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Turner syndrome: Cardiovascular abnormalities and correlation with clinical phenotype and karyotype

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ناهنجاری های مادرزادی قلب در سندرم ترنر: ارتباط آن با فنوتیپ و کاریوتیپ

خلاصه

مقدمه و هدف : سندرم ترنر شایع ترین اختلال کروموزومی جنسی محسوب می‌گردد. ناهنجاری های مادرزادی قلب در این بیماران شیوع بیشتری دارد. از آنجا که رابطه فنوتیپ و ژنوتیپ بیماران با ناهنجاری مادرزادی قلبی در کشور ما بررسی نشده است، این مطالعه به منظور بیان تجربه این مرکز انجام گردید.

روش کار: تعداد ۳۷ بیمار با تشخیص بالینی و ژنتیکی سندرم ترنر طی سال های ۱۳۷٤ تا ۱۳۸۲ در بیمارستان امام رضا(ع) وابسته به دانشگاه علوم پزشکی مشهد، که مرکز ارجاعی و سطح سوم محسوب می گردد، مورد مطالعه قرار گرفت. یافته‌های قلبی و عروقی بیماران جمع‌آوری و رابطه آن با ژنوتیپ و فنوتیپ بیماران تجزیه و تحلیل آماری شد.

نتایج: متوسط سن بیماران در هنگام تشخیص ٤/٤٨±۱۲/۸۱ سال بود. شیوع ناهنجاری های مادرزادی قلب ۲۱٪ که شایع ترین آن کوارکتاسیون آئورت بود. (ریسک نسبی و مطلق آن به ترتیب ۰/۷٥ و ۰/۱٦ بود). توزیع کاریوتیپ بیماران به صورت: ٤٥X(٦٥٪)، اختلالات ساختمان کروموزوم X (۳۰٪) و موزائیسم در ٥٪ موارد بود.
در بیماران با کاریوتیپ ٤٥X ناهنجاری های مادرزادی قلب فراوانی بیشتری داشت ($P<0.05$). در انواع موزائیسم، ناهنجاری مادرزادی قلب مشاهده نگردید. در بیماران با تغییرات ظاهری بیشتر (علائم فنوتیپیک بیشتر)، شیوع ناهنجاری های مادرزادی قلب زیادتر بود که اکثر این بیماران نیز ژنوتیپ ٤٥X داشتند.

نتیجه‌گیری: نظر به شیوع بیشتر ناهنجاری مادرزادی قلب در مبتلایان به سندرم ترنر، بررسی دقیق و دوره‌ای قلبی عروقی در تمام بیماران با فنوتیپ و ژنوتیپ های مختلف در این سندرم امری ضروریست.

کلمات کلیدی : سندرم ترنر ، ناهنجاری مادرزادی قلب ، اکو کاردیوگرافی.

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Introduction

TS is the most common chromosomal abnormalitys in females and is caused by aneuploidy disorder with only one fully functioning X chromosome (1). It presents in its classic form with a charocteristic phenotype and was first deseribed in 1938 by Dr. Henry Turner (1,3). The overall incidence is 2/4000 phenotypic females (1/2000-1/5000 in live born).

Affected systems are; cardiovascular, endocrine, lymphatic, renal, gasterointestinal, otologic, hematologic and neuropsychological involvement (2,4).

Other forms of gonadal dysgensis, syndromes, noonan's syndrome must be differentiated. The specific diagnosis can be established via both phenotypic differences, such as characteristic associated CHD, and appropriated chromosomal studies (5,6,9).

Pts with TS are known to have a higher incidence of CHD than the general population (1,2,8). Early diagnosis of TS makes possible optimal application of all procedures of substitution and symptomatic therapy and offers also psychological support to the parents and Pts (15).

Our series collected 37 Pts not cardiologically preselected, no studies have reported echocardiographic data according to the phenotype and chromosomal pattern in our country. The aim of our study was to assess the incidence and character of associated congenital malformation of the cardiovascular system and our institutinal experience.

Methods

Since 1995 to 2002, 37 unslected Pts with TS have been referred to the pediatric cardiology clinic of Imam Reza Hospital of Mashhad University of Medical Sciences.

