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Prevalenceof Papillary carcinoma thyroid in patients with toxic goitre- A descriptive study in a tertiary care centre

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ABSTRACT A descriptive study was conducted at government medical college Trivandrum to determine the prevalence of papillary carcinoma thyroid in thyroidectomy specimens of toxic goitre patients, which is thought to be on a rising trend. It also aims to find the associated pathologies which predispose to papillary carcinoma in the thyroidectomy specimens.A total of 735 patients with toxic nodular goitre were evaluated using FNAC thyroid, Ultrasonogram thyroid and histopathological examination of the specimen after total thyroidectomy. 31 of the total 735 patients who underwent thyroidectomy of toxic nodular goitre had papillary carcinoma thyroid. Thus, 4.2% of toxic nodular goitre are papillary carcinoma thyroid, 5% of the 31 papillary carcinoma thyroid patients in the study had histologically positive cervical lymph node metastases.77.4% of the Papillary Carcinoma Thyroid patients with toxic nodular goitre had associated lymphocytic thyroiditis.Of the 31 patients with papillary carcinoma thyroid, 24 (77.4%) had associated lymphocytic thyroiditis on histopathological examination, whereas only 18(2.6%) of patients without papillary carcinoma thyroid, have histopathological evidence of lymphocytic thyroiditis. Thus, there is a significant association between lymphocytic thyroiditis and papillary carcinoma thyroid in patients developing toxic nodular goitres.

KEYWORDS : papillary carcinoma thyroid, toxic goitre, lymphocytic thyroiditis

Introduction

Goitre is a very common condition in clinical practice, and hyperthyroidism and thyrotoxicosis symptoms are very frequently associated with goitre. Majority of these cases are managed medically and are on long term follow-up. But there has been an increase on the incidence of papillary carcinoma thyroid in the operated thyroidectomy specimen, which suggests that goitres-diffuse; solitary or multinodular have the potential for developing malignancy in the subsequent.

Many recent studies have revealed a high prevalence of locally advanced thyroid cancer in patients with hyperthyroidism, including cases where no preoperative suspicion of cancer was present. The study focuses on the prevalence of papillary carcinoma in cases of solitary or multinodular goitre with toxicosis. Study aims at identifying associated pathological conditions in these cases of goitre which are likely to predispose to papillary carcinoma thyroid.

Papillary carcinoma constitutes 80-90% of thyroid malignancies and occurs with equal frequency in the multinodular or single nodule gland. It is more common in women than men by a ratio of approximately 3:1 and has a median age of diagnosis of 45 years. Patients are usually asymptomatic and present with a solitary thyroid nodule or with a gland that contains multiple thyroid nodules or with a palpable cervical lymph node. Occasionally, a patient presents with symptoms worrisome for an aggressive or invasive thyroid cancer such as hoarseness, dysphagia, or haemoptysis.

Risk factors for Papillary Carcinoma thyroid include female sex, very young (<15 yrs.) or old (>65 yrs.), recent pregnancy within about 5 years, exogenous oestrogens- including lactation suppressant drugs, postmenopausal oestrogen therapy, fertility drugs, ionizing radiation and the presence of Hashimoto's thyroiditis. The influence of Hashimoto's and lymphocytichyroiditis on thyroid cancer risk is controversial, but large studies have shown an increased prevalence of lymphocytic thyroiditis in patients with papillary thyroid carcinoma.

Incidence of hyperthyroidism in patients with thyroid carcinoma is 2.8%.[9]Gulcelik et al found 12 cases of hyperthyroidism among 422 patients of thyroid carcinoma. Nine patients with papillary carcinoma, 1 patient with follicular carcinoma and 2 patients with follicular variant of papillary carcinoma presented with hyperthyroidism. None of the patients had Graves' disease.[9]

The incidence of concurrent cancer in patients with hyperthyroidism is higher at 5%. Zanella et al reported an incidence of 5.3% of thyroid cancer in a series of 202 patients of Graves' disease who underwent thyroidectomy.[10] Thyroid carcinoma was also found in 5.8% of patients of hyperthyroidism in Terzioglu's series of 138 patients. Concurrent carcinoma was greater in frequency in patients with toxic adenoma (8%) than in those with Graves' disease (6 %) and toxic nodular goitre (5 %).In study by Kalliopiet al.2008, the disease-specific mortality in the cohort of patients studied (with thyroid cancer and hyperthyroidism) was 3.3% over 4.5 years of mean follow-up. In comparison, 5-year mortality of patients with thyroid cancer in Greece has been reported at 2% (papillary) to 8% (follicular).[29] It appears therefore that patients with thyroid cancer and thyrotoxicosis have an aggressive course to their cancer as compared to those without thyrotoxicosis.

