Familial Autoimmune Thyroid Disease

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ABSTRACT

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Auto immune thyroiditis (AIT) has shown an increased prevalence in Kerala. Various studies conducted showed a significant correlation with hypothyroidism and antibody positivity. The present study was conducted to find the prevalence of thyroid auto antibodies in the immediate relatives of 74 proven AIT patients. Of the 142 relatives screened, 94% showed antibody positivity. 46% of the screened relatives were found to have hypothyroidism (with 15% newly detected cases) and 98.5% of them were antibody positive. All the newly detected cases were antibody positive. The results of our study stress the importance of estimating thyroid auto antibodies and thyroid function tests to detect early asymptomatic hypothyroidism in patients with antibody positivity.

Keywords: Autoimmune thyroiditis, Familial, Hypothyroidism, Antibody positivity

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INTRODUCTION

Hypothyroidism is a very common disorder of the thyroid gland, especially in females. The onset of the symptoms is starting in the later age, i.e., in the reproductive age, where its complications cost a lot. The most common form of hypothyroidism seen is Autoimmune Thyroiditis. Autoimmune thyroiditis has shown an increased prevalence in Kerala. Studies done in our institution showed that 70% of patients attending our clinic with thyroid problem had autoimmune thyroiditis (Grave's disease and myxedema excluded). This was a retrospective study of selected patients having histologically proven AIT.[1] Family history of thyroid disease was common in these clinic patients. A pilot study was conducted by us previously to estimate the prevalence of auto antibodies in young asymptomatic females and males. 125 males and 125 females in the age group 15-35 years were selected at random. Very high prevalence antibody positivity was found in these asymptomatic general population- 89% in females and 72% in males.[2,3] Hypothyroidism was detected in 1.8% females and 3.3% males with positive antibodies.

Another study on pregnant patients revealed the presence of thyroid auto antibodies were present in 29% cases.[4] A statistically significant correlation of hypothyroidism with antibody positive pregnant patients compared to antibody negatives was also found (p=0.005). In another study it was shown that 75% of babies born to pregnant patients with thyroid auto antibodies had positive antibodies.[5]

All these data led to us to conduct a study on the familial inheritance of autoimmune thyroiditis.

MATERIALS AND METHODS

After the approval of the Ethical Committee, this study was conducted on immediate relatives **(table 1)** of 74 index cases with proven auto immune thyroiditis- (thyroid antibody positivity & FNAC). These cases were selected randomly from the relatives who accompanied the index cases. 142 immediate relatives of 74 index cases were studied-which included 66 females and 8 males.

All of them were screened for thyroid function and antithyroid antibody status. TFT, Anti TPO and ATG antibody assays were done by fully automated analyzer (Cobase 411, Roche) the principle of the assay is Electro-chemiluminescence immune assay; on the same

Table 1. Study population

Father	Mother	Daughters	Son	Sisters	Brothers	Grand daughter	Grandson	Grandmother	Aunt	Nephew
4	17	53	48	12	3	1	1	1	1	1

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day of blood collection. All the values above the upper limit of normal were taken as positive. (Normal values: AMA/ATG: <9IU/ml; TSH: <5μIU/dl).

RESULTS

The age group of index cases varied from15-65 years.

The age wise distribution is given in **table 2.**

Table 2. Age group distribution

Age group	Male	Female	Total
15- 19 years	0	2	2
20- 29 years	1	31	32
30-39 years	4	19	23
40- 49 years	3	7	10
50- 59 years	0	5	5
>60 years	0	2	2
Total	8	66	74

50 out of 74 (68%) patients belong to the age group 20-39 years and 66 out of 74 (89%) were females.

Thyroid Function in Index Cases

Thyroid functions of Index cases areas shown in the **table 3**.

Table 3. Thyroid function of index cases

Euthyroid	Hypothyroid	hyperthyroid
47	22	5

30% index cases were hypothyroid, 6% hyperthyroid and the rest were euthyroid.

1. Antibody positivity in the relatives (table 4)

133 out of 142 [93.6%] had antibody positivity. Out of 133 individuals, 84 [63%] had both antibodies positive; 44 [33%] had only anti TPO; 5 [3.7%] had only ATG. Anti TPO was the most prevalent one which was present in 128 cases (90% of the screened cases). ATG was present in 89 (62.6%) cases. Majority had both antibodies 84 of 142 (59%). Value was considered positive when it is above the normal range.

Table 4. Antibody positivity in relatives

No. of subjects	Both Antibodies positive	Only TPO +ve	Only ATg +ve	No antibodies
142	84	44	5	9

Table 5. Thyroid function in relatives

Hypothyroid	Euthyroid	Hyperthyroid	Total
65	77	0	142

2. Thyroid function status of Relatives of index cases (table 5)

65 out of 142 cases (45.7%) had hypothyroidism. Of the 65 hypothyroid cases detected, 64 (98.5%) had antibody positivity. Only 1 male case had hypothyroidism with no antibodies. The 65 cases included 52 females and 13 males. Of Euthyroid cases, 68 individuals (85%) had positive antibodies and 9 (12%) had no antibodies. (Cases included 43 males and 34 females).

