



## Comorbid Medical Conditions in Indian Children with Down Syndrome

### KEYWORDS

Down syndrome, medical comorbidities

#### \* Anila Chacko

Assistant Professor, Departments of Paediatrics Unit 3, Christian Medical College, Vellore, Tamil Nadu, India 632004, \* Corresponding Author

#### Sumita Danda

Professor, Clinical Genetics, Christian Medical College, Vellore, Tamil Nadu, India 632004

#### Gibikote Sridhar

Professor, Radiology Christian Medical College, Vellore, Tamil Nadu, India 632004

#### Vivi M. Srivastava

: Professor, Pathology, Christian Medical College, Vellore, Tamil Nadu, India 632004

**ABSTRACT** *Objective:* To study associated medical conditions in Indian children with Down syndrome.

*Methods:* A prospective study was carried out in a tertiary care hospital where consecutive children with Down syndrome were included. The presence of associated medical comorbidities - cardiac, thyroid, hematological, auditory, ophthalmological and skeletal were assessed.

*Results:* Fifty six cytogenetically proven children with Down syndrome were enrolled in the study. Cardiac anomalies were detected in 42%. The common cardiac abnormalities were atrial septal defect, ventricular septal defect and patent ductus arteriosus. Twenty seven percent of children had thyroid abnormalities. Ophthalmologic abnormalities were detected in 46% and auditory abnormalities in 53%. Pre B Acute lymphoblastic leukaemia was identified in 5.4% of the children and 12% of the children above 3 years had atlanto-axial dislocation.

*Conclusion:* There are significant medical comorbidities in Indian children with Down syndrome. Addressing these issues early is important to improve the quality of life.

### INTRODUCTION

Down syndrome (DS) is the most frequent genetic cause of mild to moderate mental retardation. An extra chromosome 21 causes this syndrome.<sup>1</sup>

Children with DS often have other associated medical abnormalities which include cardiac, endocrine, auditory, ophthalmological, skeletal and malignancies. Their quality of life and achievement of maximum potential is optimized by early identification and a multidisciplinary approach while managing these comorbidities. Survival of children with DS has increased and more parents are now seeking care for them. The aim of this study was to identify the associated comorbid medical conditions in Indian children with DS.

### MATERIALS AND METHODS

This was a prospective study conducted in the Department of Pediatrics at Christian Medical College, Vellore, India – a tertiary care medical center. This study was approved by the institutional review board. Consecutive, cytogenetically proven children who were between the ages of 5 months to 16 years over a 1 year period were invited to participate in the study. Once informed consent was obtained, relevant history and detailed clinical examination was carried out. Blood was collected for the following investigations: complete blood count, thyroid function test, thyroid stimulating hormone and karyotyping. Lateral neck X-ray in neutral position to look for atlanto-axial dislocation was done in children older than 3 years. The children then underwent echocardiogram, eye checkup and hearing assessment by the respective specialists.

### RESULTS

Fifty six children were included in the study. There were 42

boys (75%), and 14 girls (25%) between 5 months - 14.9 years. The median age was 2.87 years.

#### Cardiac abnormalities

Fifty two children had echocardiograms done. Cardiac anomalies were detected in 22 (42%). The echocardiogram anomalies were as follows (some children had more than one abnormality): 9/22 (41%) had atrial septal defects, 8/22 (36%) had ventricular septal defects, 6/22 (27%) had patent ductus arteriosus, 2/22 (9%) had atrio-ventricular canal defects, 2/22 (9%) had other defects- mitral valve and tricuspid valve prolapse & pulmonary regurgitation with pericardial effusion. Younger children (<3 years) had more cardiac anomalies (16/27) compared to older children (6/25) (p 0.013).

#### Thyroid Abnormalities

Thyroid function test was done for all children. The profile was as follows: Mild TSH elevation (TSH between 6 – 10  $\mu$ IU/ml with normal TFT) in 16%, Hypothyroidism (TSH above 10  $\mu$ IU/ml) in 7%, hyperthyroidism in 4% and normal thyroid function in 73%. The mean TSH level was 4 $\mu$ IU/ml.

Thyroid auto antibodies were checked for the following

- a. Mild TSH elevation (3/9) all negative
- b. Hypothyroidism (3/4) all positive
- c. Hyperthyroidism (2/2) all positive

There was no significant association between the thyroid status of the children and age (p 0.24), sex (p 0.52), height as plotted on the IAP growth chart (p 0.94), height as plot-

ted on the Cronk growth chart (p 0.87), weight as plotted on the IAP chart (p 0.51), weight as plotted on the Cronk chart (p 0.59) and head circumference (p 0.62).

