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Original Article (Pages: 6095-6102)

Congenital Heart Disease in Children with Down syndrome in Kermanshah, West of Iran during 2002 - 2016

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Abstract

Background

Down syndrome is the most common chromosomal anomaly. Dysmorphic features can occur in several organs in this syndrome. Cardiac anomalies with a prevalence of 50% are the most common anomalies responsible for death during the first two years of life. We aimed to determine the prevalence of cardiac anomalies among Down syndrome patients admitted to two tertiary hospitals in Kermanshah, Iran from 2002 to 2016.

Materials and Methods

In this descriptive study, the medical records of all patients with Down syndrome admitted to two university hospitals namely Imam Ali and Imam Reza, Kermanshah city located in Western part of Iran in the study period were reviewed. All patients had received Echocardiography two-dimensional (2D). The required data including cardiac anomaly type, consanguinity of parents, maternal age, surgical interventions, and survival were collected into a checklist.

Results: During the study period, 166 patients with Down syndrome had received diagnostic and therapeutic services in the studied hospitals. There were 70 males (42.2%) and 96 females (57.8%). Familial consanguinity was documented in 95 patients (57.2%). Mean ± standard deviation (SD) maternal age at delivery was 26.33 (±4.7) years (range, 15 to 45 years). Of 166 studied patients, 123 (74.1%) had cardiac anomaly. Ventricular septal defect (VSD) was the most prevalent single defect seen in 32 (26%) patients, followed by atrial septal defect (ASD) detected in in 22 (17.8%) patients. Seventy patients (42.1%) required surgical interventions. A total of 74 patients experienced relative improvement of the symptoms. Also, seven patients (10.2%) died including five females and two males.

Conclusion: The frequency of cardiac anomalies in the studied population of Down syndrome patients was higher than former reported figures. The pattern of the anomalies is compatible with some former reports, but contradicts other reports.

Key Words: Cardiac anomaly, Congenital Heart, Down syndrome, Iran, Prevalence.

*Please cite this article as: Jalili Z, Jalili S. Congenital Heart Disease in Children with Down syndrome in Kermanshah, West of Iran during 2002-2016. Int J Pediatr 2017; 5(11): 6095-6102. DOI: **10.22038/ijp.2017.24971.2113**

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Received date: Jul.13, 2017; Accepted date: Aug. 12, 2017

1- INTRODUCTION

Down syndrome is the most prevalent autosomal chromosome anomaly in live-born neonates. The syndrome is defined by trisomy of chromosome 21 in 95% of cases and translocation or mosaic in 5% of cases (1-3). It is the most common cause of intellectual disability and almost all patients have cognitive impairment with a wide range of severity. The incidence of Down syndrome is dependent on various factors, most importantly screening programs, perinatal care, and maternal age (4, 5). Approximate incidence of own syndrome is one in 700 live births in Brazil (2) and one in 732 infants in the USA (6). In a recent systematic review including eight studies from Iran between 1990 and 2016, Down syndrome has a prevalence rate of 0.9 per 1,000 births (7). Another study from Northwestern Iran, reported Down syndrome as responsible for 4.9% of all congenital anomalies (8). There are no reports about the incidence of Down syndrome in western part of Iran.

Down syndrome is characterized by several clinical features including up slanting palpebral features, epicanthic folds, transverse palmar crease, flat facial profile, etc. Many organs can be involved in this syndrome. One of the main organs affected is the heart. In several studies, cardiac anomalies have been reported as the most common congenital defect (9). Congenital heart diseases have been reported to occur in 40 to 60% of patients with Down syndrome (2, 10), and can cause poor prognosis if not treated in a timely fashion (11). A report also proposed the association between congenital heart disease and leukemia in Down syndrome, though further studies are required (12).

The most common congenital heart diseases in Down syndrome include atrial septal defect, ventricular septal defect, Tetralogy of Fallot (TOF), and atrioventricular septal defect which is regarded as a characteristic cardiac anomaly in such patients (13, 14). In a large study in the UK over a 22-year period studying 821 infants with Down syndrome, 42% had cardiovascular anomalies (15). This figure is much higher than the rate in general population which is about 0.8% of live births (16). The importance of congenital heart diseases becomes more evident when these disorders are reported to be the most common cause of death during the first couple of years after birth in Down syndrome (17). Furthermore, these anomalies may result in severe comorbidities in patents such as congestive heart failure, pulmonary hypertension, pneumonia, etc (16).

