Letter to the Editor

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Thyroid abnormalities among Down syndrome children from Kerala, India

Sir,

Down syndrome (DS), caused by trisomy of human chromosome 21, is one of the most common chromosomal abnormalities in live born infants with a prevalence rate of 1 in 700 live births. Individuals with DS usually have comorbid conditions such as thyroid dysfunction, growth retardation, diabetes mellitus and obesity. The most frequent among these are the thyroid abnormalities which range from subclinical to overt hypothyroidism, rarely hyperthyroidism. 1-3 and Individuals with DS are more susceptible to thyroid disorders compared to the general population. Primary hypothyroidism, referred to as elevated TSH, is the most common thyroid abnormality in DS; secondary hypothyroidism indicated by normal/reduced TSH is extremely rare. The prevalence of hypothyroidism varies between 3-54% in adults with DS.4 The aim of this study was to examine the incidence of thyroid abnormalities among children with DS registered in a tertiary referral center for neurodevelopmental disorders and noncommunicable neurological disorders in Kerala, a south Indian state. 100 children with DS in the age range of 4 months-15 years, registered at Institute Communicative and Cognitive Neurosciences (ICCONS), Shoranur, Kerala during the period of 2012-2016, were recruited for the study. The mean age of the participants (57 males, 43 females) was 5.4±3.8 years. The diagnosis of DS was confirmed by karyotyping. All the participants were drug-naive at the time of blood collection. 500 µl of serum samples was used for thyroid function test (TFT) which measured the levels of TSH, triiodothyronine (T3) and thyroxine (T4) by chemiluminescence immunoassay (CLIA). The reference range for TSH, T3 and T4 were as follows, TSH: 0.4-4mIU/ml, T3: 70-170ng/dl, T4: 4.5- $12.5 \mu g/dl$.

Among the 100 DS patients tested for TFT, 33 patients (33%) had elevated levels of TSH, 16 (16%) had elevated T3, and 10 (10%) had elevated T4. None of the patients showed a decrease in TSH, while 1 patient (1%) had reduced T3, and 4 patients (4%) had reduced T4 levels. 67 patients (67%) had normal TSH, while 83 patients (83%) had normal T3 and 86 patients (86%) had normal T4 levels (Figure 1A, B, C).

The DS patients were categorized as having hypothyroid, subclinical hypothyroid and hyperthyroid status based on the following criteria: elevated TSH along with reduction in T3 and T4 indicates hypothyroidism, elevated TSH

with normal T4 indicate subclinical hypothyroidism, and T3 and T4 indicate hyperthyroidism. Hypothyroidism was further subdivided into two: elevated TSH and reduced T4 indicate primary hypothyroidism, while normal/reduced TSH and reduced T4 indicate secondary hypothyroidism. Abnormal TFT (elevated/reduced TSH, T3 or T4) profile was observed in 53 DS patients, among whom 29 (54.7%) had subclinical hypothyroidism, 1 (1.9%) had primary hypothyroidism, and 3 (5.7%) had secondary hypothyroidism. Among the remaining 20 DS patients with abnormal TFT, three had elevated TSH and T4, while 16 had elevated level of T3, and one patient had decreased T3. A significant negative correlation was observed between age of children and T3 levels (r=-0.439; p=4.92e⁻⁰⁶) (Figure 1D). There was no significant difference between males and females in TSH (t=1.08; p=0.282), T3 (t=0.47; p=0.641) and T4 (t=0.04; p=0.964) levels.

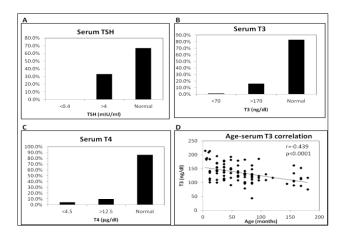


Figure 1: A) Serum TSH, B) T3, C) T4 levels in Down syndrome patients, D) negative correlation between age and serum T3 levels.

Our observation of a high frequency of subclinical hypothyroidism in DS patients is similar to that of previous reports from India¹ and elsewhere.^{2,3} We did not observe any cases of hyperthyroidism in this study. Subclinical hypothyroidism in infants and preschool children with DS is usually a transient condition, with remission in >70% of cases. The clinical significance of subclinical hypothyroidism varies. While there are reports on delayed growth and intellectual development, there are studies which report no significant impact.^{4,5} There are several hypotheses on the pathophysiological

basis of subclinical hypothyroidism in DS. Some of the proposed mechanisms for elevated TSH include hypothalamic pituitary dysfunction, thyroid resistance to TSH, or definite hypothyroidism.⁶⁻⁸ In this study, the reference range of TSH was 0.4-4mIU/ml, which is the usual standard. Since, TSH levels change markedly during childhood, pediatric reference range has been suggested as 0.6-5.5mIU/ml.9 Applying this reference range to our study, the percentage of DS patients with elevated TSH will be reduced to 15%, while 1% has decreased TSH. Age-appropriate reference ranges may be required to detect pediatric thyroid dysfunction to avoid misdiagnosis of hypothyroidism and oversight of mild subclinical hypothyroidism. Our observation of negative correlation between the age of children and serum T3 is similar to that of previous reports.¹⁰

In conclusion, a high frequency of thyroid abnormalities was observed among children with DS. Early screening programs for thyroid dysfunction are recommended to avert the medical issues associated with this condition.

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