of placentation were not recorded or the blood samples had not been available, but there was no known bias in the omissions [5].

One or more anomalies had been recorded for 55 twin pairs. Zygosity was determined for 46 of these pairs, of whom 26 (57%) were DZ and 20 (43%) were MZ. Only two of the 55 pairs were concordant for *any* anomaly. There was an excess of malformations in individuals from the MZ pairs compared with those from the DZ pairs, but this was not statistically significant ($p = 0.97$) (Table 2). There is a slight excess, again not statistically significant ($p = 0.32$), of affected monochorionic pairs (Table 3). The number of affected pairs was considered to be too small to permit extension of this analysis even to anatomic systems, let alone to specific anomalies.

In the NCPP study 219 (18.3%) of 1,195 twin individuals were malformed in contrast to 57 (4.3%) of 1,314 twin individuals in the Aberdeen study (Table 2). Major and multiple anomalies mainly accounted for the difference.

TABLE 1. Composition of the Aberdeen Twin Sample

Sex distribution		
	Twin pairs	
Sex	No.	%
Unlike	184	28.0
Like	465	70.8
Not known	8	1.2
Total	657	100.0

Distribution by zygosity and placentation

	Placentation							
	Dichorionic		Monochorionic		Not known		Total	
Zygosity	No.	%	No.	%	No.	%	No.	%
DZ	327	49.8	0	—	29	4.4	356	54.2
MZ	80	12.1	109	16.6	1	0.2	190	28.9
Not known	49	7.5	0	—	62	9.4	111	16.9
Total	456	69.4	109	16.6	92	14.0	657	100.0

TABLE 2. Distribution of Malformed Individual Twins by Zygosity

		Zygosity			
Study	Individuals	MZ	DZ	Not known	Total
Aberdeen	Malformed	20	26	11	57
	Total	380	712	222	1,314
	% malformed	5.3	3.7	5.0	4.3
NCPP	Malformed	90	91	38	219
	Total	373	617	205	1,195
	% malformed	24.1	14.7	18.5	18.3

While the number of affected twin pairs is small, especially in the present study, the two studies are in general agreement over the directions of the associations with zygosity (Table 2) and placentation (Table 3). Both studies show that congenital malformations are likely to be commoner amongst MZ than DZ pairs.

DISCUSSION

At least some of the difference in the proportion of malformed twins between the NCPP and Aberdeen studies may be attributed to differences in methods of ascertainment. Infants in the NCPP study were followed to age 7 years, whereas data from the present study only include malformations detected at birth or in the first week of life. In addition, the NCPP study was prospective, and guidelines were issued to each hospital for the criteria to be used in the diagnosis of individual malformations in both singletons [19] and twins [17]. The NCPP study also included subpopulations between which rates of both mal-

TABLE 3. Distribution of MZ Pairs of Known Placental Type by Presence or Absence of Malformations

Study	Placental type	Total	MZ pairs	
			Malformed	%
Aberdeen	Monochorionic	109	12	11.0
	Dichorionic	80	7	8.8
	Total	189	19	10.0
	% monochorionic	57.7	63.2	—
NCPP	Monochorionic	117	39	33.3
	Dichorionic	56	16	28.6
	Total	173	55	31.8
	% monochorionic	67.6	70.9	—

formation and of twinning varied markedly. Rates of malformations in the black population were particularly high for minor anomalies, for example, polydactyly.

By contrast, in Aberdeen the population was relatively homogeneous and the study was retrospective. The EUROCAT classification was used although the instructions were not always sufficiently specific or detailed to avoid uncertainties. This raises the question of the definition of anomalies to be included in any study, agreement on which is essential for comparative purposes [7,15,19].

Neither study supports the theory that a monochorionic placenta is of importance in the causation of all malformations among MZ twin pairs. Equally, neither study excludes the possibility that this type of placentation might be involved in the etiology of particular defects, as is almost certainly the case for acardia [2] and anomalies resulting from the death of one twin and subsequent disseminated intravascular coagulation [11,21].

It would appear that it is the division of the zygote and the subsequent early stages of development, rather than the type of placentation, that in some way produces a deviation from normality usually in one, less commonly in both, MZ twin conceptuses [4,21]. These observations are not understood, but it has been suggested that there may be common factors involved in the causation of MZ twinning and the production of malformations, or that MZ twinning renders the embryos more vulnerable to environmental or teratogenic agents than either DZ or singleton embryos [16,18].

CONCLUSION

The present study shows that there are differences in rates of congenital anomalies between MZ and DZ twin pairs at delivery. This finding reinforces the recommendation that the application of twin study methods in assessing the relative importance of genetic and environmental components in the etiology of congenital anomalies should be treated with caution.

ACKNOWLEDGMENTS

We would like to thank the staff of the Aberdeen Maternity Hospital for their cooperation; Mrs. D. Seedburgh for assistance in preparation of the data; and Dr. David Timlin, Medical Computer Center, Westminster Hospital for the statistical analysis.

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Correspondence: Gerald Corney, M.D., The Galton Laboratory, University College London, Wolfson House, 4 Stephenson Way, London NW1 2HE, England.