CONGENITAL MALFORMATIONS: ARE THEY MORE PREVALENT IN POPULATIONS WITH A HIGH INCIDENCE OF CONSANGUINEOUS MARRIAGES?

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There is the impression that congenital malformations are more prevalent in populations with a high intermarriage rate, including Saudi Arabia. Although some studies have been reported from other parts of the country [1-6] or neighboring countries, [7-10] none has specifically addressed the population of the Al-Hasa area in the Eastern Province, where consanguineous marriages are very common, nor specifically the relationship with consanguineous marriage. We therefore undertook a study of the congenital anomalies diagnosed within the first few days after birth in infants delivered in our institution.

Methods

Our hospital provides medical care to 80,000 company employees and their families who are all Saudi, originating and living in the Al-Hasa area, therefore constituting a genetically homogeneous population.

Congenital malformations discovered at birth or before discharge from the neonatal nursery in infants born between January 1987 and December 1992 were studied. Those discovered later were not included, as some cases were diagnosed in other hospitals without detailed information, or infants died at home before a diagnosis could be made.

The diagnosis of congenital malformations was based on clinical evaluation and all were logged. The clinical, radiological and laboratory data were entered in the medical records. Chromosomal studies were carried out in infants suspected to have a recognizable chromosome syndrome, or in the presence of an unrecognizable pattern of two or more malformations.

The classification of the severity of the malformations was similar to that used by Christianson et al. [11] They were classed as minor when they affected nonvital organs, had little or no functional effect and did not cause distress in the neonatal period. They were classed as major when they were potentially life-threatening and, if not corrected, would impair the child's development or well-being. Neonatal deaths that occurred within a few hours of birth were studied. We did not include antenatal diagnosis because, although made in some cases, other pregnancies were either managed in other institutions or had no antenatal care at all, therefore with no documentation available prior to the delivery of the affected infant. The medical records of all affected infants were reviewed.

Results

Throughout the study period, 18,146 live deliveries occurred in our institution. The incidence of intermarriage in our families was 70%, 40% of which were first-degree. As we compared the incidence of congenital malformations in our population as a whole to other reports, we did not study separately their incidence in non-consanguineous families and those with intermarriage.

Some children had more than one anomaly. A total of 674 congenital anomalies were diagnosed in 607 infants (562 live born, 20 stillborn and 25 neonatal deaths). This represents an incidence of 37.1 anomalies per 1000 total births and 35.8 per 1000 live births. The incidence of infants with congenital anomalies was 33.4 per 1000 births. Table 1 summarizes those congenital anomalies, providing details on a few discussed in this article.

Out of 674 anomalies diagnosed, 391 (58%) were classed as major, of which 25% were skeletal, 15% cardiovascular, 10% neurologic, 10% renal, 9% digestive or abdominal wall defects, 8% ocular and 6% chromosomal anomalies.

There were 60 infants with congenital heart disease (3.3 per 1000 births). The most common anomalies were ventricular septal defect, hypoplastic left heart and tetralogy of Fallot (0.6, 0.4 and 0.3 per 1000, respectively). One-third of the cases had complex cardiac anomalies.

The incidence of chromosome anomalies was 1.3 per 1000 births, constituting only 4.6% of all cases with congenital anomalies. Trisomy-21 represented 78% of all chromosomal disorders.

One hundred and five infants (17% of all malformations) required immediate evaluation for their

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TABLE 1. *Congenital anomalies.*

	Total number	Number/1000
Cardiovascular anomalies	60	3.3
Ventricular septal defect	11	0.6
Hypoplastic left heart	7	0.4
Tetralogy of Fallot	6	0.3
Endocardial cushion defects	3	0.16
Transposition of the great arteries	2	0.11
Complex anomalies	20	1.1
Thoracic anomalies	25	1.4
Diaphragmatic hernia	4	0.2
Gastrointestinal and abdominal wall anomalies	35	2
Imperforate anus	9	0.3
Omphalocele	4	0.2
Tracheoesophageal fistula	3	0.1
Genitourinary anomalies	150	8.3
Central NS anomalies	59	3.2
Neural tube defects	13	0.7
Holoprosencephaly	3	0.1
Skeletal anomalies	174	9.6
Skin anomalies	18	1
Ocular anomalies	32	2
Craniofacial anomalies	33	2
Chromosomal anomalies	24	1.3
Trisomy 21	18	1
Trisomy 13	2	0.1
Trisomy 18	1	0.05

NS=nervous system.

