Increased Frequency of Positive Antithyroid Antibody in Nodular Goiter

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Abstract:

Background: Nodular goiter is mostly a benign thyroid tumor. A change of frequency of nodular goiter in areas with sufficient iodine intake has been documented in several reports. However, contrary to common belief it may also be associated with autoimmunity is being observed recently by many investigators. **Objectives:** To observe association between thyroid autoimmunity and nodular goiter. **Methods:** This cross sectional study included two hundred cases and one hundred controls. Clinically suspected nodular thyroid patients were confirmed by USG. Selection of healthy control was done after exclusion of nodule clinically and by USG. Data were collected through a structured questionnaire. **Results:** Frequency of positive anti-thyroid antibodies was significantly higher in nodular goiter cases, when anti-TPO and anti-TG considered together (42.5% vs. 25.0%; χ^2=8.792, p=0.003) as well as individually (anti-TPO: 37.0% vs. 20.0%; χ^2=8.955, p=0.004 and anti-TG: 31.0% vs. 9.0%; χ^2=17.861, p<0.001) in the patients with nodular goiter than that of control. Conversely, there was no statistical difference between STN and MNG for antibody status when considered together (41.1vs. 42.5%; χ^2=0.093; p=0.769) or separately (for anti-TPO: 34.2% vs. 38.6%; χ^2=0.374, p=0.648 and anti TG: 27.4% vs. 33.1%; χ^2=0.698, p=0.431). Also there was no statistical disparity for frequency of positivity of the two antibodies in STN (p=0.359) and MNG (p=0.167). **Conclusion:** Significant number of nodular goiter cases was positive for anti-thyroid antibodies.

Key words: Nodular goiter, Antithyroid Antibody (Anti TPO, Anti TG)

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Introduction:

Nodular goiter is more common in iodine deficient region but also occurs in regions of iodine sufficiency reflecting multiple genetic, autoimmune and environmental influences on the pathogenesis[1]. Presence of antithyroid antibodies in clinically non autoimmune thyroid disease indicates the autoimmune nature of the disease process. High iodine intake as well as widely varying concentration of dietary iodine increases vulnerability for development of thyroid autoimmunity. Patient with thyroid enlargement i.e. simple goiter may progress to develop nodular goiter. Principle etiologic factor for endemic goiter is iodine deficiency. During iodine deficiency there is adaptive changes in the gland where the principle regulator is thyroid stimulatory hormone which on prolonged stimulation causes goiter formation. Patient may present with normal thyroid function and they may have positive anti thyroid antibody. There are evidences that inappropriate iodinization may excite thyroid autoimmunity[2]. Antithyroid antibodies are the hall mark of thyroid autoimmunity[3]. Some authorities both at home

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and abroad in their studies showed that there is significant higher frequency of positive antibody titer in nodular goiter. Results of their studies indicate a relative importance of antithyroid antibody measurement and autoimmunity in nodular goiter[4]. Pathologic significance of antithyroid antibody is not fully known, but they represent the hallmarks of the process of thyroid autoimmunity. Present study was aimed to observe the frequency of anti thyroid peroxides and anti thyroglobulin antibodies in nodular goiter cases, which may help to understand the pattern of autoimmunity in nodular goiter in this country.

Methods:

This cross sectional study was conducted in the department of Endocrinology, Bangabandhu Sheikh Mujib Medical University (BSMMU) from December 2010 to June 2012. Two hundred patients with thyroid nodule and age and gender matched one hundred controls were recruited by purposive sampling technique. Clinically suspected nodular thyroid patients confirmed by USG attending in the outpatient department considered as cases. Selection of healthy control was done after exclusion of nodule clinically and by doing USG. Informed written consents were obtained from all subjects before interviewed by using structured questionnaire. Laboratory tests (TSH, FT3, FT4 & antithyroid antibodies) were done from serum samples of both the cases and controls by chemiluminescent immunoassay in the department of Microbiology & Immunology, BSMMU. Patient with pregnancy/lactation and with serious comorbidities were excluded. Data were analyzed by the use of SPSS (Version 13) and expressed as mean ± SEM or in frequency or percentage. P value ≤ 0.05 was considered as the level of significance.

Results:

Characteristics of the studied subjects were shown in table-I.

Table -I

Characteristics of the studied subjects (n=300)

Character	Patients with goiter	Healthy Control
N	200	100
Age (M ± SE, Year)	39.64 ± 0.87	40.70 ± 1.28
Gender (M / F)	29 / 171	13 / 87
Goiter Status:		
Solitary nodule	73	-
Multinodular	127	-
Duration of goiter (M ± SE, month)	67.46 ± 7.29	-

Table-II shows, frequency of positive anti-thyroid antibodies was significantly higher ($\chi^2 = 8.792$; $p = 0.003$) in the patients with nodular goiter (42.5%) than that of control group (25.0%).