As congenital heart diseases in Down syndrome impose great risk on the patients, parents, and healthcare system, knowledge of its epidemiology and incidence in every geographical region is important. There is evidence that the incidence of cardiovascular malformations may vary based on geography, ethnicity, and environmental factors (10, 14, 18).

Kermanshah city is one of the seven largest cities in Iran with a population of about 1 million persons. It is located in the Western part of Iran in a mountainous region. Two major university hospitals with advanced cardiology services serve the population of the province (with a population of 4 million persons), and four neighboring provinces (Ilam, Lorestan, Kurdistan, and Hamedan).

Both hospitals are equipped with advanced pediatric cardiology services and many newborns with congenital heart disease are referred to these tertiary hospitals. So far, no study has been done about the incidence of congenital heart disease among Down syndrome infants in the western part of Iran. Hence, we intended to determine this incidence in this study and associated factors.

2- MATERIALS AND METHODS

2-1. Materials and Methods

In this retrospective descriptive study, the medical records of neonates with Down syndrome who were referred to two university tertiary hospitals during the study period were reviewed. Two hospitals are located in Kermanshah, Iran. Both hospitals are major referral centers with pediatric cardiology services. The study period in Imam Reza Hospital was March 2004 to December 2016. In Imam Ali Cardiology hospital, the study period was from March 2002 to December 2016.

All patients for whom the diagnosis of Down syndrome had been confirmed and were admitted to the hospitals for diagnosis and management of possible cardiac anomalies were included. Transthoracic Echocardiography two-dimensional (2D) had been performed for all of them. The medical records were primarily reviewed by a medical student supervised by a board certified pediatric cardiologist. The required variables were entered into an investigator-designed checklist. This checklist was designed by performing relevant literature review.

The first section of the checklist contained demographic variables including age, gender, birth place, and socioeconomic status. The second section contained variables including gestational age, consanguinity of patents, histories of abortion, birth weight, and medication history during pregnancy. Other neonate-related variables included echocardiography results, the type of cardiac anomaly, age at which treatment was done, requirement for surgical intervention, and survival of the neonate. Descriptive indices including frequency, percentage, mean and its standard deviation (SD) were used to express data. All analyses were done using SPSS software (ver. 20.0, IBM). The study protocol was approved by the research deputy ethics committee of Kermanshah University of Medical Sciences, Kermanshah, Iran (ID number: 91024).

3- RESULTS

During the study period (2002 to 2016), 166 patients with Down syndrome had received diagnostic and therapeutic services in the studied hospitals. There were 70 males (42.2%) and 96 females (57.8%). Mean (±SD) age of the sample was 64.6 (±4.2) months (range, 1 month to 20 years). The frequency of patients admitted in each year of the study period is depicted in **Figure. 1**.

Table.1, presents demographic information of the studied sample. The highest numbers of patents (20 cases, 22.5%) were admitted in 2011 and 2016. Familial consanguinity was documented in 95 patients (57.2%). Mean (±SD) maternal age at delivery was 26.33 (±4.7) years (range, 15 to 45 years). **Table.2** presents maternal and obstetrics factors as well as family history of cardiac diseases investigated. Fifty-three patients (32%) had birth weight of less than 2,500 grams. Cytogenetic analysis was available for 132 patients. Chromosomal analysis showed non-disjunction trisomy of chromosome 21 in 114 cases (86.3%), translocation in 14 cases (10.6%), and mosaic in four cases (3.1%). Of 166 studied patients, cardiac anomalies were diagnosed in 123 (74.1%) patients [67 (54.4%) females and 56 (45.6%) males]. Sixty-seven patients (54.4%) had one cardiac anomaly, but 56 patients (45.6%) had more than one anomaly. The total number of anomalies was 174. The various types of cardiac anomalies are presented in **Figure.2**.

