

Correlation of Thyroid auto Antibodies and Thyroid Function in Patients with Autoimmune Thyroiditis

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ABSTRACT

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Introduction: Autoimmune Thyroid Disease (AITD) or Autoimmune thyroiditis (AIT) is the most common organ specific autoimmune disorder resulting in the dysfunction of the thyroid gland (hyper or hypofunction) and includes Hashimoto's thyroiditis (HT) (or chronic autoimmune thyroiditis) which has specific histo-pathological findings.

Materials and Methods: 100 consecutive patients with a histological diagnosis of autoimmune thyroiditis or Hashimoto's thyroiditis with either symptoms of thyroid dysfunction and / or thyroid swelling who attended SUT Hospital Thyroid clinic, Pattom, Thiruvananthapuram are included in the study.

Findings: Out of 100 patients studied 64% (64 patients) were having HT and 36% were having AIT. Thyroid Peroxidase antibodies (TPO Ab) were estimated only in 95 patients; out of which 84 patients were tested positive (88%) and 11 were tested negative (12%). Anti thyroglobulin antibody (ATG Ab) estimation was done in 73 patients and 49 patients were tested positive (67%) and 24 patients were negative (33%). The ultrasound findings of the patients studied revealed 53 patients with multi nodular goitre, 20 with diffuse goitre, 2 with cystic thyroid nodules, 22 with thyroiditis features (i.e., diffuse or focal coarse echo texture in the thyroid gland – generalised or focal thyroiditis), and 3 patients with solitary nodule.

Discussion: Autoimmune thyroiditis is not a rare disease, but under diagnosed. All patients with a thyroid swelling should be subjected to TFT and antibodies estimation followed by FNAC. If all these tests are in favour of AIT, there is no need of any urgent surgery unless there is an indication such as pressure symptoms, rapid enlargement or suspicion of malignancy.

Keywords: Autoimmune Thyroiditis, Ultrasound, Antibodies

*See End Note for complete author details

INTRODUCTION

Autoimmune Thyroid Disease (AITD) or Autoimmune thyroiditis (AIT) is the most common organ specific autoimmune disorder resulting in the dysfunction of the thyroid gland (hyper or hypofunction) and includes Hashimoto's thyroiditis (HT) (or chronic autoimmune thyroiditis) which has specific histo-pathological findings.¹ AIT shows lymphocytic infiltration with large lymphoid follicles with germinal centres. In addition, if large thyroid cells having an acidophilic staining character called Hurthle or Askanazy cells are present, it is called Hashimoto's Thyroiditis (HT). All patients with histological findings of AIT and with or without histo-pathological findings of HT are included under the title AITD in this study.

The common thyroid antibodies detected in the blood are anti Thyroglobulin antibodies (ATG), Thyroid Peroxidase antibodies (TPO, previously known as Antimicrosomal antibodies- AMA) and TSH Receptor antibodies. TSH receptor antibodies (stimulating or

blocking antibodies) are more related to Grave's disease and Myxedema which also come under AITD, but not included here. In Autoimmune thyroiditis circulating anti-thyroglobulin antibodies (ATG) and anti-TPO antibodies are present in high titres in blood.

The presently accepted classification of AITD, listed in Table 1, includes HT and its variants, autoimmune atrophic thyroiditis (myxoedema) and Grave's disease (GD).² According to American Thyroid Association 5% to 7% of women worldwide develop autoimmune thyroiditis making it a relatively common disorder.³ Routine antibody estimation in patients with thyroid enlargement has revealed increased prevalence of autoimmune thyroiditis in Kerala.⁴ The so called puberty goitre seen in adolescents or multi nodular goitre in adults could be due to autoimmune thyroiditis, not diagnosed previously due to the non availability of antibody estimation.⁴ This study is aimed at finding the prevalence of Thyroid auto-antibodies (TPO and ATG) and its relation to the thyroid function in patients with a histological diagnosis of AIT or HT.

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To our knowledge such a study has not been reported from Kerala before.

Type	Clinical expression
1 Chronic autoimmune thyroiditis or Hashimoto's thyroiditis	Goitre due to lymphocytic infiltration. Hypothyroidism
2 Painless thyroiditis (postpartum/ sporadic)	Small goitre. Transient thyrotoxicosis and/or hypothyroidism
3 Atrophic thyroiditis or primary hypothyroidism	Thyroid atrophy. Hypothyroidism.
4 Grave's disease	Thyroid hypertrophy. Hyperthyroidism.

