Original Article

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Clinical Study of Carcinoma Thyroid and its Management

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Abstract

Background: Thyroid carcinoma is one of the common cancers affecting the women in their young age. They vary from being indolent to aggressive cancers. Improvements in diagnostics and understanding the pathophysiology have made the treatment more effective with good long-term results.

Objective: To study the clinical presentation and management of carcinoma thyroid in a tertiary center.

Materials and Methods: 30 patients of histopathologically proven thyroid cancers treated during the period of 2-year from September 2005 to August 2007 were studied. Detailed history and physical findings were noted, along with the investigations and treatment given.

Results: Thyroid carcinoma formed 1.5% of all cancers treated during the period. It formed 15.78% of all thyroid swellings admitted for treatment during the same period. Male:female ratio in this study was 1:5. Most of the cases of carcinoma (86%) were seen in the 21-50 years age group. All patients in this study had a goiter and only 10% of patients presented with lymphadenopathy and hoarseness of voice. Two-thirds of tumors were slowly growing with duration ranging from 3 months to 2 years. Fine-needle aspiration cytology (FNAC) was the common diagnostic test done. Most of the cancers (76.6%) were in Stage I disease. Total thyroidectomy was the most common surgery done, and papillary carcinoma was the most common histopathology seen. Transient hypocalcemia was the most common post-operative complication seen in 20% of patients.

Conclusion: Thyroid cancers affect young adult females presenting as slow growing tumors. Majority of the tumors are papillary type in the early stage with good prognosis. FNAC is a simple test to detect cancer, and total thyroidectomy is the procedure of choice for treatment.

Key words: Fine-needle aspiration cytology, Papillary carcinoma, Radio iodine, Total thyroidectomy, Thyroid carcinoma

INTRODUCTION

Thyroid cancer is the most common endocrine cancer and has the highest mortality among endocrine neoplasms except for ovarian cancer.[1] Even though thyroid cancer is more common in women than in men, death from thyroid cancer is more common in men. Thyroid cancer represents <1% of all malignancies.[2] The cumulative life-time risk of thyroid cancer in Chennai was one in 970 in males and one in 565 in females.[3]

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Thyroid cancers display a wide range of aggressiveness from the more indolent papillary cancer to the uniformly lethal anaplastic cancer. Because of the developments in diagnostic methods and pathophysiological understanding, asymptomatic stages of the disease are detected with increasing frequency, population and patients may be treated more efficiently.

The declining mortality rates are largely due to early diagnosis and effective therapy applied at an early tumor

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stage when it is most amenable to surgery and I-131 therapy. Fine-needle aspiration cytology (FNAC) plays an important role in the diagnosis of thyroid cancer and allows the clinician to plan a rational treatment strategy.

The protracted and generally favorable course of well-differentiated carcinomas complicates the evaluation of various treatment methods. There are no long-term prospective studies of the treatment of this disease. The clinical management of the well-differentiated thyroid carcinomas rests on retrospective studies and individual clinical experiences.

Many studies have recommended total or near-total thyroidectomy followed by post-operative I-131 thyroid remnant ablation for most patients with differentiated thyroid carcinoma, regardless of age, and almost everyone preferred long-term T4 therapy to doses sufficient to lower the thyroid stimulating hormone (TSH) levels to 0.01-0.5 μ units/ml. External radiation and chemotherapy play a very important role in the treatment of undifferentiated thyroid carcinoma.

MATERIALS AND METHODS

In this clinical study of thyroid cancers, cases, which were admitted in various surgical units in Victoria hospital, attached to Bangalore Medical College, Bengaluru for a period of 2-year, from September 2005 to August 2007, were studied. A total of 30 cases of histopathologically proven cases of thyroid cancers in all age groups and both sexes were included. Detailed examinations of each case were done and data entered in the proforma case sheet for analytical study.

All patients whose final histopathological diagnoses were proven benign were excluded. Patients whose FNAC revealed follicular neoplasms but the histopathology revealed follicular adenomas were also excluded.

