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A Study on Anti Thyroid Peroxidase and Anti Thyroglobulin antibodies in patients with Thyroid Dysfunction

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Abstract: *The most common cause of thyroid dysfunction in iodine sufficient areas of the world is thyroid autoimmunity. The main hallmark of autoimmune thyroid disease is the development of thyroid antibodies and the simplest way to confirm the autoimmune cause of thyroid dysfunction is the presence of significant levels of thyroid antibodies.This study was conducted at Regional Institute of Medical Sciences, Imphal to ascertain the autoimmune cause of thyroid disorders. The study was done on 50 hypothyroid or hyperthyroid patients and 50 apparently healthy subjects with no history of thyroid disease and normal thyroid function tests.Serum Anti Thyroid Peroxidase Antibody (TPOAb) and serum Anti Thyroglobulin Antibody (TgAb) were estimated by Enzyme Linked Immuno Sorbent Assay (ELISA) technique for the two groups. Thyroid antibodies were positive in 22(70.96%) out of 31 hypothyroid patients, in 14(73.68%) out of 19 hyperthyroid patients and in 6(12%) out of 50 control subjects. The mean levels of serum TPOAb and TgAb in the hypothyroid group were found to be 199.97 IU/ ml and 616.51 IU/ ml respectively and in the hyperthyroid group were found to be 142.68 IU/ ml and 749.42 IU/ ml respectively. These were significantly higher than in the control group which were 19.82 IU/ ml and 89.73IU/ ml respectively. Among the female thyroid patients 34(77.27%) were positive for thyroid antibodies while among male thyroid patients only 2(33.33%) were positive for thyroid antibodies. The findings of the study show that elevated thyroid antibodies is quite common among patients with thyroid dysfunction and females.*

Keywords*: Autoimmune thyroid disease, thyroid antibodies, hypothyroid, hyperthyroid*

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I. Introduction

The thyroid is a small gland that produces two related hormones, thyroxine (T4) and triiodothyronine (T3) which play critical role in cell differentiation during development and help maintain thermogenic and metabolic homeostasis in the adult. Disorders of the thyroid result primarily from processes that either stimulate the overproduction of thyroid hormones which is known as hyperthyroidism or cause glandular destruction and hormonal deficiency leading to hypothyroidism[1].

The most common cause of thyroid dysfunction in iodine sufficient areas is autoimmunity. Autoimmune thyroid disease is group of thyroid disorders in which autoimmune processes target various constituents of thyroid tissue including cells, receptors and enzymes[2]. It affects about 2% to 4% of women and upto 1% of men worldwide[3]. Autoimmune thyroid disease comprises a series of interrelated conditions which include hyperthyroid Graves' disease, Hashimoto's thyroiditis which cause hypothyroidism, atrophic autoimmune hypothyroidism and post partum thyroiditis. Among these diseases, Hashimoto's thyroiditis and Graves' disease are the commonest type and share many features immunologically[4]. Patients with these disorders may manifest overlapping clinical features and share immunologic and pathologic abnormalities[5]. Autoimmune hypothyroidism is the commonest cause of hypothyroidismin iodine sufficient areas of the world and Graves' disease is responsible for 60%-80%of the cases of hyperthyroidism.

The main hallmark of autoimmune thyroid disease is the development of antibodies to thyroid peroxidase (TPO), thyroglobulin (Tg) and thyroid stimulating hormone receptor (TSH-R)[6]. There are several different causes of thyroid diseases and the only simple way of confirming the autoimmune cause of thyroid dysfunction, other than biopsy is the presence of significant levels of thyroid antibodies. Both TPO antibody (TPOAb) andTg antibody (TgAb) are found in almost all patients with autoimmune hypothyroidism. TPOAb and TgAb are also present in 50% to 90% of patients with Graves' disease. A negative test for both the antibodies virtually exclude autoimmune thyroid disease as 98% of patients with autoimmune thyroid disease are positive for either antibody[7]. Patients with other thyroid diseases such as multinodular goiter and thyroid cancer may have low serum titers of thyroid antibodies but high titers are strongly suggestive of autoimmune thyroiditis or Graves' disease.

In the present study, we investigated the presence of thyroid antibodies, TPOAb and TgAb in patients with thyroid dysfunction to ascertain the autoimmune cause of thyroid disorders as not many studies had been done on thyroid autoimmunity in Manipur.

