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Research Article

Investigating the Relationship between Chromosomal Patterns and Echocardiographic Down syndrome Patients with Therapeutic Time of Congenital Heart Disease in Taleghani and Sayad-Shirazi Medical Center, Gorgan

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ABSTRACT

Introduction: Down syndrome is one of the most common chromosomal abnormalities in humans that between every 700 live births are a child with Down syndrome. Syndrome naturally occurs due to chromosome 21 trisomy and is associated usually by anomalies such as heart anomalies.
Objective: The aim of this paper is to determine the relationship between chromosomal patterns and echocardiographic Down syndrome patients with congenital heart defects in children who are treated. However, in this study, the criteria associated with other variables such as maternal gestational age, birth weight, presence of family relationship between parents and placed evaluated.
Methods: In this study, data on 50 patients referred to Gorgan Sayyad Shirazi hospital and Taleghani therapeutic educational center, the results of echocardiography and chromosome tests as well as the results of the questionnaire were collected and examined.
Results: Analysis of chromosome 50 patients (30 males and 20 females), 47 patients (94%) as trisomy 21 and in 3 patients (6%) was just translocation. Of the 50 patients, 29 of them (58%) had congenital heart decease, 29 percent of patent ductus arteriosus (PDA), 24% endocardial cushion defects in padding (AVSD), 18% atrial septal defect (ASD), 15% increase in pulmonary artery pressure (PHTN), 10% the ventricular septal defect (VSD) and 4 percent tetralogy of fallot (TOF), were observed. Family history of heart disease in 3 patients (10.6%) was positive. Gestational age at birth in 22 cases (44%) more than 35 years. The birth weight of patients with Down syndrome in 12 cases (24%) was less than 2.5 kg.
Conclusion: The diagnosis of congenital heart defects in patients with Down syndrome start prognosis and treatment of special importance, because their treatment reduces mortality and morbidity in them. Gestational age is also a risk factor in causing the disease is very important, so that the possibility of occurrence of this syndrome in mothers, who for the first time, gestational age greater than 35 years, is more heavily than other groups.

Key words: Down syndrome, congenital heart defects, echocardiography.

INTRODUCTION

Down syndrome is one of the most common chromosomal abnormalities in humans and one in every 700 live births is a child with this syndrome. [1] Several risk factors for metabolic

syndrome have been proposed, but it seems that the most important risk factor in the high incidence of gestational age is conversely, other chromosomal abnormalities, blood kinship parents and birth weight as a risk factor not considered important [2,3].

This syndrome is caused by trisomy of chromosome 21 that normally arise, including cardiac anomalies associated with multiple anomalies [4-5]. Several studies have shown that about half of children with Down syndrome have heart defects [6-7]. Characteristic heart defects in Down patients is due to abnormal development of the endocardial septal that leading to a range of atrioventricular septal defects involving heart valve [8].

The severity of these lesions is also common atrioventricular valve defects and membranous ventricular septal defect and atrial septal early with valvular abnormalities are varied [9]. It seems that the incidence of cardiac disorders associated with genes located on chromosome 21 and these genes are likely involved in the evolution of heart. [10] Specificity atrioventricular septal defects for trisomy 21 by the observation that 70% of all cases of atrial ventricular septal defects seen in Down's patients has insisted and different assumptions about the association between increased expression of the genes on chromosome 21 abnormalities in Down's patients septal and a valve has been proposed [11]. However, it should be noted that abnormalities in cardiac and respiratory infections as an important cause of early morbidity and mortality in patients with Down syndrome [12]. Thus, timely detection of defects in these patients is essential, however it seems the importance of this issue becomes clear when many studies have shown that early treatment early in patients with these defects because a significant reduction in morbidity and mortality and their inability [13-14].

One of the ways that many of the physicians emphasized in the early detection of these defects, the use of echocardiography in the diagnosis of these defects is a non-invasive method [15]. Studies have also shown that this approach, along with other non-invasive diagnostic methods such as electrocardiography and chest radiography to evaluate the full treatment typically is in the future [16]. This study aimed to investigate the relationship between genetic patterns and echocardiographic abnormalities when treating patients with Down syndrome, congenital heart disease in children referred to Gorgan Taleghani and Sayyad Shirazi hospitals. It also examines the relationship between these abnormalities in patients with chromosomal analysis, gestational age, a history of drug use in pregnancy, gender, consanguineous parents, a history of congenital heart disease in first degree relatives and the patient's weight at birth is examined.

