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Original Article

Cytological Evaluation of Thyroid and its Correlation with Thyroid Function Test and Anti-Thyroid Peroxidase in a Patient of Hashimoto's Thyroiditis

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Abstract

Background

A thyroid swelling is an enlargement of thyroid glands causes by iodine deficiency, ageing, autoimmune disease and benign or malignant tumors. Autoimmune thyroiditis is the second most common thyroid lesion diagnosed after goiter.

Materials and Methods

To find out the distribution of thyroid gland swelling in patients visiting otorhinolaryngology department of Nobel medical college and correlate serum thyroid function test and anti-thyroid peroxidase level with fine needle aspiration cytology reports.

Results

The mean age of patient with thyroid gland lesions was 40.47 ± 13.05 years. Out of 87 patients studied, the highest number of patients (37, 42.5%) was diagnosed with colloid goiter followed by autoimmune thyroiditis (29, 33.3%). The mean age of patients with autoimmune thyroiditis was found to be 38.66 ± 12.31 years. The sensitivity and specificity of anti-thyroid peroxidase antibodies for diagnosing autoimmune thyroiditis was 89.7% and 94.8% respectively.

Conclusion

Autoimmune thyroiditis has statistical correlation with serum anti-thyroid peroxidase antibodies and it can be effectively used as an alternative tool in diagnosing autoimmune thyroiditis with acceptable diagnostic accuracy.

Key words: *Autoimmune, Cytology, Thyroid*

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Introduction

A thyroid swelling is an enlargement of thyroid glands which is a common clinical presentation. The most common causes of thyroid swelling include iodine deficiency, ageing, autoimmune disease and benign or malignant tumors [1, 2]. Asymptomatic thyroid swelling is a common occurrence affecting 5 to 20% patients in endemic areas [3]. Majority of thyroid swellings are benign, whereas fewer than 5% of thyroid swellings are malignant [4].

Hashimoto's thyroiditis, a synonym of autoimmune thyroiditis or chronic lymphocytic thyroiditis, was first described by Hakaru Hashimoto in 1992 [5]. It is the second most common thyroid lesion diagnosed after goiter [6, 7]. The prevalence of Hashimoto's thyroiditis ranges from 1-4% [7]. The thyroid follicular cells are destroyed by the invasion of the thyroid by lymphocyte, plasma cells and macrophage. Thyroid peroxidase (TPO), thyrotropin receptor (TSH-R) and thyroglobulin (Tg) are target antigens of thyroid antibodies [8].

The definitive diagnosis of thyroid lesion is done by histopathology but most often Fine Needle Aspiration Cytology is used as a standard procedure as it is simple, cost effective, and minimally invasive diagnosed procedure [9].

In thyroid gland, (triiodothyronine) T3 and (thyroxin) T4 is secreted by thyroid follicles under the stimulation of thyroid stimulation hormone (TSH) which is produced by anterior pituitary gland [10] Thyroid dysfunction is evaluated based on level of these hormones. In autoimmune thyroiditis, the level of Anti-thyroid peroxidase (TPO) is increased in blood and is used as an important diagnostic tool [11]

Thyroid gland swelling is not adequately studied in Eastern Nepal. The present study is conducted to evaluate the incidence of different thyroid lesions and determine the importance of serum level of anti-TPO in relation to FT3, FT4 and TSH in diagnosing autoimmune thyroiditis.

Materials and Methods

This is a prospective and comparative study, which was conducted on the patients presented with thyroid gland swelling, attending the Outpatient department of Otorhinolaryngology, Nobel Medical College Teaching Hospital, Biratnagar, Nepal for a period of two years from Jan 2017 to Jan 2019. Written consent was obtained and Fine Needle Aspiration Cytology (FNAC) was done in all patients by department of pathology of Nobel medical college. Ethical clearance was obtained from Institutional ethics committee of Nobel medical college and teaching hospital, Biratnagar, Nepal. The sample size was calculated by the correlation 96.0% [19] in a previously reported study, hence sample size become 59 using 95% confidence interval and 90% power, but all 87 samples were considered for analysis during the study period.