II. Materials and Methods

The study was conducted in the Department of Physiology, Regional Institute of Medical Sciences (RIMS), Imphal in collaboration with the Department of Medicine, RIMS, Imphal after getting approval from the Institutional Ethics Committee. Patients with thyroid diseases who attended the Outpatient Department (OPD) of the Department of Medicine were recruited for the study. A total of 50 hypothyroid or hyperthyroid patients whose thyroid status were confirmed by estimating serum T3, T4 and TSH were taken to form the study group. Thyroid patients were initially selected irrespective of age and sex and estimation of serum T3, T4 and TSH were done. Then, the thyroid patients who are either hypothyroid or hyperthyroid were selected to form the study group and serum TPOAb and TgAb were estimated. Any subject having severe illness, physical trauma or physiological stress which can induce change in one or more aspects of thyroid function were excluded. The control group consist of 50 age and sex matched apparently healthy subjects with no history of thyroid disease, autoimmune disease and with normal thyroid function.

Informed written consent was obtained from each of the subject. A proforma was maintained for each subject wherein a brief clinical information including particulars of the subject, chief complaints, history of present and past illnesses, family, menstrual, personal, dietary and treatment history were taken and recorded. Proper general, systemic and local examinations were done and recorded in the proforma.

Venous blood samples of the subjects were collected in sterile anticoagulant free tubes. Lipemic and hemolysed samples were discarded. Serum was separated from whole blood by centrifugation and stored at 2^0 C to 8^0 C until assay. Prior to use, all samples were brought to room temperature.Estimation of serum total T3, serum total T4, serum TSH, serum TPOAb and serum TgAb were done by ELISA technique using commercially available microplate ELISA kit of Monobind Inc., USA. The normal ranges for serum T3, T4 and TSH are as follows : T3 – 0.52- 1.85 ng/ ml, T4 – 4.4-11.6 µg/ ml, TSH – 0.39- 6.16 µIU/ ml. For serum TPOAb, values > 40 IU/ ml are considered positive and for serum TgAb, values > 125 IU/ ml are considered positive. The intra-assay variation of precision was 3.8% for TPOAb and 4.0% for TgAb and the inter-assay variation was 4.5% for TPOAb and 4.9% for TgAb.

Statistical analysis: Statistical analysis was done using SPSS ver.13. Paired student's t-test and chi-square test were used to analyze the data. The level of significance was set at $p< 0.05$ and interpretations were made accordingly.

III. Results

Table 1 shows the age and sex distribution of the study group and control group. In the study group of 50 thyroid patients, 6(12%) were males and 44(88%) were females showing a female preponderance. The mean age of the subjects in the study group was 40.28 years and in the control group was 40.10 years.

Table 1: Age and sex distribution of study and control groups

Parameter		Study group (N=50)	Control group (N=50)
Sex	Male	6(12)	6(12)
	Female	44(88)	44(88)
Age (Years) Mean ± SD		40.28±11.48	40.10±12.48

Figures within parenthesis indicate percentage

Table 2 shows that all the subjects in both the study and control groups took iodine supplementation in the form of iodized salt.

Table 2: Iodine supplementation in study and control groups

Group	Taking iodized salt	Not taking Iodized salt
Study Group N= 50 (%)	50(100)	-
Control Group N= 50 (%)	50(100)	-

Table 3 shows the subjects in the study and control groups according to the thyroid status. In the study group, 31(62%) are hypothyroid and 19(38%) are hyperthyroid with no euthyroid subjects. In the control group, all the subjects are euthyroid.

Table 3: Distribution of study and control group according to thyroid status

Thyroid Status	Study group N= 50 (%)	Control group N=50 (%)
Euthyroid	-	50(100)
Hyperthyroid	19(38)	-
Hypothyroid	31(62)	-

Note :Figures within parenthesis indicate percentage

It is observed in Table 4 that, in the hypothyroid group the mean levels of serum TPOAb (199.97 IU/ ml) and serum TgAb (616.51 IU/ml) are significantly higher (p=0.000) than in the control group. Also the mean serum T3 and T4 levels are significantly lower and the mean serum TSH is significantly higher than in the control group. In the hyperthyroid group also, the mean levels of serum TPOAb (142.68 IU/ml) and serum TgAb (749.42 IU/ml) are significantly higher (p=0.000) than the control group. The mean serum T3 and T4 levels are also significantly higher than the control group while the serum TSH is lower than the control group.

