# Frequency of congenital heart disease among patients with Down's syndrome in Mosul

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## ABSTRACT

***Background:*** Down's syndrome (DS) or trisomy 21 is a chromosomal disorder frequently associated with a varied combination of morphological and structural birth defects. Individuals with Down syndrome are more prone to congenital heart defects such as atrioventricular septal defects (ASD), ventricular septal defects (VSD), isolated secundum atrial septal defects. Congenital and acquired gastrointestinal anomalies and hypothyroidism are common in patient with DS.

***Aims:*** To measure the frequency of congenital heart disease (CHD) among study population, to categorize CHD according to their anatomical location and to demonstrate socio-demographic characteristics of Down syndrome patients.

***Methods:*** Case series study design was conducted in Mosul over one year period starting from the 1st of Dec. 2011 to the 30th of Nov. 2012. Parents have been intervened by one of the investigators, and a specially designed questionnaire form were completed to each patient.

Echocardiography have been conducted to all patients included in the study by a qualified pediatric cardiologist in Echo Unit- Khansaa Teaching Hospital, the echo result was recorded in the questionnaire form. Analysis of the data was conducted by using SPSS, and excels computer systems; simple rates and ratios were calculated in order to describe the study findings.

***Results:*** The present study includes a total of 69 patients diagnosed with Down's syndrome. Two thirds of study population was below six months of age. Male gender constitutes 69.6% of study population with male to female ratio 1:0.44. 39.2% of mothers are in age group ≥40 years. Fifty patients (72.5%) with DS diagnosed to have CHD by echocardiography. ASD was the most common defect and was diagnosed among 30% of patients, followed by complete AV canal and VSD which constitutes 20% each. 14.5% of patients with DS have extra cardiac anomalies and GIT anomalies were the most frequent one.

***Conclusion:*** The incidence of congenital heart disease in patients with Down's syndrome was high in this study (72.5%). ASD was the most frequent form observed.

**Keywords:** Down's syndrome, CHD.

# نسب حدوث أمراض القلب الولادية لدى المصابين بمتلازمة داون في الموصل

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## الخلاصة

**الخلفية:** متلازمة داون او تثلث الصبغي ٢١ هو اضطراب في الكروموسومات يرتبط غالبا مع مجموعة من العيوب المورفولوجية والخلقية. ألأطفال الذين يعانون من متلازمة داون يكونون اكثر عرضة للإصابة بتشوهات خلقية في القلب (٣٠%-٥٠%) مثل

عيوب الحاجز الأذيني البطيني، عيوب الحاجز البطيني، وعيوب الحاجز الأذيني . كما أن التشوهات الخلقية للجهاز الهضمي ونقص هرمون الغدة الدرقية تعتبر شائعة للمرضى المصابين بمتلازمة داون.

**أهداف البحث:** لقياس نسبة تكرار تشوهات القلب الخلقية لمرضى متلازمة داون قيد الدراسة، لتصنيف تشوهات القلب الخلقية وفقا لموقعها التشريحي ولإظهار الخصائص الاجتماعية والديموغرافية لمرضى متلازمة داون.

**طريقة البحث:** أجريت دراسة تسلسل الحالة في مدينة الموصل للفترة من ٢٠١١/١٢/١ لغاية ٢٠١٢/١١/٣٠ (سنة واحدة) . تم تضمين جميع المرضى المصابين بمتلازمة داون في الدراسة وتم أخذ المعلومات الطبية من أحد الوالدين حسب إستمارة إستبيان خاصة. وقد أجريت فحوصات صدى القلب لجميع المرضى المشمولين بالدراسة من قبل طبيب أطفال مؤهل لإجراء هذا الفحص في مستشفى الخنساء التعليمي للأطفال. أجري تحليل البيانات بإستخدام برنامج SPSS ونظام أكسل.

