



# The Prevalence of Major Congenital Anomalies Among Live Births in Birjand, Iran

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Received 2017 December 20; Revised 2018 March 22; Accepted 2018 April 15.

## Abstract

**Background and Objectives:** Congenital anomalies can increase the neonatal mortality rate. Infants with anomalies suffer from long-term disabilities that impose heavy burdens on their families and healthcare systems. Understanding the prevalence of congenital anomalies helps health policy-makers develop better health-related policies. This study aimed to evaluate the prevalence of major congenital anomalies among live births in Birjand city, Iran.

**Methods:** This cross-sectional descriptive-analytical study was conducted on 6,000 infants who were born from September 23, 2015, to March 6, 2016, in the maternity departments in Birjand. Stillbirths and infants who died immediately after birth, i.e. before the assessment for anomalies, were excluded. On the first day of birth, a neonatologist or a pediatrician performed a careful physical examination for each infant to diagnose probable congenital anomalies. Appropriate diagnostic procedures were also used to confirm the diagnosis when needed. Then, data on the characteristics of infants were collected using a researcher-made checklist. The data were reported using descriptive statistics such as absolute frequency, relative frequency, mean, and standard deviation. Moreover, the Chi-square and Fisher's exact tests were conducted using the SPSS computer program (v. 16.0) for hypothesis testing at a significance level of less than 0.05.

**Results:** The prevalence of major congenital anomalies was 1.83 cases per 1000 live births. The prevalence rates of low birth weight and prematurity were significantly greater among infants with congenital anomalies than in their non-afflicted counterparts (45.5% vs. 15.9% and 36.4% vs. 11.1%, respectively;  $P < 0.05$ ). Around 63.6% of the anomalies were among male infants and 54.5% of parents had kinship relationships.

**Conclusions:** This study showed that the prevalence of major congenital anomalies among live births in Birjand was 1.83 cases per 1000 live births, which is less than the rates reported in other areas of Iran.

**Keywords:** Infants, Birth Weight, Congenital anomalies

## 1. Background

Congenital anomaly (CA) refers to any anatomical defect at birth. It is a major structural abnormality with serious medical, surgical, and aesthetic consequences. Respecting their intensity, CA cases are divided into two main categories of major and minor (1). Major CAs include severe anatomical anomalies which affect the ability to stay alive or the function of the afflicted organ(s) and are among the common causes of disability and death among children (2). On the other hand, minor anomalies are structural changes which need no serious treatment and are corrected using simple techniques (1).

Major CAs happen in 3% - 4% of all live births. The congenital defect in major CAs can be isolated or multiple (3). Congenital heart disease is the most common CA among infants and the leading cause of anomaly-related death.

The prevalence of congenital heart disease is 0.5% - 0.8% among full-term live infants, 10% - 25% among aborted fetuses, 3% - 4% among stillbirths, and 2% among preterm infants (4). The prevalence and the types of major CAs vary among different races due to differences in racial characteristics and environmental factors (5). For instance, the risk of CAs is greater among black people than among the white (6). Moreover, the most common CAs in Asian race are patent ductus arteriosus, cleft palate, congenital hip dislocation, ventricular septal defect, and anencephaly, while the most common CAs among white Americans, black Americans, and Chinese people include hypospadias and clubfoot, polydactyly, and cleft lip and palate, in sequence (6).

In industrial countries, CAs and genetic disorders include 2% - 5% of live births, 30% of pediatric hospital ad-

missions, and 50% of childhood deaths (7). These anomalies not only are a leading cause of abortion, but also cause preterm birth, childhood and adulthood complications, and serious reactions among parents and families (5).

The underlying etiology of most CAs is multifactorial inheritance. Other causes include monogenic defects, chromosomal abnormalities, maternal disorders, congenital infections, intrauterine factors, environmental factors, medications, nutritional factors such as acid folic deficiency, and unknown causes. Most afflicted children have no family history of CAs (1). Studies report gender (8), maternal age of more than 30, parental consanguinity, and positive family history (6) as factors contributing to CAs. Moreover, the risk of major CAs is almost 20% higher in males than in females so that the prevalence of major CAs among males and females is respectively 307 and 243 cases per 10,000 persons (8).

Treatment and rehabilitation of people with CAs are costly and are not necessarily associated with desired personal and social outcomes. Moreover, some CAs cases are associated with abortion or intrauterine fetal death. Therefore, their prevention is more cost-effective than treatment and rehabilitation (9). Interventions for identifying and managing the risk factors of CAs can prevent the heavy costs and the serious personal, financial, and social outcomes associated with the birth of an afflicted infant.

