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The Rate of Addiction in Parents of Children with Congenital Heart Disease Compared with Healthy Children

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Abstract

Background
Congenital heart diseases (CHD) are the most common congenital anomaly in children and also the leading cause of mortality from congenital anomalies. Various factors including smoking, drinking alcohol and addiction play role in development of congenital heart diseases. This study was conducted with the aim of investigation of the prevalence of addiction in parents of children with congenital heart disease compared with healthy children.

Materials and Methods
This was a case-control study conducted on 320 children with congenital heart disease aged 6 months to 16 years and 320 healthy children as control group. Children referring to Ali Asghar hospital or who were hospitalized in Imam Ali Hospital were included in the study and their demographic characteristics and their parents were collected. Data were analyzed using SPSS 20.

Results
Average age of diseased and healthy children was 4.08 ± 4.11 and 3.59 ± 2.36, respectively. The rate of addiction of father, mother and parents of children with congenital heart disease was higher than those of children in control group. The most common congenital heart disease was ventricular septal defect (VSD).

Conclusion
In overall, this study showed addiction rate of parents in children with congenital heart disease was higher.

Key Words: Addiction, Children, Congenital heart disease, Iran, Parents.

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1- INTRODUCTION

Congenital Heart Diseases (CHDs) are the common and major diseases (1), included one third of congenital diseases (2). These diseases occur due to several reasons (1), so that genetic and environmental factors are contributed to the development, and some other environmental causes are diabetes, maternal obesity, smoking and alcohol (3).

These diseases can also being a cause of growth delay in children (4); and they are the most highlighted set of top three causes of death in children (3). Therefore, to reduce the incidences of these diseases launches such as promotion in pregnancy care and improving maternal health are required (1). The highest prevalence of CHD reported in Asia (9.3 per 1,000 live births), while the observed prevalence are 8.2 and 6.9 in 1000 live births in European countries, and in North America respectively (2,5). In a retro-spective study has been shown that the prevalence of CHD was 8.9 to 11.2 in 1000 live births from 2004 to 2012 in northern areas of Iran (6). A few years back the prevalence was 12-30 in 1000 live births in Khuzestan province of the country, Iran, during 1998-2007 (7). Addiction is a chronic behavioral disorder that observed with forced need to use opioids and inability to control their consumption and accompanied with anxiety and withdrawal of the absence of consumption (8).

The prevalence of opioid addiction in pregnant women is 0.5% in Iran (9), and about 5 folds less than general women population in USA (10). About 37% of general American populations are smoking, when this percentage is 12% in pregnant women (11). Despite of efforts to reduce drug abuse, an increasing trend is observing in drug use and addiction, so that it has been became a major health problem in all societies. In fact, the main cause addiction and increasing the addicted number is that opioids are easy access (11). Using Cocaine alone or in combination with oth-er addictive substances can cause much impairment such as somatic, psychological and developmental fetus during pregnancy as well as the cardiovascular abnormalities (12).

Studies have shown that abusing nicotine during pregnancy even low-dose can cause an interfere in the process of embryo developmental (13), and smoking causes intrauterine fetal death at a ratio of one in five American pregnancies (11). Disorders due to opioid addiction have become a major health problem (14), and one of the worrying aspects is an influence on growth and development in the fetus of addicted mothers. For example, morphine is a substance with high potential to cross the placenta and affect tissues develop-pment especially cardiovascular disorders (15).

Maternal opioid consumption caused an increase in fetal and infant mortality, low birth weight and premature delivery (9). The majority of addicted mothers are in the reproductive age group (14), and these mothers are most vulnerable, because they frequently have non-planned pregn-ancies and adverse pregnancy that have many complications for the mothers and embryos (16). A study to determine the relationship between opioid use and the incidence of CHD showed that parental addiction rate was 6.5% in children with CHD compared with 2% in control (17). More chance of having congenital anomalies have been reported in children with addicted mothers than controls. Considering the high prevalence of addiction in Iran, especially in Sistan and Baluchestan province, and with respect to the role of addiction in the incidence of congenital heart disease, this study aimed to investigate the prevalence of addiction in parents of children with CHD compared with healthy children.