**النتائج:** شملت هذه الدراسة ٦٩ طفل مصاب بمتلازمة داون وكانت أعمار ثلثي الأطفال المصابين أقل من ستة شهور. كانت نسبة الذكور ٦٩.٦% ونسبة الذكور للأناث ١:٠.٤٤ .كانت أعمار ٥٩.٢% من أمهات الأطفال المصابين أكثر من أو مساوي لأربعين سنة. كانت نسبة زواج غير الأقارب ٥٣.٦% وكانت نسبة إصابة أطفال متلازمة داون بتشوهات القلب الوراثية ٧٢.٥% (٥٠ مريض) .كانت الإصابة بعيوب الحاجز الأذيني ASD هي الأكثر شيوعا (٣٠%) تلتها الإصابة بعيوب الحاجز البطيني VSD وعيوب الحاجز الأذيني البطيني AV canal (٢٠ % لكل واحد منهم). كانت نسبة الإصابة بالتشوهات الخلقية غير القلبية ١٤.٥ % ومثلت تشوهات الجهاز الهضمي النسبة الأعلى. لم تتناول ٥٩.٤ % من أمهات الأطفال المصابين بمتلازمة داون أي علاجات أثناء الحمل .

**الاستنتاجات:** كان نسبة الإصابة بتشوهات القلب الخلقية عالية في هذه الدراسة ٧٢.٥% وكانت الإصابة بعيوب الحاجز الأذيني ASD هي الأكثر تواترا.

**الكلمات المفتاحية:** متلازمة داون، أمراض القلب الوراثية.

## INTRODUCTION

Trisomy 21 or Down syndrome (DS) is a chromosomal disorder commonly related with a varied mixture of morphological and structural birth defects in the form of congenital intellectual disability, hypotonia, distinguishing body features, heart defects, and other inherited malformations. The occurrence of these morphological and functional problems vary considerably among affected individuals. [1]

In 1866, John Langdon Haydon Down first characterize DS as a dissimilar disease with intellectual impairment then in late fifties, Lejeune and Jacobs separately reported that DS resulted from additional chromosome 21. In view of the fact the condition has been known as trisomy 21. [1] This particular trisomy is the most widespread form of chromosomal abnormality, affecting about one in 700 live births [2,3]. It is characterized by the whole chromosomal aneuploidy in about ninety five percent of cases. The remaining five percent is in the form of translocations and mosaics [4]. The risk of pregnancy with DS increases with the mother's age, and it can occur with an incidence as high as one in 30 in those women older than 45 years [1].

Individuals with Down's syndrome are more prone to congenital heart defects (30-50%) such as atrioventricular septal defects, ventricular septal defects (VSD), isolated secundum atrial septal defects(ASD), patent ductus arteriosus (PDA), and tetralogy of Fallot (TOF). hereditary and acquired gastrointestinal anomalies and hypothyroidism are common [5,6]. the cardiac anomalies in mongolism appeared to be due predominantly to defects occurring in the earlier stages of cardiac development [7].

Cardiovascular complications are vital in Down's syndrome. Children who seem asymptomatic at birth and do not have a murmur may have a major cardiac defect. If augmented pulmonary vascular resistance is noted, the left-to-right shunt may be minimized, thus preventing early heart failure. However, if left undetected, this condition may lead to constant pulmonary hypertension with irreversible pulmonary vascular changes.[8] In patients with an ASD, symptoms usually occur in infancy as a result of systemic-to-pulmonary shunting, high pulmonary blood flow, and an enlarged risk of pulmonary arterial hypertension. Augmented pulmonary resistance may lead to a reversal of the systemic-to-pulmonary shunt accompanied by cyanosis [8].

Patients with Down's syndrome are considered to be at superior risk for pulmonary arterial hypertension than patients with no Down syndrome. For the reason that the low number of alveoli, the thinner media of pulmonary arterioles, and the impaired endothelial function. Timely corrective cardiac surgery is warranted to prevent irreversible pulmonary vascular lung damage [9].

### Aims of the study:

1- To measure the frequency of CHD among study populatiom.
2- To categorize CHD according to their anatomical location.
3- To demonstrate socio-demographic characteristics of Down's syndrome patients.

## PATIENTS AND METHODS

The present study was conducted in Mosul over one year period starting from the 1st of Dec. 2011 to the 30th of Nov. 2012. Case series study design was adopted in order to achieve the objectives of the present study.

