

## **Autoimmune Thyroiditis in Women of Child Bearing Age and its Association with Thyroid Function and Thyroid Antibody Status**

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### **ABSTRACT**

Thyroid disorders are prevalent in women of childbearing age and for this reason commonly present in pregnancy and the puerperium. Chronic autoimmune thyroiditis (AIT) is the most common and extensively studied organ-specific autoimmune disorder and it has important consequences on fertility, the occurrence of pregnancy complications and pregnancy outcome. Across sectional analytical study has been carried out on autoimmune thyroiditis among the women of child bearing age with suspected thyroid disorders in the Centre for Nuclear Medicine & Ultrasound, Mymensingh during the period of July, 2011 to June, 2012. The objectives of the study were to estimate the prevalence of autoimmune thyroiditis in women of child bearing age and to determine the association of autoimmune thyroiditis with thyroid function and thyroid antibody status. In the present study, 100 women of childbearing age (15-45Yrs) with any sorts of suspected thyroid disorders were included. But already diagnosed all follow up cases were excluded from the study. High Resolution Ultrasonography (HRUS) had been taken as principal modality of diagnosis of autoimmune thyroiditis. T<sub>3</sub>, T<sub>4</sub> and TSH were taken as an important indicator for thyroid function status. Serum TM-Ab (Thyroid Microsomal Antibody) level and serum Tg-Ab (Thyroglobulin Antibody) level were measured to see the thyroid antibody status. In the present study, prevalence of autoimmune thyroiditis among the women of childbearing age with suspected thyroid disorders was found 41%. According to the thyroid function status, 65.85% AIT patients were found in hypothyroid state, 29.27% in subclinical hypothyroid state and rest 4.88% were found in euthyroid state. In consideration of thyroid antibody status, 69.23% AIT patients were positive & 30.77% were negative for thyroid autoantibody. This study revealed that there were significant association of AIT with the biochemical hypothyroid state and positive thyroid antibody status.

**Key Words:** Autoimmune thyroiditis, Women of Child Bearing Age, Thyroid Function, Thyroid Antibody Status.

## INTRODUCTION

Autoimmune diseases are the leading causes of death among young and middle-aged women in the United States (1). According to the U.S. Department of Health and Human services, Office on Women's Health (2010), autoimmune diseases can affect anyone. Yet certain people are at greater risk, including women of childbearing age. More women than men have autoimmune diseases, which often start during their childbearing years (2).

Autoimmune thyroiditis or chronic autoimmune thyroiditis is a disease in which the body interprets the thyroid gland and its hormone products ( $T_3$  and  $T_4$ ) and Thyroid Stimulating Hormone (TSH) as threats and produce special antibodies that target the thyroid cells and destroy it. It presents with hypothyroidism or hyperthyroidism and the presence or absence of goiters. If goiters are present, it is understood as Hashimoto's Thyroiditis. On the other hand, if the thyroid is atrophic, it is denominated Atrophic Thyroiditis. If the symptoms of thyroiditis appear in women after parturition, it is referred to as Postpartum Thyroiditis. Silent Thyroiditis and Postpartum Thyroiditis are now believed to be manifestations of chronic autoimmune thyroiditis (3).

In developed countries, chronic autoimmune thyroiditis is the most common cause of hypothyroidism among women in their childbearing age. Antibodies responsible for compromising maternal thyroid function can cross the placenta and can compromise fetal and neonatal thyroid function. Hypothyroidism in pregnant women can adversely affect their children's subsequent neuropsychological performance. Decreases in performance can occur even when the pregnant woman's hypothyroidism is mild and probably asymptomatic (4).

Uncorrected thyroid dysfunction in pregnancy has adverse effects on fetal and maternal well-being. The deleterious effects of thyroid dysfunction can also extend beyond pregnancy and delivery to affect neuro intellectual development in the early life of the child. Demand for thyroid hormones is increased during pregnancy, which may cause a previously unnoticed thyroid disorder to worsen (5).