2- MATERIALS AND METHODS

2-1. Method

This case-control study was conducted on 640 children with equal ratio. Sampling was randomly collected from those children with CHD that were diagnosed by echocardiography and from those that referred to the hospital for routine check-up. The samples collection was hospital base so that, both case and control participants were from Ali Asghar and Ali Ibne Abitaleb hospitals in Zahedan, Iran. Cases were matched randomly to children with non-drug-dependent mothers (controls). The participant's age ranged from 6 months to 16 years. Selected participants were asked to fill out an easy question sheet related to demographic information and information about their parents' drug possession.

2-2. Sampling method

Accordance with the following formulae the sample size calculated,

$$n = \left(\frac{r+1}{r}\right)\frac{(\bar{p})(1-\bar{p})(Z_{\beta}+Z_{\alpha/2})^2}{(p_1-p_2)^2}$$

Where: P_1= parents addiction prevalence with CHD children (6.5%). P_2= parents addiction prevalence with healthy children (2%). Z_{α}= 1.96, Z_{β}= 0.84 and r=1:1.
Applying the formulae with the mentioned values for the major parameters resulted 640 samples with equal ration in case and control.

2-3. Ethical consideration

The study as a MD thesis was approved by the institutional review board and research committee of the Zahedan University of Medical Science.

2-4. Statistical Analysis

SPSS version 22.0 (SPSS Inc., Chicago, IL, USA) were used for analysis. Metric parameters were compared using independent t-test. Contingency coefficient testing was used for non-metric parameters. P-value < 0.05 was considered statistically significant.

3- RESULTS

In the present study sex distribution of participants' accordance with case-control, addicted mother, fathers or parents have shown in the **Table.1**. The table showed that from 640 participants, 48.1% were boys. From those children with addicted mother, 45.2% were boys. From those children with addicted father, 49.2% were boys. From those children with addicted parents, 46.2% were boys. The sex distribution was similar in all mentioned factors (P>0.05). Participants' weight were similar in groups made of case-control, addicted mothers, fathers or parents (P>0.05). Same trends can be observed for age, gestation. But the birth weight of participant was different accordance with addicted mothers or parents classifications; so that for those who their mothers or parents were addicted, mean birth weight was lower (2.79±0.22 vs. 2.71±0.12 in both factors). These variations were significant (t= 4.095, P<0.001) and (t= 3.716, P<0.001) in addicted mothers or parents, respectively (**Table.2**).

Table.3 showed the various relationships between case-control and addicted mothers, addicted fathers or addicted parents. In this table observed that groups of participant (case and controls), had a strong and significant relationship with addicted mothers (Contingency Coefficient = 0.174, P<0.000), fathers (contingency coefficient =0.230, P<0.0000 or parents (contingency coefficient =0.161, P<0.000).

Table.4 showed the Congenital Heart Defects distribution in children accordance with their addicted mother, father or parents. From the table observed that most of the children with CHD had ventricular septal defect (VSD) (60%), when their mothers were addicted. The frequencies were followed by atrial septal defect (ASD) (11%) in these children.

Considering CHD children with addicted father, VSD was the major heart defect (63%) and followed by ADS (9%) and tetralogy of fallot (TF) (9%). The tabled showed that CHD children with parents' addiction mostly had VSD (66%) and followed with the defect of ASD (9%).

