

# Hyperthyroidism in Down's Syndrome – A Rare Association

Manju Shrestha<sup>1</sup>, Jyoti Agrawal<sup>2</sup>, Basant Rai<sup>1</sup>, Shipra Chaudhary<sup>2</sup>

<sup>1</sup> Assistant Professor, Department of Paediatrics, BP Koirala Institute of Health Science (BPKIHS), Dharan, Nepal

<sup>2</sup> Associate Professor, Department of Paediatrics, BP Koirala Institute of Health Science (BPKIHS), Dharan, Nepal

## Article History

Received On: 22 Jul, 2022

Accepted On: 11 Apr, 2023

**Funding sources:** None

**Conflict of Interest:** None

## Keywords:

Down syndrome, Carbimazole, Hyperthyroidism

## Online Access



## DOI:

<https://doi.org/10.3126/jnps.v42i3.46894>

## Abstract

Trisomy 21 is the most common chromosomal abnormality in paediatric population, leading to intellectual disability. Hypothyroidism is regarded as commonest endocrine disease in these population. Hyperthyroidism is rare in patients with Down syndrome, but is likely to be underestimated. Hyperthyroidism treatment strategy is highly important for an undisturbed and balanced development of the children. The objective of this case report is to highlight the importance of hyperthyroidism in Down syndrome which is the rare presentation, to best of our knowledge.

## Introduction

The 21 trisomy (Down syndrome, DS) is one of the most common chromosomal disorders in paediatric practice. Thyroid dysfunctions in these patients are very common. Hypothyroidism is diagnosed in nearly 50% of DS patients and the number of patients increases with age.<sup>1</sup> The frequency of congenital hypothyroidism in children with Down Syndrome is 25 to 28 times higher than in general population.<sup>2</sup> This is probably caused by hypoplasia of the thyroid gland (Fibrosis of the gland) during fetal life.<sup>2</sup> Hyperthyroidism though rare is more prevalent in patients with DS than in the general population and has no gender predominance.<sup>3</sup> A hyperthyroid state in children is mostly caused by Grave's disease. It can also be seen in acute and subacute thyroiditis, toxic nodules, toxic multinodular goitres, and thyroid hormone ingestion, however not commonly seen.<sup>4</sup> This condition can have a threatening impact on the process of growth and psychomotor development in children and adolescents. The symptoms, including weight loss, heart arrhythmia, lack of concentration, and behavioural disturbances are distressing.<sup>5</sup> For these reasons, hyperthyroidism treatment strategy is highly important for an undisturbed and balanced development of the children. We report a ten-year-old boy of Down syndrome with hyperthyroidism for the relative rarity of this condition.

## Case report

A 10-year-old boy with a DS presented to the Endocrinology OPD for consultation of voracious appetite and intermittent passage of loose stool. His parents also gave history of 5 kg of body weight loss during 5 months and had problems with concentration. His weight was 17 kg, height was 128 cm. On physical examination, he was afebrile, with mild tachycardia with pulse rate of 110/min and blood pressure of 110/70 mm of Hg. There was a diffuse goitre measuring 10 x 6 cm (Figure 1) and mild proptosis was present. He had mouth ulcer with cheilosis and mild dysphagia (Figure 2). He was admitted and all the workup was done. His base line investigations

## \*Corresponding Author

Manju Shrestha,  
Department of Paediatrics,  
BP Koirala Institute of Health Science  
(BPKIHS), Dharan, Nepal  
Email: drmanjustha@gmail.com

Copyrights & Licensing © 2022 by author(s). This is an Open Access article distributed under Creative Commons Attribution License (CC BY NC)



were within normal limits. His chest X-ray was normal.



Figure 1. Diffuse goitre seen in the neck of the child

His ultrasonography of abdomen and echocardiography were normal. The laboratory results showed elevated levels of free T4 -108 ng / dl (0.8 - 2.3 ng / dl) and free T3 -11.15pg/ml (2.4 - 6.5 pg / ml), as well as decreased level

of TSH -0.01 mIU / ml (0.4 -3.8 mIU / ml), consistent with hyperthyroidism. His thyroid scan was done which showed increased vascularity. He was diagnosed with Grave's disease and oral carbimazole was started. He was followed up for six months for normalisation of thyroid function while on treatment (Table 1).



Figure 2. Ulcer and cheilosis of the tongue

Table 1. Serial change of values of thyroid function test TSH

Tests	Results of treatment				Reference range	Units
	On presentation	weeks 03	months 03	months 06		
T3	11.15	14.18	9.55	6.2	230-660	pg/dl
T4	108	74.62	37.5	22.5	0.8-2.3	ng/dl
TSH	0.01	0.04	0.07	0.1	0.7-6.4	pg/ml

\*TSH: Thyroid stimulating hormone, T3: Triiodothyronine, FT4: Free Thyroxine.