TABLE 2. *Congenital anomalies associated with perinatal deaths.*

	Stillbirths	Neonatal deaths
Hydrops fetalis	5	4
Anencephaly, neural tube defect	8	4
Hydrocephalus	1	0
Renal agenesis	1	0
Thoracic dystrophy or hypoplastic lungs	2	7
Turner's syndrome	1	0
Dwarfism or arthrogryposis	0	3
Diaphragmatic hernia	0	1

anomalies: 52% had cardiovascular, 31% ocular and 17% urogenital anomalies. A total of 88 infants (14.5% of all malformations) required surgery within a few days from birth: 40% were gastrointestinal or abdominal wall defects, 38% neurological and 14% ocular.

Twenty stillbirths out of 101 had congenital anomalies and 25 infants with congenital malformations died in the immediate neonatal period (Table 2).

Discussion

This study is a hospital-based survey, but, since the majority of deliveries in the area take place in hospitals, the data is a good reflection of the incidence of congenital anomalies in this genetically homogeneous population.

Major congenital anomalies constituted 58% of all cases with malformations. Immediate surgery was required in 14.5% and immediate evaluation in 17% cases of malformations, therefore highlighting the need for resources for care of affected infants.

Out of a total of 121 stillbirths, 20 (16.5%) had congenital anomalies, as did 25 (71.4%) out of 35 immediate neonatal deaths (Table 2). This underlines the significant contribution made by congenital anomalies to neonatal mortality and morbidity in this area, despite the significant improvement in health care throughout Saudi Arabia over the past few decades.

Despite the high prevalence of consanguineous marriages, the overall incidence of congenital anomalies we found was not higher than in other parts of the world. Although most anomalies had the same incidence as elsewhere, the incidence of neural tube defects was lower than in Ireland (4.6/1000)[12] and similar to the reports from other parts of Saudi Arabia (0.7/1000).[6] The incidence of trisomy-21 and -18 was also lower than that shown in the literature (1.5 and 0.12/1000 respectively).[13] As not all congenital anomalies were systematically karyotyped, it is possible that the true incidence of chromosomal disorders was underestimated in our study. Tracheoesophageal fistula, diaphragmatic hernia and congenital heart disease were also lower than in the United Arab Emirates (UAE),[8] but our study did not include heart defects diagnosed after the neonatal period. Transposition of the great arteries constituted only 3% of heart defects diagnosed in neonates compared with a reported incidence of 14%.[14]

On the other hand, the incidence of imperforate anus was higher than the 0.05/1000 in the literature and the 0.23/1000 reported from the UAE.[8] Holoprosencephaly was more frequent than in Abu Dhabi (0.045/1000).[7] Ventricular septal defect was found in 18% and endocardial cushion defects in 5% of heart defects, compared with a reported incidence of 9%-15% and 3%-4% respectively.[14,15] Complex cardiac anomalies were also high, constituting one-third of all heart defects diagnosed in the newborn period.

The inherited hematological disorders and inborn errors of metabolism were not the subject of this study. As most are autosomal recessively inherited, their incidence would be expected to be higher with consanguineous marriages. Some congenital anomalies that manifest after the neonatal period, such as various heart defects, are underestimated in this review. Nevertheless, this study provides a framework to anticipate and plan services for the prevention and treatment of some congenital anomalies in this population.

Although antenatal diagnosis and counseling is available for some of these anomalies, customs, beliefs,

cultural and religious factors are to be taken into consideration and usually override the medical aspect. If the prevention of severe anomalies is therefore not possible, it becomes even more crucial to anticipate and plan accordingly for the management of these disorders in our population. A nationwide registry for congenital malformations will constitute an important first step towards this goal.

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