

Short communication

Study of congenital heart diseases in patients with Down syndrome in Algeria

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دراسة أمراض القلب الوراثية في مرضى متلازمة داون في الجزائر

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الخلاصة: هدفت هذه الدراسة إلى وصف وتقييم نوع وتواتر وأنماط أمراض القلب الوراثية في المرضى المصابين بمتلازمة داون في مدينة سطيف بالجزائر. و متلازمة داون، أو متلازمة تثلث الصبغي 21، هو أكثر الاضطرابات الوراثية شيوعاً في العالم. وقد تم تجميع البيانات ومتابعتها من يناير/ كانون الثاني 2009 إلى ديسمبر/ كانون الأول 2013. وأجري تحليل نَسَب لتوثيق درجة القرابة الأبوية، وتحليل للخلايا الصبغية، وفحص سريري لجميع الحالات. وأظهرت النتائج أن 22 حالة (15.4% ± 0.06) من مجموع حالات متلازمة داون المعروفة والبالغ عددها 143 حالة في مراكز علاج متلازمة داون يعانون من اضطرابات وراثية في القلب، وأن 88 حالة (10.6% ± 2.2) من إجمالي 770 مريضاً مصاباً باضطرابات وراثية في القلب جمعت بياناتهم من الأقسام العامة في المستشفيات التعليمية لصحة الأم والطفل، بمدينة سطيف، يعانون من متلازمة داون. ومن بين 110 حالة، يعاني 75 مريضاً (68%) من تشوهات قلبية أحادية و 35 حالة (32%) من تشوهات قلبية متعددة. وتمثلت أكثر اضطرابات القلب الوراثية شيوعاً في اعتلال الحاجز البطيني. وختاماً، من شأن هذه الدراسة توضيح الوضع الراهن لمتلازمة داون وتحديد توزع اضطرابات القلب الوراثية في مرضى متلازمة داون في مدينة سطيف بالجزائر لإجراء مزيد من الدراسة بشأنها.

ABSTRACT This study aimed to describe and evaluate the type, frequency and patterns of congenital heart diseases (CHDs) in patients with Down Syndrome (DS) in Sétif, Algeria. Down Syndrome, or trisomy 21, is the most common genetic disorder in the world. Data were collected and followed from January 2009 to December 2013. Parental consanguinity documenting pedigree analyzing, chromosome analysis and clinical examination were carried out for all cases. Results have shown that 22 (15.4%; ± 0.06) of the total 143 known cases of DS from DS centres have CHDs and 88 (10.6%; ± 2.2) of the total 770 patients with CHDs collected from public departments at the child and maternity teaching hospital, Sétif, have DS. Among the 110 cases, 75 (68%) have single cardiac abnormalities and 35 (32%) have multiple cardiac abnormalities. The most frequent CHDs were Atrioventricular Septal Defect (AVSD). In conclusion, our study will be helpful to demonstrate the current status of DS and to identify the distribution of CHD in patients with DS in Sétif, Algeria, for further study.

Étude des cardiopathies congénitales chez des patients atteints du syndrome de Down en Algérie

RÉSUMÉ La présente étude avait pour objectif de décrire et d'évaluer le type, la fréquence et les caractéristiques des cardiopathies congénitales chez des patients atteints du syndrome de Down à Sétif (Algérie). Le syndrome de Down, ou la trisomie 21, est le trouble génétique le plus courant au monde. Des données ont été collectées et suivies entre janvier 2009 et décembre 2013. L'étude de la consanguinité des parents incluant l'analyse de l'arbre généalogique, une analyse chromosomique et un examen clinique, a été réalisée pour tous les cas. Les résultats ont montré que sur 143 cas connus de syndrome de Down provenant de centres spécialisés dans la prise en charge de ces patients, 22 (15,4 %; ± 0,06) souffraient d'une cardiopathie congénitale et que sur 770 patients atteints d'une cardiopathie congénitale venant des départements publics des hôpitaux universitaires de soins maternels et infantiles à Sétif, 88 (10,6 %; ± 2,2) étaient atteints du syndrome de Down. Parmi ces 110 cas, 75 (68 %) souffraient d'une seule anomalie cardiaque tandis que 35 (32 %) avaient plusieurs anomalies cardiaques. La cardiopathie congénitale la plus courante était la communication auriculo-ventriculaire. Pour conclure, notre étude sera utile pour mettre en évidence la situation actuelle du syndrome de Down ainsi que pour identifier la répartition des cardiopathies congénitales à Sétif (Algérie) en vue d'études ultérieures sur le sujet.

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Introduction

Congenital heart diseases (CHDs) are a leading cause of birth defects (1,2). Down syndrome, or trisomy 21, is a chromosomal disorder which is often associated with morphological and structural defects. People with Down syndrome are clinically diagnosed by the presence of a characteristic phenotype. The clinical diagnosis is confirmed by chromosome analysis (3). The risk of Down syndrome increases with increasing age of the mother (4).