Table-1: The Sex distribution of participants' accordance with case-control, addicted Mother, Fathers or Parents

Factors and their options			Gender		Total	Contingency Coefficient	P-value
			Girls	Boys			
Groups	Case	Number	164	156	320	0.062	0.114
		Percent	51.3	48.8	100.0		
	Control	Number	144	176	320		
		Percent	45.0	55.0	100		
Total		Number	Number	332	640		
		Percent	Percent	51.9%	100		
Mother addiction	No	Number	289	309	598	0.015	0.698
		Percent	48.3	51.7	100		
	Yes	Number	19	23	42		
		Percent	45.2	54.8	100		
Total		Number	Number	332	640		
		Percent	Percent	51.9	100		
Father addiction	No	Number	277	300	577	0.007	0.856
		Percent	48.0	52.0	100		
	Yes	Number	31	32	63		
		Percent	49.2	50.8	100		
Total		Number	308	332	640		
		Percent	48.1	51.9	100		
Parent addiction	No	Number	290	311	601	0.01	0.799
		percent	48.3	51.7	100		
	Yes	Number	18	21	39		
		Percent	46.2	53.8	100		
Total		Number	308	332	640		
		Percent	48.1	51.9	100		

Table-2: Independent t-test results for differences in case-control, Mother, Father and Parental addiction based on the factors of birth and at study time weight, gestational, mother and child's age and birth order

Variables	Groups	Mean	SD	t-test	P- value
Weight (kg)	Case	14.4859	10.19157	-1.126	0.261
	Control	15.3400	8.95336		
Child age (year)	Case	4.0727	4.16100	1.71	0.088
	Control	3.6118	2.43226		
Mother age (year)	Case	28.075	24.560	1.69	0.092
	Control	25.728	3.53		
Gestational age (week)	Case	37.89	2.07	0.373	0.71
	Control	37.8250	2.37159		
Birth weight (gr)	Case	2.7556	.19548	-3.43	<0.001
	Control	2.8140	.23342		
Birth order	Case	2.7531	1.60475	5.587	<0.001
	Control	2.1875	.83937		
Variables	Mother addiction	Mean	SD	t-test	P-value
Weight (kg)	No	14.9612	9.65649	0.48	0.632
	Yes	14.2262	8.74068		
Age	No	3.8212	3.36777	-0.59	0.555
	Yes	4.1429	4.03987		
Gestational age (Week)	No	37.8462	2.30208	-0.5	0.617
	Yes	38.0238	.15430		
Birth weight(gr)	Yes	38.0238	.15430	4.095	<0.001
	No	2.7903	.22145		
Birth order	Yes	2.7071	.11769	-0.761	0.447
	No	2.4599	1.27634		
	Yes	2.6190	1.73841		
Variables	Father Addiction	Mean	SD	t-test	P-value
Weight (kg)	No	15.0000	9.65953	0.694	0.488
	Yes	14.1159	9.01036		
Age (year)	No	3.8086	3.32312	-0.755	0.45
	Yes	4.1508	4.16750		
Gestational age (Week)	No	37.8406	2.34348	-0.593	0.553
	Yes	38.0159	.12599		
Birth weight(gr)	No	2.7889	.22096	1.727	0.088
	Yes	2.7476	.17493		
Birth order	No	2.4437	1.25860	-1.558	0.12
	Yes	2.7143	1.70794		
Variables	Parents' Addiction	Mean	SD	t-test	P-value
Weight (kg)	No	14.9181	9.65189	0.053	0.957
	Yes	14.8333	8.77638		
Age	No	3.8054	3.36674	-1.073	0.248
	Yes	4.4103	4.07152		
Gestational age (Week)	No	37.8469	2.29634	-0.486	0.627
	Yes	38.0256	.16013		
Birth weight (gr)	No	2.7897	.22109	3.7162	<0.001
	Yes	2.7103	.12095		
Birth order	No	2.4676	1.27907	-0.209	0.835
	Yes	2.5128	1.74525		

SD: Standard deviation.

