

Frequency of Thyroid Dysfunction and Congenital Heart Defects in Subjects with Down Syndrome

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Abstract

Objective: To explore the frequency, and types of congenital heart defects (CHD) and Thyroid disorders in children with Down syndrome (DS) in the children's hospital and the institute of child health (CHICH) Multan.

Study design: Descriptive cross-sectional.

Setting: Outpatient department (OPD) of CHICH Multan.

Material and Methods: A total of 158 Down Syndrome (DS) patients of 0 to 15 years of age, of both genders, were included in this study from October 2019 to October 2020. DS was diagnosed by specific clinical features and karyotyping. Age, sex, and mother's age were noted. Blood samples of all the patients were sent for karyotyping and serum T4 and thyroid stimulation hormone (TSH). For patients more than 36 months, blood samples were also sent for antithyroglobulin and antithyroid peroxidase antibodies. Echocardiography of all the patients was done. Data was collected and analyzed by using SPSS version 16.0.

Results: Out of 158 DS children 81 (51.5%) presented below 6 months of age, with a male to female ratio of 1:1.4. 79 (50%) mothers were between 20 to 40 years of age. Karyotyping revealed non-disjunction in 97% of cases. Cardiac abnormalities were found in 48% of DS children. The most common Type was VSD (10.9%), Thyroid abnormalities were detected in 24% of DS patients and subclinical hypothyroidism (13.9%) was most common.

Conclusion: CHD and thyroid disorders must be ruled out in all DS patients, to start early management.

Keywords: Down syndrome, congenital heart disease, hypothyroidism.

Introduction

DS is the most common chromosomal abnormality in humans with a prevalence of 1 in 700-1500 live births.¹ The basic mechanism of this syndrome is trisomy of chromosome 21 in all or some of the body cells.² Non-disjunction is responsible for 95% of cases, while translocation or mosaicism for the rest of the cases.³⁻⁵ DS is the most common genetic cause of intellectual disability worldwide and other health issues like congenital heart defects (CHD), thyroid dysfunctions, hematopoietic disorders, early-onset Alzheimer disease, gastrointestinal disorders, neuromuscular weakness, hearing and visual problems, typical facial and physical features, and a high frequency of other medical conditions.⁶⁻⁹

Thyroid dysfunction is the commonest among the endocrine abnormalities, found in 4-8% of children with Down syndrome.³ In DS patients, the spectrum of thyroid dysfunction includes overt, subclinical, or acquired hypothyroidism, as well as hyperthyroidism.¹⁰ The prevalence of thyroid disorders is higher than the general population in DS patients. These patients most commonly suffered from subclinical and congenital hypothyroidism (CH).^{1,11-15} Nermin H. Amr. reported prevalence of subclinical and congenital hypothyroidism as 7-40 and 28-35 times higher than the general population respectively.³ Hyperthyroidism is mainly due to graves' disease in DS patients.¹⁶

CH is also the preventable cause of mental retardation and increases the risk of other disorders like congenital heart and gastrointestinal as compared to DS without CH¹⁷, so early diagnoses and management of CH in DS patient can reduce the morbidity.

Another health issue in DS is CHD, which is also the main cause of morbidity and mortality in DS especially within the first two years of life.¹⁸ In DS children, variation in the prevalence of CHD, frequency, and associations of its different types have been observed not only from country to country but also among different areas of the same country. It may be due to different inclusion criteria about the size and age of the study population.

A study from Egypt reported 36.9% a Prevalence of CHD in DS.¹⁹ However, In Pakistan prevalence is reported at 41.8%.²⁰ Regarding frequency and association of CHD, Sanaa Benhaourech described atrioventricular septal defect (AVSD) (42.2%) as the most common CHD, followed by ventricular septal defect VSD (31.3%).²¹

This study aimed to determine the frequency and types of CHD and thyroid dysfunction among DS children in south Punjab and to compare our data with other studies.

Materials and Methods

This descriptive cross-sectional study was conducted in the Out-patient Department (OPD) of the CH & ICH Multan. A total of 158 DS patients of 0 to 15 years of age, of both genders, were recruited from developmental pediatrics, pediatric cardiology, and endocrinology OPD from October 2019 to October 2020.

