

A study to determine the co-existence of Hashimoto's thyroiditis and papillary thyroid cancer

¹Dr. McEnroe D Mordom, ²Dr. Benitta Francis D, ³Dr. Ajayan G, ⁴Dr. Deepak Paul

¹Assistant Professor, Department of Pediatric Surgery, Travancore Medicity, Kollam, Kerala, India

²Assistant Professor, Department of Pediatrics, Travancore Medicity, Kollam, Kerala, India

³Associate Professor, Department of General Surgery, Sree Gokulam Medical College and Research Foundation, Venjaramoodu, Kerala, India

⁴Assistant Professor, Department of General Surgery, Sree Gokulam Medical College and research Foundation, Venjaramoodu, Kerala, India

Corresponding Author:

Dr. Deepak Paul (dkpl2004@gmail.com)

Abstract

Background: Thyroid diseases are endemic in India with around 42 million people suffering from them. Hashimoto's thyroiditis is the most common autoimmune pathology of the thyroid gland. Papillary carcinoma thyroid is the most common thyroid cancer. The objective of this article is to study coexistence of Hashimoto's thyroiditis with papillary thyroid cancer.

Methods: Our study was prospective study carried out on 123 patients in the age group 14-65 in the department of surgery Sree Gokulam Medical college and research foundation Venjaramoodu during the period November 2011 to February 2013. A history was taken followed by clinical examination. They were then investigated by thyroid function test, ultrasound neck X-ray neck, X-ray chest, indirect laryngoscopy, fine needle aspiration cytology (FNAC) and anti-thyroid antibody tests. The patients were taken up for surgery and histopathology reports were correlated with the findings of FNAC and anti-thyroid antibodies.

Results: Out of the 123 patients who enrolled. For our study 115 were females. All patients presented with a swelling in the neck. FNAC showed 70(56.9%) colloid goitre, 14(11.4%) had Hashimoto's thyroiditis, 11(8.9%) follicular neoplasm and 4(3.3%) papillary thyroid cancer. 60(48.8%) of patients of 123 had abnormal Anti- TPO antibodies and 70(56.9%) had positive Anti- thyroglobulin antibody. Of the 123 patients 38(30.89%) had thyroiditis. 19(15.44%) patients had papillary thyroid cancer and 5(4%) had papillary thyroid cancer and thyroiditis at the same time. All patients with papillary carcinoma thyroid and thyroiditis were females.

Conclusion: In a country like India where thyroid diseases are endemic, benign thyroid diseases are very common. Papillary thyroid cancer is the most common thyroid cancer and according to our study has a 26.3% coexistence with Hashimoto's thyroiditis which is the commonest autoimmune thyroid disease. From this study we conclude that careful workup and surgery are recommended when dealing with patients with thyroiditis especially women.

Keywords: Hashimoto's thyroiditis, papillary carcinoma thyroid, thyroiditis, thyroid

Introduction

Thyroid diseases are quite common worldwide. India also has a significant number of thyroid related

cases. Around 42 million people in India suffer from thyroid diseases ^[1]. One of the common thyroid disorder is Hashimoto's thyroiditis. It is the most common autoimmune inflammatory pathology of the thyroid and is the main cause for auto immune hypothyroidism ^[2]. It was named after the Japanese physician Hakaru Hashimoto who first described the symptoms of patients with struma lymphomatosa, an intense infiltration of lymphocytes within the thyroid gland ^[3].