### Haematological abnormalities

The incidence of anemia was 14.3%, Thrombocytopenia (platelet count < 100 000/mm<sup>3</sup>) was detected in 4 (7.1%) of the children. Thrombocytosis (platelet count > 450 000) was detected in 3 (5.4%) of the children. Hematologic malignancy (Pre B acute lymphoblastic leukaemia) was identified in 3 (5.4%) of the children.

### Skeletal

Atlanto-axial dislocation was looked for in children older than 3 years. 3/25 (12%) had evidence of atlanto-axial dislocation.

### Ophthalmologic and hearing evaluation

Of the 56 children, 41 had ophthalmologic evaluation and 40 had complete hearing assessment. Ophthalmologic abnormalities were detected in 19/41 (46%) children and ENT related abnormalities were detected in 21/40 (53%).

The ophthalmologic abnormalities were as follows (some children had more than one abnormality): refractory error 13/41 (32%), nystagmus 4/41 (10%), cataract 3/41 (7%), squint 2/41 (5%), nasolacrimal duct obstruction 1/41 (2.4%) and brushfield spot 1/41 (2.4%).

ENT abnormalities: 10/40 (25%) had features of otitis media with effusion and 14/40 (35 %) had hearing deficit either unilateral/ bilateral.

Thirty four children had both visual and auditory evaluations. In children  $\geq 3$  years as compared to those <3 years, the prevalence of visual deficits was increased (p0.035).

## DISCUSSION

### Demography

56 children - 42 boys (75%), and 14 girls (25%) were included in the analysis. Thus the male: female ratio was 3:1. In the study by Kava<sup>2</sup> et al, the male: female ratio was 1.37:1 and in Sachdev's<sup>3</sup> study the ratio was 1.84:1. In series abroad, the male: female ratio seen in Myrelid's<sup>4</sup> study was 1.34: 1 and in Cronk's<sup>5</sup> study, it was 1.33:1.

Thus it is seen that our study had an unusually large number of boys. There was no statistical difference between the children in the different age groups with regard to their age and sex distribution. For analysis, the children were grouped into < 3 years (n=29) and  $\geq 3$  years (n=27).

### Cardiac abnormalities

Cardiac anomalies were detected in 22 (42%) of the children. This was similar to the data submitted by Bhatia<sup>6</sup> (44%). Younger children had more cardiac anomalies compared to older children. This was statistically significant (p 0.013).

Kava et al<sup>2</sup> conducted a retrospective study on 524 patients over 7.5 years. Congenital heart disease was clinically diagnosed in 96 cases (18.3%). Cardiac abnormalities were identified by colour Doppler examination and/or 2D-echocardiography in 58 cases. Ventricular septal defect (25.8%), tetralogy of Fallot (15.5%), and atrial septal defect (12.1%) were the common cardiac defects.

Bhatia et al<sup>6</sup> evaluated the utility of echocardiography in assessing the frequency and nature of cardiac malforma-

tions in fifty chromosomally proven children with Down syndrome. Endocardial-cushion-defect was the commonest anomaly, followed by ventricular septal defect.

### Thyroid Abnormalities

Since thyroid abnormalities affect growth, thyroid function test (TFT) and thyroid stimulating hormone were checked for all the children. Our findings fit in with literature where there is a wide variation in prevalence of hypothyroidism from 3 – 54% depending on the definition used.<sup>7</sup>

Thyroid auto antibodies were found to be elevated in 5 out of 6 children with hypo and hyper thyroidism. Thus it is worthwhile checking thyroid antibody status for all children with hypo and hyperthyroidism.

Selikowitz<sup>8</sup> looked at 101 children with DS over 5 years and did not find a significant difference in the growth and development of children who had compensated hypothyroidism (slightly elevated TSH) as compared to those with normal thyroid function.

### Haematological abnormalities

was detected in 8 (14%), leukaemia in 3 (5.4%), thrombocytopenia in 4 (7.1%) and thrombocytosis in 3 (5.4%) of the children.

Awasthi et al<sup>9</sup> studied 239 cases of DS. There were 15 cases (6%) with hematologic abnormalities - 2 had anemia, 1 with myelofibrosis, 1 with idiopathic thrombocytopenia and 4 with transient myeloproliferative disorder (TMD), 3 with TMD/acute leukemia and 4 with acute leukemia.<sup>49</sup> The incidence of leukaemia in our study is probably high as we are a tertiary care center with a well set up Pediatric Oncology Department.