After taking written consent from parents or guardians, detailed history was taken from parents/guardians and patients. The age, sex, and age of the mother were noted. DS was diagnosed by specific clinical features¹ and karyotyping.¹⁻²² Age was divided into 3 groups, 0-6 months, >6-36 months, and >36 months-15 years. For karyotyping, 3-5 cc venous blood was collected and sent to the laboratory.

For identifying thyroid disorders serum T4 and TSH levels of all patients were sent to hospital laboratory assessed by ACCESS-2 Immunodiagnostic system (BECKMAN COULTER) using Chemiluminescence technology. The blood sample of DS children in the age group between 36months to 15 years was also sent for Antithyroglobulin and antithyroid peroxidase antibodies. After the result, children were labelled as euthyroid if T4 and TSH were normal, overt hypothyroid if T4 was low and TSH high, subclinical hypothyroidism with normal T4 and high TSH. Autoimmune hypothyroidism was diagnosed with low T4, high TSH, and the presence of one or both Antithyroglobulin and antithyroid peroxidase antibodies. For detecting hyperthyroidism T4 was high with low or normal TSH.^{20,23}

All the DS children were sent to the pediatric cardiology department for echocardiography by a consultant cardiologist for the diagnosis of CHD and identifying its type. Wherever multiple cardiac lesions were found in the same patient, the leading lesion was taken as the main lesion. Patent foramen ovale, bicuspid aortic valve without significant aortic stenosis or regurgitation were considered as normal

All the information was noted on predesigned Performa and the collected data was analyzed through SPSS version 16.0. Descriptive statistics were applied. The frequency and percentages of all the variables were calculated. The relationship of types of CHD and thyroid disorder with DS was assessed by using the

chi-square test. P-value was calculated, which is considered significant if ≤ 0.05 .

The study was approved by the institutional ethical committee. No conflict of interest was involved in this study. No financial support was provided by the institution or pharmaceutical company. Due autonomy, beneficence, confidentiality, and non-maleficence were ensured to the patients.

Results

Out of 158 DS children most belonged to the age group 0-6 months with a male to female ratio of 1:1.4. Most mothers were between 20 to 40 years of age. Karyotyping revealed non-disjunction as a cause of trisomy in most of the children. Cardiac abnormalities were found in 48% of DS children and the most common defect was ventricular septal defect (VSD) with a p-value of < 0.01 . Thyroid abnormalities were detected in 24% of DS patients, subclinical hypothyroidism (p-value= < 0.01) was most common. The basic characteristics of patients are shown in Table 1. The frequency of congenital heart and thyroid disorders are described in Tables 2, and 3 respectively.

Table 1: Basic Characteristics (N=158)

Variables	N	%
Age		
0-6 months	81	51.1
>6-36 months	61	38.6
>36 months-15 years	16	6.3
Gender		
Male	88	55.7
Female	70	44.3
Age of mother		
<20 years	50	31.6
>20-40 years	79	50
>40 years	29	18.4
Karyotyping		
Non-disjunction	153	97
Translocation	3	1.8
Mosaic	2	1.2

Table 2: Different Types of Cardiac Lesions in Children with Down Syndrome (N=158)

Findings	n	%
Normal Heart	82	52
Cardiac lesions	76	48
Type of cardiac lesion		
Ventricular septal defect	16	10.2
Complete atrioventricular septal defect	15	9.5

Patent ductus arteriosus	14	8.9
Atrial septal defect	11	6.9
Tetralogy of Fallot	05	3.2
Severe pulmonary hypertension	04	2.6
Tricuspid Atresia	03	1.9
Univentricular heart	02	1.2
Pulmonary Atresia	01	0.6
Pulmonary Stenosis	01	0.6
Coarctation of aorta	01	0.6
Ebstein Anomaly	01	0.6

Table 3: Different Types of Thyroid Disorders in Children with Down Syndrome (N=158)

Type of Thyroid disorders	n	%
Normal (euthyroid)	120	76
Thyroid disorders	38	24
Hypothyroidism		
Overt	7	4.4
Subclinical	22	13.9
Autoimmune	4	2.5
Hyperthyroidism		
	5	3.2

