

## Study on Congenital Cardiac Defects of Down Syndrome Children

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### Abstract

**Background:** Down syndrome is one of the most common chromosomal abnormality due to the presence of all or part of a third copy of chromosome 21. Congenital heart diseases are very common in Down syndrome. Various studies described it, but the pattern is different in each study and also most are done in foreign countries only. Early screening and surgical intervention can greatly increase the quality of life and overall life span in these individuals. Only few studies are conducted in India, so we did it at India's largest pediatric hospital, Institute of child health, Chennai, Tamilnadu, India.

**Objective:** To find out the incidence and patterns of congenital heart diseases in Down syndrome and to find out the risk factors for the congenital heart diseases in Down syndrome.

**Materials and Methods:** All karyo-typically confirmed Down syndrome children are included in our study conducted in the tertiary care hospital over the period of one-year. History, examination and Echo and other tests are done. Chi square test is applied. Results are analyzed.

**Results:** Out of 112 Down syndrome children, 55 children (49.1%) are having congenital heart diseases. Incidence of CHD is more in a male with Down syndrome (55%) than in a female (45%). Ventricular Septal defect (34.5%) is the most common CHD followed by Endocardial cushion defect (21.8%). Percentage of CHD was more in trans-location (67%) than due to non-disjunction (49.5%).

**Conclusions:** Congenital heart diseases are very common in Down syndrome. Boys of consanguineous parents are having more chances of congenital heart diseases, Down syndrome children with increased maternal and paternal age are having more probability of having congenital heart diseases and down syndrome children in 3rd or more order of birth are having more chances of congenital heart diseases.

**Keywords:** Down syndrome, Congenital heart diseases.

### Introduction

Down syndrome is the most frequent chromosomal abnormality characterized by well-defined and distinctive phenotypic features and natural history. In 1866, John Langdon Down first described it [1]. It is caused by the triplicate state of all or a critical portion of chromosome 21. Incidence of Down syndrome is 1 in 800 [2]. Children with Down syndrome have multiple malformations but most common is congenital heart diseases<sup>3</sup> followed by intellectual physical growth, bone development, and dental eruption. Non-disjunction is the most common form of the genetic condition Trisomy 21 (95% of Down syndrome),

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mosaicism and translocation are other causes of Down syndrome [3,4], The incidence of Down syndrome rises with increasing maternal age, so most specialists recommend that women who become pregnant at age 35 or older undergo prenatal testing for Down syndrome [5].

David S. Newberger identified the dysmorphic signs of Down syndrome [6]. Increased incidence of about 50% compared with an incidence of 0.4% in infants with normal chromosomes was recognized by Garrod & Maude Abbot [7,1]. Out of which, 30-40% have complete Atrioventricular septal defects [7,8]. followed by ventricular septal defects, Atrial Septal defect (ostium secundum), Patent ductus arteriosus and Tetralogy of Fallot.

## Study Justification

The incidence of congenital heart defects among Down syndrome cases varies from 30 to 65% in previous studies and the incidence in our setting can be calculated. The pattern of congenital heart defects varies among geographic areas and the pattern of CHD in our tertiary care centre can be highlighted. This study will throw light on the various factors like maternal age, order of birth, consanguinity of parents, maternal genetic compositions etc. which are likely to influence the expression of CHD in Down syndrome.

## Objective of The Study

Objective of our study is to determine the incidence and pattern of congenital heart defects in children with karyotypically proved Down syndrome attending a tertiary care centre.

## Materials and Methods

This descriptive study was conducted on 112 karyotypically proved Down syndrome children admitted over the period of 1year in pediatric cardiology ward and pediatric wards at India's largest pediatric hospital, Institute of child health, Chennai. Sample size was calculated from previous studies and the prevalence of Down syndrome children admission.

## Manoeuvre

All karyotypically proved cases will be included in the study. All suspected cases of Down syndrome in the age group of 3 months -12 years, fulfilling the clinical diagnostic criteria were subjected to karyotyping. After a detailed history and physical examination, the cases were subjected to Chest X-ray, ECG and Two-dimensional Echocardiography with colour Doppler by experienced Pediatric Cardiologist using Hewlett Packard Sonos phased array imaging system with 5.0 MHz and 3.7 MHz transducers. Statistical analysis was done using chi square test and p value < 0.05 is considered significant.

## Results

### Observations

112 Down syndrome cases were recruited into the study. Among them 55 cases had congenital heart disease (49.1%) (Table 1). 60 male cases and 52 female cases were recruited into the study with a Male-female ratio of 1: 0.87. It was

found that 55% of male Down syndrome cases had CHD, whereas only 42.3% of female cases had CHD. (The p value of 0.19 is not statistically significant).

## Genetic Composition and CHD Among the Cases

About 92% (103/112) of cases belonged to Non-disjunction, among which 49.5% had CHD. Translocation was noted in 8 cases (7%) among them about 67% had CHD. Mosaicism is noted in only one case who did not have any CHD. (The p value of 0.68 is not statistically significant) (Table 2).

32% of Down syndrome children born of the first order had CHD. In the second order birth about 51% cases had CHD, whereas 20 cases (71%) born of the third order had CHD. (The p value of 0.005 is statistically significant).

## Consanguinity of Parents

All the 3 Down syndrome children (100%) who are off springs of 2nd degree consanguineous parents had congenital heart defects. 58.1% of children with down syndrome born to 3rd degree consanguineous parents had CHD. It dropped to 43.6% when parents are non-consanguineous. (The p value of 0.08 is significant).

## Maternal Age

In the maternal age group of 20-25 years 30.6% of children with Down syndrome are having CHD. In the age group of 26-30 years, 51% of Down syndrome children had CHD. When the maternal age was above 31 years the chances of CHD in Down syndrome increased to 71.4%. (The p value of 0.02 is statistically significant).

