CLINICOPATHOLOGICAL STUDY AND MANAGEMENT OF THYROID MALIGNANCIES

By

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation **"CLINICOPATHOLOGICAL STUDY AND MANAGEMENT OF THYROID MALIGNANCIES"** is a bonafide and genuine research work carried out by me under the guidance of PROF P RAGUMANI., M.S., Professor, Department of General Surgery, MMC& RGGGH, CHENNAI.

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is a bonafide

research work done by Dr. M B SRIDEV in partial fulfillment of the

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LIST OF ABBREVIATIONS

AGES	--	Age, grade of tumour, extent of tumour, size
AMES	--	Age, metastatic disease, extra thyroidal extension, size
ATC	--	Anaplastic thyroid cancer
DAMES	--	DNA content, age, metastatic disease, extra thyroidal extension, size
DFS	--	Disease free survival
FNAC	--	Find Needle Aspiration Cytology
MACIS	--	Metastasis, age, completeness of surgery, invasion, tumor
MALT	--	Mucosa associated lymphoid tissue
MEN	--	Multiple endocrine neoplasia
MNG	--	Multi nodular goiter
MTC	--	Medullary thyroid carcinoma
NHL	--	Non-Hodgkin’s lymphoma
PS	--	Prognostic score
PTC	--	Papillary thyroid carcinoma
RAI	--	Radioactive iodine
RLN	--	Recurrent laryngeal nerve
SNT	--	Solitary nodule thyroid
Tg	--	Thyroglobulin
TSH	--	Thyroid stimulating hormone

ABSTRACT

BACKGROUND AND OBJECTIVES

Thyroid cancer is overwhelmingly the most common type of endocrine malignancy accounting for majority of death due to endocrine cause. It is a heterogenous group of tumours that show considerate variability in histological appearance, in biological behaviour. Clinically it presents as any other benign condition of thyroid in its early stages. So success in treatment of this condition lies largely upon early diagnosis and appropriate management. Hence this study is done to evaluate the modes of presentation, incidence of various pathological types, accuracy of FNAC in the diagnosis and surgical management.

METHODOLOGY

Patient presenting with sign and symptoms of carcinoma thyroid, who were clinically evaluated and confirmed by FNAC were chosen for the study. Patients less than 12 years of age and those who were previously treated for any other thyroid ailments were excluded from the study.

RESULTS

The occurrence of carcinoma thyroid is maximum in 4th decade, female patients outnumbering males. FNAC was found to be simple, cost effective and reliable investigation with overall diagnostic accuracy of 98%. Most of the well differentiated carcinomas were categorised into low risk group of AMES classification**.**

INTERPRETATION AND CONCLUSION

FNAC is a practical and accurate investigation that provides tissue diagnosis. The overall approach in management of thyroid malignancy is multi modal comprehensive therapy which is mainly dominated by surgical treatment. The extent of surgery depends on clinical staging, cytology and risk categorisation**.**

KEY WORDS: Thyroid carcinoma; Papillary carcinoma; FNAC

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Tamil Nadu Dr. M. G. R. Medical University

by

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INTRODUCTION

Thyroid cancer is overwhelmingly the most common type of endocrine malignancy, accounting for majority of deaths due to endocrine cancers. The majority of the patients with carcinoma of the thyroid have differentiated cancer varying in history from a pure papillary carcinoma to a follicular carcinoma and in most instances mixed papillary and follicular variants. Differentiated carcinoma of the thyroid gland is most prevalent in young adults with a female to male ratio of 2:1.

Cancer of the thyroid gland represents a spectrum of different histological entities with diverse clinical behaviour. Generally there is a very low progression from differentiated carcinoma to anaplastic carcinoma. However, this transition takes decades to takes place in most instances. The clinical evaluation of thyroid nodule is a common problem confronting the clinicians. The vast majority of such nodules are benign, but such a thyroid swelling may harbour malignancy demands prompt and accurate diagnosis. The natural history of thyroid carcinomas allows the surgeon to perform a more prolonged and thoughtful preoperative workup and evaluation.

Appropriate management is essential to achieve the optimal therapeutic success. The fine needle aspiration cytology is now the corner

stone of investigation for many of these patients and evaluation and subsequent treatment usually involve assessment by a multidisciplinary team fully conversant in all aspects of thyroid cancer therapy. The clinical management of the well-differentiated thyroid carcinomas rests on retrospective studies and individual clinical experience.