Given the high costs associated with CA management, healthcare authorities need reliable statistical data about the prevalence. Yet, there is no reliable data about the prevalence of CAs in Birjand city, Iran. On the other hand, due to the differences in the prevalence of CAs in different geographic areas, prevalence-related data collected in other countries and even in cities of the same country cannot be reliably generalized to other countries and cities. Therefore, local studies are needed to provide credible information about the prevalence of CAs (10). The present study aimed to evaluate the prevalence of major CAs among live births in Birjand city, Iran.

## 2. Methods

This was a cross-sectional descriptive-analytical study. All live infants born from September 23, 2015, to March 6, 2016, in the maternity departments in Birjand (including the maternity wards of Shahid Rahimi, Boo-Ali, and Valiasr hospitals) were approached. On the first day of their birth, a neonatologist or pediatrician carefully examined the infants for CA diagnosis. The infants who died during the first minutes after birth were excluded because the diagnosis of CAs needed an autopsy. Suspected CA cases during the physical examination were more examined through appropriate diagnostic procedures. Then, a checklist was

used to collect data from both healthy and CA-afflicted infants regarding their gender, gestational age at birth, mode of delivery, birth weight, parity, maternal age, parents' kinship relationships, and parents' educational status.

The SPSS computer program (v. 16.0) was used for data analysis. The data were reported using descriptive statistics such as absolute frequency, relative frequency, mean, and standard deviation. Moreover, the Chi-square and the Fisher's exact tests were conducted for hypothesis testing at a significance level of less than 0.05.

This article came from a thesis approved by the ethics committee of Birjand University of Medical Sciences, Birjand, Iran (with the code of IR.BUMS.REC.1394.428).

## 3. Results

In total, the number of live births in Birjand city during the six-month course of the study was 6,000, from which 11 cases were afflicted by major CAs. In other words, the prevalence of major CAs in the present study was 1.83 cases per 1000 live births. CAs included hydrocephalus, thanatophoric dysplasia, cerebral anomalies, omphalocele, omphalocele with cleft lip and palate, myelomeningocele with bladder exstrophy, pulmonary hypoplasia with esophageal atresia and cardiac dextroposition, skeletal dysplasia with ventricular septal defect and upper limbs agenesis, dysmorphic syndrome with atrial septal defect and patent ductus arteriosus, and two cases of asphyxiating thoracic dystrophy. Table 1 shows the observed CAs based on the afflicted infants' gender.

CA-afflicted infants were seven males (63.6%) and four females (36.4%). The overall prevalence of major CAs among male and female participants was 0.2% and 0.1%, respectively. Of course, the difference was not statistically significant ( $P = 0.4$ ). CA-afflicted infants were seven full-term (63.6%) and four preterm (36.4%) infants. The mean of gestational age at birth was  $36.8 \pm 2.6$  weeks. The overall prevalence of major CAs among full-term and preterm infants was 0.1% and 0.7%, respectively. The difference was statistically significant. In other words, major CA prevalence was significantly greater among preterm infants than in their non-afflicted counterparts ( $P = 0.004$ ). Five CA-afflicted infants were born through normal vaginal delivery (45.5%) and six through cesarean section (54.5%). The overall prevalence of major CAs among infants who were born through normal vaginal delivery and cesarean section was 0.1% and 0.3%, respectively, with no statistically significant difference ( $P = 0.11$ ).

Participants with major CAs were five low-birth-weight infants with a weight of 1500 - 2500 g (45.5%) and six infants with a normal birth weight of 2,500 - 3,500 g (54.5%). The

**Table 1.** The Frequency Distribution of Major CAs in Both Genders<sup>a</sup>

CAs	Female	Male	Total
Asphyxiating thoracic dystrophy	0	2 (28.6)	2 (18.2)
Hydrocephalus	1 (25)	0	1 (9.1)
Thanatophoric dysplasia	1 (25)	0	1 (9.1)
Cerebral anomalies	1 (25)	0	1 (9.1)
Omphalocele	0	1 (14.3)	1 (9.1)
Omphalocele with cleft lip and palate	0	1 (14.3)	1 (9.1)
Myelomeningocele with bladder exstrophy	1 (25)	0	1 (9.1)
Pulmonary hypoplasia with esophageal atresia and cardiac dextroposition	0	1 (14.3)	1 (9.1)
Skeletal dysplasia with ventricular septal defect and upper limbs agenesis	0	1 (14.3)	1 (9.1)
Dysmorphic syndrome with an atrial septal defect and patent ductus arteriosus	0	1 (14.3)	1 (9.1)
<b>Total</b>	<b>4 (100)</b>	<b>7 (100)</b>	<b>11 (100)</b>

