EASILY IDENTIFIABLE CONGENTAL ANOMALIES: PREVALENCE AND RISK FACTORS

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Abstract- To determine easily identifiable congenital anomalies (CA) prevalence and risk factors in the first 24 hours of life in a cross-sectional study we assessed 2291 liveborn neonates at four teaching hospitals from September 1999 until March 2000 in the south of Tehran. Data were collected by a structured form which contained neonatal characters including sex, gestational age, birth weight, history of CA in siblings, type of CA if there was any and maternal characters including maternal age, history of chronic illness, history of reproduction (including gravidity, parity, infertility and abortion) and conditions during recent pregnancy (including multiple gestation, vaginal bleeding, drug taking, smoking, exposure to X-ray and gestational illness). The prevalence of CA was 2.3% (55 cases). There were 29 males (52.7%) and 26 females (47.3%). Seventeen cases (30.9%) and 15 cases (27.3%) were low birth weight (LBW) and premature, respectively. There was positive history of CA in siblings of only 2 cases (3.6%). Mother of one case (1.8%) had history of drug ingestion during pregnancy. 14.5% (8) and 9.1% (5) of cases, mothers had chronic or gestational illnesses, respectively. Overall musculoskeletal system (30.59%), central nervous system (18.82%) and genital anomalies (16.48%) were accounted as the most common CA. There was statistical significance between CA and birth weight (Odds ratio[OR] 2.51, Confidence Interval[CI] 1.17-5.37).

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Key Words: Congenital anomalies, congenital malformations, CNS anomalies, CDH, congenital eye malformation, cleft lip, cleft palate, limb reduction defects, maternal age, gravidity, parity, drug taking, teratogen

INTRODUCTION

Congenital anomalies (CA) are one of the major causes of stillbirths and neonatal death all over the world. Moreover they are perhaps even more important as causes of physical defects and disabilities. CA can be separated into those that represent a single primary defect in development and those that represent a multiple malformation syndrome. For most of single primary defect the etiology is unknown, however most are explained on the basis of multi-factorial inheritance. Multiple malformation syndromes are caused by chromosomal abnormalities, by teratogens and by single gene defects inherited in Mendelian patterns. The present study was performed to determine the prevalence and risk factors of CA during the first 24 hours of life. Early recognition of CA on one side is important for planning care, because for some CA such as tracheo-esophageal fistula, diaphragmatic hernia, choanal atresia and intestinal obstruction immediate medical and surgical therapies are essential for survival.

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On the other side, recognition of risk factors of CA could be useful in reducing the prevalence of preventable anomalies.

MATERIALS AND METHODS

2291 live born neonates who were delivered at 4 teaching hospitals in the south of Tehran from September 1999 till March 2000 were included in this cross-sectional study. All of the newborns were examined by a pediatrician during the first 24 hours of life and whenever there was any deviation from normal physical structure it was recorded. Data collection were performed by means of a structured form which contained two parts. The first part was about maternal characters and included age, history of chronic illnesses, history of reproduction (including gravidity, parity, infertility and abortion) and conditions during recent pregnancy (including drug ingestion, smoking, exposure to X-ray, multiple gestation, vaginal bleeding and gestational illnesses). These data were obtained by interviewing neonates' mothers. The second part was about neonatal characters including gestational age (GA), birth weight (BW), sex, history of CA in siblings, existance of CA and type of it which were collected

from medical records. Data analysis was performed by SPSS for Windows program (ver. 10). κ^2 test, Fisher exact test and multiple logistic regression were used for univariate and multivariate analysis respectively.

RESULTS

In this study 2291 live born neonates were assessed. Distribution of maternal and neonatal characters were summarized in table 1. 275 (12%) and 384 (16.08%)neonates were low birth weight (LBW) and premature respectively. Among chronic maternal illnesses, thyroid diseases [hypothyroidism (54,16.1%), simple goiter (35,10.4%)], heart diseases (25,7.4%), and hypertension (20,5.9%) were the most frequent illnesses. Diabetes (72,26.8%), urinary tract infection (64,23.88%) and preclampsia (61,22.7%) emerged as the commonest maternal gestational illnesses. Overall 63 mothers (2.75%) had positive history of drug ingestion during pregnancy out of whom 15 cases (23.8%) consumed more than one drug. The most common consuming drug was levothyroxin (24,38%). Only one CA (CDH) was found among neonates of mothers with positive history of drug ingestion (levothyroxin) during pregnancy.