Among all cases of CHDs, 4–10% have Down syndrome and 40–50% of people with Down syndrome have CHDs (5). They are the most common cause of death in people with Down syndrome in the first 2 years of life (6–8). Therefore, echocardiography is recommended for early detection of CHDs, which may help to prevent many complications. Single heart defects are usually found in people with Down syndrome but multiple defects are also found. In the United States of America and Europe, atrioventricular septal defect is reportedly the most common CHD associated with Down syndrome (9–13). In Asian communities, ventricular septal defect is the most common defect (14,15) whereas in Latin America, atrial septal defect is reportedly the most common defect (11,16).

In recent decades, there has been a substantial increase in the life expectancy of children with Down syndrome in general (17). This increase in life expectancy is mainly due to the successful early surgical treatment of CHD in children with Down syndrome (9,17–20).

There have been no previous studies about CHDs in patients with Down syndrome in Algeria. The aim of this study, therefore, was to determine the type and distribution of CHDs in young patients with Down syndrome in Sétif, eastern Algeria.

Methods

Study design, setting and participants

This case series study examined the type, frequency and patterns of CHDs in young people (< 21 years) with Down syndrome in Sétif. General health care in the area is provided by the Central University Hospital, 12 hospitals, 70 health centres and 320 primary health care centres. There are 6 centres for children and young people (5–20 years) with Down syndrome and other conditions with intellectual disability.

Our study population consisted of all Down syndrome patients with CHDs in Sétif. Patients were drawn from the 6 Down syndrome centres and the university hospital. Primary care physicians in the other hospitals, health centres and primary health care centres have not been trained to treat Down syndrome patients with CHDs so these patients are all referred to these 2 places.

The recruitment period spanned 18 months (January 2009 to June 2010) in order to have a large representative sample. Patients were followed until December 2013. Eligible patients were Sétif residents aged < 21 years, and both sexes were included. Patients with other genetic disorders and Down syndrome without CHDs were excluded.

All Down syndrome patients < 21 years in the 6 Down syndrome centres ($n = 143$) were examined to determine if they had CHDs. In addition, all patients with CHDs < 21 years at the paediatric department of the university hospital of Sétif ($n = 770$) were examined to determine if they had Down syndrome. For comparison, we also included Down syndrome patients without CHDs from the 6 centres who agreed to participate.

Data collection

All potential cases underwent full clinical assessment including phenotypic features that suggested Down syndrome, such as hypotonia, brachycephaly,

small low-set ears, upslanting creases and a gap between the first and second toes. Those with Down syndrome and CHDs, and the Down syndrome patients without CHDs from the centres who agreed to participate had a detailed medical history taken of age, sex, consanguinity and family history with special emphasis on maternal and paternal ages. The diagnosis of Down syndrome was confirmed by chromosome analysis and all patients were examined by plain chest X-ray, electrocardiogram and ultrasound of the heart (2-D echocardiography). The echocardiography examination was performed at the cardiology department using a GE Vivid 3 ultrasound machine.

Statistical analysis

SPSS, version 16 was used for analysis. Descriptive statistics were done and data are presented as means and standard deviations (SD) or proportions.

Ethical considerations

This study was approved by the University Hospital and the Faculty of Medicine of Sétif University. Informed consent was given by the guardians of all the participants; none declined.

Results

Among 143 patients with Down syndrome < 21 years at the 6 centres, 22 (15.4%) had CHDs. Of 770 patients with CHDs < 21 years at the paediatric department of the university hospital, 88 (11.4%) had Down syndrome. Thus, a total of 110 people < 21 years with Down syndrome and CHDs were included in the study. In addition, 66 Down syndrome patients without CHDs agreed to participate for comparison.

Table 1 shows the demographic characteristic of the patients: their ages ranged from 3 months to 20 years, with a mean age of 4.3 (SD 0.5) years, 60

Table 1 Demographic characteristics of Down syndrome patients with congenital heart diseases

Demographic characteristic	No. (n = 110)	%
Age groups (years)		
< 2	40	36
2–4	37	34
5–14	27	24
15–20	6	5
Mean (SD) (years)	4.3 (0.5)	
Sex		
Female	50	45
Male	60	55
Consanguinity		
Yes	13	12
No	97	88

(55%) were male and 13 (12%) had consanguineous parents.

The mean ages of the mothers and fathers of the patients were 36.6 and 43.2 years respectively.

Table 2 compares maternal age and parental consanguinity of Down syndrome patients with and without CHDs. Maternal age 40–49 years was significantly associated with CHDs in Down syndrome patients ($P=0.03$) but first and second degree consanguinity was not ($P=0.12$ and 0.1 respectively).

Table 3 show the types of CHD among the Down syndrome patients

with CHDs. Of the 110 patients, 75 (68%) had a single cardiac abnormality, while 35 (32%) had multiple cardiac abnormalities. The most common CHDs were atrioventricular septal defect isolated (30%) or combined with other cardiac abnormalities (44%), ventricular septal defect (17%), atrial septal defect (7%) and patent ductus arteriosus (6%).