The study required certain investigations to be conducted on the patient viz, routine blood investigations, thyroid profile, radiography of the chest, and neck, FNAC of the thyroid gland and lymph nodes. Ultrasound of the neck was done in all cases to determine whether thyroid swellings are multinodular or solitary nodules and to determine the cervical nodal involvement. Computed tomography scan was done when needed. Indirect laryngoscopy was done in all patients to determine the status of the vocal cords specifically their movements. All the patients underwent surgery after proper consent. Most of the patients were discharged with a clean and healthy wound except a few with post-operative complications.

RESULTS

Thyroid carcinoma formed about 0.17% of all surgical admissions and 1.5% of all cancers admitted during the period. Thyroid carcinoma formed 15.78% of all thyroid swellings admitted to the hospital during the period (Table 1).

No of female patients were 25 and male patients 5. Male:female ratio in this study was 1:5 (Table 2).

In this study, most of the cases (86%) of carcinoma thyroid occurred in the age group of 21-50 years, with the average age being 36 years with a minimum of 19 years and a maximum of 70 years. Only 2 cases (6.6%) were seen after 50 years of age (Table 3).

In this study, all patients (100%) presented with a swelling of the thyroid. Only 10% of patients had hoarseness of voice, which was the most common pressure effect. Features of hyperthyroidism were present in 6.6% of patients. Palpable lymph nodes were present in 10% of cases (Table 4).

Most of the patients (73.3%) presented with symptoms during the past 3 months to 2 years. Only 6.6% of cases had swelling for >5 years. None of the patients had a symptom more than 10 years (Table 5).

Table 1: Incidence

Total no of patients	No of patients	Percentage
Total number of surgical admissions	16897	0.17
Total number of all cancers	1965	1.5
Total number of thyroid cases	190	15.78

Table 2: Sex ratio

Type of carcinoma	Female	Male
Papillary carcinoma	17	4
Follicular carcinoma	6	1
Anaplastic carcinoma	1	0
Medullary carcinoma	1	0
Others	0	0
Total	25	5

Table 3: Age distribution

Age (years)	Papillary	Follicular	Anaplastic	Medullary	Others	Total
0-10	-	-	-	-	-	-
11-20	1	1	-	-	-	2
21-30	5	1	-	-	-	6
31-40	10	2	1	1	-	14
41-50	4	2	-	-	-	6
51-60	-	1	-	-	-	1
61-70	1	-	-	-	-	1
71-80	-	-	-	-	-	-

Two-thirds (66.6%) of the tumors were slow growing, and one-third (33.3%) were fast growing tumors.

22 patients (73.3%) had a firm gland, 7 patients (23.3%) had a hard gland and only 1 patient (3.3%) presented with a soft gland on palpation.

FNAC detected papillary carcinoma in 11 patients (36.6%), follicular neoplasm in 6 patients (20%), and 1 patient each of anaplastic and medullary carcinoma. Rests of the thyroid glands (36.6%) were reported as nodular or colloid goiter (Table 6).

Indirect laryngoscopy was done in all cases. 5 patients (16.66%) showed unilateral vocal cord palsy commonly being on the left side. Bilateral vocal cord movements were equal in the rest of the patients (83.3%).

X-ray neck was done in all the cases. Calcification in thyroid swelling was seen in 2 cases (6.6%) and tracheal deviation in 2 cases (6.6%). Other cases presented as soft tissue swellings (86.6%).

18 patients (60%) presented as multinodular goiter, whereas 12 patients (40%) presented as a solitary thyroid nodule (Graph 1).

Table 4: Clinical features

Clinical features	Number of cases	Percentage
Thyroid swelling	30	100
Dysphagia	1	3.3
Dyspnea	0	0
Hoarseness of voice	3	10
Thyrotoxicosis	2	6.6
Lymph node mass	3	10

Table 5: Duration of symptoms

Duration	Number of cases	Percentage
Up to 3 months	3	10
>3-6 months	7	23.3
>6 months-1 year	6	20
>1-2 years	9	30
>2-5 years	3	10
>5-10 years	2	6.6
>10 years	0	0