METHOD

100 consecutive patients with a histological diagnosis of autoimmune thyroiditis or Hashimotos thyroiditis with either symptoms of thyroid dysfunction and / or thyroid swelling who attended SUT Hospital Thyroid clinic, Pattom, Thiruvananthapuram are included in the study.

Besides detailed clinical examination, the following investigations were done in all patients: Blood routine, Random blood sugar, Fasting lipids, Thyroid Function tests (T3, T4, TSH) Thyroid Peroxidase Antibodies (TPO), Anti Thyroglobulin Antibodies (ATG), Ultrasound Thyroid scan and FNAC Thyroid. TFT and antibodies were estimated by chemiluminiscent method.⁵ The normal values of TFT and antibodies in our laboratory are given below: T3: 1.10 – 2.8 nmol/L; T4: 65 – 140 nmol/L; TSH:0.4–5.0 μ IU/ml; AMA:<9.0IU/ml; ATG:<60IU/ml.

RESULTS

Out of 100 patients studied 64% (64 patients) were having HT and 36% were having AIT. 94 were females and 6 were males (Table 2). For analysis of the data both HT and AIT were considered under the heading of autoimmune thyroid disease (AITD) as stated previously.

Age group	Male	Female	Total	%
<20 years	3	0	3	3
20 – 29 yrs	0	29	29	29
30 -39 yrs	3	30	33	33
40 -49 yrs	0	20	20	20
>50 yrs	0	15	15	15
Total	6	94	100	100

Range (16 – 64 years)

The age group of the patients studied ranges from 16 years to 64 years; in which 3 were less than 20 years of age and all these patients were males.

65% patients were less than 40 years of age, however these ages could not be considered as the age of onset because in many patients the thyroid problem started years before they came to see us

Antibody positivity and thyroid function

Thyroid Peroxidase antibodies (TPO Ab) were estimated only in 95 patients; out of which 84 patients were tested positive (88%) and 11 were tested negative (12%). Anti thyroglobulin antibody (ATG Ab) estimation was done in 73 patients and 49 patients were tested positive (67%) and 24 patients were negative (33%). Of the 84 patients who were TPO +ve, 40 were hypothyroid (47%); 5 were hyperthyroid (6%) and 39 were euthyroid (47%). However all TPO Ab negative patients were euthyroid (100%) enhancing the positive predictive value of TPO Ab positivity and thyroid dysfunction (Table 3).

Table 3. Relationship b/w antibody positivity and thyroid dysfunction (Total patients 100)

Antibody	Done	+ve (no. of ts.)	+ve %	P value*
TPO	95	84	88	0.0008
ATG	73	49	67	

*This difference is statistically significant.

In 49 ATG positive patients, 25 patients were hypothyroid (52%); 4 were hyperthyroid (8%) and 20 (40%) were euthyroid. But in the 24 ATG negative patients also, hypothyroidism was seen in 13 cases (54%) and hyperthyroidism in 1 patient (Table 4).

Table 4. Thyroid Function Status – (total patients 100)

Hypothyroid %	Hyperthyroid %	Euthyroid %
40	10	50

At the time of first visit to our clinic, 40% of patients were having hypothyroidism, 10% in hyperthyroid state and 50% were euthyroid. TPO antibodies are found to have more sensitivity as compared to ATG (88% v/s 67%), (Table 5) in predicting hypothyroidism.

Ultrasound findings

The ultrasound findings of the patients studied revealed 53 patients with multi nodular goitre, 20 with diffuse goitre, 2 with cystic thyroid nodules, 22 with thyroiditis features (i.e., diffuse or focal coarse echo texture in the thyroid gland – generalised or focal thyroiditis), and 3

Table 5. Antibody positivity and thyroid dysfunction*

Anti-body	Status	No. of pts.	Hypothyroid % & no. of pts.	Hyperthyroid % & no. of pts.	Euthyroid % & no. of pts.
TPO	+ve	84	47% (40)	6% (5)	47% (39)
	-ve	11	0	0	100% (11)
ATG	+ve	49	52% (25)	8% (4)	40% (20)
	-ve	24	54% (13)	4% (1)	42% (10)

*In one patient with hyperthyroidism, TPO was negative, but ATG was positive. In another patient with hyperthyroidism, TPO was positive, but ATG was negative.