Finally, there is a great variability in the duration of follow up in these relatively slow growing lesions. This is a time bound study of cases, which presented with thyroid carcinoma to **MADRAS MEDICAL COLLEGE AND RGGGH, CHENNAI.**

OBJECTIVES

1. To study the clinical presentation of thyroid malignancies.

2. To study the relative incidence of various pathological types of thyroid malignancies.

3. Correlation of FNAC with HPE.

4. To study the various surgical modes of management of thyroid malignancies.

REVIEW OF LITERATURE

The name thyroid is derived from the Greek description of a shield-shaped gland in the anterior aspect of the neck (thyreoides). **Andres Vasalieus** (1514-1564 A.D.), who is credited as the "Father of Anatomy" gave the first description of thyroid gland. Classic anatomic descriptions of the thyroid were available in the 16th and 17th centuries, but the function of the gland was not well understood. By the 19th century, pathologic enlargement of the thyroid, or goiter, was described. Iodine-rich seaweed was used to treat this condition. Direct surgical approaches to thyroid masses had frighteningly high complication and mortality rates.

In the late 19th century, two surgeon-physiologists revolutionized treatment of thyroid diseases. **Theodor Billroth and Emil Theodor Kocher** established large clinics in Europe and, through development of skilled surgical techniques combined with newer anaesthetic and antiseptic principles, provided surgical results that proved the safety and efficacy of thyroid surgery for benign and malignant problems. As a result of his pioneering developments in the understanding of thyroid physiology, Kocher received the Nobel Prize in 1909.

The 20th century started with the contributions of Kocher and Billroth. In rapid succession, the understanding of altered physiology, including hypothyroidism, hyperthyroidism, and thyroid cancer, and advances in imaging, epidemiology, and most recently, minimally invasive diagnostic and surgical techniques have taken place. These advances have allowed the diagnosis and treatment of thyroid diseases to become rapid, cost-effective, low-morbidity procedures.

Duffy 1950 reported the link between child irradiation to head and neck and occurrence of thyroid carcinoma as radiation was routinely used for therapy of acne, tonsils, enlarged thymus. By 1960, radiation therapy for benign condition was abandoned. FNAC of thyroid was first described in the 1930's by Martin and Ellis.

In 1950, the technique of FNAC was popularized in Scandinavia. It is Zajieek, the first pathologist to embrace FNAC in collaboration with Franzen at the Karolinska hospital defined the precise diagnostic criteria and determined the diagnostic accuracy.

At Johns Hopkins University Hospital, William S. Halsted revolutionized surgical treatment and education and made an enormous contribution to the operative treatment of both the thyroid and parathyroid glands. Since then a number of important advances have been made in the

diagnosis and management of patients with thyroid tumors, including the development of antithyroid drugs, fine needle aspiration biopsy, radioiodine treatment, and various imaging modalities.

PIONEERS IN THYROID SURGERY

FIG 1: THEODORE BILLROTH{1829-1894}

FIG 2: EMIL THEODORE KOCHER{1841-1917}

EMBRYOLOGY

The thyroid gland arises as an out pouching of the primitive foregut around the third week of gestation. It originates at the base of the tongue in the vicinity of the foramen caecum. Endoderm cells in the floor of the pharyngeal anlage thicken to form the median thyroid anlage. During its descent the median anal age remains connected via thyroglossal duct. Paired lateral anlages originate from the fourth branchial pouch and fuse with the median anal age at fifth week of gestation. Thyroid follicles are initially apparent by eight weeks and colloid formation begins by the 11th week of gestation.

SURGICAL ANATOMY AND RELATIONSHIPS

The adult thyroid gland is brown in colour and firm in consistency, and is located posterior to the strap muscles. The normal thyroid gland weighs approximately 20 g, but gland weight varies with body weight and iodine intake. The thyroid lobes are located adjacent to the thyroid cartilage and connected in the midline by an isthmus that is located just inferior to the cricoid cartilage. A pyramidal lobe is present in about 50% of patients. The thyroid lobes extend to the mid thyroid cartilage superiorly and lie adjacent to the carotid sheaths and sternocleidomastoid muscles laterally. The strap muscles (sternohyoid, sternothyroid, and

superior belly of the omohyoid) are located anteriorly and are innervated by the ansacervicalis (ansahypoglossi). The thyroid gland is enveloped by a loosely connecting fascia that is formed from the partition of the deep cervical fascia into anterior and posterior divisions. The true capsule of the thyroid is a thin, densely adherent fibrous layer that sends out septa that invaginate into the gland, forming pseudolobules. The thyroid capsule is condensed into the posterior suspensory or Berry's ligament near the cricoid cartilage and upper tracheal rings.