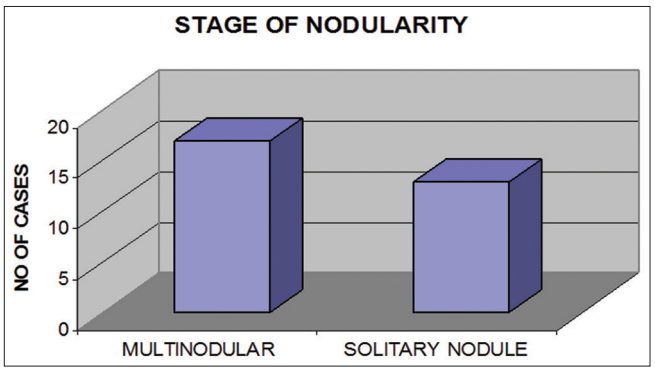
Table 6: FNAC results

FNAC diagnosis	Number of patients	Percentage
Papillary carcinoma	11	36.6
Follicular neoplasm	6	20
Anaplastic carcinoma	1	3.3
Medullary carcinoma	1	3.3
Nodular goiter	9	30
Colloid goiter	2	6.6

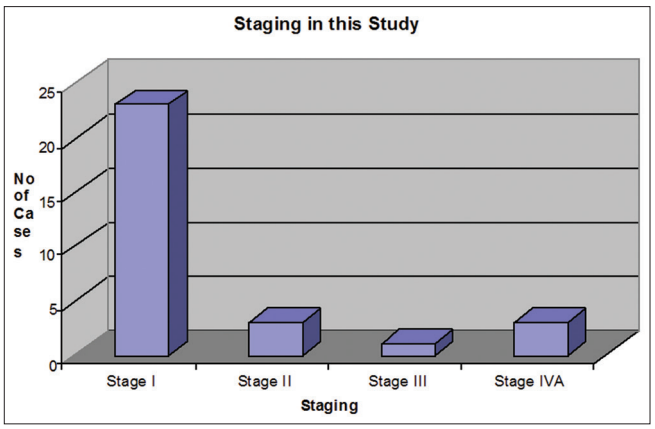
FNAC: Fine-needle aspiration cytology

Most of the cases after investigations and pathological reporting were found to be in Stage I (76.6% of cases). Stage II and IVA was the next commonly seen stage with 10% of cases each in the study (Graph 2).

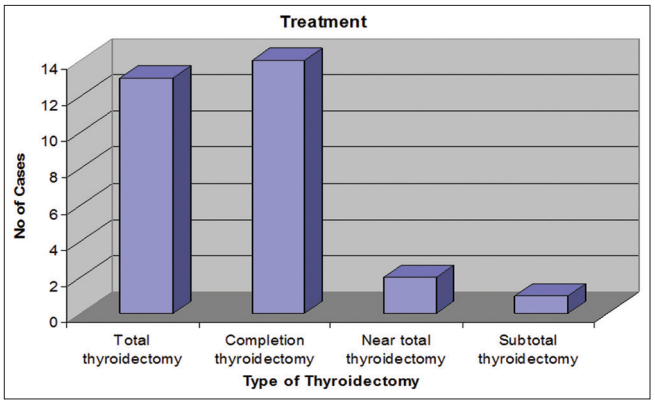
The most commonly performed surgical procedure was completion thyroidectomy in 14 patients (46.6%), followed by total thyroidectomy in 13 patients (43.3%). 2 patients (6.6%) underwent near-total thyroidectomy leaving the thyroid tissue adjacent to the recurrent laryngeal nerve (Graph 3).



Graph 1: Ultrasound results



Graph 2: Staging of carcinoma



Graph 3: Surgical procedure

Patients who were diagnosed as follicular neoplasm by FNAC underwent hemithyroidectomy initially and later a completion thyroidectomy for proven cases.

Patients with FNAC diagnosis as nodular goiter underwent subtotal thyroidectomy followed by completion thyroidectomy later. Only 1 patient underwent subtotal thyroidectomy, as she was low risk for her disease.

The predominant variety of thyroid cancer in our study was papillary carcinoma in 21 patients (70%), and next common was follicular carcinoma in 7 patients (23.3%). None of the other variants of papillary and follicular carcinomas were found in the histopathological study. One patient each of medullary carcinoma and anaplastic carcinoma patients was treated (Graph 4).