Low thyroid reserve due to autoimmune thyroiditis is increasingly recognized as a serious health problem: 1) Thyroid autoimmunity increases the probability of spontaneous fetal loss. 2) Thyroid failure due to autoimmune thyroiditis, often mild and subclinical, can lead to permanent and significant impairment in neuropsychological performance of the offspring. 3) Evidence is emerging that as women age with sub clinical hypothyroidism, as a sequel of post partum thyroiditis, predisposes them to cardiovascular disorder.

The prevalence of post partum thyroiditis ranges from 5-7%. Postpartum thyroiditis is an acute stage of autoimmune thyroid destruction with subsequent repair in the context of an existing and ongoing process of thyroid auto-sensitization. This process frequently leads to a gradual development of permanent thyroid failure. The recognition of the true nature of this process, combined with recently described detrimental effects of a low thyroid reserve due to autoimmune thyroiditis, has important repercussions on clinical practice especially in women of childbearing age (6).

Benoist, et al. stated that more than 1.9 billion people of all ages were iodine deficient in the world; of them prevalence was lowest (10%) in the Americas and highest (57%) in the Europe and less than fifty percent (40%) in South East Asia (7).

Iodine deficiency was found to be hyper-endemic in Bangladesh in 1993 in the national survey on goitre. Some subsequent investigations in the country attributed endemic goitre to widespread iodine deficiency. A few recent studies have observed the frequency of thyroid autoimmunity and cancer to be higher than it was before iodine prophylaxis in some countries. High iodine intake, as well as widely varying concentration of dietary iodine, day-to-day increases vulnerability of developing thyroid autoimmunity (8).

The study on prevalence of antithyroid microsomal antibody in thyroid patients of endemic goitre area by Mahmood, et al. at CNMU, Mymensingh revealed that the great majority (89.28%) of the study subjects (both male & female) had Hashimoto's thyroiditis or generalized features of autoimmune thyroid disorder (AITD). Among the total study population, female rated higher (59%) with anti-microsomal antibody (TM-Ab) and highest number of cases (> 90%) were found in 30-35 yrs of age group (9).

Autoimmune thyroiditis in women of childbearing age is such a clinical condition, which needs special attention. The concept of post partum thyroiditis being a mild and transient disorder is now changing. The recognition of the true nature of postpartum thyroiditis that is an acute phase in an ongoing and chronic thyroid autoimmune process, and the negative consequences of such a chronic process for offspring of affected mothers and for the mothers themselves, in the long run, are reasons to consider screening.

In context of Bangladesh, very few data & research findings are available about this health problem. So considering all these facts the present research work had been done.

The general objective of the study was to estimate the prevalence of Autoimmune Thyroiditis among the women of child bearing age with suspected thyroid disorders and to determine the association of Autoimmune Thyroiditis with thyroid function and thyroid antibody status.

The specific Objectives were:

1. To perform the High Resolution Ultrasound (HRUS) of thyroid glands of the study subjects to diagnose Autoimmune Thyroiditis.
2. To estimate the prevalence of Autoimmune Thyroiditis among the women of child bearing age with suspected thyroid disorders.
3. To measure the thyroid hormone profiles and thyroid autoantibody levels among the study subjects.
4. To establish the association of Autoimmune Thyroiditis with thyroid function status and thyroid antibody status.

#### **MATERIALS AND METHODS:**

This cross sectional analytical study was carried out for one year starting from July, 2011 to June, 2012 in Centre for Nuclear Medicine & Ultrasound (CNMU), Mymensingh. Female patients of childbearing age with suspected thyroid disorders, attending Centre for nuclear medicine & Ultrasound, Mymensingh.

Women of childbearing age (15-45 yrs) having any sorts of suspected thyroid disorders were included. But already diagnosed or follow up cases of any thyroid disorders were excluded from the study to avoid repetition.