<sup>a</sup>Values are expressed as No. (%).

mean weight among infants was  $2661.4 \pm 699.8$  grams. The prevalence of low birth weight and normal birth weight among infants with major CAs was 0.5% and 0.1%, respectively, with a statistically significant between-group difference ( $P = 0.003$ ). CA-afflicted infants were born from three primiparous mothers (27.3%) and eight multiparous mothers (72.7%). The prevalence of major CAs was not significantly different between the infants of primiparous and multiparous mothers ( $P = 0.86$ ). Maternal age was 25 or less in four cases of CAs (36.4%), 25 - 30 in two cases (18.2%), 30 - 35 in two cases (18.2%), and more than 35 in three cases (27.3%). The overall prevalence of major CAs among the infants of mothers in these four age groups was 0.2, 0.1, 0.2, and 0.3, respectively, with no statistically significant difference between the groups ( $P = 0.63$ ). The total mean of maternal age was  $30 \pm 7.54$ . Only one afflicted infant had a positive family history of CAs (9.1%). There was a kinship relationship between the parents in six cases of major CAs (54.5%). The overall prevalence of major CAs among infants with and without parental kinship relationships was 0.3% and 0.1%, respectively, with no statistically significant between-group difference ( $P = 0.07$ ). Four infants with major CAs died during the first month after birth (36.4%) (Table 2).

#### 4. Discussion

This study evaluated the prevalence of major CAs among live births in Birjand city, Iran. The prevalence was 1.83 cases per 1000 live births. There is no comprehensive

**Table 2.** The Prevalence of Major CAs Based on Participants' and Their Parents' Characteristics<sup>a</sup>

CA Affliction Characteristics	Yes	No	P Value
<b>Gender</b>			0.409
Male	7 (0.2)	3053 (8.99)	
Female	4 (0.1)	2911 (99.9)	
<b>Gestational age</b>			0.004
Full-term	7 (0.1)	5358 (99.9)	
Preterm	4 (0.7)	606 (99.3)	
<b>Mode of delivery</b>			0.111
Vaginal	5 (0.1)	4049 (99.9)	
Cesarean	6 (0.3)	1915 (99.71)	
<b>Birth weight, g</b>			0.003
< 2,500	5 (0.1)	4803 (99.9)	
$\geq$ 2,500	6 (0.5)	1161 (99.71)	
<b>Parity</b>			0.86
Primiparous	3 (0.2)	1770 (99.8)	
Multiparous	8 (0.21)	4194 (99.8)	
<b>Maternal age, y</b>			0.63
< 25	4 (0.2)	1831 (99.8)	
25 - 30	2 (0.1)	1881 (99.9)	
30 - 35	2 (0.2)	1306 (99.8)	
$\geq$ 35	3 (0.3)	946 (99.7)	
<b>Consanguineous marriage</b>			0.07
Yes	6 (0.3)	1797 (99.7)	
No	5 (0.1)	4167 (99.9)	

<sup>a</sup>Values are expressed as No. (%).

study into CA prevalence in Iran for the purpose of comparison. Most studies in this area were conducted using varying methodologies and in different areas throughout the country.

In overall, the prevalence of CAs in our study was less than in other areas of the world and other areas of Iran. For instance, the prevalence of CAs per 1000 live births was 46.5 and 34.57 cases in Saudi Arabia (11), 13.43 and 12.6 in China (12, 13), 7.33 cases in Taiwan (14), 22.2 cases in India (5), 28.7 cases in Korea (15), 26.12 cases in Thailand (16), 2.9 cases in Turkey (17), and 9.3 cases in Libya (18). Moreover, the European surveillance of congenital anomalies (EURO-CAT) reported that the prevalence of major CAs in 2003 - 2007 in Europe was 23.9 cases per 1000 births (19). The center for disease control and prevention also reported that around 3% of all births in the United States are affected by CAs (20). Studies in Iran also showed that the prevalence of major CAs in Tehran was 18 cases per 1000 births

(6), while the prevalence of obvious major CAs per 1000 births was 8.5 - 17 cases among different ethnic groups in Gorgan (9), 8.2 cases in Ardebil (10), 8.92 - 2046 cases in different areas of Golestan province (21), and 18 cases in Sistan (22). The CA prevalence in an earlier study in Birjand was also as high as 5.34 cases per 1000 live births (23). These wide variations in CA prevalence in different areas of Iran and the world are attributable to a wide range of reasons such as the differences in the populations, samples, and lengths of the studies, as well as the differences among different societies respecting the risk factors of CAs such as consanguineous marriage, environmental exposure to teratogens, consumption of essential supplements during pregnancy, maternal age, ethnicity, and maternal history of cigarette smoking (24-27).