BLOOD SUPPLY

The supply and drainage of blood to and from the thyroid involves two pairs of arteries, three pairs of veins, and a dense network of connecting vessels that mesh throughout the capsule of the gland. The superior thyroid artery begins as the first branch of the external carotid artery in 80% of individuals and from the common carotid artery in the remainders. The superior thyroid artery goes to the superior pole of the gland where it divides to lie in the anterior and posterior surface of the lobe. The superior thyroid artery usually lie posterolaterally and parallel to the external branch of the superior laryngeal nerve. It is surgically significant that there is perhaps 1 cm of the superior thyroid artery between the gland and the anterior take off of the external laryngeal

nerve. This space allows safe clamping of the vessel. The inferior thyroid arteries branch directly from the thyrocervical trunk, and they are the only structures in the lower neck to cross the long axis of the common carotid artery deep to the vessel. The artery usually gives off one or two branches, one directed cephalically to the superior parathyroid gland and another inferiorly to the inferior parathyroid gland. Because this blood supply to the delicate parathyroid gland is critical to their function, ligation of the inferior thyroid artery should take place beyond these take off sites. A variable (3%) a third artery, thyroid ima, artery arise from brachio cephalic artery or aortic ach and ascends anterior to trachea.

NERVES

The thyroid gland is closely associated with two nerves- the recurrent laryngeal and the external laryngeal nerves. The right recurrent laryngeal nerve leaves the vagus at the base of the neck, loops around the subclavian artery, and then extends into the thyroid bed 2 cm lateral to the trachea. The left recurrent laryngeal nerve has somewhat different course than the right; it leaves the vagus nerve at the level of the aortic arch and passes inferior and posterior to the arch, lateral to the ductus arteriosus. It then passes posterior to the carotid sheath and into the thyroid bed, where it is closer to and parallel to the tracheoesophageal groove than its

counterpart on the other side of the neck. Recurrent nerve run behind the artery in 53% on right and 69% on left and run anterior to artery in 37% on right and 24% on left. It is easily susceptible to stretching when the thyroid lobe is retracted anteriorly near the berry ligament. Unusually the non-recurrent laryngeal nerve can arise directly from the vagus and pass directly into the thyroid this non-recurrent anatomy is found in 1-1.5% of patients. Even more infrequently, there may be recurrent and non-recurrent laryngeal nerves. These two nerves usually join in a position beneath the lower pole of the thyroid. The superior laryngeal nerves arise from the vagus nerve at the base of the skull and descend towards the superior pole of the thyroid along the internal carotid artery. The smaller external branch travels along the lateral surface of the inferior pharyngeal constrictor muscle and usually descends anteriorly and medially along with the superior thyroid artery. Within 1 cm of the superior thyroid artery's entrance into the thyroid, the nerve takes a medial course and enters into the cricothyroid muscle. The nerve is not usually visualized during surgery as it has already entered the inferior pharyngeal muscle fascia. This nerve is at risk of severed or entrapped if the superior pole vessels are ligated too above the superior pole of the thyroid.

Cernea and colleagues proposed a classification system to describe the relationship of this nerve to the superior thyroid vessels . The type 2a variant, in which the nerve crosses below the tip of the thyroid superior pole, occurs in up to 20% of individuals and places the nerve at a greater risk of injury.

LYMPHATIC DRAINAGE

The thyroid gland is endowed with an extensive network of lymphatics. Intra glandular lymphatic vessels connect both thyroid lobes through the isthmus and also drain to perithyroidal structures and lymph nodes. Regional lymph nodes include pretracheal, paratracheal, perithyroidal, RLN, superior mediastinal, retropharyngeal, esophageal, and upper, middle, and lower jugular chain nodes. These lymph nodes can be classified into seven levels as depicted in . The central compartment includes nodes located in the area between the two carotid sheaths, whereas nodes lateral to the vessels are present in the lateral compartment. Thyroid cancers may metastasize to any of these regions, although metastases to submaxillary nodes (level I) are rare (<1%). There also can be "skip" metastases to nodes in the ipsilateral neck.