Table-3: The Relationship between belonging groups and addicted mothers, addicted fathers or addicted parents

Factors	Options	Case		Control		Total	
		Frequency	%	Frequency	%	Frequency	%
Addicted Mothers	No	285	89.1%	313	97.8%	598	93.4%
	Yes	35	10.9%	7	2.2%	42	6.6%
Total		320	100.0%	320	100.0%	640	100.0%
Contingency Coefficient= 0.174				P <0.001			
Addicted Fathers	No	266	83.1%	311	97.2%	577	90.2%
	Yes	54	16.9%	9	2.8%	63	9.8%
Total		320	100.0%	320	100.0%	640	100.0%
Contingency Coefficient=0.230				P <0.001			
Addicted Parents	No	288	90.0%	313	97.8%	601	93.9%
	Yes	32	10.0%	7	2.2%	39	6.1%
Total		320	100.0%	320	100.0%	640	100.0%
Contingency Coefficient= 0.161				P<0.001			

Table-4: Congenital Heart Defects distribution in children accordance with their addicted mother, father or parents

Congenital Heart Defects	Mother Addiction				Father Addiction				Parents Addiction				Total	
	No		Yes		No		Yes		No		Yes			
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
VSD	132	46	21	60	119	45	34	63	132	46	21	66	153	48
ASD	45	16	4	11	44	17	5	9	46	16	3	9	49	15
TF	22	8	2	6	19	7	5	9	22	8	2	6	24	8
PDA	34	12	2	6	34	13	2	4	35	12	1	3	36	11
ASD+VSD	7	2	1	3	7	3	1	2	8	3	0	0	8	3
VSD+PDA	2	1	0	0	2	1	0	0	2	1	0	0	2	1
PS	2	1	0	0	2	1	0	0	2	1	0	0	2	1
ASD+PDA	3	1	0	0	3	1	0	0	3	1	0	0	3	1
VSD+PS	3	1	0	0	3	1	0	0	3	1	0	0	3	1
ASD+VSD+PDA	1	0	2	6	1	0	2	4	1	0	2	6	3	1
PS	7	2	1	3	6	2	2	4	7	2	1	3	8	3
ASD+PS	3	1	0	0	3	1	0	0	3	1	0	0	3	1
DORV	3	1	0	0	3	1	0	0	3	1	0	0	3	1
TGA	7	2	0	0	6	2	1	2	7	2	0	0	7	2
MR	3	1	1	3	3	1	1	2	3	1	1	3	4	1
TR	4	1	0	0	4	2	0	0	4	1	0	0	4	1
TAPVC	1	0	0	0	1	0	0	0	1	0	0	0	1	0
CoA	2	1	0	0	2	1	0	0	2	1	0	0	2	1
AS	4	1	1	3	4	2	1	2	4	1	1	3	5	2
Total	285	100	35	100	266	100	54	100	288	100	32	100	320	100
Cyanotic	33	12	2	6	29	11	6	11	33	11	2	6	35	11
A cyanotic	252	88	33	94	237	89	48	89	255	89	30	94	285	89

VSD: Ventricular Septal Defect; ASD: Atrial Septal Defect; TF: Tetralogy of Fallot; PDA: Patent Ductus Arteriosus; PS: Pulmonary stenosis; DORV: Double Outlet Right Ventricle; TGA: Transposition of Great Arteries; MR: Mitral Regurgitation; TR: Tricuspid Regurgitation; TAPVC: Total Anomalous Pulmonary Venus Connection; CoA: Coarctation of Aorta; AS: Aortic Stenosis.

4- DISCUSSION

In the present study more fathers were addicted compared mothers. The prevalence of addiction in parents was higher in CHD children. From the results, observed that most of the children with CHD had VSD and then ASD. Considering CHD children with addicted father, VSD was the major heart defect and followed by ADS. CHDs are the most common congenital anomalies in infants and they are the leading causes of death. The average prevalence of opium addiction was 4 in 1000 adults aged 15-64 years in Europe which one third of them are women in childbearing age (18). During the last decade the prevalence of opioid addiction has been increased from 0.19% in 2000 to 0.58% in 2009 in America (19). Addiction in pregnant may causes fetal and maternal complications that mothers affected by psychological and physical disorders included of depression, anxiety and other mood disorders, hepatitis C (50% of intravenous drug users), infected with HIV (1-4% of drug injection) and fetal complications, including placental insufficiency developmental disorders and tissue growth, preterm delivery and low birth weight newborns with low Apgar scores and more (20).