The 11 major CA cases observed in the present study were related to the musculoskeletal, cardiovascular, central nervous, urinary, and respiratory systems, as well as cleft lip and palate. Six infants suffered from isolated CAs (54.5%), while five infants were afflicted by multiple CAs (45.5%). Similarly, a study in Saudi Arabia showed that 66.6% of major CAs were isolated and 33.4% were multiple. The most common CAs in Saudi Arabia were urinary (11, 28) and cranial anomalies (11). A study in Turkey also reported that 76% of CAs were isolated and 24% of them were multiple (29). The most prevalent CAs in Turkey were related to the cardiovascular system (29), central nervous and musculoskeletal systems, and cleft lip and palate (17). However, a study in Libya found that most CAs were multiple (56.1%) and more than two-thirds of them were of chromosomal, musculoskeletal, or central nervous types (18). Studies in Iran also reported that the most common CAs in Golestan province and Birjand city were cardiovascular CAs (21), and cardiopulmonary and skeletal CAs (23), respectively. Moreover, CAs in Tehran (6), Gorgan (9), and Ardebil (10) were mostly musculoskeletal.

Our findings revealed that the CA prevalence was not significantly correlated with infants' gender. Contrarily, most previous studies reported the higher prevalence of CAs among males (1, 2, 9, 23). Moreover, we found no significant correlation between CA prevalence and maternal age, even though the mean age was greater among mothers with CA-afflicted children than in mothers of non-afflicted infants. Similarly, several earlier studies reported the insignificant correlation of maternal age with CA prevalence (15, 30-32). However, two studies reported that the age of parents, particularly mother, is directly correlated with the prevalence of some CAs (33, 34).

The findings of the present study also indicated that the parents of more than half of the CA-afflicted infants (54.5%) had kinship relationships, while this rate among the parents of non-afflicted infants was 30.1%. Consan-

guineous marriage is a risk factor for CAs (7, 10). Previous studies also reported that the rate of kinship relationships among the parents of CA-afflicted infants was 58.5% in Birjand (28) and 40% in Saudi Arabia (28). Studies in the Middle East and North Africa also confirmed the greater risk of CAs among parents with consanguineous marriage (6, 35-38). Moreover, a study in Ardebil reported a significant correlation between parental kinship relationship and CA affliction among infants (10). However, this relationship was not statistically significant in the present study.

Most mothers of CA-afflicted infants in the present study were multiparous (72.7%). This rate in an earlier study in Birjand was 60.2% (23). However, there was no statistically significant relationship between parity and CA affliction in our study. Another study in Iran also reported no significant relationship between CA affliction and the number of pregnancies (30). A study noted that the belief of greater likelihood of CAs among the first infants is false (39).

We also found a significantly higher prevalence of low birth weight and prematurity among CA-afflicted infants compared to non-afflicted infants (45.5% vs. 15.96% and 36.4% vs. 11.1%, respectively). In line with our findings, an earlier study reported that the prevalence of low birth weight among afflicted infants was 45.7%. However, the rate of prematurity among afflicted children in another study was 29%, which is much lower than the rate in our study (31). In overall, most previous studies reported that low birth weight and prematurity are associated with higher CA prevalence (18, 39-42).

The mortality rate among children with major CAs in the present study was 36.4%. This rate in a study in Saudi Arabia was 34.9% (11). The mortality rate in our study was greater than the rate reported by studies in Turkey (14% - 15.5%) (17, 29) and Denmark (1.61%) (43) and less than the rate reported by studies conducted in Birjand (78%) (23) and Libya (49.1%) (18).

#### 4.1. Limitations

Like most studies, this study faced several limitations such as small sample size, short sampling period, small geographical coverage, and incompleteness of infants' medical records. We solely studied 6000 infants who were born during a six-month period in 2015 - 2016. Conducting the study for longer periods of time and on larger samples of infants recruited from different geographical areas could produce more reliable results. The incomplete medical records of some infants also required us to exclude them from the study. Another limitation was the exclusion of five infants who experienced early death before our assessment for CAs. Besides, based on the national rules in Iran,

CA-afflicted pregnancies can be terminated before the gestational age of sixteen. Such pregnancy termination might have affected our results respecting the prevalence of CAs. Thus, studies are needed to determine the overall prevalence of CAs.

#### 4.2. Conclusions

This study showed that the prevalence of CAs among live births in Birjand was 1.83 cases per 1000 live births, which is less than the rates reported in other areas of Iran. Identification and management of the risk factors for CAs, as well as more comprehensive prenatal care services, can help reduce the rate of CAs.

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