This emphasizes the need for thorough evaluation of thyroid to exclude malignancy even in a clinical setting of hyperthyroidism. The data presented here raise questions as to how intensively patients presenting with hyperthyroidism should be investigated for the presence of coincidental thyroid cancer. Although there is insufficient evidence to base recommendations for any change in practice, clinicians managing patients with hyperthyroidism need to be aware of the possible increased risk of thyroid cancer in this patient group; in particular, the proposition that hot nodules are associated with exceedingly low probability of malignancy[16-19] needs to be re-evaluated in prospective studies.

Materials and methods

735 patients with controlled thyrotoxicity who underwent thyroidectomy were included in the study. Preoperative investigations studied wereSerum T3, T4, TSH level, FNAC thyroid, USG Thyroid. Doppler USG thyroid was not considered in the study due to lack of availability of the same in the hospital setup and due to financial considerations.FNAC results were considered in all cases. FNAC was performed after explaining the procedure to the patient and taking an informed consent. The area was cleaned with

povidone iodine solution. A 22-guage needle and a 10 ml syringe were used for suction. In nodules showing cystic changes FNAC was obtained from the solid area of the nodule. Inmultinodular goitre, FNAC was obtained either from a suspicious nodule (poorly defined margins, hypoechogenicity) or from the largest representative nodule. After localizing the lesion, the needle was introduced tangential to the probe at the selected depth. In cases in which FNAC results were indeterminate or showed inadequate material a repeat FNAC was obtained. None of the patients suffered any complication after FNAC.FNAC finding could be nodular goitre, thyroiditis or papillary carcinoma. Results of Serum ant thyroglobulin or antinuclear antibodies were found positive in 1.4% of patients and hence noted as chronic autoimmune thyroiditis. However, serum ant thyroglobulin or antinuclear antibody estimation was not part of our research protocol.

High-frequency, real-time ultrasonography of thyroid was done and distinguishing features such as echogenicity, margins and micro calcification were studied. Ultra sonogram also routinely evaluated presence of significant cervical lymphadenopathy.

Surgery was near total thyroidectomy, done under general anaesthesia. Total Thyroidectomy was done after controlling the serum thyroid levels with carbimazole and propranolol for a period of 3- 7 months.Total thyroidectomy was performed following the identification and the preservation of the recurrent laryngeal nerves and of the parathyroid glands. All the specimens were sent for histopathological examination. The patients were closely monitored during the immediate postoperative period for complications like haemorrhage, respiratory obstruction; vocal cord paralysis, thyroid crisis and infection.Details of the Histopathological Examination of Thyroid Specimen were collected.

- ***Histopathological Examination of Thyroid Specimen***

All thyroid tissue samples were oriented, cut in parallel longitudinal slices each 5 mm thick and fixed in 10%neutral buffered formalin for 24 hours. After fixation the samples were finely cut and paraffin embedded. For solitary encapsulated nodules measuring up to 5 cm, an additional section was taken for each additional centimeter in diameter, including the tumor capsule and adjacent thyroid tissue. For multinodulargoiters, one section of each nodule (up to five nodules) was taken and more than one section for larger nodules. Samples were routinely processed after paraffin embedding. Normal tissue adjacent to neoplastic areas was also evaluated.Agreement of FNAC findings and ultrasonogram findings with the histopathological findings were also examined. The prevalence of papillary carcinoma concurrent with thyrotoxicosis was studied. The probable cause for the increasing co-existence of papillary carcinoma thyroid and hyperthyroidism was studied.