Each PT received a noninvasive cardiac evaluation by a pediatric cardiologist, including clinical examination, electrocardigram, transthoracic echocardiogram (M mode, 2D, color and doppler evaluation). One patient with ASD underwent corrective cardiac surgery.

The absolute and relative prevalence of various CHD in Turner patients were calculated and compared with that for the general population (1,2,5,6).

Results

The mean age at the time of diagnosis was 12.81×4.48 years (3-25 years)(Fig 1). Karyotype distribution was: 45,X (65%), X-structural abnormalities (30%), and X-mosaism (5%).

The prevalence of CHD was 21% (8/1000 in general population); two of them had multiple abnormalities.

Coarctation of Aorta was the most prevalent anomaly (16%, 372 times more frequent), followed by aortic valve disease (11%, 85 times more frequent) (Table 1).

When we consider the relative prevalence of the different cardiac anamolies in Turner PTS with CHD, it can be seen that Coarctation of Aorta and Aortic valve disease is significantly higher in T.S with CHD than in the general population ($P<0.5$). 45,X Karyotype have the highest prevalence of CHD followed byX-structural abnormalities (25% and 18% respectively).

The PTS with severe dysmorphic sign's had 45,X karyotype and showed asignificant higher relative risk of cardiac malformation ($P<0.05$). Frequency of major morphologic signs are shown in Fig 2. All of the PTS had short stature.

There is no significant correlation between each sign and CHD ($P>0.05$). 45,X karyotype have the highest prevalence of dysmorphic signs followed by X-structural abnormalities (22/24 and 6/11 of PTS had more than two defined major dysmorphic signs respectively) ($P<0.05$). PTS with X-mosaism have lower prevalence (2/37) and less severe dysmorphic signs (no one had more than two major dysmorphic signs).

Discussion

The mean age at the time of diagnosis was 12.81×4.48 years. That showed delayed diagnosis. In Savendahl and co-workers study the mean age at diagnosis for the 81 patient with Turner Syndrome was 4.2×5.6 years and ranged from prenatal life to 16.8 years (14).

An echocardiographic diagnosis made in time may be of decisive importance for the prevention of complication and proper management. Karyotype distribution was similar to other studies (4,5,7,9,10,11). PTS with TS are known

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to have a higher incidence of CHD than the general population. Most of the studies are based on a cardiologically preselected series. Our study collects a nonselected series (1,3,6,8,9). The prevalence of CHD was 21% vs 0.8% in the general population, which agree with other published unselected series (22-35%) (8,9). Coarctation of the aorta was the most common cardiac anomaly, with a prevalence of 16%. Similar percentages have been reported by other authors (5,7,13) whereas an even higher frequency (ranging from 25% to 34%) has been reported. The second most frequent anomaly was BAV and aortic valve disease found in 11% (8% and 3% respectively) of our Pts. It is known that : Bicuspid aortic valve may become stenotic or incompetent with advancing age. The prevalence of : Bicuspid aortic valve in the general population may be as high as 1-2% of the general population. PAPVC, that is first in some studies, was not seen in our study. Floppy mitral valve was seen in 38% of Pts (six times more frequent). In comparison with general population, a higher incidence of each type of CHD was observed. Coarctation of Aorta was first, being 372 times more common than in the general population, followed by aortic valve disease (85 times) and : Bicuspid aortic valve (6 times).

Conclusion

There is an absolute higher prevalence of CHD in Pts with TS, Anaccurate noninvasive cardiologic evaluation is necessary in all Pts with TS. Early diagnosis and proper management may be decisive importance for the prevention of complication.

Abbreviation

Pts: Patients
PAPVC: Partial anomalous pulmonary venous connection
CHD: Congenital heart defect
TS: Turner Syndrome
CoA: Coarctation of Aorta
BAV: Bicuspid aortic valve

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Table 1: Absolute and relative prevalence of congenital heart defects (CHD) in Turner patients (TS) and general population (GP)

	Absolute prevalence				Relative prevalence	
	TS		GP	TS/GP	GP	P
	(N)	(%)	(%)	Ratio	(%)	
CHD	8	21	0.8	26.25	---	---
CoA	6	16	0.043	372	---	<0.05
BAV	3	8	1.28	6.25	---	---
AOVD	1	3	0.035	85.71	7	<0.05
ASD	1	3	0.064	46.87	10.3	>0.05
MVP	14	38	6	6.33	---	---