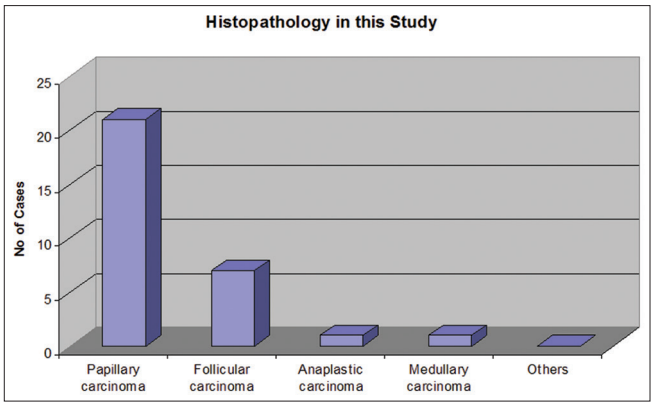
3 patients (10%) presented with lymph node secondaries along with primary in the thyroid. All these patients belonged to papillary carcinoma. None of the other thyroid cancers had cervical lymph node involvement.

2 patients underwent unilateral functional neck dissection. One patient had infiltration of sternocleidomastoid, spinal accessory nerve, and internal jugular vein, who underwent radical neck dissection. 1 patient with medullary carcinoma underwent prophylactic central neck dissection.

All the patients were observed in the immediate post-operative period for any complications. Transient hypoparathyroidism was the most common complication noted in 6 patients (20%). Serum calcium was estimated if the Trousseau's sign (inducing carpopedal spasm by occlusion of the arm with a blood pressure cuff for 3 min) was positive.

All symptomatic hypocalcemic patients were treated with 10 ml of 10% calcium gluconate given slowly intravenously. Less severe cases were treated with oral calcium supplements along with Vitamin D. All patients recovered in the immediate post-operative period. 2 patients (6.6%) had wound infection who improved with antibiotics and dressings. None of the patients had recurrent laryngeal nerve injury postoperatively in our study. No other complications were observed in this study. None of the patients who had immediate post-operative hypocalcemia developed hypocalcemia on a long-term (Table 7).

All the patients with differentiated thyroid cancers were referred to higher centers for radioiodine therapy. One patient who presented with medullary carcinoma was advised a regular follow-up with calcitonin assay. The patient with anaplastic carcinoma was referred for external beam radiotherapy in Victoria hospital. The patient with anaplastic cancer survived for about 6 months.



Graph 4: Histopathology of thyroid carcinoma

Table 7: Surgical complications

Complication	Number of patients	Percentage
Transient hypoparathyroidism	6	20
Wound infection	2	6.6
Recurrent laryngeal nerve palsy	0	0
Others	0	0

The patients with medullary and anaplastic carcinoma treated with total thyroidectomy were started on replacement doses of thyroxine, whereas those with differentiated thyroid cancer were not started on thyroxine, as they were referred for radioiodine ablation.

DISCUSSION

In the US, thyroid malignancies account for 0.6% of male and 1.6% of female malignancies.[4] In India, thyroid malignancies constitute 1.2% and 1.9% of malignancies in men and women, respectively.[5] It is less common in children but still accounts for 1.4% of childhood malignancies. In our study, thyroid carcinoma accounts for 1.5% of all cancer cases. In reality because of the fact that many thyroid cancers never become clinically apparent, and as such are never diagnosed, the true incidence is not known. In an autopsy study, Fukunaga and Yatani reported data from multiple countries that there was an 11% overall incidence of occult thyroid cancer.[6]

Women are affected more than men, and the ratio is somewhere around 3:2, whereas in our study it was 5:1. Surprisingly, a nodule in man is more likely to be malignant than in a woman.

Overall papillary cancer is more common than follicular which is more common than medullary which is more common that anaplastic cancer. In general, papillary carcinoma peaks in early adult life and then gradually decreases in frequency, whereas the incidence of follicular carcinoma tends to peak sometime later. Anaplastic cancer occurs later in life than differentiated cancers.

