

INCIDENCE AND OUTCOME OF HASHIMOTO'S THYROIDITIS IN NODULAR GOITER- AN INSTITUTIONAL STUDY

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ABSTRACT

BACKGROUND

Thyroid disease is most common endocrine disorder and is different from other endocrine diseases because of its visible swelling and ease of diagnosis. In India, significant burden of thyroid diseases exists with an estimation of around 42 million cases. The thyroid status and autoimmune disease status of adult Indian population is largely unknown.

The main aim of this study was to generate valuable epidemiological data regarding the prevalence of Hashimoto's Thyroiditis (HT) in northern population of Kerala, to study the different histopathological type of malignancy in FNAC (fine-needle aspiration cytology) proven HT, to assess thyroid autoimmunity, goitrogens along with environmental factors in the development of thyroiditis.

MATERIALS AND METHODS

The present study was conducted in Department of General Surgery, Government Medical College, Kozhikode, Kerala, between January 2015 to June 2016. It included cross-sectional analysis of cytomorphology of fine-needle aspiration cytology material of 200 patients presenting with thyroid nodule in the Department of General Surgery.

RESULTS

The commonest age group affected was 40-50 yrs. The female patients (92%) outnumbered the male patients (8%). The cytomorphological analysis of 200 patients revealed 25.5% cases have HT and a few patients with nodular colloid goiter were found to have associated HT, which makes overall prevalence of 28%. Incidence of coexistent papillary carcinoma with Hashimoto's thyroiditis is 3.9%.

CONCLUSION

Higher prevalence of autoimmune thyroiditis in females maybe linked with both genetic and environmental factors. There is co-existence of HT and papillary carcinoma; therefore, HT patients need to be carefully followed up. The high TSH values was exclusively found in patients with FNAC proven HT (63%), which is in concordance with existing literature. HT is the most common cause of hypothyroidism.

KEYWORDS

Nodular Goiter, Hashimoto's Thyroiditis, Fine-Needle Aspiration Cytology, Papillary Carcinoma.

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BACKGROUND

Hashimoto's thyroiditis is now considered the most prevalent autoimmune disease as well as the most common endocrine disorder. It was initially described in 1912, but only rarely reported until the early 1950s. In India, thyroid disorders are the second commonest endocrine disease next to diabetes mellitus and its prevalence is much higher in females. Autoimmune thyroid disease is the most common organ-

specific autoimmune disorder resulting in dysfunction of the thyroid gland.¹

The term thyroiditis encompasses a group of many relatively common inflammatory thyroid disorders. The thyroid gland maybe subject to inflammatory change in a variety of conditions, which maybe focal or diffuse and are often associated with thyroid dysfunction.

The incidence of thyroiditis once considered rare is reported to be increasing.² The incidence varies depending on the geographical location, type of study, and sex of the patient.

Hashimoto's thyroiditis is an multifactorial autoimmune disease of the thyroid gland that has a characteristic pathological appearance.³ The main feature is infiltration with haematopoietic cells, mainly lymphocytes, organised in lymphoid follicles that often show prominent germinal centres. Other features include transformation of normal thyrocytes into Hurthle cells in some areas, destruction and

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atrophy of thyrocytes in other areas and interstitial fibrosis. These histological findings vary significantly among patients so that a clinicopathologic spectrum of conditions, rather than a single disease, falls under the term Hashimoto's thyroiditis. This spectrum now includes the classical, fibrosing, juvenile, painless, and Hashitoxicosis variants.

The occurrence of thyroglobulin antibodies in the serum of patients with autoimmune thyroid disease was first described by Roitt et al.^{4,5} Subsequently, antibodies to microsomal antigen, second colloid antigen and cell surface antigen were described. The most commonly measured antibodies in patients with autoimmune thyroid disease include antithyroglobulin and antimicrosomal antibodies.⁶

Fine-needle aspiration cytology provides an accurate and safe method of cytological diagnosis of thyroid pathology. Recent appreciation of sensitivity and specificity of fine-needle aspiration cytology is growing and has drastically altered the approach to the management of thyroid swelling. The extensive availability, simplicity and rapidity of containing the diagnosis with minimum complications has led to the approval of fine-needle aspiration cytology as a diagnostic tool.^{7,8}

The present study was undertaken to evaluate the incidence of Hashimoto's thyroiditis in the given cohort of patients from Government Medical College, Calicut, Kerala, presented with nodular goitre in relation with age and sex and the different histopathological type of malignancy in histopathologically proven HT.