It was decided to include all patients who are diagnosed to have Down's syndrome by a qualified pediatrician through their consultation to pediatric units in Al-Khansaa Teaching Hospital in Mosul during the study period.

Informed consent has been taken from the parents before inclusion to the study.

Parents have been intervened by one of the investigators, and a specially designed questionnaire form were completed to each patient including age, gender, mother's age, father's age, child rank, drug history during pregnancy, family history of CHD. Furthermore echocardiography have been conducted to all patients included in the study by a qualified pediatric cardiologist in Echo Unit- Khansaa Teaching Hospital, the echo result was recorded in the questionnaire form.

Analysis of the data was conducted by using SPSS, and excels computer systems; simple rates and ratios were calculated in order to describe the study findings.

## RESULTS

The present study includes a total of 69 patients diagnosed with Down's syndrome. **Table 1** depict the characteristics of study population, it is clear from the table that two thirds of study population were below six months of age, on the other hand 20.3% of study population were above 1 year of age. Moreover male gender constitutes 69.6% of study population with male to female ratio 1:0.44, also the table shows that 39.2% and 58.0% of mothers and fathers respectively were in age group ≥40 years; age group 30-40 years constitutes 33.3% and 26.0% of mothers and fathers respectively. Regarding parents consanguinity the table illustrate that more than half of study population (53.6%) gave a negative history for parents consanguinity. Majority of patients have negative family history for CHD, only 10.1% of study population have a positive family history of CHD, see table (1).

**Table 1.** Sociodemographic characteristics of study population, Mosul 2013.

| Characteristic N=69 | No. | % |
|---|---|---|
| **Age (months)** | | |
| 0-6 | 46 | 66.7 |
| 6-12 | 9 | 13.0 |
| ≥12 | 14 | 20.3 |
| **Gender** | | |
| Male | 48 | 69.6 |
| Female | 21 | 30.4 |
| **Mother's age** | | |
| <20 | 6 | 8.7 |
| 20-30 | 13 | 18.8 |
| 30-40 | 23 | 33.3 |
| ≥ 40 | 27 | 39.2 |
| **Father's age** | | |
| <20 | 1 | 1.5 |
| 20-30 | 10 | 14.5 |
| 30-40 | 18 | 26.0 |
| ≥ 40 | 40 | 58.0 |
| **Parents consanguinity** | | |
| Yes | 32 | 46.4 |
| No | 37 | 53.6 |
| **Child rank** | | |
| 1-2 | 20 | 29.0 |
| 3-4 | 14 | 20.3 |
| 5-6 | 9 | 13.0 |
| 7+ | 26 | 37.7 |
| **Family history of CHD** | | |
| Positive | 7 | 10.1 |
| Negative | 62 | 89.9 |

**Table 2** give a picture of distribution of Down's syndrome patients according to CHD, it is evident that fifty patients (72.5%) diagnosed to have CHD by echocardiography. Atrioseptal defect (ASD) was the most common defect and was diagnosed among 30% of patients, followed by complete AV canal and ventricular septal defect (VSD) which constitutes 20% each. On the other hand tetrology of Fallot (TOF) and patent ductus arteriosus (PDA) were diagnosed only in 4 patients (8%) and 3 patients (6%) respectively.

**Table 3** portray the distribution of Down's syndrome patients according to other congenital anomalies, it is obvious that only 10 patients (14.5%) have other congenital anomalies. Intestinal atrasia was diagnosed among 4 patients also anal atrasia was observed in 4 patients; moreover polycystic kidney and hydrocephalus were found in one patient for each.