Case Selection

Inclusion Criteria: All the consenting patients of either age or sex with thyroid gland swelling. Exclusion Criteria: History of systemic disease like cardiac disease, hepatic disease and chronic kidney disease, Any contraindication of FNAC such as bleeding diathesis and skin infection in area of fine-needle aspiration, Patient's refusal.

A total of 87 patients attending otorhinolaryngology department with thyroid gland swelling were enrolled in our study after proper informed written consent. Detailed history taking, clinical examination and laboratory investigation was done, and age and sex were recorded for demographic comparison. All patients were subjected to blood sampling for estimation of free T3 (FT3), free T4 (FT4), thyroid stimulating hormone (TSH) and anti-TPO antibodies.

With informed written consent FNAC was done under aseptic precautions with 24 G needle from thyroid lesions. Procedure was not performed under USG guidance. A minimum of two passes were made and the contents of needle were expressed onto clean glass slides and fixed with 95% alcohol and staining was done by Giemsa stain. In case of insufficient aspirate, repeat aspiration was done. After examination of smear under light microscope by pathologist in department of pathology, results were reported. The diagnostic criteria used by Bhatia et al [6] were used to diagnose autoimmune thyroiditis in FNAC as shown in Table 1.

Table 1: Grading of thyroiditis on cytological material

Grade	Morphological features
Grade 0	No lymphoid cells.
Grade 1 (Mild)	Few lymphoid cells infiltrating the follicles/increased number of lymphocytes in the background.
Grade 2 (Moderate)	Moderate lymphocytic infiltration or mild lymphocytic infiltration with Hurthle cell change/ giant cells/ anisonucleosis.
Grade 3 (Severe)	Florid lymphocytic inflammation with germinal center formation, very few follicular cells left.

Ft3, FT4, TSH and anti-TPO antibodies were analyzed by Siemens XP fully automated hormone assay using chemiluminescence assay. The normal values for FT3, FT4, TSH and anti-TPO was taken as 1.08-3.14 nmol/L, 0.8-2.3ng/dl, 0.4-4.0 mIU/L and 7-50 IU/mL respectively.

The results of the study were statistically analyzed using SPSS version 25, using chisquare test, Fisher's exact test and independent sample t test. Results on continuous measurements are presented as mean ± standard deviation (min-max) and results on categorical measurements are presented in percentage and frequency. The sensitivity, specificity and diagnostic accuracy of anti-TPO antibodies were calculated. A p-value of <0.05 was considered statistically significant.

Results

A total of 87 patients with thyroid gland swelling were studied of which 29 patients were diagnosed as autoimmune thyroiditis in cytological examination. The mean age of patient with thyroid gland lesions was 40.47 ± 13.05 years with minimum age of 14 years and maximum age of 77 years.

Out of 87 patients studied, the highest numbers of patients (37, 42.5%) were diagnosed with colloid goiter followed by autoimmune thyroiditis (29, 33.3%), papillary carcinoma (6, 6.9%), papillary adenoma (5, 5.7%), follicular carcinoma (4, 4.6%), hyperplastic goiter (3, 3.4%) and De Quervain's thyroiditis (3, 3.4%). On further analysis of cytological reports, the incidence of thyroid gland lesion was highest in 31-40 years age groups (39.1%) followed by 41-50 years (24.1%), 51-60 years (14.9%), 21-30 years (9.2%), <20 years (6.9%) and >60 years (5.7%). The incidence of autoimmune thyroiditis is highest in 31-40 years age group (32.43%) followed by 41-50 years (21.62%), 51-60 years and 21-30 years (8.11%).