MATERIALS AND METHODS

Subjects

The Department of General Surgery in Government Medical College, Calicut, is situated in the northern part of Kerala is tertiary referral centre for thyroid disease and patients being referred here for further evaluation. This is descriptive study of 200 patients who visited the General Surgery Department with nodular goiter.

METHODOLOGY

Study Design- Descriptive- Cross-sectional study.
Duration- One and a half years from January 2015 to June 2016.
Sample Size- 200.

Inclusion Criteria

1. Clinically diagnosed case of nodular goitre from Government Medical College, Calicut.
2. Patients above the age of 13.

Exclusion Criteria

1. Patients having other head and neck malignancies.
2. Patients below the age of 12.
3. Patients diagnosed to have other type of thyroiditis.

Procedure

Cross-sectional analysis of the histopathological and fine-needle aspiration cytology reports of the diagnosed case of nodular goitre.

Study Tools

- Case sheets of patients.
- FNAC reports.
- Histopathological reports.

Statistical Methods

- Microsoft Excel and Word 2007 for data entry.
- SPSS 18 software for data analysis.

RESULTS AND ANALYSIS

Distribution of nodular goitre according to sex in this study.

Gender	Frequency	Percentage (%)
Male	19	9.5
Female	181	90.5
Total	200	100

Table 1. Distribution of Nodular Goitre According to Age Group

*mean age of the population was 43.29 years.

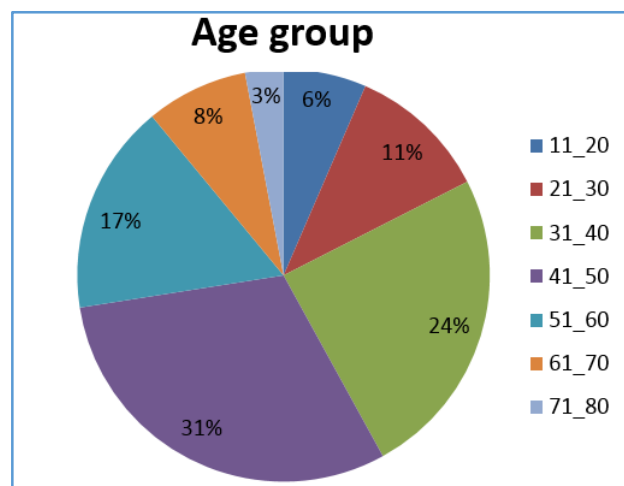


Chart 1

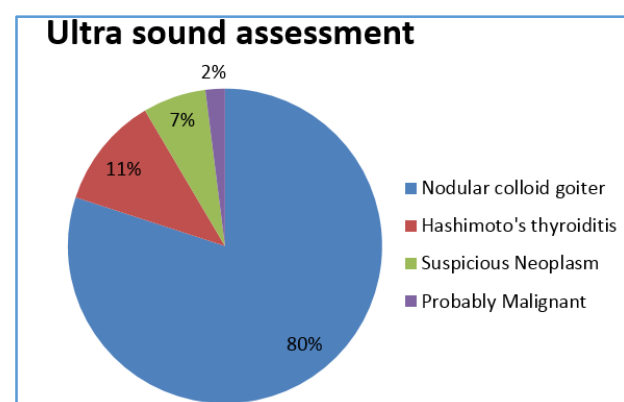


Chart 2. Ultrasound Assessment

Management	Frequency	Percentage (%)
Medical management/follow up	132	66.0
Surgery	68	34.0
Total	200	100

Table 2. Management

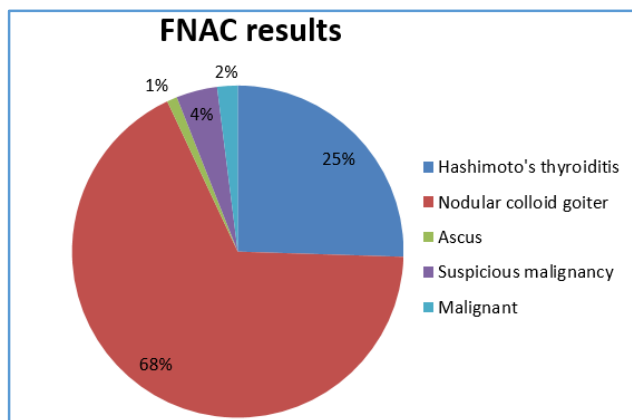


Chart 3. FNAC

Histopathology Report	Frequency	Percentage (%)
Hashimoto's thyroiditis	2	1.0
Nodular colloid goiter	42	20.7
Papillary carcinoma	12	6.1
Follicular Carcinoma	4	2.0
Papillary carcinoma with Hashimoto's thyroiditis	2	1.0
Nodular colloid goiter with Hashimoto's thyroiditis	6	3.0
No HPR report	132	66.2
Total	200	100.0