Table 4 shows the distribution of atrioventricular septal defect and ventricular septal defect in the Down syndrome patients by sex. No significant difference by sex was found for either

atrioventricular septal defect or ventricular septal defect ($P > 0.05$).

Discussion

Our study confirms some data reported by other studies on CHDs in people with Down syndrome (13,21). The frequency and distribution of CHDs in Down syndrome varies with geographical region (1). Ours is the first study of CHDs in patients with Down syndrome in a state of Algeria. In our study, the prevalence of CHDs was 15.4% among the Down syndrome patients aged between 5 and 20 years at the Down syndrome centres. This may be because more deaths occurred in patients with Down syndrome and CHDs in the absence of early surgery. The frequency of CHDs in Down syndrome patients observed in our study is less than that reported in Korea (57%), Sudan (43%) and Oman (57%) (16,22,23). However, these studies included infants with a mean age of 3 months versus 52 months in our study. In the hospital sample, among 770 patients with CHDs aged between 3 and 48 months, 11.4% had Down syndrome, which is similar to the prevalence reported in previous studies (4–10%) (1,5,21).

Table 2 Maternal age and parental consanguinity among Down syndrome (DS) patients with and without congenital heart diseases (CHDs)

Variable	DS patients with CHDs (n = 110)	P-value	DS patients without CHDs (n = 66)	P-value
	No. (%)		No. (%)	
Maternal age group (years)				
19–24	10 (9)		9 (14)	
25–29	10 (9)	0.19	4 (6)	0.25
30–34	19 (17)	0.25	7 (11)	0.12
35–39	22 (20)	0.07	17 (26)	0.21
40–49	49 (44)	0.03	29 (44)	0.10
Consanguinity degree				
First degree	8 (7)	0.12	6 (9)	0.25
Second degree	5 (5)	0.10	6 (9)	0.24
None	97 (88)		54 (82)	

Statistical significance at $P < 0.05$.

Table 3 Types of congenital heart diseases in patients with Down syndrome

Type of congenital heart disease	No. (n = 110)	%
Single heart defect	75	68
AVSD	33	30
VSD	19	17
ASD	8	7
PDA	7	6
TOF	4	4
CoA	1	1
MR	3	3
Combined heart defects	35	32
AVSD + PDA	10	9
AVSD + PS	4	4
AVSD + TOF	1	1
AVSD + VPR	1	1
VSD + ASD	4	4
VSD + ASD + PDA	1	1
VSD + PDA	6	5
VSD + PS	1	1
ASD + PDA	6	5
ASD + PS	1	1

ASD = atrial septal defect, AVSD = atrioventricular septal defect, CoA = coarctation of the aorta, PDA = patent ductus arteriosus, MR = mitral regurgitation, PS = pulmonary stenosis, TOF = tetralogy of Fallot, VPR = venous pulmonary return, VSD = ventricular septal defect.

Table 4 Distribution of atrioventricular septal defect and ventricular septal defect in the Down syndrome patients by sex

Congenital heart disease	No.	%	P-value
Atrioventricular septal defect			
Male	26	53	0.21
Female	23	47	0.10
Total	49	100	
Ventricular septal defect			
Male	18	58	0.09
Female	13	42	0.15
Total	31	100	

Consanguineous marriage is common in the Middle East and Arab countries, especially in small and rural areas. In the current study, the consanguinity rate among the parents of the Down syndrome patients with CHDs was 12%. This differs from the rate reported

in Saudi Arabia (57.8%) (24) and other countries. (25–29).

We found a statistically significant relationship between maternal age 40–49 years and Down syndrome with CHDs; however there was no significant difference with mothers \leq 39 years.

Our data differ from those reported in Korean and Lebanese studies; they found that mothers \geq 35 years old were more likely to give birth Down syndrome child with a CHD than infants with Down syndrome born to mothers who were $<$ 35 years of age (15,16).

The most common CHDs in our study were atrioventricular septal defect isolated or combined with other cardiac abnormalities, ventricular septal defect, atrial septal defect and patent ductus arteriosus. This is similar to findings of studies in Europe and the United States of America (12,13). However, atrial septal defect was the most common defect reported as in a Korean study (30.5%) (16). In Saudi Arabia, ventricular septal defect was the most common defect (14), while in Singapore patent foramen ovale predominated (30).

In the absence of newborn screening in Algeria, we could only draw patients from Down syndrome centres and the department of paediatrics of the university hospital. So our patients may not be representative of all Down syndrome patients and the prevalence found is only therefore an approximate figure.

Conclusion

This is the first study to document the types, distribution and frequency of CHDs in Algerian patients with Down syndrome. The most frequent CHD diagnosed was atrioventricular septal defect. High maternal age appears to be a risk factor for CHDs in Down syndrome patients in the Algeria population. The characteristics of CHDs in Down syndrome patients from Sétif are similar to those reported worldwide.

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