Opioids, particularly morphine as a main and effective material in opium is the most effective material that transferred in large amounts to the fetus through the placenta and accumulated in fetal tissues especially heart. Teratogenic effects of opium and its derivatives on cell proliferation have been proven in the first phase of pregnancy and probably have similar effects on other embryonic organs so that the cardiovascular organs are the most involved (21). On the other hand, several studies have shown the effects of drugs, especially opium on brain. Since heart and brain have a common embryonic origin in the cephalic fetal, and also separation of cushion endocardial cells from neural crest cells, can be proved that there probably are opium teratogenic effects on the heart (22).

In view of the above mentioned documents and also taking into account the effects of opioids, especially opium on migration and cell proliferation in the first 20 weeks of pregnancy, as well as their influence on cell differentiation can prove and demonstrate teratogenicity opium effect on the cardiovascular system (21). Given a rising prevalence of drug addiction in pregnant women and its consequences has been became this phenomenon a major health problem (20). According to the results of the present study numbers of patients children who their fathers were addicted were more than the number of patients' children who their mothers were addicted. Same trends observed in the control children.

These results were not in the same line with shahramian's results. Shahramian's reported that children with one addicted parent were lower than children who had both parents addicted (23). Saleh Gargari resulted that neonatal anomalies were considerably higher in neonates with addicted mothers than neonates with no addicted mothers. Many anomalies has been reported in neonates with addicted mothers such as clubfoot, micropenis, macrocephaly, cardiac anomalies, great tongue, limb anomalies, hypospadias and polydactyly (24).

The present study showed that the rate of congenital heart defects were more in children with addicted parents compared to their counterparts and as well revealed that the most rate of CHD was for children with fathers that consumed opium and followed by children who their mothers had this behavior disorder. Shahramian reported that rate of CHD was more in children with addicted mothers on eating and smoking opium (23). In CHD children, ventricular septal defects (VSD) were more frequent and followed by atrial septal defect (ASD).

These findings were consistent with Shahramian results, so that in their study the most common CHD was VSD.

Vucinovic demonstrated that in children with addicted mothers, the most common anomalies were ASD, Transposition of Great Arteries (TGA), and Hypoplastic Left Heart Syndrome (HLHS) (22). In the present study from all children with VSD, the majority had addicted father and more less had addicted mothers. From children with ASD, only a few had addicted mothers. From the present results revealed that the average weights of children with CHD were significantly lower than healthy children who indicate that CHD can lead to growth retardation and malnutrition.

Children with CHD are at risk of malnutrition due to inadequate energy, increase metabolism or both (25). Impaired in absorption can also play an important role in malnutrition in children with CHD.

A child with CHD goes to a reduction in receiving energy and increased in metabolic needs and consequently malnutrition and delayed in growth due increasing cardio-respiratory work, fatigue and loss of appetite, dyspnea, tachypnea, chronic hypoxia (26). It is shown that the developmental status of infants with CHD are strongly related to their growth, especially weight (27). In a study that conducted in Taiwan demonstrated that children with CHD in respect to height (52%) and weight (73%) had higher percent under the fifth percentile compared to control children (28). Vucinovic resulted that the risk of anomalies in children with addicted mothers was 4 times more than in children from non- addicted mothers (22), and Shahramian found this value as 10 times. The chance of this risk in our study approximately was similar to Saeeidi study.

4-1. Limitations of the study

Limitations of the study were retrospective design, as well as the case–control setting. None the less, by matching for maternal age in case and control, ethnicity, smoking status and mode of conception, we ruled out known confounding factors that have been shown to influence fetal heart rate.

5- CONCLUSION

Findings of the present study showed that the drug abuse in parents of CHD children was more than parents with healthy children. Birth weight of children was different accordance with their parents' addiction status. Those who their parents were addicted, mean birth weight was lower. Ventricular septal defect was the major heart defect in children who their parents were addicted. Given the high prevalence of addiction in this region of Iran and taking into account the role of addiction in the incidence of congenital heart disease, by trying to reduce the rate of addicted parents, can reduce the rate of children with congenital heart disease.

6- CONFLICT OF INTEREST: None.

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