Table 4. Histopathology Report

TSH Values	Frequency	Percentage (%)
Low	26	13.0
Normal	142	71.0
High	32	16.0
Total	200	100

Table 3. TSH Values

Age Group	FNAC						
		HT	Nodular Colloid	Ascus	Suspicious Malignancy	Malignant	Total
11-20	Count	1	8	0	3	1	13
	% within age group	7.7%	61.5%	.0%	23.1%	7.7%	100.0%
	% within FNAC	2.0%	5.9%	.0%	37.5%	25.0%	6.5%
21-30	Count	2	17	2	1	0	22
	% within age group	9.1%	77.3%	9.1%	4.5%	.0%	100.0%
	% within FNAC	3.9%	12.6%	100.0%	12.5%	.0%	11.0%
31-40	Count	12	34	0	2	1	49
	% within age group	24.5%	69.4%	.0%	4.1%	2.0%	100.0%
	% within FNAC	23.5%	25.2%	.0%	25.0%	25.0%	24.5%
41-50	Count	17	43	0	1	0	61
	% within age group	27.9%	70.5%	.0%	1.6%	.0%	100.0%
	% within FNAC	33.3%	31.9%	.0%	12.5%	.0%	30.5%
51-60	Count	14	18	0	1	0	33
	% within age group	42.4%	54.5%	.0%	3.0%	.0%	100.0%
	% within FNAC	27.5%	13.3%	.0%	12.5%	.0%	16.5%
61-70	Count	4	10	0	0	2	16
	% within age group	25.0%	62.5%	.0%	.0%	12.5%	100.0%
	% within FNAC	7.8%	7.4%	.0%	.0%	50.0%	8.0%
71-80	Count	1	5	0	0	0	6
	% within age group	16.7%	83.3%	.0%	.0%	.0%	100.0%
	% within FNAC	2.0%	3.7%	.0%	.0%	.0%	3.0%
Total	Count	51	135	2	8	4	200
	% within age group	25.5%	67.5%	1.0%	4.0%	2.0%	100.0%
	% within FNAC	100%	100%	100%	100%	100%	100%

Table 5. Comparison Between Age Group Affected and FNAC Results

*The results were significant at chi-square value 52.77 at df 24 and P value of 0.01.

It was noticed that the HT group and nodular colloid goiter were more common among the middle age group while the malignant lesions were more common in the older group.

AGE GROUP AND HASHIMOTO'S THYROIDITIS

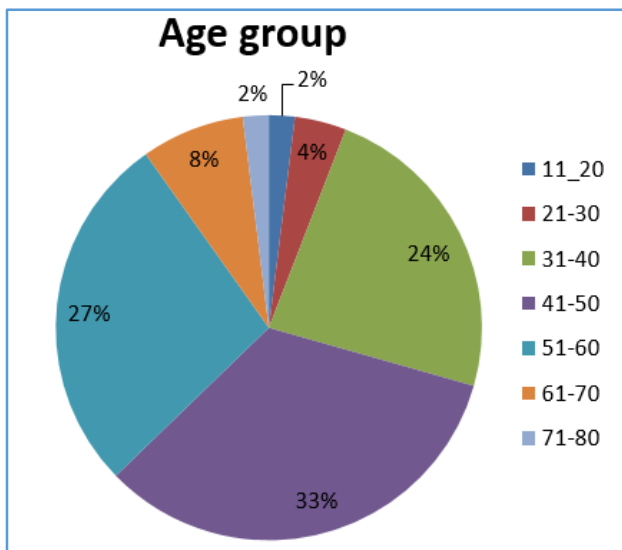


Chart 4

FNAC								
Gender			HT	Nodular Colloid	Ascus	Suspicious Malignancy	Malignant	Total
	Male	Count	4	14	0	1	0	19
		% within sex	21.1%	73.7%	.0%	5.3%	.0%	100.0%
		% within FNAC	7.8%	10.4%	.0%	12.5%	.0%	9.5%
	Female	Count	47	121	2	7	4	181
		% within sex	26.0%	66.9%	1.1%	3.9%	2.2%	100.0%
	% within FNAC	92.2%	89.6%	100.0%	87.5%	100.0%	90.5%	
Total	Count	51	135	2	8	4	200	
	% within sex	25.5%	67.5%	1.0%	4.0%	2.0%	100.0%	
	% within FNAC	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	

Table 6. Comparison Between Gender and FNAC Results

There is no significant difference among the groups with respect to gender distribution as majority of the sample were females.