On further analysis of FNAC reports, mean age of patients with autoimmune thyroiditis was found to me 38.66 ± 12.31 years with minimum age of 16 years and maximum age of 74 years. The comparison of incidence of autoimmune thyroiditis and other thyroid gland lesions in various age groups did not show statistically significant difference (p=0.930) as shown in Table 2.

Table 2: Comparison of age groups of patients with FNAC findings of thyroid lesions

	FNAC findings						p-value
	Autoimmune thyroiditis			Others			
Age groups	Male	Female	Total	Male	Female	Total	
<20 years	0	2	**2(6.9%)**	1	3	**4(6.9%)**	
21-30 years	0	3	**3(10.3%)**	2	3	**5(8.6%)**	
31-40 years	2	10	**12(41.4%)**	4	18	**22(37.9%)**	**0.930**
41-50 years	0	8	**8(27.6%)**	2	11	**13(22.4%)**	
51-60 years	0	3	**3(10.3%)**	2	8	**10(17.2%)**	
>60 years	0	1	**1(3.4%)**	1	3	**4(6.9%)**	
Total	**2(6.9%)**	**27(93.1%)**	**29(100%)**	**12(20.7%)**	**46(79.3%)**	**58(100%)**	

The incidence of autoimmune thyroiditis in male and female was 6.9% and 93.1% respectively with male to female ratio of 1:13.5. Similarly, the incidence of thyroid lesions other than autoimmune thyroiditis in male and female was 20.7% and 79.3% respectively with male to female ratio of 1:3.83. However, the difference was not statistically significant (p=0.086) as shown in Table 3.

Table 3: Comparison of sex of patients with FNAC findings of thyroid lesions

	FNAC findings		p-value
	Autoimmune thyroiditis	Others	
Sex			
Male	2(6.9%)	12(20.7%)	**0.086**
Female	27(93.1%)	46(79.3%)	
Total	**29(100%)**	**58(100%)**	

The sensitivity and specificity of Anti-TPO antibodies for diagnosing autoimmune thyroiditis was found to be 89.7% and 94.8% respectively with overall diagnostic accuracy of 93.1% as shown in Table 4.

Table 4: Correlation of Anti TPO antibodies and FNAC findings

		FNAC findings	
		Autoimmune thyroiditis	Others
Anti TPO	**Positive**	26(89.7%)	3(5.2%)
	Negative	3(10.3%)	55(94.8%)

On further analysis of patients with autoimmune thyroiditis, thyroid dysfunction was observed in 23 patients, whereas 6 patients were euthyroid. The most common thyroid dysfunction was hypothyroidism (44.8%), followed by subclinical hypothyroidism (31.0%), euthyroid (20.7%) and hyperthyroidism (3.4%) as shown in Table 5.

Table 5: Pattern of thyroid dysfunction among the patients with Hashimoto's thyroiditis

Thyroid dysfunction	Numbers (%)
Hypothyroid	13(44.8%)
Subclinical hypothyroid	9(31.0%)
Euthyroid	6(20.7%)
Hyperthyroid	1(3.4%)
Total	**29(100%)**

The grading of autoimmune thyroiditis was analyzed, which showed highest number of autoimmune thyroid lesions in grade 3 (13), followed by grade 2 (7), grade 1 (5) and grade 0 (4) as shown in Table 6.The correlation of grading of autoimmune thyroiditis with anti-TPO antibodies and TSH level was studied. TSH and anti-TPO antibodies was increased in grade 3 which is statistically significant (p=0.033). On further analysis, the significance is gradually increasing from grade 1 (p=0.243) to grade 3 (p=0.033) as shown in Table 6.