### Ophthalmologic and hearing evaluation

Ophthalmologic abnormalities were seen in 19/41 (46%) children and hearing abnormalities in 21/40 (53%) children. As the age increased, the prevalence of visual deficits increased (p0.035). One possibility is that detection of visual deficits is easier as the child grows older. However prevalence of 61% visual deficits in children over three years is very high.

Roizen<sup>1</sup> concluded that ophthalmologic disorders are found in about 38% of children less than 12 months, and 80% of those between 5 -12 years. The most frequent disorders found in children are refractive errors (35-76%), strabismus (27-57%), and nystagmus (20%).

Another interesting finding was that visual abnormalities were commoner in those who were below the 25<sup>th</sup> percentile in weight as per the IAP charts (p0.02).

47 children were evaluated for hearing abnormalities. Out of these, 7 children went to ENT outpatient clinic, but did not complete their evaluation and so were excluded. 21 of the remaining had abnormal findings. Roizen<sup>1</sup> stated hearing loss to be between 38 – 78%.

Thirty four children had both ENT and ophthalmological evaluations. The interesting finding was that those who had auditory deficits did not have visual deficits and vice versa. This was statistically significant (p 0.04)

### Skeletal abnormalities

3/25 (12%) who were older than 3 years were identified to have atlantoaxial dislocation. 2 were boys and 1 was a girl.

One of the children had surgical stabilization of the spine.

This is similar to the data by Pueschel et al who studied 404 patients with DS - 14.6% had atlantoaxial instability (an Atlanto Dens interval greater than 5 mm), but only 1.5% (n=6) had symptoms and underwent surgical stabilization of the cervical spine.<sup>10</sup>

#### CONCLUSION:

The prevalence of comorbid medical conditions in Indian children with DS is high. About half the children have auditory, ophthalmological and cardiac abnormalities and a quarter have thyroid abnormalities. Other disorders are hematological and skeletal. This information is useful in alerting the Physician to what we can expect in Indian children with DS and thus improving the quality of care.

Conflicts of interest: None

Funding source: **Christian Medical College, Vellore Fluid Research Grant**

#### BIBLIOGRAPHY

1. Roizen NJ, Patterson D. Down's syndrome. *Lancet*. 2003 Apr 12; 361(9365):1281-9.
2. Kava MP, Tullu MS, Muranjan MN, Girisha KM. Down syndrome: clinical profile from India. *Arch Med Res*. 2004 Jan-Feb; 35(1):31-5.
3. Sachdev HS, Menon PS, Verma IC, Ghai OP. Physical growth of children with Down syndrome in India. *Indian J Pediatr*. 1981 Jan-Feb; 48(390):85-9.
4. Myreliid A, Gustafsson J, Ollars B, Anneren G. Growth charts for Down's syndrome from birth to 18 years of age. *Arch Dis Child*. 2002 Aug; 87(2):97-103.
5. Cronk C, Crocker AC, Pueschel SM, Shea AM, Zackai E, Pickens G, et al. Growth charts for children with Down syndrome: 1 month to 18 years of age. *Pediatrics* 1988 Jan; 81(1):102-10
6. Bhatia S, Verma IC, Shrivastava S. Congenital heart disease in Down syndrome: an echocardiographic study. *Indian Pediatr*. 1992 Sep; 29(9):1113-6.
7. Shaw CK, Thapalial A, Nanda S, Shaw P. Thyroid dysfunction in Down syndrome. *Kathmandu Univ Med J (KUMJ)*. 2006 Apr-Jun; 4(2):182-6
8. Selikowitz M. A five-year longitudinal study of thyroid function in children with Down syndrome. *Dev Med Child Neurol*. 1993 May; 35(5):396-401.
9. Awasthi A, Das R, Varma N, Ahluwalia J, Gupta A, Marwaha RK, et al. Hematological disorders in Down syndrome: ten-year experience at a Tertiary Care Centre in North India. *Pediatr Hematol Oncol*. 2005 Sep; 22(6):507-12
10. Pueschel SM, Scola FH. Atlantoaxial instability in individuals with Down syndrome: epidemiologic, radiographic, and clinical studies. *Pediatrics*. 1987 Oct;80(4):555-60.
11. Poeschel SM, Scola FH. Atlantoaxial instability in individuals with Down syndrome: epidemiologic, radiographic, and clinical studies. *Pediatrics*. 1987 Oct;80(4):555-60.