As observed, ventricular septal defect (VSD) was the most prevalent single defect anomaly seen in 32 patients (26%) patients [18 (56.2%) females and 14 (43.8%) males], followed by atrial septal defect (ASD) detected in 22 (17.8%) patients [14 (63.6%) females and 8

(36.4%) males]. The most common clinical findings were in order dyspnea (100 patients), repetitive pulmonary infections (80 patients), increased respiratory rate (66 patients), fatigue (58 patients), weight disorders (50 patients), cyanosis (17 patients), and heart failure (13 patients). Mean (±SD) age of treatment was 38.6 [(±20.38) months (range, 1 month to 20 years)]. Mean (±SD) admission duration was 8.7 [(±5.63) days (range, one day to 33 days)]. Seventy patients (42.1%) required surgical interventions. A total of 74 patients experienced relative improvement of the symptoms. Seven patients (10.2%) died including five females and two males.

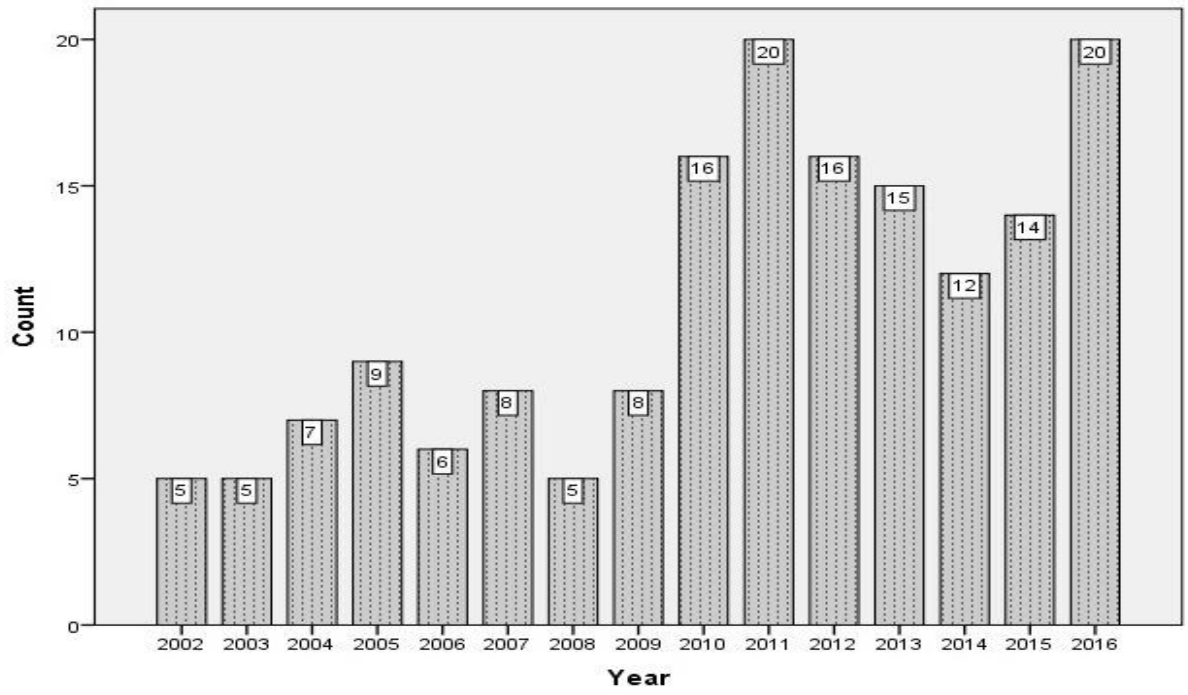

Fig.1: Frequency of 166 patients with Down syndrome based on the year admitted at two hospitals in Kermanshah, Iran from 2002 to 2016.

Table-1: Demographic characteristics of 166 patients with Down syndrome who were admitted at two hospitals in Kermanshah, Iran from 2002 to 2016

Variables	Sub-group	Frequency	Percentage
Age group	< 5 years	112	67.5%
	5-10 years	24	14.5%
	> 10 years	30	18%
Birth place	Kermanshah province	136	82%
	Lorestan province	6	3.6%
	Ilam province	9	5.4%
	Hamedan province	3	1.8%
	Kurdistan province	12	7.2%
Socio-economic status	Good	8	4.8%
	Fair	108	65%
	Poor	50	30.2%

Table-2: Maternal characteristics of 166 patients with Down syndrome who were admitted at two hospitals in Kermanshah, Iran from 2002 to 2016

Variables		Frequency	Percentage
Age groups	< 20 years	50	30.1%
	21 to 30 years	56	33.8%
	> 30 years	60	36.1%
History of abortion		30	18%
Number of abortions	1	24	80%
	≥ 2	6	20%
Medication use during pregnancy		74	44.6%
Family history of cardiac disease		45	27.1%
Cardiac disease in the family	IHD	22	49%
	CHF	7	15.5%
	MVP	6	13.3%
	HOCM	1	2.2%
	Multiple	9	20%

Abbreviations: IHD: ischemic heart disease; CHF: congestive heart failure; MVP: mitral valve prolapse; HOCM: hypertrophic obstructive cardiomyopathy.