## Paternal Age

In the paternal age group of 21-30 years, the risk of CHD in Down syndrome offspring is 39.2%. But in the age group of 31-40 years the risk rises to 55.9% and when the age is 40 and above there is 100% chances of CHD in down syndrome children. (The p value was calculated to be 0.08 is significant).

## Pattern of CHD in Down Syndrome

Ventricular Septal defect is the most common defect identified in 34.5% of down syndrome children with CHD followed by Endocardial cushion defect 21.8% and Atrial Septal defect in 20% of cases. Patent ductus arteriosus was

**Table 1:** Sex distribution.

	CHD		NO CHD		Total	
	N	%	N	%	N	%
Male	33	55	27	45	60	100
Female	22	42	30	58	52	100
Total	55	49	57	51	112	100

**Table 2:** Order of birth.

	CHD		NO CHD		Total	
	N	%	N	%	N	%
First	13	32	28	68	41	100
Second	22	51	21	49	33	100
Third	20	71	8	29	28	100

**Table 3:** Comparison of types of CHD of various studies.

	Our Study	Laursen Hb [17]	Tubman Trj [18]
Vsd	34.50%	49%	21.50%
Endocardial Cushion Defect	22%	19%	29%
Asd	20%	4%	20%
Pda	14.50%	6%	16.70%

detected in 14.5% of cases. Tetralogy of Fallot was found in 2 cases and one case had Coarctation of Aorta and another had Dextrocardia with situs inversus totalis.

## Discussion

Congenital heart disease is the common cause for long term morbidity and mortality in Down syndrome. Between 40-50% of babies with Down syndrome have congenital heart defects. Of these 30-40% have complete Atrioventricular septal defects followed by ASD (25%) and VSD (22%) [9,4].

The incidence of Congenital heart defects among down syndrome children in our present study is 49.1%. Various published studies have reported frequencies ranging from 30-65%. Study by Wells GL et al [10] in the University of Alabama showed an incidence of 48% close to our statistics. In a similar study by Bhatia S. et al [11] in the All India Institute of Medical Sciences, New Delhi, the incidence was 44%. The incidence of CHD in Down syndrome varies among geographical areas. The incidence of CHD in our present study is comparable to that conducted in Alabama, Atlanta, France and Saudi Arabia.

The male-female ratio in our study is 1:0.85, which corresponds to the study done by Venugopalan et al [12] in Oman, 55% of male children with Down syndrome had CHD. In 92% of cases, the cause for Down syndrome is a Non-disjunction.

Half of them had CHD. A trans-location (14, 21) was found in 5 cases and 40% of them had CHD. Trans-location (21, 22) was detected in 3 cases and 2 of them had CHD. One child was found to be mosaic and no CHD was detected. In a study by Wells GL et al [10] in the University of Alabama, 49 (48%) had heart defects; 47 of these had Trisomy 21 and 2 had unbalanced trans-location karyotypes. Of the 53 (52%) who did not have heart defects, all had Trisomy except 1 with a mosaic karyotype and 1 with a trans-location karyotype. So trans-location carries more risk of being born with a CHD. Consanguinity increases the risk of CHD in the general population. Likewise, when the Down syndrome children are born of consanguineous marriage they are having more chances of being born with a CHD. In our study all the cases of 2nd degree consanguinity had CHD. 58% of cases born of 3rd degree Consanguinity had CHD. Among non-consanguineous parentage only 43% had CHD. Consanguineous marriage is common in Arab countries, exceeding 50% in some communities. In a study by Venugopalan et al [12] in Oman, it was found that in high consanguineous areas the incidence of CHD in Down is more like in Turkey where it is 65% and in Oman it is 60%.

As maternal age advances, the risk of giving birth to a Down Syndrome child also increases. In our present study, in the age group 21-25 it is 30% of down syndrome children

are having CHD and in 26-30 it is 51%. The risk is higher in the age group more than 31 years, where 71% of babies born had CHD. It is statistically significant.

Studies by Maria et al [13] give no evidence that paternal age can be considered a risk factor for the conception of a child with Down syndrome. In our study when the paternal age was between 21-30 years, the incidence of CHD was 39% and in the 31-40 age group it was 55%. In 2 cases, the paternal age was above 40 years and both of them had CHD. It is not statistically significant [14-16].

In our present study, Ventricular septal defect (VSD) is the most common abnormality accounting for 34.5% of CHD followed by Endocardial cushion defect (22%). Even though most studies point to Atrioventricular septal defect (AVSD) as the most common abnormality, there are studies depicting VSD as the most common defect. Laursen [17] found VSD in 49% of 80 Down syndrome children with Congenital heart disease. Atrioventricular canal was found in 15% (Table 3).

## Summary and Conclusion

Incidence of Congenital Heart defects in Down syndrome is 49.2%. Incidence of CHD is more in a male with Down syndrome (55%) than in a female (45%). Ventricular Septal defect (34.5%) is the most common CHD followed by Endocardial cushion defect (21.8%). Percentage of CHD was more in trans-location (67%) than due to non-disjunction (49.5%). As the order of birth increases, the chance of congenital cardiac defect also increases so we have to prevent high order of birth by the implementation of family planning. Advanced maternal age is not only a risk factor for increased incidence of Down syndrome, but also an independent risk factor for CHD. Risk of CHD in down syndrome is 100% when born to 2nd degree Consanguineous parentage and 58.1% to 3rd degree consanguineous parents. So, we have to prevent consanguineous marriages. We have to do antenatal screening test for elderly parents to prevent Down syndrome.

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