Non-random, purposive sampling included total 100 subjects.

All relevant data collected during the investigations were recorded on a pre-designed data collection sheet for each patient. Enlarged, diffusely hypoechoic, inhomogeneous tissue echotexture with or without internal septations on HRUS of thyroid gland is the basis of diagnosis of Autoimmune Thyroiditis. HRUS were done using ACCUVIX V 10, Medison, Korea with 5 to 13 MHz linear array transducer & Nemio 10, Toshiba, Medical system, Tokyo, Japan with 7 to 11 MHz linear array transducer.

Serum T<sub>3</sub>, T<sub>4</sub> and TSH were done in all patients. Serum T<sub>3</sub> and T<sub>4</sub> were done by Radioimmunoassay (RIA) and serum TSH was done by Immunoradiometric assay (IRMA). Estimation of serum thyroid microsomal antibody (TM-Ab) and thyroglobulin antibody (Tg-Ab) were done in all study subjects by RIA.

The collected data were compiled and subjected to relevant statistical analyses through the SPSS program. Chi- square tests were done to establish the association of AIT with other findings. The results of all tests were considered significant at p<0.05.

**Ethical consideration:** The nature & purpose of the study was such that no physical, psychological, social or legal risk was likely to be posed to the subjects. Subjects were inquired about relevant topics only to supplement the recorded data. The aims & objectives of the study were explained to the patients, consents were acquired & patients were assured that all information & records will be kept confidential.

## RESULTS

**Table 1: Number and percentage distribution of the patients according to the diagnosis based on HRUS (n=100)**

Diagnosis	Number of patients (n)	Percentage (%)
AIT	41	41
Non-AIT	59	59
<b>Total</b>	<b>100</b>	<b>100</b>

According to the diagnosis based on HRUS findings, the patients were categorized as AIT and Non-AIT. 41% patients were diagnosed as AIT and 59% patients were diagnosed as Non-AIT.

**Table 2: Number & percentage distribution of AIT patients according to the thyroid function status (n=41)**

Thyroid Function Status	Number of patients	Percentage (%)
Hypothyroid	27	65.85
Subclinical Hypothyroid	12	29.27
Euthyroid	2	4.88
Subclinical Hyperthyroid	0	0.00
Hyperthyroid	0	0.00
<b>Total</b>	<b>41</b>	<b>100.00</b>

In this study, among the 41% AIT patients, 27(65.85%) patients presented in overt hypothyroid state, 12(29.27%) patients in subclinical hypothyroid state and 2(4.88%) patients presented in euthyroid state. No AIT patients were found in hyperthyroid or subclinical hyperthyroid state.

**Table 3: Association of AIT with biochemical hypothyroid state (n=100)**

Hypothyroid state (Hypothyroid+Subclinical Hypothyroid)	AIT n (%)	Non-AIT n (%)	Total n (%)	p-Value
Present	39 (39%)	11 (11%)	50 (50%)	<b>&lt;0.001</b>
Absent	2 (2%)	48 (48%)	50 (50%)	
<b>Total</b>	<b>41 (41%)</b>	<b>59 (59%)</b>	<b>100(100%)</b>	

\* Chi-Square test was done to measure the level of significance.

In this study, 39(39%) AIT patients and 11(11%) Non-AIT patients were in hypothyroid state. Chi-Square test demonstrated a significant association of AIT with the biochemical hypothyroid state ( $p<0.001$ ).

**Table 4: Number & percentage distribution of AIT patients according to the thyroid antibody status (n=39)**

Thyroid Antibody Status	Number of patients	Percentage (%)
Positive	27	69.23
Negative	12	30.77
<b>Total</b>	<b>39</b>	<b>100.00</b>

Among the AIT patients, 27(69.23%) patients were thyroid autoantibody positive and 12(30.77%) patients were negative.