METHODS

Children with Down syndrome that between 2014-2015 referred to the Pediatric in Sayyad Shirazi and Taleghani hospital in a retrospective study were examined. Information on these patients, the files in the hospital and echocardiography results were obtained, in the form of a questionnaire which included gender, gestational age, family relationship with both parents, history of abortion, birth weight, gestational age, maternal history of drug in the mother during pregnancy, family history of heart disease, the patient's condition in terms of chromosomal analysis, the patient's condition in terms of cardiac abnormalities, based on echocardiography this is done by a pediatric cardiologist. Information on babies and test results in a database was stored.

Statistical analysis was performed using SPSS software. In this study, 50 patients with Down syndrome who were referred to our hospital during the years 2014 to 2015 were studied. 30 patients (60%) were male. The variables studied in children include the presence and type of congenital heart malformations, chromosomal analysis, gender, patient birth weight, family history of heart disease in patients is shown in Table 1. The variables included maternal age at birth of the patient's drug history during pregnancy; consanguinity between parents is shown in Table 2.

Frequency	Patient Characteristics
	Gender
30 (60%)	Boy
20 (40%)	Girl
	Chromosomal analysis
47 (94%)	Trisomy 21
3 (6%)	Translocation
	Congenital heart disease patients
29 (58%)	Yes
21 (42%)	No
	Birth weight
12 (24%)	Less than 2.5 kg
38 (76%)	More than 2.5 kg
	Family history of heart disease
5 (10%)	Positive
45 (90%)	Negative

Table 1. Demographic characteristics and genetic study of children with Down syndrome

The echocardiographic study was conducted in 50 patients with Down syndrome in this article, the most common abnormality was found, Endocardial Cushion Defect (AVSD) and Patent Ductus Arteriosus (PDA), which is about 40% of them will be included.

Other abnormalities were: Ventricular Septal Defect (VSD), Pulmonary Hypertension (PHTN), Atrial Septal Defect (ASD) and Tetralogy of Fallot (TOF).

The following conclusions after studying 29 subjects (from 50 subjects) who have cardiac abnormalities, the result is as follows. It should be noted that a large number of patients, more than one defect was observed in Figure 1 you can see it.

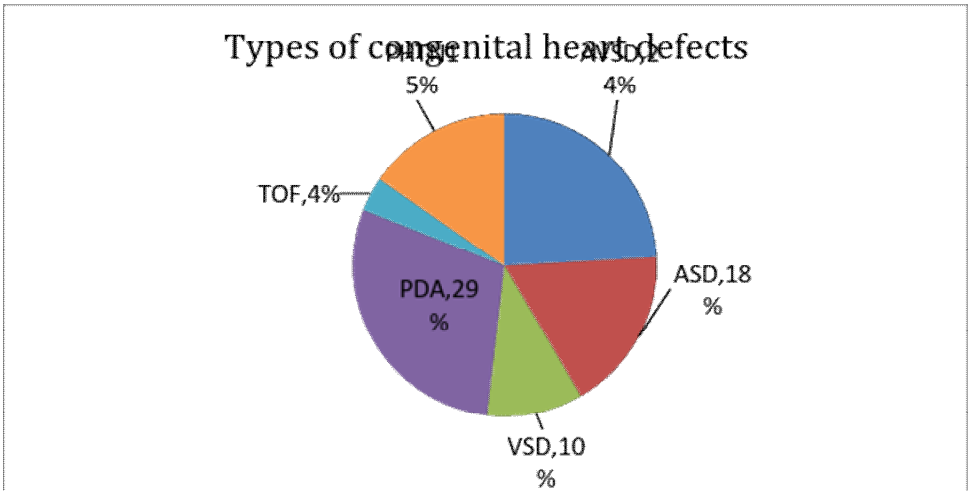

Figure 1: distribution of congenital cardiac abnormalities in patients

Frequency	Characteristics
	Maternal age at birth of child
28 (56%)	Less than 35 years
22 (44%)	More than 35 years
	History of drug use during pregnancy
9 (18%)	Yes
41 (82%)	No
10(20%) 40 (80%)	Family of mother and the child's father Has Has not

Table 2: Demographic characteristics and medical histories of mothers of children with Down syndrome study

RESULTS & DISCUSSION

Here we examine the hypotheses. The usual assumptions are described in the following two hypotheses. Recall that for the assumptions of the tests we use SPSS statistical software and criteria for acceptance or rejection based on the amount of P-Value is usually compared with $\alpha = 0.05$. In Table 3 the results are hypotheses.