Table 6: Grading of autoimmune thyroiditis and correlation of grading of autoimmune thyroiditis with anti-TPO and TSH level

	Lymphocyte grade							Total
	0+	1+	p-value	2+	p-value	3+	p-value	
Anti-TPO increase TSH increase	3	3		5		10		21
Anti-TPO increase TSH normal	1	1	0.243	1	0.119	1	**0.033***	4
Anti-TPO increase TSH low	0	1		0		0		1
Anti-TPO normal TSH increase	0	0		1		2		3
Total	**4**	**5**		**7**		**13**		**29**

Statistically significant*

The mean value of Anti-TPO antibodies in autoimmune thyroiditis was found to be 93.03 ± 29.25 IU/ml, whereas in non-autoimmune thyroiditis, it was found to be 32.69 ± 21.47 IU/ml. The difference is statistically significant ($p<0.001$).

Discussion

This is a study conducted on patients with thyroid gland swelling in Nobel Medical College, Biratnagar, Nepal with respect to biochemical markers including FT3, FT4, TSH and anti-TPO antibody.

The mean age of patient with thyroid gland lesions was 40.47 ± 13.05 years with minimum age of 14 years and maximum age of 77 years which is comparable to the study done by Yang et al [12], Staii et al [13]. According to the study conducted in Maharajgnj, Nepal by Karki et al. mean age of thyroid swelling was 40.4 years, which is in accordance to our study [14]. In the present study, the incidence of thyroid gland lesion was highest in 31-40 years age groups (39.1%) followed by 41-50 years (24.1%) and 51-60 years (14.9%) which is similar to the study done by Karki et al. which showed 20-50 years as common age of thyroid gland swelling [14].

The highest number of patients were diagnosed with colloid goiter (37, 42.5%) followed by autoimmune thyroiditis (29, 33.3%), whereas in a study conducted by S. Chandanwale et al., colloid goiter seen in 65.3% of cases but thyroiditis was seen in only 12.6% of cases [15]. However, comparable to our study, autoimmune thyroiditis was seen in 35.4% of cases in study conducted by Chehade et al [1]. Similar to the observation reported by Devi J et al [16] and Chandanwale et al [15], papillary carcinoma was the most common neoplastic lesion followed by follicular carcinoma in present study.

The mean age of patients with autoimmune thyroiditis was found to me 38.66 ± 12.31 years which is comparable to the study conducted by Saha et al [17], but 9 years less than that of study done by staii et al [13]. The present study showed that autoimmune thyroiditis is more common in female with male to female ratio of 1:13.5, which is in accordance with study done by Shetty et al. which showed male to female ratio of 1:14.7 [18].

The most common thyroid dysfunction was clinical hypothyroidism (44.8%), followed by subclinical hypothyroidism (31.0%), euthyroid (20.7%) and hyperthyroidism (3.4%) in patients with autoimmune thyroiditis. However, in contrast to present study, most patients were euthyroid in study conducted by Staii et al [13].

The sensitivity and specificity of Anti-TPO antibodies for diagnosing autoimmune thyroiditis was found to be 89.7% and 94.8% respectively which is higher compared to study conducted by Karki et al [14]. However Engler et al. has reported 96% sensitivity of anti TPO antibody in autoimmune thyroiditis [19].

The correlation of grading of autoimmune thyroiditis with anti-TPO antibodies and TSH level was studied which showed increased level of anti TPO antibodies and TSH level in higher grade of autoimmune thyroiditis which is comparable to study done by Sood et al [20]. Two patients with increased anti-TPO without lymphoid infiltration and normal level of TSH were present in our study. The study conducted by Cappa M et al. showed that in early stage of autoimmune thyroiditis, TSH may be normal with increased level of anti-TPO antibody [21].

Conclusion

The incidence of thyroid gland swelling is higher in 31-40 years age groups with highest incidence of colloid goiter followed by autoimmune thyroiditis. Autoimmune thyroiditis is commonly found in female with male to female ratio of 1:13.5. Autoimmune thyroiditis has statistical correlation with serum anti-TPO antibodies, and with its high sensitivity and specificity, it can be effectively used as an alternative tool in diagnosing autoimmune thyroiditis with acceptable diagnostic accuracy.

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