FNAC								
Management			Hashimoto's	Nodular Colloid	Ascus	Suspicious Malignancy	Malignant	Total
	Medical/follow up	Count	46	86	0	0	0	132
		% within Management	34.8%	65.2%	.0%	.0%	.0%	100.0%
		% within FNAC	90.2%	63.7%	.0%	.0%	.0%	66.0%
	Surgery	Count	5	49	2	8	4	68
		% within Management	7.4%	72.1%	2.9%	11.8%	5.9%	100.0%
	% within FNAC	9.8%	36.3%	100.0%	100.0%	100.0%	34.0%	
Total	Count	51	135	2	8	4	200	
	% within Management	25.5%	67.5%	1.0%	4.0%	2.0%	100.0%	
	% within FNAC	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	

Table 7. Comparison Between Management and FNAC Results

The results were significant at a chi-square value of 40.79 with df 4 and P value of <0.05. There is a significant difference in the management of patients with thyroid nodule. 90.2% of Hashimoto's thyroiditis were managed medically while 36.1% of nodular colloid goiter was operated.

		FNAC						
			HT	Nodular colloid	Ascus	Suspicious Malignancy	Malignant	Total
TSH	Low	Count	9	17	0	0	0	26
		% within TSH	34.6%	65.4%	.0%	.0%	.0%	100.0%
		% within FNAC	17.6%	12.6%	.0%	.0%	.0%	13.0%
	Normal	Count	10	118	2	8	4	142
		% within TSH	7.0%	83.1%	1.4%	5.6%	2.8%	100.0%
		% within FNAC	19.6%	87.4%	100.0%	100.0%	100.0%	71.0%
	High	Count	32	0	0	0	0	32
		% within TSH	100%	.0%	.0%	.0%	.0%	100.0%
		% within FNAC	62.7%	.0%	.0%	.0%	.0%	16.0%
Total		Count	51	135	2	8	4	200
		% within TSH	25.5%	67.5%	1.0%	4.0%	2.0%	100.0%
		% within FNAC	100%	100.0%	100.0%	100.0%	100.0%	100.0%

Table 8. Comparison Between TSH Values and FNAC Results

The results were significant at a chi-square value of 121 at df 8 and P value of <0.05 Hashimoto's thyroiditis group was the only group in which elevated TSH (hypothyroidism) was noticed with 62.7% of them affected.

		FNAC						
			HT	Nodular Colloid	Ascus	Suspicious Malignancy	Malignant	Total
HPR	HT	Count	2	0	0	0	0	2
		% within HPR	100.0%	.0%	.0%	.0%	.0%	100.0 %
		% within FNAC	3.9%	.0%	.0%	.0%	.0%	1.0%
	Nodular colloid goiter	Count	1	40	1	0	0	42
		% within HPR	2.4%	95.2%	2.4%	.0%	.0%	100.0 %
		% within FNAC	2.0%	29.6%	50.0%	.0%	.0%	21.0%
	Papillary carcinoma	Count	0	3	0	6	3	12
		% within HPR	.0%	25.0%	.0%	50.0%	25.0%	100.0 %
		% within FNAC	.0%	2.2%	.0%	75.0%	75.0%	6.0%
	Follicular carcinoma	Count	0	1	0	2	1	4
		% within HPR	.0%	25.0%	.0%	50.0%	25.0%	100.0 %
		% within FNAC	.0%	.7%	.0%	25.0%	25.0%	2.0%
	Papillary carcinoma with HT	Count	2	0	0	0	0	2
		% within HPR	100.0%	.0%	.0%	.0%	.0%	100.0 %
		% within FNAC	3.9%	.0%	.0%	.0%	.0%	1.0%
	Nodular colloid goiter with HT	Count	0	5	1	0	0	6
		% within HPR	.0%	83.3%	16.7%	.0%	.0%	100.0 %
		% within FNAC	.0%	3.7%	50.0%	.0%	.0%	3.0%

	No HPR results	Count	46	86	0	0	0	132
		% within HPR	34.8%	65.2%	.0%	.0%	.0%	100.0%
		% within FNAC	90.2%	63.7%	.0%	.0%	.0%	66.0%
Total		Count	51	135	2	8	4	200
		% within HPR	25.5%	67.5%	1.0%	4.0%	2.0%	100.0%
		% within FNAC	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
Table 9. Comparison Between HPR Results and FNAC Results								

Results were significant at a chi-square value of 194 with df 24 and P value of <0.05.