The result: a rejection of the assumption (such as P-Value> 0.05)

Hypotheses 1: There is a significant relationship between the incidences of congenital heart defects in patients with Down syndrome by chromosome analysis?	
P-Value= 0.621	Result: rejection of the hypotheses (Because P-Value > 0.05)
Hypotheses 2: There is a significant relationship between the incidences of congenital heart defects in patients with Down syndrome and the mother's age during pregnancy?	
P-Value= 0.015	Result: accept of the hypotheses
Hypotheses 3: There is a significant relationship between the incidences of congenital heart defects in Down syndrome patients with a history of maternal drug use during pregnancy?	
P-Value= 0.423	Result: rejection of the hypotheses
Hypotheses 4: There is a significant relationship between the incidences of congenital heart defects in patients with Down syndrome parents?	
P-Value= 0.312	Result: rejection of the hypotheses
Hypotheses 5: There is a significant relationship between the incidences of congenital heart defects in patients with Down syndrome in first degree family history of heart disease?	
P-Value= 0.621	Result: rejection of the hypotheses
Hypotheses 6: There is a significant relationship between the incidences of congenital heart defects in patients with Down syndrome with gender?	
P-Value= 0.525	Result: rejection of the hypotheses
Hypotheses 7: There is a significant relationship between the incidences of congenital heart defects in patients with Down syndrome with the patient's weight at birth?	
P-Value= 0.041	Result: accept of the hypotheses

Table 3: Results of the hypotheses

According to the table above, we conclude that there are two hypotheses and their importance is increasingly clear to us:

1) Factor for gestational age, heart abnormalities in children with Down syndrome, is very important and gestational age above 35 years can be effective in creating these anomalies.

2) There is a significant relationship between birth weight children with Down syndrome with congenital heart malformations.

In other words, children with Down syndrome with birth weight less than 2.5 kg are more at risk of having congenital heart defects.

The main issue thoroughly examines the following hypothesis.

"Is there a significant relationship between Chromosomal patterns and echocardiographic in Down syndrome patients with the treatment of congenital heart anomalies in children admitted to hospital?"

As noted above, one of 50 patients with Down syndrome, 47 patients (94%) chromosomal pattern of trisomy 21, and the rest of the 3 patients (6%) were translocation pattern. However:

A: Of the 47 patients, who had a pattern of trisomy 21, 27 patients (57.4%) suffered from heart abnormalities and 20 patients (42.6%) were healthy.

B: Of the three people, who were moving pattern, 2 patients (66.7%) suffered from heart defects and one (33.3%) has also been healthy. Most groups also generally the initial treatment is done for them, are infants less than 1 month of age, respectively. In Table 4, the start time of great treat patients with heart disorders, are:

Frequency%	Frequency	Start treatment
58.6	17	From birth to 1 month
41.2	7	From 1 to 3 months
17.2	5	Over 3 months
100	29	Total

Table 4: Prevalence start time treats patients with heart disorders

On the other hand it should be noted, whenever echocardiographic testing is done, when treatment is started and depending on the age of the patient at the time of treatment, the patient's condition changes. So in general, the patient's condition after receiving treatment in three ways congenital heart abnormalities improve themselves has shown that the relative improvement occurred or, or a change has been made and the patient was referred for surgery or other tasks or the patient has died this is shown in Table 5.

Patient's condition after treatment		
Recovery (As partial or complete)	No change (referral for surgery and other things)	Death
20person	7 person	2 person

Table 5: patient status after treatment

The exact time to start treatment for kidney patients, who were suffering from congenital heart problems, the resolution of the future status of these patients is presented in Table 6.

The patient's condition	Treatment time		
	From birth to 1 month	Between 1 to 3 months	More than 3 months
Recovery (20 persons)	14 persons	3 persons	3 persons
Referral for surgery (7 persons)	1 person	3 persons	3 persons
Death (2 persons)	-	1 person	1 person

Table 6: the future status of patients with congenital heart problem by separation

As is found from Table 6, of the 20 people who were suffering from congenital heart problems, 14 patients (70%) with early detection of abnormalities in their heart by echocardiography tests, less than 1 month old at the time of these patients, prescribe medication and other measures, found the road to recovery and their heart abnormality was eliminated. So it can be concluded as soon as possible if treatment is started, can improve congenital heart abnormalities in these patients will help. However, due to chromosomal patterns and ejection fraction in patients treated Table 6. Also, according to Table 6, treatment prognosis distribution with chromosomal and echocardiographic patterns are identified separately in Table 7.

