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HYPOTHYROIDISM IN PAEDIATRIC AGE GROUP – A LONGITUDINAL STUDY

Community Medicine

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ABSTRACT

This longitudinal study was conducted at a teaching hospital in a metropolitan city in Western India on 42 patients (33 girls: 78.57% and 9 boys: 21.43%) who had confirmed diagnosis of autoimmune thyroiditis. The mean age of girls was 9.48 +/- 2.83 years, while that for boys was 9.67 +/- 2.74 years. Nearly 50% of patients had family history of thyroid dysfunction. The mothers of 17 patients were affected with hypothyroidism and 5 out of these 17 mothers (29.41%) had thyroid antibodies. Paternal history of thyroid dysfunction was reported in 4 families and in one family; there was a history of thyrotoxicosis in father and grandfather. Goitre was the most frequent clinical finding; other common findings were dry skin, short stature and bradycardia. On follow-up, all children had improved clinical and biochemical parameters. Catch-up growth was observed, with growth rate increasing 2 to 3 fold above the normal for age.

KEYWORDS

Autoimmune thyroiditis, Goitre, Hashimoto's thyroiditis, Hypothyroidism, Thyroid

INTRODUCTION

The prevalence of mild sub-clinical hypothyroidism in children and adolescents ranges between 1.7% and 2.9%, [1, 2] and resolves spontaneously or may persist without progressing to overt hypothyroidism. The causes of persistent sub-clinical hypothyroidism include – Hashimoto's disease, obesity and overweight, genetic syndromes, iodine deficiency and excess, medications and ionizing radiation, and chemical exposures. If no clear aetiology can be identified, the condition is labelled as being "idiopathic".

Autoimmune thyroiditis, also called Lymphocytic Thyroiditis or Hashimoto Thyroiditis, is seen in children above the age of 5 years and in adolescents (4-7 times more common in girls). [3, 4] This condition is seen in children with genetic conditions, such as, Down syndrome or Turner syndrome, [5] and in patients with other autoimmune diseases, such as, celiac disease or type-1 diabetes mellitus. [5, 6]

A mild increase in thyroid-stimulating hormone (TSH) levels is found in overweight and obese children, [7, 8] which may be an adaptive response designed to reduce the availability of energy for conversion into fat. [8] These abnormalities return to normal after weight loss. Thus, the increase in TSH levels in obese persons is reversible and seems to be an outcome and not the cause of obesity. [8-10] Thyroxine therapy is not necessary in obese children with a mild increase in TSH levels. [11]

25.3% to 60.0% of children with Down syndrome may have sub-clinical hypothyroidism. [12] Pseudohypoparathyroidism type 1a is another genetic disorder that is associated with sub-clinical hypothyroidism. [13] In moderate to severe iodine deficiency, goitre and overt hypothyroidism can develop and on the other hand, excess iodine intake may also increase the incidence of sub-clinical hypothyroidism. [14] Iodine-containing medications, [15] iatrogenic iodine excess from radiographic contrast, [16] treatment with iodine (131I) radio-isotope, [17] cough suppressants and nutritional supplements containing iodine, [18] interferon (IFN)-α therapy, [19] antiepileptic drugs (phenobarbital, phenytoin, carbamazepine, and valproic acid), [20] and lithium therapy [21] can also impair thyroid function. Several chemicals (perfluorinated chemicals, polychlorinated biphenyls and dioxins, bisphenol A, perchlorate, and phthalates), [22] food, and consumer products, can interfere with thyroid function by acting on different points of regulation of thyroid hormone. [23] Dioxins and polychlorinated biphenyls may cross the placenta and get excreted in breast milk. [22]

The purpose of the present study was to document the clinical spectrum of autoimmune thyroiditis in children and adolescents, to study their investigational profile and correlate with clinical findings and to follow up all the participants included in the study.

MATERIALS AND METHODS

This longitudinal study was conducted on children and adolescents of either gender, up to 18 years of age, who had confirmed diagnosis of autoimmune thyroiditis at a teaching hospital in a metropolitan city in Western India. Patients with acute and sub-acute thyroiditis were excluded. After explaining about the study and obtaining written informed consent from parents / guardians, the details of history, family history and examination findings at initial presentation and the results of all investigation were recorded. Careful clinical examination was done and anthropometric measurements were recorded. Standard charts [24] were used for grading height, weight, weight-for-height and height-for-age. The grading system of the World Health Organization [25] was used for grading goitre size. Standard radio immunoassay kits estimated serum levels of T3 and T4, the sensitivity of the assays being 0.24ng/ml and 0.5µg/ml, respectively. Serum TSH was assayed by immunoradiometric (IRMA) assay with a sensitivity of 0.07µIU/ml and the laboratory normal range was 0.2-5.1µIU/ml. Antithyroglobulib (ATG) and microsomal (AMA) antibodies were tested by serodia kits macrohemagglutination test (Fujirebio Inc, Tokyo, Japan) with appropriate controls. Titres of more than 1 in 100 were considered positive for ATG and AMA in children.

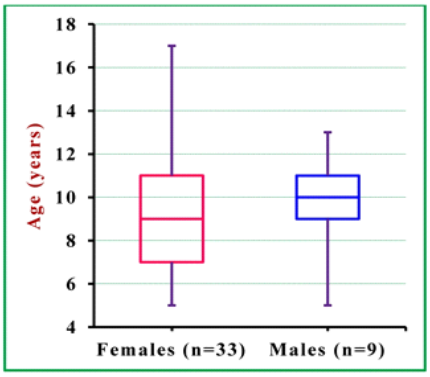
Initial follow up was always advised 6-8 weeks after instituting therapy, when serum T3, T4 and TSH were re-estimated and clinical examination carried out, with upward and downward revision of the dose as required. During follow up height, weight, improvement in symptoms and signs including size of the goitre was recorded and any side effects of therapy were assessed.