**Table 5: Association of AIT with positive thyroid antibody status (n=96)**

Thyroid Antibody Status	AIT n (%)	Non-AIT n (%)	Total n (%)	p-Value
Positive	27 (28.13%)	13 (13.54%)	40 (41.67%)	<b>&lt;0.001</b>
Negative	12 (12.50%)	44 (45.83%)	56 (58.33%)	
<b>Total</b>	<b>39 (40.63%)</b>	<b>57 (59.37%)</b>	<b>96 (100.00%)</b>	

\* Chi-Square test was done to measure the level of significance.

The result showed that among the 100 thyroid disordered patients, 96 were investigated for the thyroid antibody status. In case of 4 patients, thyroid antibody could not be done due to missing. Among the AIT patients, 27(28.13%) were thyroid autoantibody positive and 12(12.5%) were

thyroid autoantibody negative. And among the Non-AIT patients, 13(13.54%) were thyroid autoantibody positive and 44(45.83%) were thyroid autoantibody negative. Chi-square test demonstrated a significant association of AIT with the positive thyroid antibody status ( $p<0.001$ ).

## **DISCUSSION:**

In the present study HRUS had been taken as principal modality for diagnosis of autoimmune thyroiditis based on several studies (10,11,12,13,14). Normal thyroid shows homogenous echotexture and the level of echogenicity is more than that of surrounding muscles. Presence of diffuse hypoechoic, inhomogeneous echotexture that is almost equal to or less than that of surrounding muscles, multiple small irregular echopenic, and linear echogenic areas and irregularity of thyroid borders are seen in autoimmune thyroiditis (10). Estimates of the prevalence of thyroid dysfunction depend upon methodological factors, classifications of hypothyroidism, geographic and environmental factors including iodine intake status and composition of the community examined by age, ethnicity and gender, making comparisons between studies of limited value (15).

In a countrywide screening among the healthy young girls in post iodization phase in India, the overall prevalence of Juvenile Autoimmune Thyroiditis (JAT) was 2.1%, of which Hashimoto's Thyroiditis (HT) was 1.6% and Focal Lymphocytic Thyroiditis (FLT) was 0.56%; and among the goitrous girls, JAT was 7.5% which included HT in 5.6% and FLT in 1.9% respectively (16). The overall prevalence of JAT in 2801 schoolgirls surveyed by Jaksic, et al. (1994) was 0.6%, whereas the goiter-specific prevalence was 12.4% (17). In a previous study on autoimmune thyroiditis among the puberty onset goitre based on HRUS by Chakraborty (2006) in CNMU, Mymensingh, the prevalence of autoimmune thyroiditis was found 36% (18). In the present study, the prevalence of AIT among the women of child bearing age with suspected thyroid disorders was 41.0% on the basis of HRUS.

In a study on autoimmune thyroiditis in young girls in India, Marwaha, et al. (2000) found that 5.2% and 13.8% of girls with FNAC proven JAT had overt and sub-clinical hypothyroidism, respectively; 5.9% and 15.7% of girls who were diagnosed as JAT on serological criteria, had overt hypothyroidism and sub-clinical hypothyroidism respectively (16).

In a study on prevalence of thyroid microsomal antibody (TM-Ab) in thyroid patients in CNMU, Mymensingh, Mahmood, et al. (2004) found that thyroid antimicrosomal antibody (TM-Ab) was positive in 89.28% patients who had sonographic features of Hashimoto's thyroiditis or generalized

feature of AIT in HRUS with hypothyroid state. TM-Ab was found positive in 33.33% of patients who had HRUS features of AIT with euthyroid state (9).

In another study in CNMU, Mymensingh by Chakraborty (2006) on autoimmune thyroiditis among the puberty onset goitre found that among the total 36 AIT patients, 19 patients (52.78%) were hypothyroid, 8 patients (22.22%) were subclinical hypothyroid and 9 (25%) patients were biochemically euthyroid. None of the AIT patients were found in hyperthyroid or subclinical hyperthyroid state (18).