Papillary carcinoma was noticed in 10% of the FNAC suspected HT while 3.8% of the FNAC suspected nodular colloid goiter had an HPR report with features of HT.

DISCUSSION

The thyroid nodule is a common entity. While autopsy data indicate a 50% prevalence of thyroid nodules larger than one centimetre in patients without clinical evidence of thyroid disease, the prevalence of palpable nodules is only 4 to 7%.⁹

Gender

The current study depicts that the incidence of thyroid nodule to be more in females than males. This is similar to the results from previous studies about thyroid nodules.^{10,11} In cross-sectional surveys, the prevalence of diffuse goitre is greatest in premenopausal women and the ratio of women-to-men is at least 5:1.¹²

Females were dominantly affected with HT with 92.2%. Previous report by Weetman AP¹³ in 2001 has shown a male-to-female ratio ranging from 1:5 to 1:11 among various age groups in the incidence of Hashimoto’s thyroiditis. Dayan CM et al¹⁴ in 1996 has suggested that women are 5-20 times more affected than men in case of Hashimoto’s thyroiditis. Lorini R et al¹⁵ in 2006 suggested that up to 95% of those affected by chronic lymphocytic thyroiditis are females. It is noted that female predisposition for Hashimoto’s thyroiditis is common across the age groups with even female children being affected more than male children.^{16,17,18} Numerous epidemiological studies have indicated that females present with positive thyroid antibodies up to three times more often than males.

Age

Mean age group of the sample was 43.29. This has reflected the existing literature on the age at presentation of thyroid nodule in many studies.¹⁹⁻²⁰ The age group commonly affected was between 41-50. The results were slightly higher when compared with other studies from India.¹⁹⁻²⁰

TSH Values and Hashimoto’s Thyroiditis

Most of the patients with the nodules (71%) were found to be euthyroid, 16% had a high TSH value and 13% had a low value for serum TSH. The high TSH value was exclusively

found in patients with an FNAC proven HT. Most of the patients with a low TSH values were having a diagnosis of nodular colloid goitre and HT was found in a fraction (17.6%) of them. Malignant nodules were found only in patients with a euthyroid status.

HT represents the most common cause of hypothyroidism in the general population.²¹ In regions where iodine intake is adequate, the high incidence of anti-TSH antibodies and thyroid gland destruction leads to a state of hypothyroidism in these individuals.²² Low concentrations of thyroid hormones with high TSH and circulating thyroid auto antibodies (against peroxidase in 70-90% of cases and against Tg in 40-70% of cases) virtually confirms the diagnosis of chronic lymphocytic thyroiditis.²²

Hashimoto’s and Low TSH values

The relation between circulating thyroid antibodies and TSH levels were classically described in the Whickham cohort study.²⁰ The 20-year follow-up of the Whickham cohort provided incidence data and allowed the determination of risk factors for spontaneous hypothyroidism in this period.²⁰ The mean annual incidence of spontaneous hypothyroidism during the 20-year follow-up period was 3.5 per 1000 and 0.6 per 1000 in surviving women and men, respectively.²⁰ Either raised serum TSH or positive thyroid antibodies alone or in combination were associated with a significantly increased risk of developing hypothyroidism. The probability of developing hypothyroidism was higher in those women who had serum TSH concentrations >2.0 mU/l and high-serum titres of antithyroid microsomal antibodies during the first survey.²⁰ All studies indicate that the higher the serum TSH value, the greater the likelihood of development of overt hypothyroidism in subjects with chronic autoimmune thyroiditis.²³

Assessment of Thyroid Nodule

Ultrasound Assessment

80% of the nodules were having benign characteristics in USG and 11.5% had features suggestive of Hashimoto’s thyroiditis. 6.5% of the nodules were suspicious.