**Table 2.** Distribution of Down syndrome patients according to CHD, Mosul 2013.

| **Congenital heart disease N=69** | **No.** | **%** |
|---|---|---|
| Present | 50 | 72.5 |
| Not present | 19 | 27.5 |
| **Type of CHD N=50** | | |
| ASD | 15 | 30 |
| Complete AV canal | 10 | 20 |
| VSD | 10 | 20 |
| ASD and VSD | 5 | 10 |
| TOF | 4 | 8 |
| Incomplete AV canal | 3 | 6 |
| PDA | 3 | 6 |

**Table 3.** Distribution of Down syndrome patients according to other congenital anomalies, Mosul 2013.

| **Congenital Anomalies N=69** | **No.** | **%** |
|---|---|---|
| Present | 10 | 14.5 |
| Not present | 59 | 85.5 |
| **Type of Congenital anomalies N=10** | | |
| Intestinal atrasia | 4 | 40 |
| Anal atrasia | 4 | 40 |
| Polycystic kidney | 1 | 10 |
| Hydrocephalus | 1 | 10 |

**Tables 4** describe the distribution of Down's syndrome patients according to history of mother's drug intake during pregnancy, it is clear that 59.4% of mothers have a negative history of drug intake during pregnancy of this child. Twenty eight mothers have a history of drug intake during pregnancy, 18 mothers of them state that they take antibiotics, 5 mothers and 3 mothers ingest methyl dopa and progesterone respectively.

**Table 4.** Distribution of Down syndrome patients according to history of mother's drug intake during pregnancy, Mosul 2013.

| **History of drug intake during pregnancy N=69** | **No.** | **%** |
|---|---|---|
| Present | 28 | 40.6 |
| Not present | 41 | 59.4 |
| **Type of drug intake N=28** | | |
| Antibiotics | 18 | 64.3 |
| Methyl Dopa | 5 | 17.9 |
| Progesterone | 3 | 10.6 |
| Beta agonist | 1 | 3.6 |
| Non-steroidal anti inflammatory | 1 | 3.6 |

## DISCUSSION

Congenital heart disease is common in patients with DS and the incidence vary between 30%-70% [7,10], the introduction of 2DE and Doppler echo provided means of early and accurate diagnosis of CHD.[11]

The incidence of congenital heart disease in this study found to be 72.5% which is higher than that reported by other studies from Malaysia 50%[12], Sudan 48%[13], Mexico 58%[14], and Saudi Arabia 63%[15]. The high incidence of CHD in this study may attribute to the fact that this study was performed in a referral echo center for Mosul.

Down's syndrome is associated with advance maternal age[5,6] and this agree with the present study in which 39.2% of cases of DS occurs in mothers aged 40 years and above. The majority of our patients were diagnosed with congenital heart disease during the first year of life (79.7%), and this agrees with other study done in Mexico[14]. Male sex was predominant (69.6%) and this agrees with other study done in Lebanon[16]. Parent's consanguinity was less common in patients with DS and CHD (46.4%) and this agrees with other study from Lebanon which showed that the risk

of congenital cardiac anomalies was not associated with parents consanguinity [17].

Isolated ASD, VSD and complete AV canal accounted for 70% of the cardiac abnormalities observed in Down syndrome. The most frequent was isolated ASD (30%) followed by VSD and complete AV canal (20% for each). With regard to ASD, value reported in the present study in Mosul agrees with studies from Mexico[14] and Libya 23% [1], and disagree with others from Lebanon[17], Ireland[18] Malaysia[12], and Tunis[19]. The types of cardiac malformation in DS can be determined by different factors like: Genetic factors, specific embryological mechanisms, and cell characteristics. Nevertheless, ethnic and geographic factors may also influence the formation of these abnormalities [14].

The most frequent extra cardiac malformations observed in the present study were related to the digestive tract (80%) with intestinal atrasia and anal atrasia were the most frequent forms (40% for each) a finding consistent with results reported in literatures from Saudi Arabia[15] and India [20].

The present study revealed that 59.4% of mothers have a negative history of drug intake during pregnancy of the Down's child and this agrees with the fact that the only maternal risk factors are advance age and chromosomal translocation[9, 21].

## CONCLUSION

The incidence of congenital heart disease in patients with Down's syndrome was high in the present study (72.5%). ASD, complete AV canal and VSD accounted for 70% of Down syndrome heart abnormalities in the present study setting. Isolated ASD was the most frequent lesion (30%). GIT anomaly was the most frequent extra cardiac anomalies observed.

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