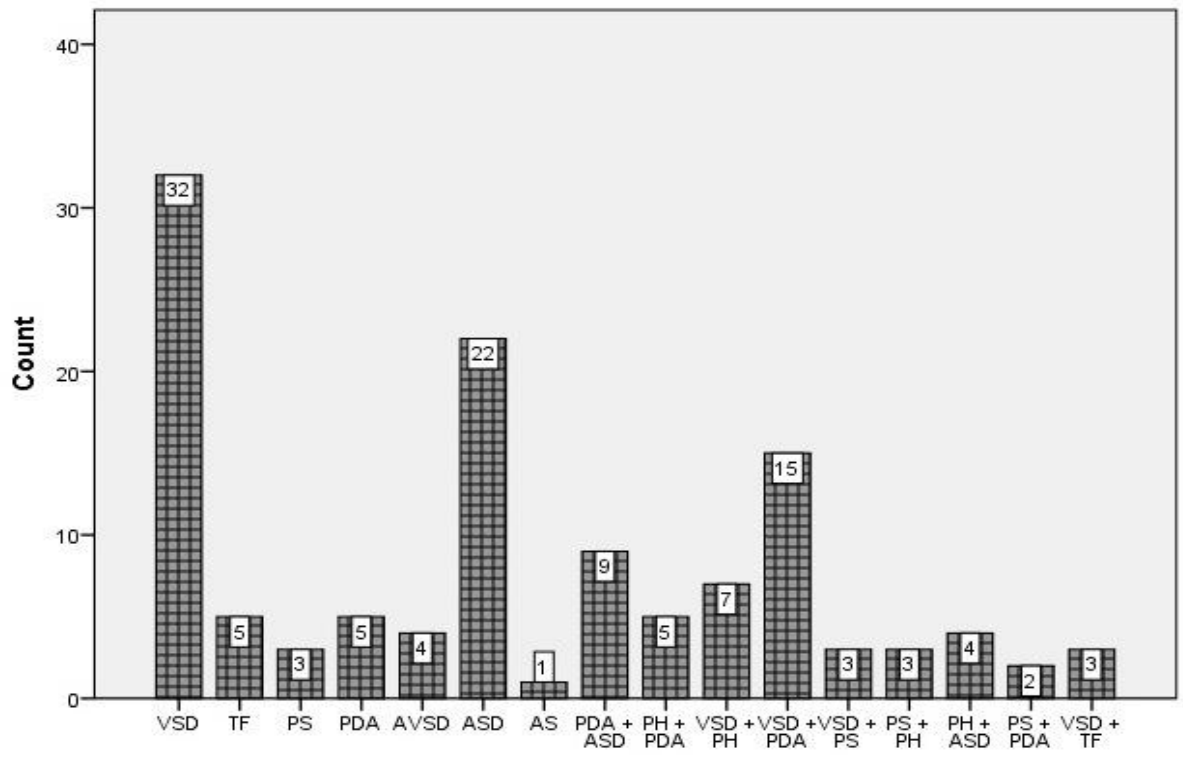

Fig.2: Frequency of various forms of cardiac anomalies among 123 patients with Down syndrome admitted at two hospitals in Kermanshah, Iran from 2002 to 2016.

Abbreviations: VSD: ventricular septal defect; TF: tetralogy of Fallot; PS: pulmonary stenosis; PDA:patent ductus arteriosus; AVSD: atrioventricular septa defect; ASD: atrial septal defect; AS= aortic stenosis; PH: pulmonary hypertension.

4- DISCUSSION

In this study, we determined the prevalence of cardiac anomalies among patients with Down syndrome in the Western part of Iran. To the best of our knowledge, this is the first report from Western Iran in the literature. The prevalence of cardiac anomalies in this study (74.1%) seems to be higher than previously reported rate which is about 40 to 60%. Overall, most studies from Europe, North America, Asia, and Africa have reported this statistic as more than 50%. There are limited studies about the prevalence of cardiac anomalies in Down syndrome in Iran.