Table 4: Mean thyroid hormones and thyroid antibody levels in study and control groups

Parameters	Study group (N=50)		Control group (N=50)
	Hypothyroid (N=31)	Hyperthyroid (N=19)	
T3 (ng/ ml) Mean±SD	0.84±0.43*	3.39±1.83*	1.16±0.31
T4 (µg/ ml) Mean±SD	3.25±2.00*	14.00±6.35*	7.10±1.73
TSH (µIU/ ml) Mean±SD	15.51±9.16*	0.24±0.57*	2.01±1.48
TPOAb (IU/ ml) Mean±SD	199.97±101.05*	142.68±108.52*	19.82±9.73
TgAb(IU/ ml) Mean±SD	616.51±590.74*	749.42±742.90*	89.73±73.53

*indicate significant (p< 0.05) value

Table 5 shows the sex-wise distribution of the study group with respect to thyroid antibodies. It is seen that 77.27% of the females are positive for thyroid antibodies which is significantly higher (p=0.025) than among males where only 33.33% are positive for thyroid antibodies.

Table 5 : Sex-wise distribution of study group with respect to thyroid antibody

Sex	Thyroid Antibody (TPOAb/TgAb)		$\chi 2$ value	p-value
	Positive (%)	Negative (%)		
Female (N=44)	34 (77.27)	10 (22.72)	5.057	0.025
Male (N=6)	2 (33.33)	4 (66.66)		

* indicate significant (p<0.05) value
Note : Figures within parenthesis indicate percentage

Table 6 shows the frequency of thyroid antibodies in the study and control groups. It is observed that thyroid antibodies are positive in 22 (70.96%) hypothyroid subjects and in 14 (73.68%) hyperthyroid subjects which are significantly higher (p=0.000) than in control group where only 6 (12%) are positive for thyroid antibodies.

Table 6 : Frequency of thyroid antibodies in study and control groups

Thyroid Antibody (TPOAb/TgAb)	Study group (N=50)		Control group (N=50)
	Hypothyroid (N=31)	Hyperthyroid (N=19)	
Positive	22*(70.96)	14*(73.68)	6 (12)
Negative	9 (19.03)	5 (26.31)	44 (88)

*indicate significant (p< 0.05) value

Note : Figures within parenthesis indicate percentage

IV. Discussion

In the present study, the mean age of the study group (40.28 years) and that of the control group (40.10 years) are similar as also the sex distribution of the two groups. However, in the study group, it is seen that there is female preponderance with 44(88%) of the thyroid patients being females and only 6(12%) being males which is similar to the finding in a study done in Nigerian patients[8].

It was reported by in a study that more than 95% of households in Imphal West District of Manipur consume iodized salt at adequate level and that there was no biochemical iodine deficiency[9]. In our study also, which has been done in the same district, it is observed that all the subjects take iodine supplementation in the form of iodized salt. This is important as excess iodine intake is a risk factor for autoimmune thyroid disease[10]. In various studies, an increase of autoimmune diseases of the thyroid has been noted after introduction of iodine prophylaxis[11, 12]. A possible explanation is that enhanced iodine intake increase the antigenecity of thyroglobulin (Tg) by formation of iodinated Tg epitopes or even generation of pathogenetic Tg epitopes that are normally cryptic[13].

In our study the mean levels of serum TPOAb of hyperthyroid subjects (142.68 IU/ ml) and hypothyroid subjects (199.97 IU/ ml) are significantly higher compared to the control group (19.82 IU/ ml). In case of serum TgAb also, it is significantly higher in hyperthyroid subjects (749.42 IU/ ml) and hypothyroid subjects (616.51 IU/ml) than in the control group. These are in agreement with the findings of a study done in Iran on patients with thyroid disorders[14].

It is observed that, in the study group, 77.27% of the females are positive for thyroid antibodies which is significantly more than in males in whom only 33.33% are positive. Other workers have also reported that thyroid antibodies are more common in females[15,16,17]. This may be due to the effect of sex hormones on the function of mammalian immune system which may play a role in the genesis of autoimmunity. Estrogen has specific effects on maturing B and T-lymphocytes which renders the surveillance screens of negative selection and tolerance induction less effective[18].

In the present study, positive thyroid antibodies is present in 70.96% and 73.68% of the patients with hypothyroidism and hyperthyroidism respectively and 12% in the control group. Aminorroaya et al also reported similar findings with positive thyroid antibodies in 75.5% and 73.6% of the patients with hypothyroidism amd hyperthyroidism respectively[14].

V. Conclusion

The present study has shown that majority of the thyroid patients have positive thyroid antibodies and that it is more common among females. Thus, it can be concluded that thyroid autoimmunity is quite common among the patients with thyroid dysfunction who were studied and is also more common in females than in males.

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