

## Progression of Thyrotropinemia in Overweight and Obese Children From Puducherry, India

SRINIVASAN THIAGARAJAN,<sup>1</sup> THIRUNAVUKKARASU ARUN BABU<sup>2</sup> AND RAJESHWAR BALAJI<sup>1</sup>

From Departments of Pediatrics, <sup>1</sup>Indira Gandhi Medical College and Research Institute (IGMC&RI), Puducherry, India; and

<sup>2</sup>All India Institute of Medical Sciences, Mangalagiri, Andhra Pradesh, India.

### Correspondence to:

Dr Thirunavukarasu Arun Babu,  
Associate Professor, Department of  
Pediatrics, AIIMS, Mangalagiri, 522  
503, Andhra Pradesh, India.

\*babuarun@yahoo.co.in

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**Objective:** To assess the progression of thyrotropinemia to overt hypothyroidism in overweight and obese children. **Methods:** 150 overweight and obese children aged 5-15 years were enrolled. Free T4 and thyroid stimulating hormone (TSH) were done at enrollment and for those with TSH >5 mIU/L, TSH levels were repeated after 1 year. **Results:** The mean (SD) body mass index (BMI) and TSH were 23.8 (3.19) kg/m<sup>2</sup> and 2.70 (2.44) mIU/L, respectively. 17 children had thyrotropinemia (TSH between 10-15mIU/L); 10 (84.6%) of these children attained normal TSH levels at one year follow-up, and none progressed to overt hypothyroidism (TSH >15 mIU/L). **Conclusion:** Levels of 5-15 mIU/L are common in asymptomatic overweight and obese children. Majority of these children revert back to normal TSH levels on follow-up.

**Keywords:** Body mass index, Metabolic syndrome, Sub-clinical hypothyroidism, Thyroid stimulating hormone.

Comprehensive National Nutrition Survey (CNNS) 2016-18 reported that 4% of all school age children and 5% of adolescents were overweight based on body mass index (BMI) [1]. Subclinical hypothyroidism (SCH) is very common in overweight and obese children and has an estimated prevalence of about 9% compared to 6.1% in non-obese children in India [2-4]. Risk factors for SCH are female sex, Hashimoto thyroiditis, reduced iodide intake, radiation exposure, etc [2].

Diagnosing SCH in obese children remains controversial as increased TSH levels (thyrotropinemia) are frequently present in obese children [4,5]. Although, the exact mechanism of TSH elevation in obesity is unclear, some studies have attributed thyrotropinemia to increased deiodinase levels converting T4 to T3 as a compensatory mechanism to increase basal metabolic rate, and reduced expression of TSH and T4 receptors in adipose tissue of obese children [6]. Two large population-based studies from India reporting normograms for TSH in normal Indian children are available [3], but there is no consensus in cut-off levels of TSH for obese children [7,8].

Thyroxine replacement for marginal elevations of TSH in childhood obesity has questionable benefits [9]. Obesity may be associated with TSH surge but it does not signify hypothyroidism in all cases. It is unclear if SCH (thyrotropinemia) progresses into overt hypothyroidism in

obese children [2]. Though there are various studies evaluating the intriguing relationship between fT4 and BMI in childhood obesity, the findings are inconsistent [6-8]. Therefore, we studied the progression of thyrotropinemia (SCH) to overt hypothyroidism in obese and overweight children.

### METHODS

This longitudinal study was conducted from July, 2018 to July, 2019 at a tertiary care pediatric hospital in Puducherry, India. Children between 5-15 years of age attending the pediatric out patient department with body mass index (BMI) more than 23 kg/m<sup>2</sup> adult equivalent according to standards for Indian children [10]. Children with BMI between 23 to 27 kg/m<sup>2</sup> and >27 kg/m<sup>2</sup> were categorized as overweight and obese, respectively. Children on anti-thyroid medication, family history of thyroid disorders, and sick children with acute illness requiring admission were excluded from the study. Approval from Institute's research and ethics committee were obtained before commencement of the study. Informed written consent was obtained from the parents and assent from older children.