The characteristic US appearance of Hashimoto’s thyroiditis is focal or diffuse glandular enlargement with coarse, heterogeneous and hypoechoic parenchymal echo pattern. Presence of multiple discrete hypoechoic micronodules (1-6 mm size) is strongly suggestive of chronic thyroiditis. Fine echogenic fibrous septae may produce a

pseudolobulated appearance of the parenchyma. Colour Doppler may demonstrate slight to markedly increased vascularity of the thyroid parenchyma.²⁴

The sensitivity of USG along with Doppler in detection of HT is high (65-95%) in previous studies.²⁵ But, the sensitivity of USG towards Hashimoto's thyroiditis in our study was poor detecting less than half of the cases (25.5% vs. 11.5%), but it was comparable with other studies, which does not use colour Doppler screening. USG is not routinely recommended for screening in adults as blood level of autoantibodies and TSH levels are more sensitive for Hashimoto's thyroiditis. USG is a preferred investigation for lymphocytic thyroiditis in children.²⁶

Fine-Needle Aspiration Cytology

FNAC still remains the most important method for detecting malignancy in the management and monitoring of thyroid nodules. It has a high sensitivity (65 to 98%) and specificity (72 to 100%) and it has a false-positive rate for cancer detection of 0 to 7% and a false-negative rate of 1 to 11%. Physician experience is quite important for performing this procedure and US-guided FNAC is preferable. Similarly, pathologist experience in interpreting the aspirated material can guide the therapeutic approach. The procedure is relatively simple, quick, safe, low-cost and devoid of significant complications.²⁷⁻²⁸

FNAC in the current study detects 67.5% of nodules to be of nodular colloid type 25.5% as HT 4% had a suspicious lesion while 1% had characteristics of a malignant lesion.

Prevalence of Hashimoto's Disease

Lymphocytic thyroiditis was detected in 25.5% cases on FNAC. A few of the patients with nodular colloid goitre were found to have associated lymphocytic thyroiditis, which makes the overall prevalence of HT in the present study as 28%. The prevalence of HT in a previous study done in India was similar to the present study.²⁹

HT Coexisting with Nodular Colloid Goitre

Hashimoto's thyroiditis may coexist with colloid goitre giving a cytologic picture of a distinct double population of lymphocytes with a background of colloid. The present study shows an incidence of 3.7% of nodular colloid goitres coexisting with pathological features of HT. This reflects the study done by Kollur et al where the incidence was 1.5% with colloid goitres along with features of lymphocytic thyroiditis.³⁰

Hashimoto's Thyroiditis and Malignancy

In the current study, follicular carcinoma was found in around 2% of the cases. Mostly, the FNAC findings were suspicious in such patient. Papillary carcinoma was detected in 7% of the nodules. Papillary carcinoma with associated features of lymphocytic thyroiditis is found in 1% of the total sample.

Papillary thyroid cancer and Hashimoto's thyroiditis reported incidence rates of coexisting thyroid neoplasia with Hashimoto's ranged between 3-14%. As already noted,

there is an increased incidence of papillary carcinoma (4%) in HT, this is not an isolated finding. A Turkish retrospective study of endocrinology clinic patients diagnosed with the prevalence of papillary thyroid cancer³¹ in HT.

Management of Thyroid Nodules

Most (66%) of the thyroid nodules were managed with medicines or were kept under follow up. Surgical intervention was predominantly performed in patients with a suspicious lesion or a proven malignancy in FNAC. FNAC proven colloid goitre were also operated in 36.3% of the cases, but patients with HT were least likely to be operated at 7.4%. This reflects the previous data with respect to management of thyroid nodule.

CONCLUSION

1. Hashimoto's thyroiditis is the most common type of thyroiditis and its incidence is increasing.
2. Majority of patients were females (93%) with maximum incidence in fourth decade of life (33%).
3. The high TSH values was exclusively found in patients with FNAC proven HT (63%), which is in concordance with existing literature. HT is the most common cause of hypothyroidism.
4. The sensitivity of USG along with Doppler in detection of Hashimoto's thyroiditis is high (65-95%) in previous studies. But, the sensitivity of USG towards Hashimoto's thyroiditis in our study was poor detecting less than half of the cases (25.5% vs. 11.5%).
5. Association of Hashimoto's thyroiditis to toxicity was noted and most of HT patients are managed medically 93%.
6. FNAC proven HT who underwent surgery, 4% had concomitant papillary carcinoma, which correlated with previous study; therefore, HT patients need to be carefully followed up.

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