In one study, all 32 patients who were referred to a major university hospital in Tehran had cardiac anomalies (19), but we found that three-fourth of the patients had cardiac anomaly. Also, in contrast to our results that VSD was the most common, the mentioned study (19) reported that endocardial cushion defect (found in half of patients) was the most common anomaly followed by VSD (21% of patients), ASD (18.7%), and TOF (6.2%); we detected five patients (4%) with TOF. Instead, a combination of VSD and PDA (patent ductus arteriosus) was the third most common anomaly in our sample.

Another report from Hormozgan, South of Iran, in 2014 showed that among 55 Down syndrome patients, ASD (41.8%), VSD (14.5%), AVSD (12%) were the most common cardiac anomalies, respectively (20). Presence of cardiac anomaly increases mortality and morbidity significantly during the first year of life. The pattern of cardiac anomalies varies in different studies. For example in Guatemala (21), PDA was reported as the most common anomaly (28%) followed by VSD (27%) among 349 patients of whom 54% had associated cardiac anomalies. In Saudi Arabia (22), atrioventricular septal defect (AVSD) was the most common anomaly reported in 40.7% of 302 children. This rate is much higher than our results. We had only four patients with AVSD. A report from Morocco is in agreement with ours as the VSD was number one anomaly seen in 27% of the sample (10). Another consideration is the proportion of patients with single defect. Here, more than 50% of the cases had single cardiac defect. However, in some studies single defect was reported to occur in less than 10% of patients (23). In agreement with our results, a study from China reported that 36% of the cases had multiple lesions (24).

Maternal age is a known risk factor for Down syndrome. Interestingly the mean maternal age in this study (26.3 years) was lower than previously reported data. This was reported as a median of 39 years from Morocco (10), or 36 years in Jamaica (25), and 32 years in Brazil (1). Here, about 10% of the patients died in the follow-up reports. This result also varies in different places presumably affected by several factors. For example, in Europe, it has been suggested that cardiac anomaly per se is not a significant factor for mortality. Instead children with Down syndrome and cardiac anomaly die because of diseases specific to neonatal period as in general population such as asphyxia, prematurity, and low birth weight (3).

Congenital heart disease has a well-established association with Down syndrome. There are differences in various studies. These can be related to many factors such as prenatal care, environmental factors, screening programs, and in many instances the true reason of this discrepancy may not be found (26). These data suggest that further studies are required in a nation-wide spectrum to register more details, especially perinatal care and follow-up records for better understanding of the outcome of the anomalies. We here used findings detected by echocardiography. Echocardiography is the definitive method

to diagnose most cardiac anomalies in Down syndrome. In a recent study on the usefulness of screening of all Down syndrome patients with echocardiography (27), the authors concluded that physical examination, electrocardiogram (ECG), and chest X-ray are acceptable methods to screen such patients to find those who can benefit from echocardiography.

We faced some limitations in this study. The presented study is not a population-based study which certainly provides more accurate estimation of the prevalence of Down syndrome in a particular geographical area and the occurrence of cardiac anomalies. We only included patients who were referred to our hospitals during the study period. It is likely that some patients in the area have been managed in other hospitals in other provincial centers or the capital city, Tehran. It is also possible that some Down syndrome patients lost their life without the chance of receiving diagnostic services to find out cardiac anomalies.

However, as there are limited studies in this field, not only in the western part of Iran, but also throughout the nation, we think that the presented statistics provide a basis for further studies to determine more details about the epidemiology of cardiac anomalies in Down syndrome and furthermore to follow the patients in longer time periods. This will enable to determine the socioeconomic and health care system costs of these congenital malformations.

5- CONCLUSION

The frequency of cardiac anomalies in the studied population of Down syndrome patients (74%) was higher than former reported figures foreign countries (50%), and lower than a former single study from Iran which reported 100% of patients to have cardiac defect. The pattern of the anomalies is compatible with some former reports from Iran that ASD and VSD are the two most commonly reported anomalies, but contradicts other reports. It seems that the pattern of cardiac anomalies in Down syndrome follows a heterogeneous distribution in various geographical regions. It is suggested that further studies performed to figure out the contribution of possible factors and outcome of any of the specific anomalies.

6- CONFLICT OF INTEREST: None.

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