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Original Research Article

The evaluation of sub clinical hypothyroidism in children and adolescents

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ABSTRACT

Background: Sub clinical hypothyroidism is defined as thyroid stimulating hormone (TSH) >4.2 mIU/ml with a normal level of free T3 and free T4. The prevalence of sub clinical hypothyroidism in adults' ranges from 1-10%, being higher in the elderly and in females. In children and adolescents, the prevalence is estimated to be less than 2%. Usually children and adolescents with sub clinical hypothyroidism have minimal signs and symptoms and the diagnosis is mostly made incidentally. Objective of the study was evaluation of clinical and etiological characteristics of children and adolescents with sub clinical hypothyroidism and to look at long term consequences in terms of progression to overt hypothyroidism.
Methods: Children in the age group of 5-18 years who were referred to the Department of Thyroid and Endocrine Research of Institute of Nuclear Medicine and Allied Sciences (INMAS), from April 2022 to October 2024 with the diagnosis of sub clinical hypothyroidism were recruited for the study. They were followed up for a period of two years.
Results: 52 cases of sub clinical hypothyroidism included 33 girls and 19 boys in the age group of 5-18 years. At the end of two year follow up period, in 67.3% of our patients, TSH reverted to normal range spontaneously without any treatment and only 17 patients (32.7%) progressed to overt hypothyroidism and were initiated levothyroxine replacement therapy.
Conclusions: Sub clinical hypothyroidism in children is a benign and self-limiting condition with low rate of progression to overt hypothyroidism.

Keywords: Sub clinical hypothyroidism, Adolescents and children, Mild thyroid failure

INTRODUCTION

Sub clinical hypothyroidism is defined biochemically as a serum thyroid stimulating hormone (TSH) concentration above the statistically defined upper limit of the reference range and a serum free thyroxine (FT4) concentration within its reference range.[1]

The prevalence of sub clinical hypothyroidism in adults' ranges from 1-10%, being higher in the elderly and in females.[1] In children and adolescents, the prevalence is estimated to be less than 2%.[2] Usually children and adolescents with sub clinical hypothyroidism have minimal signs and symptoms and the diagnosis is mostly made incidentally. In adults, sub clinical hypothyroidism is frequently associated with co morbid conditions like coronary artery disease, dyslipidemia, insulin resistance and non-alcoholic fatty liver disease.[3-11]

The natural history and long term progression of subclinical hypothyroidism in not very clear. Most children with sub clinical hypothyroidism normalize their TSH values and only a small percentage progress to overt hypothyroidism.[12] There are very few studies from India looking at the long-term progression of sub clinical hypothyroidism in children. Therefore, the aim of our study was to analyze the signs and symptoms of sub

clinical hypothyroidism in children and adolescents and also look at its long term consequences including its progression towards overt hypothyroidism.

METHODS

Study subjects

The study was performed in Department of Thyroid and Endocrine Research of Institute of Nuclear Medicine and Allied Sciences (INMAS). Children in the age group of 5-18 years who were referred to the Department of Thyroid and Endocrine Research of INMAS, from April 2022 to October 2024 with the diagnosis of sub clinical hypothyroidism were recruited for the study. In this prospective study the entire cohort was followed up for a period of two years.

52 children in the age group of 5-18 years with biochemical evidence of sub clinical hypothyroidism were enrolled in the study. Children who were taking anti-epileptic medication, glucocorticoids or lithium carbonate were not enrolled for the study. Children with congenital hypothyroidism, type 1 diabetes mellitus and Down's syndrome were also excluded from the study. The local ethical committee approved the study and informed consent was obtained from the parents of the patients.

Measurement

The entire study cohort was asked in detail about the clinical history pertaining to various symptoms of thyroid illness like constipation, inability to gain height, dryness of skin, loss of hair, menstrual disorders and poor concentration. Family history of thyroid disorder was also inquired from all the subjects. They were subjected to anthropometric evaluation, which included measurement of height, weight, and body mass index. Presence of goiter was noted by palpation in all the subjects. Biochemical evaluation included free T3, free T4, TSH and TPO antibody. All the patients were followed for a period of two years. Ultrasound of thyroid was done and hypoechogenecity on ultrasound was considered to be a marker of autoimmunity. Sub clinical hypothyroidism was diagnosed in children if TSH was >4.2 mIu/ml (in two consecutive assays) with a normal free T4.

Statistical analysis

Statistical analysis was performed using statistical package for the social sciences (SPSS) software. Categorical variables were presented as percentages. Continuous variables were represented as mean±standard deviation. A p value of <0.005 was considered statistically significant.