Major

Middle jugular nodes: level III

Lower jugular nodes: level IV

Posterior triangle nodes: level V

Lesser

Pretracheal and paratracheal nodes: level VI

Superior mediastinal nodes: level VII

Fig 3 -Thyroid gland { anterior view}

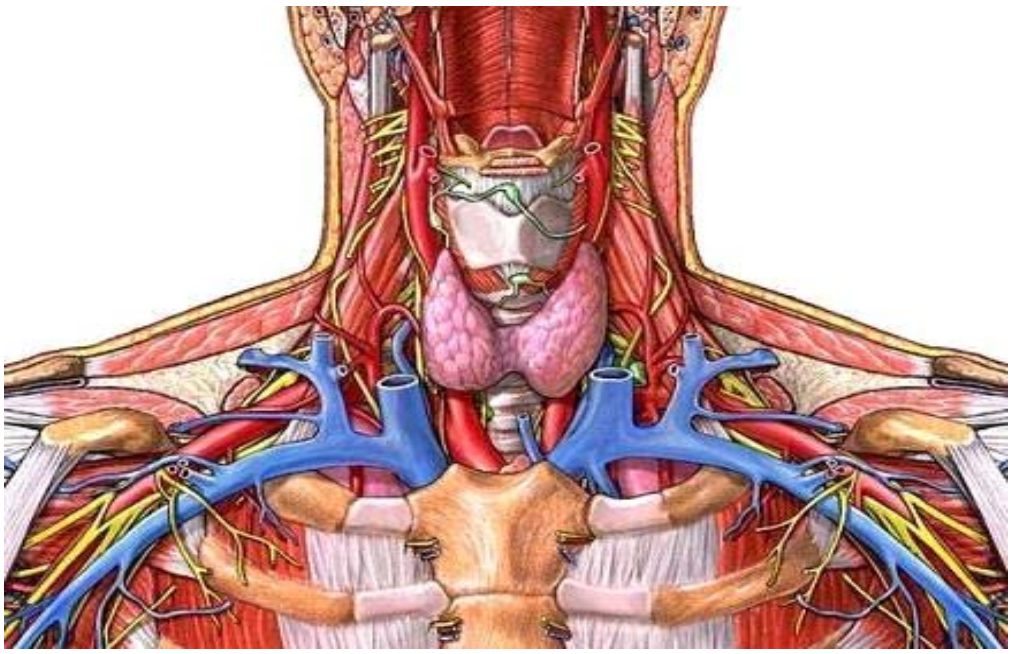
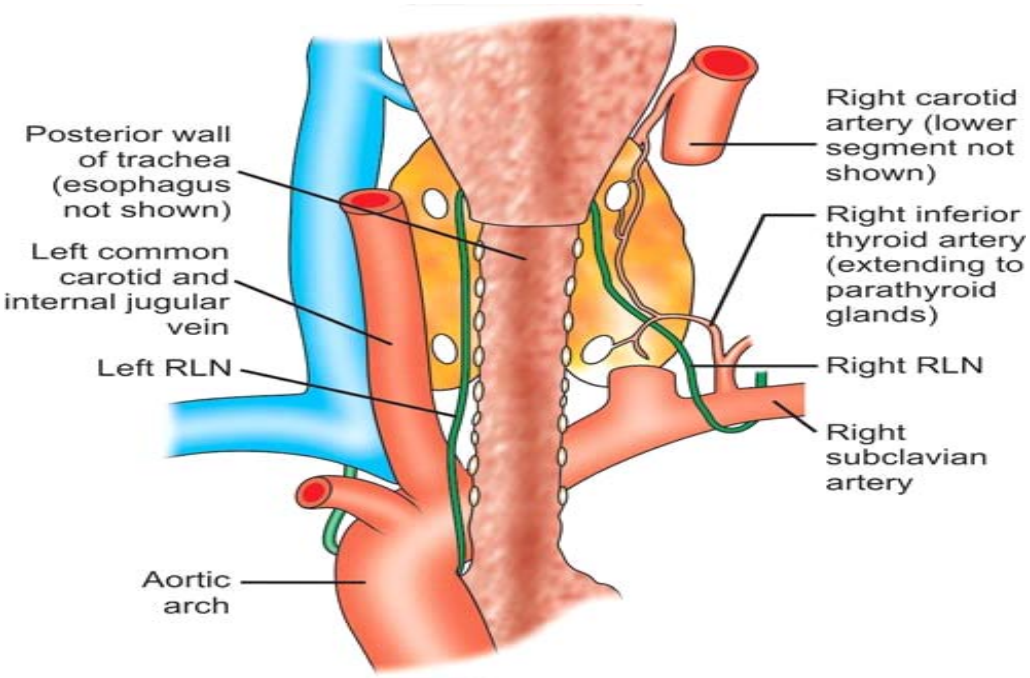


