

## Original Research Article

# Raised incidence of autoimmune thyroiditis among females in 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> decades: a randomized study

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### ABSTRACT

**Background:** Autoimmune thyroid disease (AITD), a mutual organ specific autoimmune disorder is seen mostly in women between 30-50 years of age. The rationale behind the study is to determine increased incidences of autoimmune thyroiditis. The objective of the present study was to evaluate the incidence of autoimmune thyroiditis and thyroid dysfunction in healthy females with no previously known thyroid disease, in an urban area.

**Methods:** The study was conducted on female volunteers with no known thyroid disease. 370 subjects among the hospital's medical and administration personnel were recruited. All underwent thyroid ultrasound (US) and thyroid anti-peroxidase (TPOAb) and anti-thyroglobulin (TgAb) antibodies were measured. Hypoechoogenicity and thyroid volume were determined by sonography.

**Results:** the incidence of autoimmune thyroiditis was 23.2% and 20-30 years were most commonly affected (P = 0.008); when including cases of atrophic thyroid, the frequency decreased to 14.7%.

**Conclusions:** The frequency of autoimmune thyroiditis is clearly elevated in the studied population. Further studies are necessary in order to define the increased incidence of autoimmune thyroid disease.

**Keywords:** Atrophic thyroiditis, Autoimmune thyroiditis, Incidence

### INTRODUCTION

Autoimmune thyroid disease (AITD), a mutual organ specific autoimmune disorder is seen mostly in women between 30-50 years of age. Thyroid autoimmunity can cause numerous forms of thyroiditis extending from hypothyroidism (Hashimoto's thyroiditis) to hyperthyroidism (Graves' disease). Prevalence rate of autoimmune facilitated hypothyroidism is around 0.8 per 100 and 95% among them are women. About 2 to 4 percent of women and up to 1% of men are affected worldwide, and the prevalence rate increases with advancing age.<sup>1</sup> Graves' disease is about one tenth as mutual as hypothyroidism and inclines to occur more in younger entities. Both these disorders segment many immunologic topographies and the disease may progress from one state to other as the autoimmune process

changes. Genetic, environmental and endogenous factors are responsible for commencement of thyroid autoimmunity. Numerous studies show a higher frequency of AITD in family members of patients with autoimmune hypothyroidism and Graves' disease.<sup>2</sup>

It has been well recognized that the incidence of AITD is comparative to dietary iodine content. In Europe the prevalence of GD increases with national iodine intake programs. In the current scenario the only confirmed genetic factor lies in HLA complex (HLA DR-3) and the T cell regulatory gene (CTLA 4) for thyroid autoimmunity.<sup>3</sup> Several environmental factors like viral infection, smoking, stress & iodine intake are associated with the disease progression. The growth of antibodies to thyroid peroxidase (TPO) thyroglobulin (TG) and Thyroid stimulating hormone receptor (TSH R) is the

main trademark of AITD. Circulating T lymphocytes are increased in AITD and thyroid gland is infiltrated with CD4+ and CD8+ T cells.<sup>4</sup>

Wide varieties of cytokines are produced by infiltrated immune cells, which mediate cytotoxicity leading to thyroid cell destruction. Circulating antibodies to TPO and TG are measured by immunofluorescence, hemagglutination, ELISA and RIA.<sup>5</sup> TSHR antibodies of Graves' disease can be measured in bioassays or indirectly in assays that detect antibody binding to the receptor.

The purpose of this study was to evaluate the incidents of autoimmune thyroiditis and thyroid dysfunction in female individuals with no known thyroid disease, in an urban area.

## METHODS

This is a randomized cross-sectional study with universal sampling technique, that encompassed healthy female volunteers in three groups 20-30 years, 30-40 years and >40 years with no previous personal history of thyroid disease and not currently pregnant or lactating. They were recruited among the administrative, nursing and resident personnel in our tertiary care hospital.

All volunteers signed an informed consent form to contribute in the study. They responded a questionnaire on their family history in terms of thyroid disease, their personal pathological history and comorbidities, and their use of drugs or contact with iodinated contrast media for radiological procedures. Helpers that had been exposed to iodinated products or substances inside the previous 12 weeks were excluded from the study.

A thyroid ultrasound was done on all partakers with portable equipment and a 7.5 MHz lineal transducer; the procedure was conducted by a single investigator to avoid inter-observer variations. The volume of each thyroid lobe was considered with the formula (mL): width×height×length×0.52 and the sum of both lobe measurements equals the thyroid volume.<sup>6</sup> Whether the thyroid gland's echogenicity was normal or decreased was resolute by comparing the brightness of the thyroid echoes with that of the adjacent neck muscles.

Thyroid hypoechoogenicity was classified as follows: grade 1 or mild when compared to normal thyroid tissue, grade 3 or severe, referred to echogenicity like that of the sternocleidomastoid muscle. Changes in echo pattern intermediate to grade 1 and 3 were classified as moderate, grade 2.<sup>7</sup> Echogenicity was considered decreased, only if it was diffuse and the gland was completely compromised; focal echogenicities were not considered.