Exposure to radiation is the only proved thyroid carcinogen. This was first recognized by Duffy and Fitzgerald in 1950.[7] A 10-20 years post radiation latency period was reported earlier, but this has not been noted in the pediatric thyroid cancer cases that have resulted from the chernobyl nuclear disaster in the Ukraine in 1986, where there has been a dramatic increase in such cancers as early as 1989.[8,9] A 3-5 years latency was noted between radiation exposure and tumor development. About 90% of radiation exposed thyroid cancers were found to be papillary thyroid cancers. More recently radiotherapy to the neck in adults resulted in the subsequent development of the anaplastic carcinoma. In addition, thyroid carcinoma is arising as a secondary carcinoma in survivors of Hodgkin's disease.

In countries where there is adequate iodine intake, the well-differentiated thyroid carcinomas constitute 80% of all thyroid cancers. In areas with iodine deficiency, an elective increase in follicular and anaplastic cancers is the rule, but no definite demonstration is made. Chronic stimulation by increased TSH level leads to hyperplasia and possibly carcinomatous degeneration in iodine deficient countries.[10]

Medullary thyroid carcinoma is familial in 10% to 30% of cases. Here, they are part of distinct clinical syndromes - multiple endocrine neoplasia type 2A (MEN 2A), MEN 2B, and familial medullary thyroid cancer (FMTC).

The incidence of malignancy in the thyroid nodule was found to be 3-4%, especially the patients with a history of irradiation, family history, male sex, and rapidly growing tumors.[11] A higher risk of differentiated thyroid carcinoma is found in patients with Graves' disease and cold thyroid nodules, which are more aggressive.

Thyroid cancer most commonly presents as a single neck mass noted incidentally.

A thyroid mass in a child no matter its size or consistency is highly suspicious of malignancy. Regardless of sex, mass in advanced years is likely to be malignant.

Hard and fixed nodules though associated with thyroiditis must be viewed with suspicion for malignancy.

Papillary and follicular carcinomas present as a firm to hard, solitary thyroid nodule, whereas undifferentiated cancer is characterized by a stony hard, irregular nodular gland fixed to the underlying tissues. Solid lesions have a 21% risk of malignancy, cystic 7% and mixed lesions 12%. 5-10% of multiple nodules and 10-20% of solitary nodules are malignant.[12,13]

Papillary carcinoma known for its lymphatic spread presents with cervical lymphadenopathy alone in 20% of cases and thyroid swelling with lymph nodes in 13% of cases. Children and young adults more often have palpable nodal metastases. Many studies reported a 30-40% incidence of cervical nodal metastasis when therapeutic nodal dissections were performed. In medullary carcinoma, metastases are mostly found in the neck and mediastinal lymph nodes and may calcify.[14]

Large multinodular goiters with or without substernal extension can cause tracheal shift or impingement and alteration of the airway. Local compressive symptoms are a rule in the case of anaplastic cancer and can include stridor, dysphagia, dyspnea and even superior vena cava syndrome.

Papillary carcinomas rarely spread by bloodstream, commonly in the skull, spine, and long bones. They can be pulsatile especially the skull. X-ray shows destructive bony lesion.[15]

A serum level of thyroglobulin more than 10 times the upper limit of normal is highly suggestive of cancer.[16] The plasma calcitonin has the most direct diagnostic value in determining the nature of the thyroid mass; it is elevated in almost all patients with MTC.[17,18] Mutation of ret proto-oncogene are associated in 95% of hereditary MTC, MEN 2A, MEN 2B, and FMTC.[19]

Of all the diagnostic methods, FNA and cytological evaluation are the easiest, least expensive, and most accurate method for diagnosing a thyroid nodule, and their value is universally acknowledged.[20,21] The accuracy of this technique depends on the experience of the cytopathologist. It may approach 95%.

Diagnostic ultrasonography using B-mode gray scale provides remarkable anatomic information about the thyroid gland. Because of its simplicity and ability to distinguish between solid and cystic lesions, it is often the first modality to evaluate a thyroid mass in the euthyroid patient. Good quality ultrasound using 7.5-10 MHz transducers provides excellent detail of the superficial gland but requires enough penetration to evaluate posteriorly to the level of the spine. Ultrasonography can detect lesions as small as 3 mm diameter, impalpable nodules, and subtle multinodularity that is not clinically detectable. Punctate or microcalcifications are not common in nodules and repeatedly have high specificity for thyroid cancer (95.2%) but low sensitivity (59.3%) and diagnostic accuracy of 83.3%. They may represent psammoma bodies in papillary cancer.