In the present study, according to the thyroid function status, among the total 41 AIT patients, 27 patients (65.85%) were hypothyroid and 12 patients (29.27%) were sub-clinical hypothyroid. Only 2 AIT patients (4.88%) were euthyroid and no AIT patients were found in hyperthyroid or subclinical hyperthyroid state. This study revealed that there was a significant association of AIT with biochemical hypothyroid state ( $p < 0.001$ ).

Similar result was found in a study by Marwaha, et al. (2000) in India among the young girls, where none of the patients with HT had either overt hyperthyroidism or subclinical hyperthyroidism (16). Aryal, et al. (2010) in Kathmandu University Hospital, Nepal studied with 825 subjects; the prevalence of thyroid dysfunction was 25%. Females had more thyroid dysfunction than males. Hypothyroidism (8%) and subclinical hypothyroidism (8%) had higher prevalence compared to subclinical hyperthyroidism (6%) and hyperthyroidism (3%) (15). In a countrywide screening of goitrous healthy young girls in India, by Marwaha, et al. (2000), it was found that among the girls with HT, both TM-Ab and Tg-Ab were positive in 39.5%, TM-Ab alone in 67.4% and Tg-Ab alone in 41.8% cases. And among the girls with FLT, individually TM-Ab and Tg-Ab were positive in 33.3% cases respectively and together in 28.5% cases of FLT. However in goitrous girls without autoimmune thyroiditis, TM-Ab was positive in 8.7% and Tg-Ab in 7.3% cases (16).

In a study on status of antithyroid antibodies in thyroid patients in Bangladesh by Hasanat, et al. (2000) found that among the clinically suspected AITD patients, 63.0% with Hashimoto's thyroiditis and 44.7% with atrophic thyroiditis were positive for antithyroid antibodies (8). In a study on subclinical hypothyroidism and autoimmune thyroiditis in pregnancy in South Indian subjects, TPO antibodies were positive in 8.5% of the study subjects. Among the 14 women with hypothyroidism, 8(57.1%) were TPO antibody positive and among the 481 euthyroid women, 34(7.1%) had TPO antibody positive (19). In the study in CNMU, Mymensingh on the prevalence of antithyroid microsomal antibody in thyroid patients of endemic goitre area in

Bangladesh by Mahmood, et al. found that among the total 221 patients, 126(57.01%) patients were positive for TM-Ab. Among the all female thyroid patients, 59% were positive for TM-Ab, whereas 51.67% of all male thyroid patients were positive. Highest 89.28% patients with sonographic features of AIT with hypothyroidism were found positive for TM-Ab (9). In another study on autoimmune thyroiditis among the puberty onset goitre in CNMU, Mymensingh by Chakraborty (2006), found that among the total 36 AIT patients 29 (80.6%) were thyroid antibody positive and 7 (19.4%) were thyroid antibody negative (18).

In the present study, out of total 39 AIT patients, 27 (69.23%) patients were positive for thyroid autoantibody and 12 (30.77%) patients were negative for thyroid autoantibody. There was a significant association of AIT with the positive thyroid antibody status ( $p < 0.001$ ).

## **CONCLUSION**

In conclusion, this study revealed that the prevalence of AIT among the women of childbearing age with suspected thyroid disorders was 41% and AIT was associated with biochemical hypothyroid state and positive thyroid antibody status.

In comparison to other diseases for which screening is recommended, 41% prevalence of AIT among the women of child bearing age with suspected thyroid disorders seems to be high enough to justify screening in women of childbearing age.

Further population based epidemiological studies are needed to establish the accurate prevalence and predominant etiological factors of thyroid dysfunction in this region of the country. The study recommends screening in the population of women of child bearing age for autoimmune thyroiditis by HRUS with thyroid dysfunction & thyroid autoantibody status to ensure early diagnosis and treatment and thereby to reduce the burden of the disease.

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