Table 6. Ultrasound scan findings

Multi nodular goitre	53
Diffuse goitre	20
Cystic thyroid nodule	2
Thyroiditis features*	22
Solitary nodule	3
Total	100

*see text

patients with solitary nodule. Histological evidence of papillary carcinoma was seen in these 3 patients with AITD (Table 6).

DISCUSSION

The first thyroid autoantibody discovered was anti-thyroglobulin antibody (ATG Ab) in 1956. Antibodies to antigens present in the cytoplasm of thyroid follicular cells (AMA) were detected in 1976. These "cytoplasmic" antigens (microsomal antigens) were the same as the enzyme thyroid peroxidase and hence these antibodies are also called thyroid peroxidase antibodies (TPOAbs). TPOAbs appeared to be much more prevalent than ATG Antibodies.^{6,7}

The prevalence of AIT is increasing and an analysis of our patient's data showed that about 70% of the patients presenting with thyroid problems to our clinic did have AIT.⁴ The prevalence of positive thyroid antibodies previously reported by us was 29% in pregnant patients.⁸

While hypothyroidism is the characteristic abnormality in AITD, the inflammatory state early in the course may cause thyroid follicular destruction and thyroid hormonal release resulting in transient hyperthyroidism. These antibodies can even lyse the thyroid cells. B cells present the thyroid antigen to T cells. T cells secrete cytokines which activate a variety of other immune cells, and has a role in antibody production (Th₂ cells) and apoptotic destruction of thyroid cells by activating cytotoxic T cells (Th₁ cells).

Genetic and environmental factors such as toxins, bacterial and viral infections or iodine excess, appear to interact leading to the appearance of autoantigens and accumulation of antigen-presenting cells (APCs) in the thyroid. Consequently, due to loss of immune tolerance, auto-reactive immune cells (T lymphocytes) activated by APCs, invade the thyroid gland interacting with the thyroid cells and the apoptotic pathways are activated by certain cytokines produced locally by the T lymphocytes. It is likely that the regulation of apoptosis during this interaction between the invading lymphocytes and the defending thyroid cells, may play an important role in the clinical expression of AITD.

94% of the patients in this study were females; 85% in the reproductive age group. Since thyroid dysfunction can lead to antenatal and neonatal complications, the diagnosis and correction of thyroid disorder is very important in pregnant patients. Thyroid auto immunity is a risk factor for pregnancy loss.⁹ Some authors have reported that thyroxine therapy in euthyroid TPO +ve pregnancies (AMA+ve) could improve miscarriage rate by 75% and premature deliveries by 69%.¹⁰ The prevalence of thyroid antibodies also increases the risk of postpartum thyroiditis.

Majority of the patients showed multinodularity in the thyroid (53% of patients) in US scan. 20% were with diffuse goitre. 3% of the patients were found to have papillary Ca thyroid, and hence FNAC of thyroid from multiple sites is a must in view of the association of papillary Ca with AITD. Twenty percent of the patients did not have any thyroid swelling but showed evidence of thyroiditis in the ultrasound thyroid scan.

In three patients with histologically proven AIT, no auto antibodies were detected in the blood suggesting that AIT could not be completely excluded in patients with no antibodies.

Positive antibodies were also detected in the neonates of 2 patients with positive antibodies (both TPO/ATG). Since we have not done neonatal antibody screening routinely in all the patients post partum, no conclusion could be drawn from this finding.

CONCLUSION

Autoimmune thyroiditis is not a rare disease, but under diagnosed. All patients with a thyroid swelling should be subjected to TFT and antibodies estimation followed by FNAC. If all these tests are in favour of AIT, there is no need of any urgent surgery unless

there is an indication such as pressure symptoms, rapid enlargement or suspicion of malignancy.

Although hypothyroidism was the frequent thyroid dysfunction in patients with positive TPO (47%) and ATG (52%) antibodies, it may be noted that, in none of the patients with TPO negativity, thyroid dysfunction (hypo or hyper) was detected. However in 54% of patients with negative ATG, hypothyroidism was detected which proves that TPO Ab is more sensitive than ATG in predicting hypothyroidism. Similarly the sensitivity of TPO Ab was more than ATG in autoimmune thyroiditis (88% v/s 67%; p value 0.0008).

It is well recognised that AITD is correlated with intake of excess iodine and hence the increase in prevalence of thyroiditis could be related to iodine rich salt intake, which needed further research.

END NOTE

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