Table 1. Descriptive statistics

Character	Mean	Std. Deviation	Min	Max
Maternal Age	25.69	5.54	14	44
Gravidity	2.12	1.35	1	11
Parity	0.95	1.19	0	9
Birth Weight	3033.06	609.16	550	5800
Gestational Age	38.20	2.60	23	44

Table 2. Distribution of easily identifiable congenital anomalies (CA) by neonatal and material characters

Characters	Congenital anomalies		Characters	Congenital anomalies	
	+	-		+	-
	No (%)	No (%)		No (%)	No (%)
Maternal characters			**Maternal characters**		
Age			**Gestational characters**		
≤ 40	54 (2.4)	2204 (97.6)	+	5 (1.9)	263 (98.1)
> 40	1 (2.9)	33 (97.1)	-	50 (2.5)	1974 (97.5)
History of abortion			**Vaginal bleeding**		
+	12 (3.8)	305 (96.2)	+	5 (5)	96 (95)
-	43 (2.2)	1932 (97.8)	-	50 (2.3)	2141 (97.7)
Chronic illness			**Drug taking**		
+	8 (2.4)	327 (97.6)	+	1 (1.58)	62 (98.42)
-	47 (2.4)	1910 (97.6)	-	54 (2.42)	2174 (97.58)
History of infertility			**Neonatal characters**		
+	0 (0)	120 (100)	**Sex**		
-	55 (2.5)	2117 (97.5)	Male	29 (2.5)	1152 (97.5)
Gravity			Female	26 (2.3)	1084 (97.7)
1	21 (2.2)	917 (97.8)	**Gestational age**		
≥ 2	34 (2.5)	1320 (97.5)	< 37	15 (3.9)	369 (96.1)
Parity			≥ 37	40 (2.1)	1868 (97.9)
1	25 (2.4)	1010 (97.6)	**Birth weight**		
≥ 2	30 (2.4)	1227 (97.6)	< 2500	17 (5)	321 (95)
Multiple gestation			≥ 2500	38 (1.9)	1916 (98.1)
+	3 (3)	98 (97)	**CA in siblings**		
-	52 (2.4)	2139 (97.6)	+	2 (5.4)	35 (94.6)
			-	53 (2.4)	2202 (97.6)

Table 3. Distribution of easily identifiable congenital anomalies (CA) by system according to ICD-10 calssification

CA by system	No	Incidence per 1000 live birth	CA by system	No	Incidence per 1000 live birth
Q^{00}-Q^{07}			**Q^{38}-Q^{45}**		
Central nervous system			**Other CA of Digestive system**		
Anencephaly	3	1.30	High arched palate	1	0.44
Meningoencephalocele	2	0.88	Atresia of esophagus with TE Fistula	1	0.44
Microcephaly	3	1.30	**Q^{50}-Q^{56}**		
Hydrocephalus	6	2.61	**Genital system**		
Meningocele	1	0.44	Imperforate hymen	1	0.44
Meningocele with hydrocephalus	1	0.44	CA of clitoris	1	0.44
Q^{10}-Q^{18}			Ectopic testis	1	0.44
Eye, Ear, Face and Neck			Undescended testicle, unilateral	3	2.54
Anophthalmos	1	0.44	Undescended testicle, bilateral	2	1.69
Microphthalmos	1	0.44	Hypospadias	4	3.38
Macrophthalmos	1	0.44	Congenital hydrocele	2	1.69
Cataract	1	0.44	**Q^{65}-Q^{79}**		
Corneal opacity	1	0.44	**Musculoskeletal system**		
Low set ears	1	0.44	CDH	8	3.49
Micrognathism (Mandibular)	3	1.30	Talipes equinovarus	6	2.61
CA of neck, unspecified	2	0.88	Metatarsus varus	1	0.44
Q^{20}-Q^{28}			Metatarsus valgus	1	0.44
Circulatory system			Deformity of feet, unspecified	1	0.44
VSD and ASD	1	0.44	Polydactyly	1	0.44
CA of heart, unspecified	1	0.44	Syndactyly	3	1.38
Q^{30}-Q^{34}			Shortening of upper limb	2	0.88
Respiratory system			Other reduction defect of upper limb	1	0.44
Hypoplasia of lung	1	0.44	CA of limbs, unspecified	2	0.88
Choanal atresia	1	0.44	Deformity of chest wall	2	0.88
Deviation of nasal septum	1	0.44	Diaphragmatic hernia	1	0.44
CA of nose, unspecified	1	0.44	Omphalocele	1	0.44
Q^{35}-Q^{37}			**Q^{90}-Q^{99}**		
Cleft lip and Cleft palate			**Chromosomal abnormalities**		
Cleft palate, Median	1	0.44	Down's syndrome	1	0.44
Cleft lip	2	0.88			
Cleft palata with cleft lip	2	0.88			

There was no positive history of smoking or X-ray exposure in mothers during pregnancy. The other descriptive statistics are shown in table 2. The prevalence of easily identifiable CA was 24.1 per 1000 live born neonates (55 cases). Distribution of CA by system according to ICD-10 classification has been shown in table 3. Thirty-six (65.5%) and 19 (34.5%) neonates had single and multiple CA respectively. Musculoskeletal (26, 30.59%), central nervous system (16, 18.82%) and genital anomalies (14,16.48%) respectively were the most common anomalies repectively.