Discussion

This study is conducted to know the frequency of CHD and thyroid disorders in DS children presenting to OPD. Most of the children were presented below 6 months of life which is similar to some other studies conducted in children's hospitals Lahore²⁰ and Brazil.²⁴ Chromosomal analysis is still a gold standard for the diagnosis of DS. Karyotyping revealed trisomy by non-disjunction as a most common finding in our study which is favored by the results of other studies of Pakistan^{20,25} and Egypt.²⁶ Mostly the mothers of DS children belongs to 20-40 years of age, while Mia Sotonica et al describes the highest occurrence of DS with mothers from 30 to 39 years old with trisomy as a major type of down syndrome (86.6%).²⁷

In the present study frequency of CHD is 48%, which is almost similar to the prevalence found in Lahore (41.8%).²⁰ Studies done in other countries like Egypt¹⁹, Nigeria²⁸, Iran²⁹, and Thailand³⁰ also reported a high prevalence of CHD in DS i.e. 36.9%, 79.7%, 74.1%, 67.8% respectively. Regarding types of CHD we found mostly isolated lesions, VSD the most common i.e. 10.2%, followed by AVSD 9.5%, PDA 8.9%, and ASD 6.9%. Other less common CHD were severe pulmonary hypertension 2.6%, Tricuspid Atresia 1.9%, Univentricular heart 1.2%, Ebstein Anomaly 0.6%. Studies in Lahore²⁰ and Egypt also described the same results, in isolated cardiac lesions, the most common is

VSD (41% & 14.7% respectively).¹⁹ While some other studies in Thailand³⁰, Guatemala³¹, and Nigeria²⁸, showed AVSD as the most common defect, (12.5%, 11.6%, 39.2% respectively). We found PDA as 3rd most common defect while studies of Nigeria²⁸ and USA³² do not find any isolated PDA case. We have only one case of coarctation of the aorta but the study at Lahore²⁰ does not find any case, while the Thai³⁰ study has 2 cases. Pulmonary stenosis, Pulmonary atresia, pulmonary HTN, Ebstein anomaly, and univentricular heart are diagnosed in this study although in low proportions other studies do not describe these as an isolated lesion,^{31,28} in comparison local study only diagnose PS and pulmonary HTN in few cases.²⁰ Tetralogy of Fallot (3.2%), and TGA+ VSD +PS (1.2%) are multiple cardiac defects found in our study. Another national study found VSD+PDA, VSD+ASD, AVSD+PDA, VSD+bilateral superior vena cava, and VSD+double outlet right ventricle. While an international study found VSD+PDA and VSD+ASD as multiple cardiac lesions.^{19,20}

The present study detects thyroid disorders in 24% of DS children which is similar to other study²⁰, while others conducted by lughatti in Italy, Ali et al in Kuwait, and Unachak in Thailand show a higher prevalence of this association^{33,34,35} Hypothyroidism (overt) is mainly found in 4.4% of DS children which is consistent with other studies in Lahore, Thailand, and Nepal.^{20,35,36} Subclinical hypothyroidism is diagnosed in 13.9% of DS children which co-relate with other studies (prevalence ranging between 12.5-32.5%),^{20,34,35,36,37,38,39} Subclinical hypothyroidism is asymptomatic, Diagnosis of all types of hypothyroidism in children with DS is important as it requires timely treatment in the form of thyroxin replacement therapy to prevent further intellectual deterioration. We have a very low frequency of autoimmune defect i.e. 2.5% which is favored by others too.^{20,39}

Hyperthyroidism was only detected in 3.2% of cases. Other studies also indicate that the prevalence of hyperthyroidism is less common as compared to hypothyroidism in DS patients.^{20,34,35,36,37,38,39}

Limitations

It was a Single-center study without long-term follow-up. We did not focus on the impact of thyroid dysfunction or cardiac lesions on the patients. A multi-center study will long term follow up and the impact of co-morbidities on DS patients should be planned.

Conclusion

CHD and thyroid disorders are commonly present in DS children. The clinical manifestations of CHD like cyanosis, tachypnea, tachycardia, abnormal precordial impulse, or a murmur may not appear so early in DS children, similarly, hypothyroidism also remains asymptomatic in most patients. So diagnostic investigations like (X-ray chest, electrocardiography, and echocardiography, Thyroid profile) must be carried out on all DS patients to rule out cardiac and thyroid lesions and to start early management. Early detection and management of these defects can decrease mortality and morbidity and can improve the quality of life of these patients.

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