Hashimoto's thyroiditis (HT) is more prevalent in female population (M/F ratio of 1:20) is seen in each age group and may also affect children and adolescents ^[4]. Its etiopathogenesis strongly indicates an autoimmune background, associated with T-helper lymphocyte (CD4+) activation by class II human leukocyte antigen system cells (MHC class II: HLA-DR3, HLA-DR4, HLA-DR5). On the one hand, the cells recruit cytotoxic lymphocytes (Tc, CD8+), thus facilitating a release of cytokines that damage thyroid follicular cells and, on the other hand, activating B lymphocytes; they facilitate production of specific ant microsomal, anti-thyroglobulin, or anti-TSH receptor antibodies. Described for the first time in 1912, the disease may have two distinct histological forms: atrophic and nodular. Clinically, in the majority of cases, it is characterized by hypothyroidism, although in a small number of patients, it may be preceded by symptoms of hyperthyroidism. The association between coexistence of Hashimoto thyroiditis and papillary thyroid cancer (PTC) was first described by Dailey *et al.* in 1955 ^[5]. In India thyroid diseases are endemic. The most common thyroid cancer is papillary thyroid cancer ^[6]. In Kerala the number of cases of papillary thyroid cancer are on the rise ^[7]. The objective of this article is to study coexistence of HT with papillary thyroid cancer.

Methods

A prospective study was carried out on 123 patients with enlarged thyroid swelling between 14-65 year age group, attending department of surgery, Sree Gokulam Medical College and research foundation, Venjaramoodu, Trivandrum during the period of November 2011 to February 2013. Patients with features of toxicity and those treated conservatively are excluded from the study. All patients were examined clinically after taking a detailed history. Then, they were investigated by thyroid function test (TFT), ultrasound neck, X-ray neck, X-ray chest, indirect laryngoscopy, FNAC and anti-thyroid antibody tests. The results of FNAC were interpreted according to THY grading. The thyroid antibodies test results were interpreted according to radio immune assay test. Patients who were toxic and not willing for surgery were excluded from the study. Then, all the patients were subjected to surgery and histopathological examination (HPE) of the specimen obtained. Finally, the histopathology reports were correlated with the findings of FNAC and anti-thyroid antibodies in order to evaluate their sensitivity, specificity and predictive values by statistical methods.

Inclusion criteria

1. All patients (14- 65 years) who were planned for surgery.

Exclusion criteria

1. Patients with features of toxicity.
2. Cases which are treated conservatively.

Study design: Prospective prediction model.

Study population

Patients attending the hospital with thyroid swellings and have undergone clinical examination, investigations and surgery.

Sample size

By standard statistical formulas and from the incidence of thyroid cases obtained by the pilot study the sample size is fixed at 70.

Data collection and analysis

- Structured questionnaire.
- Data analysed by summary statistics.

Results

During the study period 123 cases of enlarged thyroid underwent surgery, out of which 115 were females and 8 male patients. These patients were evaluated by clinical examination, investigations and recorded. The age of the patient in the study ranged from 14-65 years, the youngest being 16 years old and oldest being 65 years. Maximum cases being in between 30-50 with mean age of 42.3 years. Of the 123 patients who were part of the study 115(93.5%) were females and 8(6.5%) were males. Majority 39% of patients had symptoms for a duration of 1-3 years. 78(63.4%) patients were on thyroxine supplements prior to surgery.

All the patients presented with swelling in front of neck in the thyroid region. In addition to swelling in the neck 12 patients presented with pain over the swelling, 2 patients had difficulty in breathing and 2 had hoarseness of voice. 5 patients presented with thyroid swelling and cervical lymph nodes. 4 patients showed positive Pemberton's test suggestive of retrosternal extension.

After doing FNAC majority of the cases 70(56.9%) had colloid goitre. 14(11.4%) had Hashimoto's thyroiditis, 11(8.9%) follicular neoplasm and 4(3.3%) papillary thyroid cancer. (Table 1)

FNAC	Frequency	Percent
Colloid Goitre	70	56.9
Lymphocytic thyroiditis	24	19.5
Hashimoto's thyroiditis	14	11.4
Follicular neoplasm	11	8.9
Papillary carcinoma	4	3.3

60(48.8%) of patients of 123 had abnormal Anti-TPO antibodies and 70(56.9%) had positive Anti-thyroglobulin antibody. (TABLE 2, Table 3)

Anti-TPO	Frequency	Percent
Normal	63	51.2
Abnormal	60	48.8
Mean \pm SD	128.8 \pm 165.1	