The data were entered in Microsoft Excel spreadsheet (Microsoft Corporation, Redmond, WA, USA). The percentages were calculated for categorical data. For continuous data, the arithmetic mean and standard deviation were calculated. 95% Confidence interval (CI) was stated as: [Mean-(1.96)*Standard Error)] - [Mean+(1.96)* Standard Error)].

RESULTS AND DISCUSSION

There were a total of 42 patients (33 girls: 78.57% and 9 boys: 21.43%) in this study. The mean age of girls was 9.48 +/- 2.83 years (95% CI:

8.52 – 10.45 years), while that for boys was 9.67 +/- 2.74 years (95% CI: 7.88 – 11.46 years).



The minimum and third quartile of the age distribution was identical for patients of both genders; median and first quartile was higher for males and the maximum age was higher for females. (Fig-1).

Table-1: Frequencies of presenting complaints

Major Complaints	No. of patients (n=42)
Weight gain	19 (45.24%)
Lethargy	17 (40.48%)
Poor growth	13 (30.95%)
Goitre	09 (21.43%)
Constipation	08 (19.05%)
Adverse effect on schooling	07 (16.67%)
Cold intolerance	06 (14.29%)
Dry skin	06 (14.29%)
Puffiness of face	04 (09.52%)
Hair loss	02 (04.76%)

History: The frequencies of the presenting complaints are depicted in Table-1. One child presented with history of delayed development, one child with history of hyperactive behavior; one girl presented with history of premature adrenarche, which on subsequent follow up was non-progressive. One boy had a history of sertoli cell tumor for which he was operated and declared as cured. Down syndrome was diagnosed in one patient, showing association of thyroid dysfunction with trisomy 21. One patient was on treatment for Asperger's syndrome with autism. Nearly 50% of patients had family history of thyroid dysfunction. The mothers of 17 patients were affected with hypothyroidism, out of which, 5 mothers had thyroid antibodies. Paternal history of thyroid dysfunction was reported in 4 families and in one family; there was a history of thyrotoxicosis in father and grandfather.

Anthropometry: Out of 42 children, 13 (30.95%) had presented with failure to gain height. The height was less than 3rd percentile in 12 (28.57%) patients. Weight of 34 (80.95%) children was between 3rd and 97th percentile. Failure to gain weight was observed only in 3 (7.14%).

Clinical examination: Goitre was seen in 23 (54.76%): Grades Ia, Ib and II in 21 (50%) and Grade III in 2 (4.76%). Other features were: dry skin: in 13 (30.95%), facial puffiness: 4 (9.52%), pallor: 9 (21.42%), delayed reflexes: 3 (7.14%), bradycardia: 6 (14.28%), hypertrichosis: 5 (11.90%) and delayed dentition: 2 (4.76%).

Table-2: Mean serum levels of thyroid-related hormones before and during follow-up

Baseline & Follow-up	Serum TSH (mIU/mL)	Serum T3 (ng/dL)	Free T3 (pmol/L)	Serum T4 (µg/dL)	Free T4 (pmol/L)
Baseline (at presentation)	131.04 +/- 145.98	99.88 +/- 57.89	1.92 +/- 1.26	3.95 +/- 3.12	1.19 +/- 2.18
3 months	33.17 +/- 106.57	141.78 +/- 49.24	4.98 +/- 2.08	8.07 +/- 2.89	3.56 +/- 6.96
1 year	5.13 +/- 5.59	123.70 +/- 42.34	3.59 +/- 0.94	8.39 +/- 2.33	2.76 +/- 4.40
2 year	4.39 +/- 5.54	146.27 +/- 35.58	4.56 +/- 2.45	8.47 +/- 2.39	2.97 +/- 5.14
4 year	3.28 +/- 3.95	145.88 +/- 31.77	2.9 +/- 0.56	9.25 +/- 1.59	1.11 +/- 0.24
6 year	2.42 +/- 2.41	128.8 +/- 1.13	2.5 +/- 0.99	8.7 +/- 1.27	1.16 +/- 0.14

Hormone levels: The mean serum levels of thyroid-related hormones at presentation ("baseline") and during follow-up are mentioned in Table-2.

Follow-ups: In 30 (71.42%), thyroid hormone and TSH had normalized at the end of 3 months of treatment. Catch growth was observed, with growth rate increasing 2 to 3 fold above the normal for age. Treatment was stopped in three children who had maintained euthyroid status clinically and biochemically over the treatment period of 2-3 years along with decline in the antibody titres. The treatment was stopped for a period of 4-6 weeks and the children were recalled for re-assessment. Recurrence of clinical as well as biochemical parameters was seen in 2 cases and treatment was restarted. The treatment was stopped in one 12-year old female who had normal biochemical profile with no symptoms or signs suggestive of hypothyroidism. On regular follow up, she continued to remain euthyroid.

CONCLUSION

This study was conducted on 42 patients (33 girls: 78.57% and 9 boys: 21.43%) aged between 5 years and 18 years. Nearly 50% of patients had family history of thyroid dysfunction. The mothers of 17 patients were affected with hypothyroidism and 5 out of these 17 mothers (29.41%) had thyroid antibodies. Paternal history of thyroid dysfunction was reported in 4 families and in one family; there was a history of thyrotoxicosis in father and grandfather.

Goitre was the most frequent clinical finding; other common findings were dry skin, short stature and bradycardia. On follow-up, all children had improved clinical and biochemical parameters. Catch-up growth was observed, with growth rate increasing 2 to 3 fold above the normal for age.

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