## Discussion

Although DS patients are predisposed to autoimmune diseases, hyperthyroidism in these patients is rarely reported in medical literature. In DS, hyperthyroidism is more common (6.4%) than in the general paediatric population.<sup>6</sup> Clinical characteristics of hyperthyroidism in people with DS are similar to those found in general population with except on for the following: earlier presentation, no gender predominance, more frequent association with other autoimmune diseases, higher frequency of antecedent Hashimoto's thyroiditis, less severe clinical course, and less frequent thyroid eye disease. The reported incidence of hyperthyroidism in DS is much higher, varying between 1: 113 and 1: 141 live births.<sup>7</sup> The presence of hyperthyroidism increases the risk of the presence of other anomalies

including congenital cardiac disease, respiratory distress syndrome, and gastrointestinal anomalies.<sup>8</sup> The presence of congenital hyperthyroidism in DS further increases the risk of congenital anomalies especially gastrointestinal and cardiovascular anomalies when compared to patients with DS without congenital hyperthyroidism.<sup>9</sup>

Patients with Down syndrome are frequently observed to have TSH levels in the higher normal range, and T4 levels in the lower normal range.<sup>10</sup> The most common manifestations of hyperthyroidism include nervousness, insomnia, fatigue, hot and dry skin, excessive sweating, tachycardia, palpitation, weight loss, polyphagia, diarrhoea, tremors and heat intolerance. Regarding goitre, Graves' disease it is typically diffuse (97%). It can be asymmetrical or lobular with variable volume. But there is a finding considered exclusive of the disease: the presence of "thrilling" murmur

of the gland, produced by the notable increase in local blood flow. Any patient presenting with a diffuse goitre and hyperthyroidism should raise the hypothesis of Graves' disease as a diagnosis until otherwise proven.<sup>8-10</sup>

Initial treatment in the population of children and adolescents is antithyroid pharmacotherapy (methimazole).<sup>7-8</sup> Response to the treatment is good, but remission is not often achieved. An aggressive antithyroid therapy can be dangerous, and is contraindicated with concomitant infections.<sup>8</sup> One of the most serious side effect of using thionamids is agranulocytosis.<sup>9</sup> Other major side effects include: lupus-like syndrome (vasculitis), hepatitis, and liver failure. Occurrence of any of these side effects is an indication for considering RAI or surgery.<sup>5</sup> In our case, treatment with carbimazole resulted good remission. RAI in DS remains open for debate because of the risk of cancer. Radioiodine therapy is chosen in some cases, for instance when the thionamide therapy has failed, or when there are some contraindications, or when quick remission of hyperthyroidism is required. Side effects are temporary nausea and mild pain in the area of thyroid gland.<sup>9-10</sup>

## Conclusions

Hyperthyroidism though rare is more prevalent in patients with DS than in the general population and has no gender predominance. High clinical suspicion of this condition is needed to achieve early diagnosis and treatment. Different treatment modalities carry different remission rates and the choice of treatment modality should be individualized.

## References

1. Karlsson B, Gustafsson J, Hedov G, Ivarsson SA, Annerén G. Thyroid dysfunction in Down's syndrome: relation to age and thyroid autoimmunity. *Arch Dis Child*. 1998 Sep 1;79(3):242-5. DOI: 10.1136/adc.79.3.242
2. Fort P, Lifshitz F, Bellisario R, Davis J, Lanes R, Pugliese M, et al. Abnormalities of thyroid function in infants with Down syndrome. *J Pediatr*. 1984;104:545-549. DOI: 10.1016/s0022-3476(84)80544-2
3. Goday Arno A, Cerda Esteva M, Flores Le Roux JA, Chillaron Jordan JJ, Corretger JM, Cano Pérez JF, et al. Hyperthyroidism in a population with Down syndrome (DS). *Clin Endocrinol (Oxf)* 71: 110-114. DOI: 10.1111/j.1365-2265.2008.03419.x
4. Rivkees SA. Pediatric Graves' disease, management in the post-propylthiouracil Era. *Int J Pediatr Endocrinol*. 2014;2014(1),10. DOI:10.1186/1687-9856-2014-10
5. Rivkees SA, Sklar C, Freemark M. Clinical review 99, The management of Graves' disease in children, with special emphasis on radioiodine treatment. *J Clin Endocrinol Metab*. 1998;83:3767-3776. DOI:10.1210/jcem.83.11.5239
6. De Luca F, Corrias A, Salerno M, Wasniewska M, Gastaldi R, Cassio A, et al. Peculiarities of Graves' disease in children and adolescents with Down's syndrome. *Eur J Endocrinol*. 2010;162,591-595. DOI: 10.1530/EJE-09-0751. PMID: 19955260.
7. Burch HB, Wartofsky L. Graves' ophthalmopathy: current concepts regarding pathogenesis and management. *Endocr Rev*. 1993 Dec;14(6):747-93. DOI: 10.1210/edrv-14-6-747. PMID: 8119236.
8. Marchal JP, Maurice-Stam H, Ikelaar NA, Klouwer FC, Verhorstert KW, Witteveen ME, et al. Effects of early thyroxine treatment on development and growth at age 10.7 Years: follow-up of a randomized placebo-controlled trial in children with Down syndrome. *J Clin Endocrinol Metab* 2014; 99: E2722-E2729. DOI: 10.1210/jc.2014-2849
9. Gimenez-Barcons M, Casteras A, Armengol Mdel P, Porta E, Correa PA, Marin A, et al. Autoimmune predisposition in Down syndrome may result from a partial central tolerance failure due to insufficient intrathymic expression of AIRE and peripheral antigens. *J Immunol* 2014; 193: 3872-3879. DOI: 10.4049/jimmunol.1400223
10. Khan SH, Mahajan A, Rather TA. Radioactive Iodine-131 as a definitive treatment in rare association of Down syndrome with hyperthyroidism: a case report and review of literature. *Indian J Nucl Med* 2017; 32: 19-24. DOI:10.4103/0972-3919.198458