PAPVC: Partial anomalous pulmonary venous connection
CHD: Congenital heart defect
CoA: Coarctation of Aorta
AOVD : aortic valve disease
MVP: mitral valve prolapse
TS: Turner syndrome
BAV: Bicuspid aortic valve
ASD: atrial septal defect

FIG 1 . AGE GROUP DISTRIBUTION (TURNER SYNDROME)

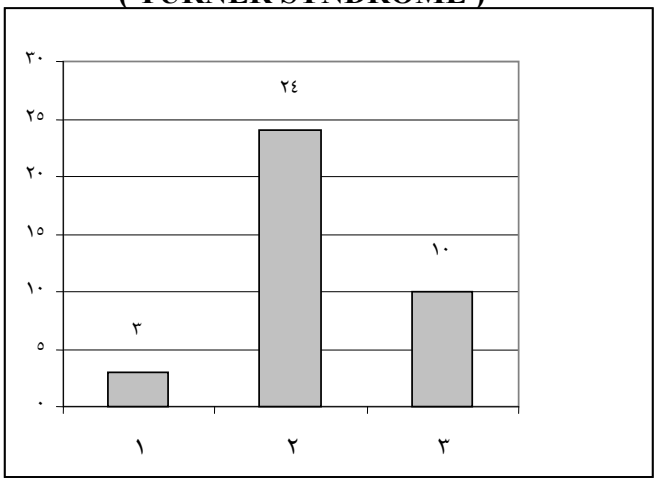
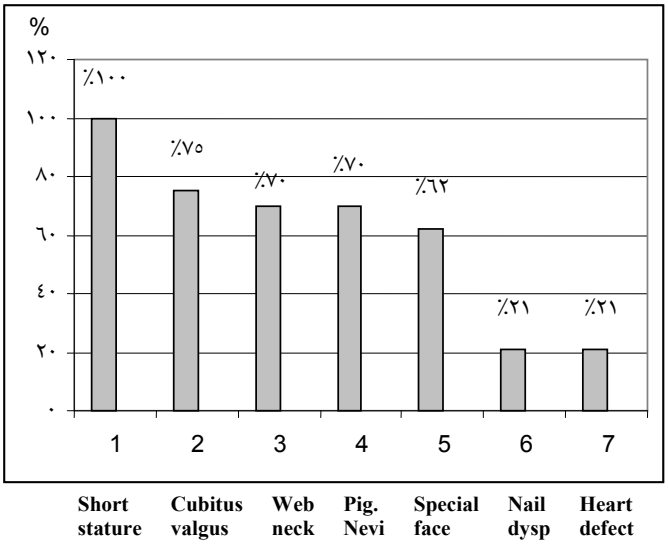


FIG.2. FREQUENCY OF MAJOR DYSMORPHIC SIGN'S (TURNER SYNDROME)



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Abstract

Introduction and Objective: Turner Syndrome (TS) is the most common sex chromosomal abnormality. Patients (Pts) with TS are known to have higher incidence of congenital heart disease (CHD) than the general population. No studies have reported echocardiographic data according to the phenotype and chromosomal pattern in our country. The aim of our study was to assess an institutional experience.

Materials & Methods: During 1995 to 2002, 37 unselected Pts with TS underwent cardiologic evaluation at the Imam-Reza Hospital. Karyotype distribution was: 45,X (65%), X-structural abnormalities (30%) and X-mosaism (5%).

Results: The mean age at the time of diagnosis was 12.81±4.48 years. The prevalence of CHD was 21%. Coarctation of Aorta (CoA) was the most prevalent CHD. (Absolute and relative risk was 16% and 75% respectively) The Pts with 45, X karyotype had the greatest prevalence of CHD, and the PTS with X-mosaism showed no signs of CHD. The Pts with severe dysmorphic signs had 45,X karyotype and showed a significant higer relative risk of cardiac malformations.

Conclusion: There is an absolute higher prevalence of CHD in Pts with TS. An accurate, periodic cardiologic evaluation is necessary in all Pts with TS.

Key Words: Turner Syndrome, Congenital heart disease, Echocardiography, Coarctation of aorta.

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