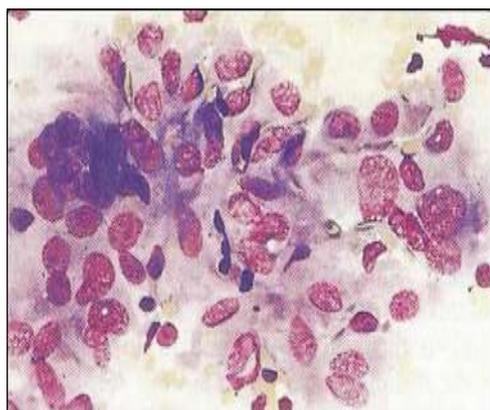
Anti Tg	Frequency	Percent
Negative	53	43.1
Positive	70	56.9
Mean \pm SD	601.1 \pm 854.1	

On histopathology 47(38.21%) had colloid goitre which was the majority. There were 5 cases of papillary thyroid cancer with concomitant thyroiditis. (Table 4)

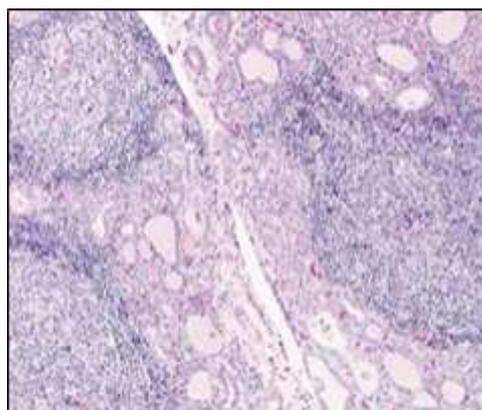
HPR	Frequency	Percentage
Colloid goitre	47	38.21
Colloid goitre + lymphocytic thyroiditis	3	0.02
Colloid goitre + follicular adenoma	1	0.01
Follicular adenoma	10	0.08
Lymphocytic thyroiditis	25	20.32
Hashimoto's thyroiditis	13	10.56
Papillary carcinoma	13	10.56
Papillary carcinoma + Hashimoto's thyroiditis	4	0.03
Papillary carcinoma + lymphocytic thyroiditis	1	0.01
Papillary carcinoma + colloid goitre	1	0.01
Hurthle cell neoplasm	3	0.02
Lymphocytic thyroiditis + follicular adenoma	1	0.01
Follicular adenoma + hurthle cell neoplasm	1	0.01

Of the 123 patients 38(30.89%) had thyroiditis. 19(15.44%) patients had papillary thyroid cancer and 5(4%) had papillary thyroid cancer and thyroiditis at the same time.

Hashimoto's thyroiditis

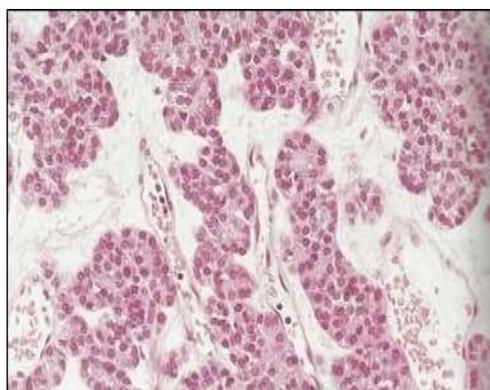


A

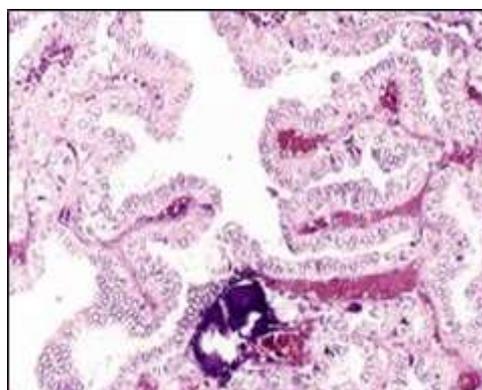


B

Papillary carcinoma



A



B

Discussion

In our study the age of the patient ranged from 14-65 years with a median of 42 years. This is comparable

to a study by Tabaqchali *et al.* [8]. Of the 123 patients in our study 115 were females and only 8 were males. The female male ratio was 14.47:1. This was comparable other studies. In a study by Afroze *et al.* it was 16.5:1 [9].