RESULTS

The median age at presentation was eight years. Figure 1 shows the patient complaints at the time of initial recruitment. Out of 52 patients, 33 were girls and remaining 19 were boys. The median age at the time of initial presentation was 8 years. The mean value of free T4 ± standard deviation was 17.12±1.6 and the mean TSH was 6.96±3.2. Table 1 shows the baseline characteristics of the study group differentiated by gender.

Table 1: Baseline characteristics of the study cohort.

Characteristics	Girls (n=33)	Boys (n=19)	P value
Age mean	8.84±3.30	8.47±2.52	NS
TSH (mean±SD)	6.9±1.5	7.14±1.7	NS
FT4 (mean±SD)	18.3±3.14	17.2±2.28	NS
Positive family history (%)	3 (9.09)	1 (5.2)	NS
Presence of TPO antibodies (%)	6 (18.18)	4 (15.78)	0.39

These children were followed up for 2 years. At the end of 2 years, 35 patients (67.3%) had reverted to euthyroid state without levothyroxine replacement. 17 patients eventually progressed to overt hypothyroid state and they were initiated with levothyroxine replacement.

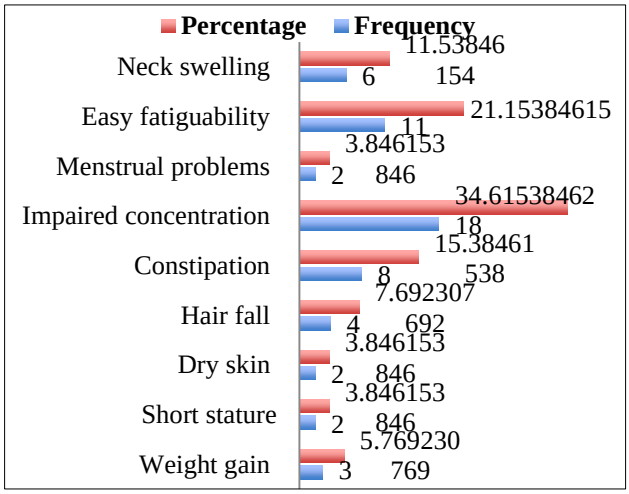

Figure 1: Showing symptoms in patients with sub clinical hypothyroidism.

Table 2: Predictors of progression to overt hypothyroidism in children and adolescents.

S. no.	Predictors
1	Presence of autoimmunity (presence of TPO antibodies)
2	Female sex
3	Family history of thyroid disorders
4	Family history of other autoimmune disorders (celiac disease)
5	Presence of goiter
6	Presence of genetic syndromes (i.e., Down syndrome)
7	High TSH levels at diagnosis

DISCUSSION

Our study aimed at evaluating the natural course of sub clinical hypothyroidism in children and adolescents with a view to establish norms for initiation of levothyroxine replacement in this age group.

The definition of subclinical hypothyroidism is entirely biochemical and establishing the upper limit of normal reference range especially in children is a big challenge. In our center the upper limit of TSH reference interval was 4.2 mIu/ml regardless of age. Lazar et al in their study have used a cut off 5.5 mIu/ml while Hanauton et al cited a cut off value of 4.1 mIu/ml.[13]

The signs and symptoms of sub clinical hypothyroidism are neither specific nor sensitive. Ganelik et al from their study concluded that patients with sub clinical hypothyroidism were usually diagnosed incidentally by biochemical evaluation of thyroid profile. Sub clinical hypothyroidism is actually a biochemical entity characterized by mild elevation of TSH with normal T3 & T4 and therefore patients may not present with clinical signs of hypothyroidism. In our study the most frequent complaint was impaired or poor concentration followed by easy fatigability. Presence of goiter was the most important sign in our children with subclinical hypothyroidism.

Normalization of TSH levels

In our study a vast majority of our patients (67.3%) normalized the TSH and became euthyroid without any treatment. Only 17 patients (32.7%) progressed to overt hypothyroidism and were initiated levothyroxine therapy.

In another study published by Wasniewska et al, natural progression of sub clinical hypothyroidism was studied in 127 girls for 5 years. Girls diagnosed with idiopathic sub clinical hypothyroidism had a higher rate of normalization of TSH.[14] 23.09% still had TSH above the upper limit of reference interval but none of them had TSH >10 mIu/ml. Out of the remaining only 2.6% had a further of TSH >10 mIu/ml which needed replacement therapy.