A fasting venous blood sample was obtained from all participants, between 07:00 and 10:00 hrs; after centrifugation, serum was placed in aliquots and frozen at

-20°C until processing. Thyroid hormone reference values were attained from the 2.5<sup>th</sup> and 97.5<sup>th</sup> percentiles in 282 individuals with no thyroid disease or family history of thyroid disease, no anti-thyroid antibodies and or thyroid nodules.<sup>8</sup>

Autoimmune thyroiditis (AT) was analyzed if the TPOAb and/or TgAb were abnormally high and the thyroid's diffuse hypoechoogenicity was ≥grade 2 (moderate or Severe); the separate presence of any of these findings were not considered diagnostic of AT.<sup>6,9</sup> Another manifestation included the diagnosis of autoimmune atrophic thyroiditis was individuals with a thyroid volume <5.0 ml regardless of the presence or lack of abnormally elevated anti-thyroid antibodies.<sup>6,10</sup>

The concentrations of TPOAb and TgAb were measured in serum by radioimmunoassay (RIA). TgAb had an analytical sensitivity of 2.0 IU/mL and values below 30 IU/mL were considered normal, the intra-assay CV was <8.3% and the inter-assay CV was <12.8%. The assay used for TPOAb had an analytical sensitivity of 1.9 IU/mL and values below 100 IU/mL were considered normal, the intra-assay CV was <9.31% and the inter-assay CV was <12.4%. The study was approved by Institutional Ethics committee.

## Statistical analysis

The recorded observations were analysed using Epi Info 7 software. Nominal categorical variables are presented as frequencies and proportions. Group comparisons were established with Fisher's exact T test and the Mann Whitney U test, depending on the case.  $p < 0.05$  was considered statistically significant.

## RESULTS

Table 1 shows among 370 study participants the most common age group volunteered for the study was 20-30 years around 50% followed by 30-40 years. The median age group was found to be 27 years and ranging between 20 to 67 years. As seen TPO Ab and Tg Ab was found to be significantly associated with age group 30-40 years ( $p < 0.05$ ).

Structural abnormalities of the thyroid detected by thyroid scan; 81(21%) subjects had nodules, mostly single. Only 12 volunteers of >40 years had more than one nodule (17%), 31 (15%) which was also found statistically significant.

As per Table 2 thyroid dysfunction was determined which suggest 23.2% of overall autoimmune thyroiditis incidents in which it highest among the 2nd decade female age group and was statistically significant ( $p = 0.08$ ). Atrophic thyroiditis was also seen among study participants and the incidence was found to be 14.3% overall and was also highest among female age group 20-30 years ( $p = 0.0001$ ).

**Table 1: Demographic characteristics and thyroid profile of study participants (n=370).**

Variables	Total	20-30 years (N=186)	30-40 years (N=114)	>40 years (N=70)	P-value
Mean age (years)		27	36	44	0.15
Family history of thyroid disorder	68	20	32	16	0.18
TPO Ab	81 (21%)	27 (14.5%)	42 (36.8%)	12 (17%)	0.001*
TgAb	91 (23%)	31 (15%)	46 (38%)	14 (17.5%)	0.02*
TPOAb/TgAb	87 (22%)	29 (14.8%)	45 (37%)	13 (17.3%)	0.005*

\*p<0.05 is considered statistically significant.

**Table 2: Autoimmune thyroiditis in the study participants.**

Variables	Total	20-30 years	30-40 years	>40 years	P-value
Autoimmune thyroiditis	86 (23.2%)	42 (22.5%)	24 (21%)	20 (28.5%)	0.008*
Atrophic thyroiditis	53 (14.3%)	24 (12.9%)	17 (14.9%)	12 (17.1%)	0.0001*

\*p<0.05 is considered statistically significant.

## DISCUSSION

In the present study, authors found a group of participants with similar characteristics to those reported in large thyroid epidemiological studies; however, the average age in present study was which highlights some of our findings, that tend to increase with age of individuals.<sup>8</sup> The incidence of autoimmune thyroiditis was like that found in other studies although most of these were conducted in children and hence its incidence was higher.<sup>9,10</sup> Other studies that consider both autoimmune and atrophic thyroiditis as we have included both entities in our studied population, 15.7% of individuals had these characteristics, a similar number to that reported in the literature (15.6% - 19.5%).<sup>11,12</sup> Atrophic thyroiditis refers to the end-stage of destructive autoimmune thyroiditis.<sup>13</sup> The frequency of thyroid hypoechogenicity was also high and notably it was more common in females as also reported in studies evaluating geographic areas with normal or excessive iodine intake but greater than that reported in areas with iodine deficiency.<sup>14,15</sup> It is currently clear that decreased thyroid echogenicity is a strong predictor of autoimmune thyroid disease.<sup>7</sup> The number of individuals with elevated anti-thyroid antibodies is remarkably like that reported in some studies or even superior.<sup>2,16</sup> The discovery of nodules in present study primarily reflects our population's intake status and coincides with the measurements obtained in the sample population that according to the ICCIDD/WHO, has a more than adequate iodine intake and agrees with the data registered in our country by the WHO.<sup>17</sup>

## CONCLUSION

Present study demonstrates an increased incidence of autoimmune thyroiditis as well as direct and indirect findings suggesting an increase in thyroid autoimmunity in young females; this increase may perhaps be associated to a more than adequate dietary iodine intake.

Additional and wider studies exploring these factors including urinary iodine excretion in our population are necessary.

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