Results

a. Sample characteristics

Age of the 735 patients ranged from 21 to 70 years. Mean age was 39 years. The peak incidence (38.1%) of nodular thyroid goitre in toxic patients was found in the 4th decade. 92.7% of the toxic goitre patients were females. 7.3% of patients were males.Though serum T3, T4 were elevated, and TSH suppressed in all of these patients, only 4.8% of patients had symptoms of thyrotoxicosis. 3.4% of patients had clinically or sonologically detected significant cervical lymph node enlargement.2.4% of patients were on treatment with oral thyroid medication for hypothyroidism.96.1% of nodular goitre patients with toxic symptoms were housewives.10.7% of all the patients had a positive history of goitre in the family. The family history includes nodular or diffuse thyroid swellings. 59.3% of the patients took anti thyroid medication for 4- 5 months before attaining euthyroid status.93.3% of the total 735 patients had colloid goitre on histopathological examination of the total thyroidectomy specimens.

6.7% of patients had findings of lymphocytic thyroiditis associated with colloid goitre. Of these, 5.3% had lymphocytic thyroiditis on HPE and 1.4% had Hashimoto's thyroiditis. The diagnosis of Hashimoto's thyroiditis was made in 10 patients based on the presence of serum ant thyroglobulin and anti-microsomal antibodies in cases with lymphocytic thyroiditis on histopathological study.

b. Prevalence of Papillary Carcinoma Thyroid among Toxic nodular goitre patients.

Table 1: Frequency and percentage distribution of papillary carcinoma thyroid

(n=735)

	Frequency (n)	Percentage (%)
Papillary Carcinoma Thyroid	31	4.2
Colloid Goitre	704	95.8
Total	735	100

Table 1 show that 31 out of the total 735 patients who underwent thyroidectomy of toxic nodular goitre had papillary carcinoma thyroid. Thus, 4.2% of toxic nodular goitre are papillary carcinoma thyroid.

c. Associated Pathology (HPE) in Papillary Carcinoma Thyroid among Toxic goitre patients.

Table 2: Frequency and percentage distribution of subjects with papillary carcinoma according to associated HPE findings

(n=31)

Associated HPE finding	Frequency (n)	Percentage (%)
Lymphocytic Thyroiditis	21	67.8
Colloid goitre alone	7	22.6
Hashimoto's Thyroiditis	3	9.6
Total	31	100

Table 2 show that; of the total 735 patients with toxic nodular goitre, 31 were diagnosed histopathologically as Papillary Carcinoma Thyroid. Among these, 22.6% of cases showed colloid goitre. 3 patients had clinically detected antimicrosomal or antithyroglobulin antibodies, and hence were categorised under the group, Hashimoto's thyroiditis (9.6%). 21(67.8%) of cases showed associated lymphocytic thyroiditis. Since the 3 cases of Hashimoto's thyroiditis also showed lymphocytic thyroiditis, the total percentage of lymphocytic thyroiditis associated with Papillary Carcinoma Thyroid is 77.4%. 22.6% of cases shown colloid goitre.

Discussion

In our study, 31 of the total 735 patients who underwent thyroidectomy of toxic nodular goitre had papillary carcinoma thyroid. Thus, 4.2% of toxic nodular goitre, in our study are papillary carcinoma thyroid. Cerci et al. compared the thyroid cancer incidence in patients with toxic and non-toxic multinodulargoiter and found that the incidence of malignancy was 9% in the toxic and 10.58% in the non-toxic multinodulargoitre group. Papillary carcinoma had a prevalence of 3.8% in toxic goitre group. Our study had a slightly higher prevalence rate, thus confirming the increase in the cases associated with toxic nodular goitre. It is possible that this observation may represent referral patterns to a tertiary centre, with low-risk coincidental cancers being managed locally.

An association between lymphocytic thyroiditis and differentiated thyroid cancer has been reported by several authors from the 1950s up to the present time.In our study, of the total 735 patients with toxic nodular goitre, 31 were diagnosed histopathologically as Papillary Carcinoma Thyroid. Among these, 22.6% of cases showed colloid goitre. 24 patients or 77.4% of cases showed associated lymphocytic thyroiditis. In patients with thyroid carcinomas, the incidence rate of association with lymphocytic thyroiditis is 1.99

times higher in those with papillary carcinoma thyroid than in subjects with other histopathological forms of thyroid carcinomas. The results from the study raise the question as to how intensively patients presenting with hyperthyroidism should be investigated for the presence of coincidental thyroid cancer. Clinicians managing patients with hyperthyroidism need to be aware of the possible increased risk of thyroid cancer in this patient group.

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