The prevalence of CA was higher in male, premature, LBW neonates or those had a positive history of CA in their siblings (Table 1). Despite significant relation between CA and GA ($P< 0.03$) or BW ($P< 0.001$) in univariate analysis, when multiple logistic regression was used only BW was statistically significant (OR: 2.5l, C1: 1.17-5.37). Therefore it seems GA is not an independent variable for CA. There was no significant relation between CA and the other neonatal or maternal characters.

DISCUSSION

As mentioned, the prevalence rate of CA in our study was 24.1 per 1000 live births. Our figure is higher than studies performed in the United Arab Emirates (10.5/1000) (1), China (11.5/1000) (2) and Lebanon (16.5/1000) (3), it is simillar to a study performed at Arash Hospital in Tehran (21.2/1000) (4) and less than a study performed at Shariati and Imam Khomeini Hospitals in Tehran (28/1000) (5). The causes of inconsistency between our results and other studies are probably as below: first of all, many referral and complicated pregnancies are admitted at our hospitals. Secondly the number of prenatal diagnosis and termination of pregnancy are very low at our hospitals similar to other hospitals in Iran. Our findings about the most frequent CA is compatible to studies in South of Beirut (3), and South India (6), but in Libyan Jamahiriya (7) and in China (2) CNS anomalies were the most common CA. Determining the causes of this difference needs in designing more extensive studies especially with regard to maternal physical characters, geographic area of settlement and other environmental factors. According to this research the prevalence of CNS anomalies is higher than the figures in South Australia (8), in the United States (9) and in China (10). In recent decades prenatal diagnosis and termination of pregnancies resulted in essencial reduction in CNS CA at birth in developed countries (8). The prevalence of cleft palate and cleft lip with or without cleft palate is simillar to the figures in Mexico (11), in Europe (12) and in Hagberg, et al study (l3). Moreover the frequency of congenital eye malformations among our neonates was close to the figures in other studies (14,15). Also limb reduction defects occured in France (A) and Spain (17) as frequent as our cases. The prevalence of hypospadias and undescended testis in our male neonates were simillar to the figures in other studies (18-20). With regard to low prevalence of these latter CA, it seems larger sample size is needed to clarify the more exact prevalence rate of CA by systems. Overall in this study not only the prevalence of CA, but also the prevalence of CNS anomalies were more than the figures in other studies. First of all there are different settings between our study's population and other studies' concerning genetic factors, geographical area of settlement, socioeconomic status, maternal nutritional status and habits, prenatal health care services and a large number of environmental and chemical factors which could not be measured and study of each of these factors necessitated performing at least another study. Secondly the number of prenatal diagnosis and medical termination of pregnancies are very limited in our hospitals in comparison with other countries. Ultimately many referral cases have been admitted in these teaching general hospitals which might overestimate our figures. As expected in this study CA of internal organs (eg digestive system, heart and circulatory system, urinary system and internal genital organs) has been undetected due to invisible nature of these systems or because of asymptomatic neonates in particular during the first 24 hours of life. As in our study, other studies have shown significant relationship between CA and BW (6,21,22), but contrary to our results GA were reported as a risk factor for CA (2,6,22,23). Similar to our results maternal age (2), parity (2) and multiple pregnancy (24) were not independent risk factors for CA. A study in India (6) reported significant relationship between positive history of previous abortion, drug intake, maternal illness and CA. This inconsistency might be explained by our small sample size with regard to maternal factors' distribution. Ultimately we recommend performing larger prospective studies on CA both in Tehran and in the country as a whole. Furthermore it is necessary to use more developed diagnostic procedures to determine the exact prevalence rate of minor and major CA in all systems in live births, thereby secondary preventive measures could be initiated as soon as possible to reduce the mortality of babies with life-threatening CA as well as developing high quality health care facilities and offering a support service of rehabilitation for newborns surviving with handicaps and disabilities. Moreover some CA are functional or developmental, so they are not detectable on physical examination especially during the first 24 hours of life. Thus monitoring of growth and development of newborns in serial follow up visits helps not only to determine the actual prevalence rate of CA, but also to offer on time medical care, treatments or educational services.

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