In India autoimmunity is a key factor that determines the progression of subclinical hypothyroidism to hypothyroidism. In our study 6 girls who tested positive for anti-thyroid antibodies progressed to overt hypothyroidism. Our results were in agreement with Wasnieska et al who studied the long term progression of a large cohort of girls with subclinical hypothyroidism and found that underlying Hashimoto thyroiditis was the main factor to become overtly hypothyroid or require levothyroxine replacement treatment.[15]

In a study performed at our institute in year 2008, Gopalakrishnan et al evaluated 32 children with subclinical (autoimmune) thyroid disorder for natural history and progression to overt hypothyroidism, all these children were followed up for 2 years. In this study TSH normalized in 21.9%, 12.5% of children developed hypothyroidism and 65.6% remained stable as SCH.[16]

CONCLUSION

Subclinical hypothyroidism when it occurs in adolescents and children has a low risk of evolution to overt hypothyroidism and therefore these children should be followed up and reassessed with thyroid function tests evert six months without initiating therapeutic interventions in them.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Biondi B, Cooper DS. The clinical significance of subclinical thyroid dysfunction. Endocr Rev. 2008;29(1):76-131.
2. Wu T, Flowers JW, Tudiver F, Wilson JL, Punyasavatsut N. Subclinical thyroid disorders and cognitive performance among adolescents in the United States. BMC Pediatr. 2006;6:12.
3. Duntas LH, Wartofsky L. Cardiovascular risk and sub clinical hypothyroidism: focus on lipids and new emerging risk factors-what is the evidence? Thyroid. 2007;17(11):1075-81.
4. Wang C. The relationship between type 2 diabetes mellitus and related thyroid diseases. J Diabetes Res. 2013;2013:390534.
5. Razvi S, Weaver JU, Vanderpump MP, Pearce SH. The incidence of ischemic heart disease and mortality in people with subclinical hypothyroidism: reanalysis of the Whickham survey cohort. J Clin Endocrinol Metab. 2010;95(4):1734-40.
6. Bindels AJ, Westendorp RG, Frolich M, Seidell JC, Blokstra A, Smelt AH. The prevalence of subclinical hypothyroidism at different total plasma cholesterol levels in middle aged men and women: a need for case-finding? Clin Endocrinol (Oxf). 1999;50(2):217-20.
7. Pearce EN. Hypothyroidism and dyslipidemia: modern concepts and approaches. Curr Cardiol Rep. 2004;6(6):451-6.
8. Pearce EN. Update in lipid alterations in subclinical hypothyroidism. J Clin Endocrinol Metab. 2012;97(2):326-33.
9. Rizos CV, Elisaf MS, Liberopoulos EN. Effects of thyroid dysfunction on lipid profile. Open Cardiovasc Med J. 2011;5:76-84.
10. Peppa M, Betsi G, Dimitriadis G. Lipid abnormalities and cardiometabolic risk in patients with overt and subclinical thyroid disease. J Lipids. 2011;2011:575840.
11. Asvold BO, Vatten LJ, Nilsen TI, Bjoro T. The association between TSH within the reference range

and serum lipid concentrations in a population-based study. the HUNT study. Eur J Endocrinol. 2007;156(2):181-6.
12. Rapa A, Monzani A, Moia S, Vivenza D, Bellone S, Petri A, et al. Subclinical hypothyroidism in children and adolescents: a wide range of clinical, biochemical, and genetic factors involved. J Clin Endocrinol Metab. 2009;94(7):2414-20.
13. Lazar L, Frumkin R, Battat E, Lebenthal Y, Philip M. Natural history of thyroid function tests over 5 years in a large pediatric cohort. J Clin Endocrinol Metabolism. 2009;94(5):1678-82.
14. Wasniewska M, Corrias A, Aversa T. Comparative evaluation of therapy with L-thyroxine versus no treatment in children with idiopathic and mild subclinical hypothyroidism. Hormone Res Paediatr. 2012;77(6):376-81.
15. Wasniewska M, Aversa T, Salerno M, Corrias A, Messina MF, Mussa A, et al. Five-year prospective evaluation of thyroid function in girls with subclinical mild hypothyroidism of different etiology. Eur J Endocrinol. 2015;173:801-8.
16. Sripati G, Chugh PK, Chhillar M, Ambardar VK, Sahoo M, Sankar R. Goitrous autoimmune thyroiditis in a pediatric population: A longitudinal study. Pediatrics. 2008;122:e670-4.

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