An elevated or rising thyroglobulin is highly specific and sensitive marker of recurrent follicular thyroid carcinoma.

Calcitonin is a specific and sensitive marker for post-operative monitoring in medullary thyroid carcinoma. Elevated concentrations are seen consistently in metastatic or nodal recurrence and the rising titer over time predicts the disease that may be progressing.

In general, 3 surgical procedures are advocated by experts - hemithyroidectomy, near-total thyroidectomy, and total thyroidectomy.[22]

Total thyroidectomy is the treatment of choice for virtually all patients with papillary thyroid carcinoma (PTC) when post-operative radio iodine therapy is being considered. This basically includes all patients except those with occult PTC (<1 cm). When a total thyroidectomy cannot be performed without injury to the recurrent laryngeal nerve or parathyroid glands, the near-total thyroidectomy is performed, and the small amount or thyroid tissue left behind can subsequently be ablated with radioactive iodine.

80% of patients with PTC have cervical lymph node metastases. The survival rates for patients who are given therapeutic node dissection and prophylactic node dissection are essentially same. Hence, only a therapeutic lymph node dissection is performed. In those patients with palpable lymph node metastases, all the lymph nodes in the central compartment are removed and with evidence of lateral lymph node metastases, a functional neck dissection is performed to remove all the fibrofatty tissue with the lymph nodes, but all the motor (phrenic, vagus, and spinal accessory) and sensory nerves, as well as the sternocleidomastoid and internal jugular vein, are preserved unless invaded by the tumor.[23]

Some experts recommend radio iodine therapy for all patients of PTC except for those with occult papillary, whereas others advocate it only for high-risk patients. The serum TSH levels, amount of residual normal thyroid tissue, the degree of differentiation of the PTC and the patient's age add to affect the amount of radioactive iodine uptake.[24] Most often it is administered 4-6 weeks after thyroidectomy with the patient in the hypothyroid state to maximize TSH-stimulated iodine uptake and whole body iodine retention.

Serum TSH must be elevated to at least 30 mIU/L and negative pregnancy test in women of childbearing age is followed by oral administration of I-131, 30-50 mCi of I-131 (low dose) for low risk, and 100-200 mCi of I-131 (high dose) for high-risk patients. In addition, TSH stimulates thyroglobulin synthesis and secretion and increases radioactive iodine uptake in thyroid cancers, which documents its stimulating role in patients. Hence, patients given an effective thyroxine hormone suppressive therapy (<0.1 mu/ml) have improved survival, lower recurrence rate, and lower mortality.

The follow-up of patients with differentiated thyroid carcinoma includes physical examination, monitoring of thyroglobulin level, I-131 whole body scanning, radiographic imaging, and functional nuclear imaging.

For medullary carcinoma, total thyroidectomy only offers the prospect of definitive cure both in primary and locally recurrent disease, irrespective of the tumor size. All nodes positive MTC without distant metastases clinically are treated by total thyroidectomy with micro dissection of the bilateral central and lateral neck compartments. Calcitonin and carcinoembryonic antigen levels should be assessed at approximately 4 weeks after surgery. A persistent or re-elevating level may indicate locoregional failure or metastases.[25]

Anaplastic carcinoma is devastating, and the treatment results are discouraging. In spite of surgery, radiotherapy, and chemotherapy, almost all the patients die of cancer-related death. The median survival of anaplastic thyroid cancer is 4-5 months.

CONCLUSION

Thyroid cancer is a disease of young adults, constituting about 1.5% of all cancers detected and more commonly seen in females. Most of the cancers present as a slow growing goiter for few months to few years duration. Most of the cancers are of papillary carcinoma type accounting up to 70% of cases. FNAC detects the majority of the cancers and is an important diagnostic test. Thyroid cancers have a good prognosis as most of the patients present as Stage I disease. Lymph nodal involvement is seen in about 10% of patients, and most of the patients require total thyroidectomy with or without lymph node dissection followed by radio iodine ablation as treatment. Prognosis is good for differentiated thyroid cancers and medullary carcinoma, whereas anaplastic carcinoma behaves aggressively and has a poor prognosis.

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