Table-II

Status of antithyroid antibodies in the studied subjects(n=300)

Subjects	Antibody status		
	+ve	-ve	p
Patients with goitre (n=200)	85 (42.5)	115 (57.5)	0.003
Control (n = 100)	25 (25.0)	75 (75.0)	

(Within parenthesis are percentages over row total)

As is displayed in Table-III, when compared between solitary and multinodular goiter, there was no statistical difference between these two subgroups (STN vs. MNG:

41.1 vs. 42.5%; $\chi^2 = 0.093$; p = 0.769). There were no significant discordance for the two antibodies in STN (p = 0.059) or in MNG (P = 0.074) groups.

Table- III

Frequency of positive antithyroid antibody among STN and MNG (n=200)

Type of goitre (STN or MNG)	Status of antibody			p
	+ve	-ve		
STN	30 (41.1%)	43 (58.9%)	73	0.769
MNG	55 (43.3%)	72 (56.7%)	127	
Total (n=200)	85(42.5%)	115 (57.5%)		

STN = Solitary thyroid nodule; MNG = Multinodular goiter.

There was significant disparity in the control group for these two antibodies and it was found that anti TPO was more frequently positive (Table- IV).

Table- IV

Concordance of positivity of anti-TPO and anti- TG antibodies in the studied subjects. (n=300)

Subject group	Both +ve	Only TPO +ve	only TG +ve	Both -ve	Total	P
STN	13	12	7	41	73	0.359
MNG	36	13	6	72	127	0.167
Goiter (n= 200)	49	25	13	113	200	0.074
Control (n= 100)	5	49	13	76	100	0.019

Frequency of positive antibody was higher among hypothyroid (27.1% vs. 7.0%), but lower in the euthyroid patients (47.1% vs. 68.7%) whereas positivity and negativity of antibody were near equal in hyperthyroid patients (25.9% vs. 24.3%) (Table - V).

Table-V

Functional status of studied subjects with antibody status:

Functional Status of the patient	Antibody status +ve	-ve	Total
Euthyroid	40 (47.1)	79 (68.7)	119
Hyperthyroid	22 (25.9)	28 (24.3)	50
Hypothyroid	23 (27.1)	8 (7.0)	31
Total	85	115	200

$\chi 2 = 16.634$; $p < 0.001$ (Within parenthesis are percentages over column total)

Discussion:

Nodular thyroid patients were found to be frequently positive for antithyroid antibodies compared the whole controls. About 42.5% patients were positive for thyroid autoimmunity compared to only 25% in apparently healthy controls. The overall autoimmunity seems heightened than that was found previously[2]. It has been observed excess and acutely increased iodine intake is sometimes associated with thyroid abnormalities including thyroid autoimmunity[5]. Universal prophylaxis by iodized salt has been introduced in Bangladesh to correct mass iodine deficiency[5]. Should iodine prophylaxis interfere and trigger autoimmunity and that should affect all types of thyroid problems as well as the control subjects. The observed increased frequency of antithyroid antibodies in healthy control subjects might have been attributable to

some extent by the phenomenon of iodine installation as mentioned above. Moreover increasing use of iodized salt might have changed the pattern of prevalence of thyroid disorders. However it is not certain whether this would explain the increased frequency of thyroid autoimmunity in nodular goiter in this study, because non nodular thyroid patients are studied here.

Concentration of antithyroid peroxides and antithyroglobulin antibodies were found to be higher in nodular goiter than control subjects. Investigators have reported similar autoimmune phenomenon in toxic multinodular goiter[2]. This has also been observed by others irrespective of functional status[6]. Thus it seems justifiable to believe that the autoimmune phenomenon has changed in thyroid disease.

Among the studied patients, 119 (59.5%) were euthyroid, 31(15.5%) were hypothyroid and the rest 50 (25%) were hyperthyroid; this findings are comparable to the findings of previous studies in IPGMR[7], Dhaka. Patients with abnormal thyroid function, both hypothyroid and hyperthyroid, were also more frequently positive for antithyroid antibodies. Thus autoimmunity and functional aberration may be the outcome of same causal factor in these thyroid problems. Hence patients with functional abnormalities should be tested for antithyroid antibodies. Universal salt iodized in agreement with WHO recommendations has been greatly emphasized in Bangladesh. It had been assumed that most of the thyroid problems may be attributable to the deficiency of iodine. This was also the suspicion by other investigators who carried out studies on thyroid problems in this country[8]. Present study did not include any iodine estimation. Therefore relations of the present issue of autoimmunity and nodularity of thyroid disease in context to iodinization program cannot be assumed from the present study.

It appeared that antithyroid antibodies are good markers of thyroid autoimmunity which is in agreement with the conventional belief[9]. There was good concordance between the two antibodies which was true for both the thyroid patients and control subjects. Moreover, by logistic regression analysis it was found that both the antibodies were individually independent predictor for autoimmunity. Thus it could be assumed that autoimmunity of thyroid equally involve these two antibodies. Therefore to evaluate autoimmunity in a thyroid patient, any of the two or both the antibodies may be considered.

Conclusions:

In the present study the overall frequency of thyroid autoimmunity was found higher than that as is conventionally believed. It was concluded that frequency of antithyroid antibodies are higher than that as is usually assumed and should be assayed in nodular goiter irrespective of variety of nodule, especially if there is functional aberration. On further study, it could be clearly recommended about the importance and validity of the estimation of antithyroid antibodies in nodular goiter for thyroid autoimmunity.

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