All children were checked for presence of goiter and symptoms of hypothyroidism like constipation, dry skin, cold intolerance, hair loss, hoarse voice and growth retardation. Weight, height, waist circumference and hip circumference measurements were recorded. Enrolled

children were screened for hypothyroidism with free T4 (fT4) and TSH values following overnight fasting of 12 hour. fT4 and TSH levels were estimated by chemiluminescence method using immunoassay analyzer. Based on a school based Indian study, the reference values of mean fT4 were 1.13-1.34 ng/dL for boys and 1.11-1.22 ng/dL for girls, and TSH 2.57-3.6 mIU/l for boys and 1.83-3.58 mIU/L for girls [4]. Children with TSH >15 mIU/L irrespective of symptoms and TSH between 10 -15 mIU/L with symptoms of hypothyroidism were treated with thyroxine [11]. Lifestyle modifications like healthy eating patterns, increased physical activity and decreased sedentary behavior were advised to all participants. Children with SCH (TSH 5-15 mIU/L) were followed up for a period of one year and serum TSH levels were repeated.

**Statistical analysis:** Data entry was done in MS Excel 2010. Data was analyzed using SPSS version 16.0. Pearson correlation coefficient was used for correlation studies. Wilcoxon signed rank test was applied for comparing baseline and follow-up variables. Values of  $P < 0.05$  were considered statistically significant.

## RESULTS

Among 150 overweight and obese children (49.3% males; mean age, 10.2 year) included in our study, 132 (88%) children were found to have a TSH value of 0-5 mIU/L (euthyroid); 17 (11.3%) had a TSH value corresponding to SCH levels with 15 (10%) having TSH between 5-10 mIU/L). One child (0.66%) had TSH >15 mIU/L diagnosed as overt hypothyroidism and started on thyroxine. The mean fT4 in subgroups with TSH 5-10 and 10-15 mIU/L were 1.40 and 1.78 ng/dL, respectively. The mean (SD) BMI and TSH of the study group were 23.78 (3.19) and 2.70 (2.44) mIU/L, respectively. There was no association of TSH level with overweight or obese children ( $P=0.56$ ). The correlation coefficient of BMI with fT4 and TSH were  $r=0.08$  and  $r=0.016$  (both  $P > 0.05$ ), respectively.

On follow-up of 17 children with SCH, 10 (84.6%) had become euthyroid and 7 (15.4%) remained at subclinical hypothyroid levels. None progressed to overt hypothyroidism. The mean (SD) baseline and following TSH values were 6.33 (2.15) and 4.92 (2.14) ( $P=0.47$ ). Comparison of mean baseline BMI with follow-up BMI is given in **Table I**. No correlation was found between weight loss and TSH change ( $r=0.138$ ;  $P=0.598$ ).

## DISCUSSION

Our study revealed majority (84.6 %) of obese kids with SCH (TSH 5-15 mIU/L) reverted back to euthyroid state within one year. In another study from India, among 40 children (aged 2-16 years) presenting with subclinical hypothyroidism, majority (52.5%) became euthyroid after

**Table I Baseline and Follow-up Body Mass Index (BMI) in Overweight and Obese Children Aged 5-15 Year With Initial Thyroid Stimulating Hormone Level 5-15 mIU/L (N=17)**

Baseline TSH, mIU/L	BMI, kg/m <sup>2</sup>		P value
	Baseline mean (SD)	Follow up mean (SD)	
TSH 5-10	22.48 (2.2)	22.49 (2.1)	0.56
TSH 10-15	25.62 (3.4)	25.59 (3.1)	0.42

the follow-up period of 3 months to 1 year, which was similar to our findings [14]. TSH levels decreased in more than 80% of obese children following life style interventions for obesity without thyroxine therapy [15]. Weight reduction and TSH normalization were attained only with diet and life style modifications [15]. In our study, though TSH levels normalized in most of the children, majority had no weight reduction on follow-up. This was mainly attributed to lack of compliance to life style modifications and lack of regular follow-up.

In this study, we found poor correlation between BMI and TSH/T4 levels, whereas Ghergherehchi, *et al.* [12] demonstrated that levels of TSH and fT4 were significantly higher in children with obesity compared with the control [12]. In a study published from South Korea, BMI was positively correlated with serum concentrations of TSH and negatively correlated with serum concentrations of fT4 after adjusting for age [13]. In this study, we could not demonstrate the relationship between baseline BMI and baseline TSH, which is discordant with many similar studies, which have confirmed the increasing TSH levels with BMI. Similarly, fT4 levels were not associated with BMI in our study though some studies revealed a positive or negative correlation with BMI [12,13].

Relatively smaller sample size and lack of autoimmune thyroid profile data in the study population are some of the limitations of this study. Further multi-centric studies with long term follow-up are needed to detail the cause of hypothyroidism among obese children, and course of thyrotropinemia in adolescence and young adulthood.

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### WHAT THIS STUDY ADDS?

- Subclinical hypothyroid levels of TSH (5-15 mIU/L) were common in overweight and obese children, and reverted back to normal after a one-year follow-up.

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