After clinical examination and laboratory tests, patients were subjected to FNAC and based on FNAC criteria for individual disease. Colloid goitre accounted for 70 cases. Hashimoto and lymphocytic were reported separately both together accounted for 38 cases. 11 cases were reported as follicular neoplasm Only 4 cases were reported as papillary carcinoma. The sensitivity of FNAC in the study ranged between 65-96% while the specificity was above 95%. The accuracy of FNAC was above 80%. This was comparable to other studies [10, 11]. There was a substantial agreement between FNAC and HPR results taking HPR as gold standard.

Anti TPO and Anti tg were done in all cases, the normal value of Anti TPO < 25 which accounted for 63 cases, 60 cases showed abnormal Anti TPO values. The normal value of Anti tg was <1:100 titre, 70 cases showed abnormal values and was grouped as positive.

The association between HPR and Anti thyroid antibodies showed a positive association in case of thyroiditis. Association of antibody titres compared to histological findings were detected in 96% in case of Tg antibody and 73% in TPO antibody [11]. The sensitivity for predicting thyroiditis by Anti TPO was 66 and specificity was 61.8 with positive predictive value of 52 with accuracy of 63.4. The sensitivity for predicting thyroiditis by Anti Tg was 63.8 and specificity was 47.4 with positive predictive value of 42.9 with accuracy of 53.7. This is in line with studies by Hasabat *et al.* and Lakshamana Rao *et al.* with a positivity rate of 63% and 83.34% [12, 13].

Based on HPR findings, 123 cases were reported in 13 categories. Maximum being colloid goitre. Thyroiditis was diagnosed as Hashimoto's and lymphocytic thyroiditis. Both accounted for 38 cases. In 12 cases, there were 2 findings each. 3 cases had colloid goitre with lymphocytic thyroiditis. 4 of the cases had papillary carcinoma with Hashimoto's thyroiditis and 1 case each for papillary carcinoma with lymphocytic thyroiditis, papillary carcinoma with colloid goitre, colloid goitre with follicular adenoma, lymphocytic thyroiditis with follicular adenoma and follicular adenoma with hurthle cell neoplasm. The commonest benign pathology associated with papillary carcinoma in many studies is shown to be Hashimoto's thyroiditis. In a study by Bradly *et al.*, the incidence of incidental papillary carcinoma in benign conditions was 12% with Hashimoto's thyroiditis being associated with the highest rate [14]. In the present study 5 cases had papillary carcinoma with thyroiditis (26.3%). All patients with papillary carcinoma thyroid and thyroiditis were females. This shows there was a 26.3% chance of papillary thyroid cancer in patients undergoing thyroidectomy. This was comparable to a study done by Repplinger *et al.* (30%) [6]. There was an incidence of papillary thyroid cancer in patients with thyroiditis in 26.7%, 28.7% and 30% in studies by Cipolla *et al.*, Yoon *et al.* and Kebebew *et al.* [15, 16, 17]. These finding are in line with our study.

Conclusion

In a country like India where thyroid diseases are endemic, benign thyroid diseases are very common. Papillary thyroid cancer is the most common thyroid cancer and according to our study has a 26.3% coexistence with Hashimoto's thyroiditis which is the commonest auto immune thyroid disease. From this study we conclude that careful workup and surgery are recommended when dealing with patients with thyroiditis especially women.