3. Newly detected hypothyroid cases

Of the 65 hypothyroid cases 10 were newly detected to have hypothyroidism; ie.15.4% - 5 daughters, 2 sons, 1 nephew, 2 mothers. 8 cases were <25 years and 2 cases were >60 years.

4. Antibody positivity

All the 10 cases were antibody positive (100%). 9 individuals had both antibodies positive (90%); 1 had only Anti Tg antibodies.

5. Relation between hypothyroid index cases and hypothyroidism among screened relatives

1. All the relatives of hypothyroid index cases were found to be one/both antibody positive. All the individuals had anti TPO positivity.
2. 60.5% (23 out of 38) of relatives of hypothyroid index cases were hypothyroid.
3. Of the 65 hypothyroid relatives screened, 35.4% had hypothyroid index cases.
4. Of the 10 newly detected hypothyroid relatives, 4 (40%) had hypothyroid index cases.

DISCUSSION

Autoimmune thyroiditis (AITD) is being increasingly diagnosed with greater awareness and is one of the commonest chronic non-communicable diseases. In the last three decades, technological advances in radioimmunoassay and imaging techniques with fine needle aspiration cytology (FNAC) have helped in accurately diagnosing thyroid diseases. AITD is the most common organ specific autoimmune disorders, resulting in dysfunction of the thyroid gland. Disorders like Chronic Autoimmune / Hashimotos thyroiditis, Postpartum/ Sporadic Thyroiditis/ Sub acute Thyroiditis, Atrophic Thyroiditis/ Myxoedema, Graves's disease share antibodies against Thyroid Peroxidase (TPO Ab), Thyroglobulin (TG Ab) and TSH receptors (TSHR Ab). Review of literature published on the incidence of

thyroid dysfunction in AITD revealed an incidence rate of hypothyroidism varied between 2.2 / 100,000/ year and 498.4/ 100000 / year and that of hyperthyroidism varied from 0.7 / 100000 / year and 99 / 100000 / year.[6]

This study is first of its kind done in Kerala state of India.

The evidence appears strong that autoimmune thyroiditis is a familial disorder. In this study, where 142 immediate relatives of 74 index cases were studied, 95.6% had antibody positivity. Anti TPO was the most prevalent one (90%). 45.8% cases (65/142) were detected to have hypothyroidism of which 15.4% cases were newly detected. Of these, 70% were children of index cases. As thyroid dysfunction can lead to antenatal and neonatal complications due to the transmission of antibodies to the next generation- the detection of thyroid antibodies and subsequent development of hypothyroidism is very important in female patients.

In a similar study, Devi Dayal et al evaluated 50 first degree relatives of 50 children with AIT, observed a higher mean TSH levels in fathers. Only 18% of the subjects were found to be positive for anti TPO antibodies in their series.[7] In another study of Hall R. and Stanbury J. B., clinical thyroid disease was present in 33% of siblings of their patients with autoimmune thyroiditis.[8]

Each patient with AITD may have a background inherited predisposition to autoimmunity. With additional environmental and hormonal factors that trigger or contribute to the development of the disease Cytotoxic T- lymphocyte Antigen- 4 (CTLA-4), an immuno- modulatory molecule expressed on the surface of activated T cell, is a key negative regulator. CTLA-4 gene is a major candidate gene for autoimmune thyroiditis.[9] CD 40 gene and Protein Tyrosine Phosphatase 22 (PTPN22) gene are also associated with AITD.[10] Environmental factors also trigger the development of autoimmunity. High dietary iodine intake enhances thyroglobulin immune reactivity.[11]

The cause of the increased prevalence of thyroid antibodies in the general population is unknown. Familial incidence could be due to trans-placental transfer of antibodies from the mother to the child as reported earlier. High prevalence of autoimmunity could be also due to the excess of dietary iodine as a result of compulsory iodine supplementation as reported by Weiping et al from China.[12] But till today this hypothesis is not experimentally proven.

CONCLUSION

In conclusion, a significant number of immediate relatives of subjects with AIT, had antibody positivity (93.6%). 10 (15.4%) of the hypothyroid cases detected in the relatives were newly detected and 70% of them were children of index cases. The relatives of all the hypothyroid index cases studied were antibody positive-100% had anti TPO positivity. The results in our study, stress the importance to do thyroid antibodies and TSH to detect early asymptomatic hypothyroidism and or to predict future hypothyroidism in patients with AIT and antibody positivity.

END NOTE

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Editor's Remarks: This article deals with a problem seen in increasing numbers these days – Auto Immune Thyroiditis. The present study was conducted to find the prevalence of thyroid auto antibodies in the immediate relatives of 74 proven AIT patients. The study stresses the importance of estimating thyroid auto antibodies and thyroid function tests to detect early asymptomatic hypothyroidism in patients with antibody positivity.

Conflict of Interest: None declared

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