Patient's condition	Chromosomal pattern			Echocardiography pattern	
Recovery (20 persons)	ASD (8 persons, 40%)	PDA (6 persons, 30%)	Other abnormalities (6 persons, 28%)	Trisomy 21 (19 persons, 95%)	Translocation (1 person, 5%)
Referral for surgery (7 persons)	AVSD (5 persons, 71%)		Other abnormalities (2 persons, 29%)	Trisomy 21 (6 persons, 85%)	Translocation (1 person 15%)
Death (2 persons)	Large AVSD (1 person, 50%)		Large PDA (1 person, 50%)	Trisomy 21 (1 person, 100%)	Translocation (0%)

Table 7: Distribution prognosis, treatment with chromosomal patterns and echocardiography

DISCUSSION

This study examines the relationship between patterns ejection fraction in patients with Down syndrome is a congenital heart abnormality at the time of treatment. As study findings show Trisomy 21 Down syndrome patients in this study is the most common cause which is fully compatible with the findings of other studies (95%) [17]. Numerous studies have shown that about half of patients with Down syndrome have congenital heart malformations. Our study also showed that 58 percent of Down's patients also suffer from congenital heart abnormalities which has been done with other studies, is compatible [18].

Due to the high risk of congenital heart defects in patients with Down syndrome, they have a lot of heart treatment centers and units are evaluated. The important point is that the most important cause of morbidity and mortality in patients with congenital heart abnormalities, Down syndrome, especially during the first two

years of life [19]. On the other hand it should be noted that extensive studies regarding the evaluation of early treatment of congenital heart abnormalities either medical or surgical patients was conducted and many of them on the issue of early treatment, especially surgical treatment of these disorders in these patients improves quality of life and increase lifespan and reduce mortality and morbidity of this disease have very different opinions [20].

It seems that early detection of cardiovascular abnormalities and knowing the type of congenital defect in the selection of appropriate treatment strategies in these patients is of utmost importance. In this study we evaluate the frequency and types of congenital heart abnormalities in these categories of patients. Echocardiographic study was conducted in 50 patients with Down syndrome in this study, endocardial cushion defects were the most common abnormality and patent ductus arteriosus that a total of more than half of patients. This finding is consistent with other studies [21]. For example, in our study, open ductus arteriosus was about 29 percent this finding is consistent with other studies that have reported rates of these abnormalities in about 17 percent is close to some extent [22]. On the other hand endocardial cushion defect and Down syndrome seems that the correlation is acceptable; Endocardial cushion defect because the prevalence of Down syndrome with congenital heart disease who are not in much lower and is about 5%, whereas in our study this case, about 25% of cardiac anomalies included. On the other hand genetic and molecular studies in patients have shown that the main characteristic heart defects in Down syndrome is caused by abnormal development in the heart of endocardial cushions which leads to atrial or ventricular septal soft involve a wide range of cardiac malformation and heart valves [23]. Endocardial cushion defect after, cardiac abnormalities common in patients, in addition to increased pulmonary arterial pressure, abdominal septal defects and defect atrial septal was respectively 18 and 10 percent of patients were found. This rate is similar to other studies in this field. Vida et al in a study conducted in 2005 on these patients, abdominal septal defects and defects showed that the prevalence of atrial septal in patients with Down syndrome 27.5% and 12.7% respectively [24]. In the other study, Kava et al (2004) reported that the prevalence of abdominal septal defects and atrial septal defect in these patients were 25.8% and 12.1% respectively [22]. In our study, the prevalence of Tetralogy of Fallot was about 4% of patients with other studies that the rate of abnormalities in Down's patients between 14 and 20 percent have reported, is different. however, that more studies are needed to clarify these differences seem necessary [22]. In our evaluation of the patients in the study, only 3 patients (6%) had a history of heart disease in your family. Only 9 (18%) had a history of drug use by the mother during pregnancy that does not seem to the variables associated with cardiac abnormalities found in these patients. However, more detailed studies with larger amount is needed in this area, as do environmental factors on the incidence of heart abnormalities in Down's patients are not fully understood.

Farid et al also study in Sweden during 1995 to 1998 conducted has reported that 17% of Down's patients had low birth weight equal to 2,500 g that is roughly consistent with our results by 24% have been reported [25]. It also found that people with Down syndrome has birth weight less than 2,500 grams, is somewhat effective in creating their heart abnormality and should be the subject more carefully. Maternal age at birth in 44% of patients is older than 35 years. In a similar study conducted in 2005 by Ahmad et al also showed that patients average age of mother at birth of 29.8 years [26]. However, it should be noted that a proven risk factor in this disease, gestational age is high and this, more serious follow-up of pregnant women at older ages. Other items can be a risk factor for this disease, blood kinship parents [27]. In the present study, a total of 20% of parents with one or two were first cousins; although this rate is lower than other studies that need further research in this area is necessary.

CONCLUSION

Due to the fact that a high percentage of patients with Down syndrome have congenital heart anomalies and on the other hand, these patients respond well to specific treatments and reconstructive surgery, this timely assessment of patients with noninvasive methods such as these abnormalities by echocardiography seems important.

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