References

1. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian J Endocrinol Metab [Internet]. 2011 Jul;15(2):S78-81. Available from: <https://pubmed.ncbi.nlm.nih.gov/21966658>
2. Graceffa G, Patrone R, Vieni S, Campanella S, Calamia S, Laise I, *et al.* Association between

- Hashimoto's thyroiditis and papillary thyroid carcinoma: a retrospective analysis of 305 patients. *BMC Endocr Disord* [Internet]. 2019 May;19(1):26. Available from: <https://pubmed.ncbi.nlm.nih.gov/31142293>
3. Böhles H. Thyroiditis lymphomatosa Hashimoto, 1912. In: *Historische Fälle aus der Medizin*. Springer, 2020, 195-201.
 4. Calcaterra V, Nappi RE, Regalbuto C, De Silvestri A, Incardona A, Amariti R, *et al*. Gender Differences at the Onset of Autoimmune Thyroid Diseases in Children and Adolescents. *Front Endocrinol (Lausanne)* [Internet]. 2020 Apr;11:229. Available from: <https://pubmed.ncbi.nlm.nih.gov/32362875>
 5. Dailey ME, Lindsay S, Skahen R. Relation of thyroid neoplasms to Hashimoto disease of the thyroid gland. *AMA Arch Surg*. 1955 Feb;70(2):291-7.
 6. Replinger D, Bargren A, Zhang YW, Adler JT, Haymart M, Chen H. Is Hashimoto's thyroiditis a risk factor for papillary thyroid cancer? *J Surg. Res*. 2008;150(1):49-52.
 7. Aravindan KP. Papillary thyroid cancer: Why the increase and what can be done? *Indian J Cancer*. 2017;54(3):491.
 8. Tabaqchali MA, Hanson JM, Johnson SJ, Wadehra V, Lennard TW, Proud G. Thyroid aspiration cytology in Newcastle: a six year cytology/histology correlation study. *Ann R Coll. Surg. Engl*. 2000 May;82(3):149-55.
 9. Afroze N, Kayani N, Hasan SH. Role of fine needle aspiration cytology in the diagnosis of palpable thyroid lesions. *Indian J Pathol Microbiol*. 2002 Jul;45(3):241-6.
 10. Cai XJ, Valiyaparambath N, Nixon P, Waghorn A, Giles T, Helliwell T. Ultrasound-guided fine needle aspiration cytology in the diagnosis and management of thyroid nodules. *Cytopathology*. 2006 Oct;17(5):251-6.
 11. Kim DW, Lee EJ, Kim SH, Kim TH, Lee SH, Kim DH, *et al*. Ultrasound-guided fine-needle aspiration biopsy of thyroid nodules: comparison in efficacy according to nodule size. *Thyroid*. 2009 Jan;19(1):27-31.
 12. Hasanat MA, Rumi MAK, Alam MN, Hasan KN, Salimullah M, Salam MA, *et al*. Status of antithyroid antibodies in Bangladesh. *Postgrad Med J*. 2000;76(896):345-9.
 13. Shankar O, Balraj N, Rakesh G. Clinical study of Hashimoto's thyroiditis. *IAIM* [11], 2016.
 14. Bradley DP, Reddy V, Prinz RA, Gattuso P. Incidental papillary carcinoma in patients treated surgically for benign thyroid diseases. *Surgery*. 2009 Dec;146(6):1099-104.
 15. Cipolla C, Sandonato L, Graceffa G, Fricano S, Torcivia A, Vieni S, *et al*. Hashimoto thyroiditis coexistent with papillary thyroid carcinoma. *Am Surg*. 2005 Oct;71(10):874-8.
 16. Yoon YH, Kim HJ, Lee JW, Kim JM, Koo BS. The clinicopathologic differences in papillary thyroid carcinoma with or without co-existing chronic lymphocytic thyroiditis. *Eur Arch oto-rhinolaryngology Off J Eur Fed Oto-Rhino-Laryngological Soc. Affil. with Ger Soc Oto-Rhino-Laryngology-Head Neck Surg*. 2012 Mar;269(3):1013-7.
 17. Kebebew E, Treseler PA, Ituarte PH, Clark OH. Coexisting chronic lymphocytic thyroiditis and papillary thyroid cancer revisited. *World J Surg*. 2001 May;25(5):632-7.