Fig 4 Thyroid anatomy-- nerves



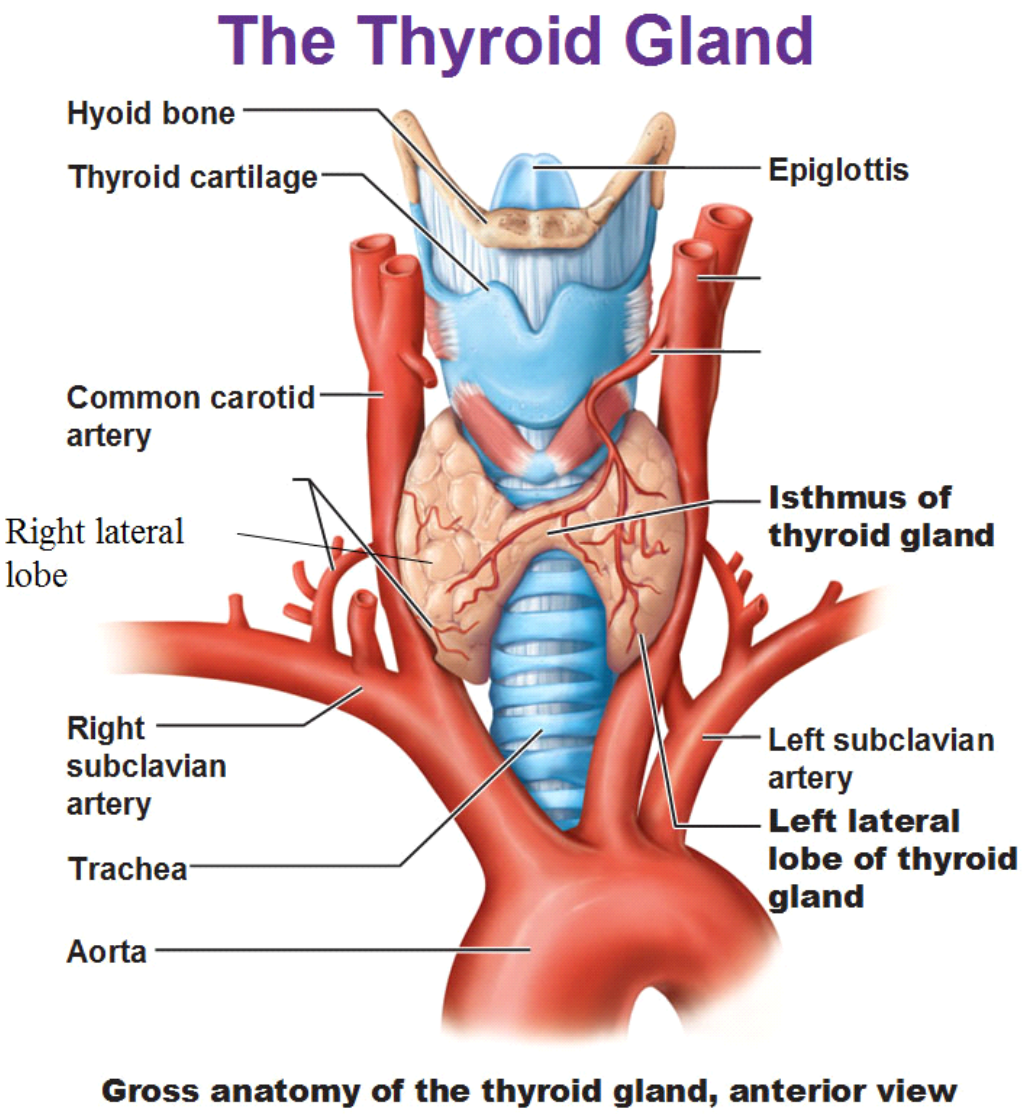
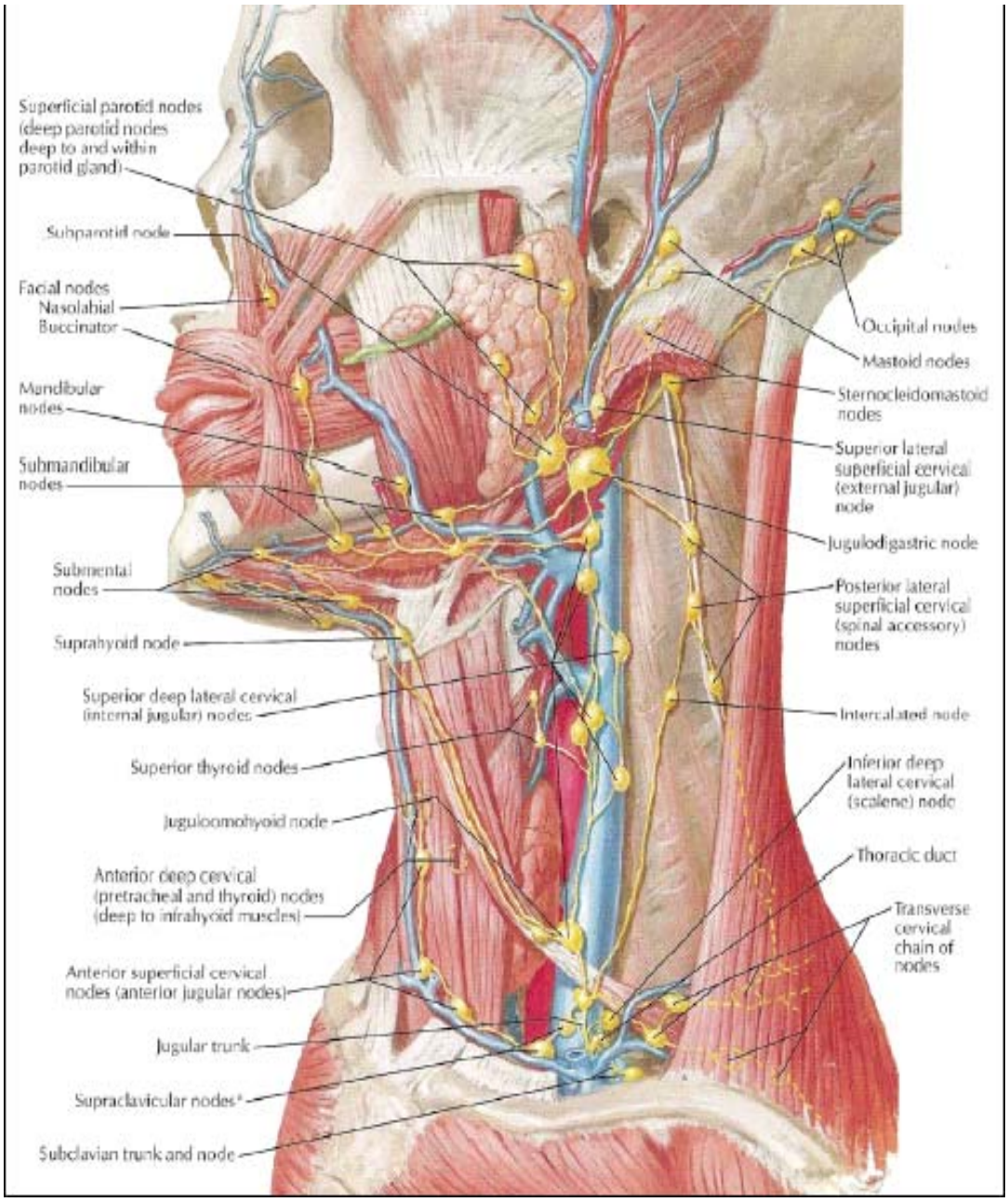


Fig 5 Gross Anatomy-- Thyroid Gland

Fig 6 Head And Neck Lymphatics



EPIDEMIOLOGY

The Indian Council of Medical Research established the National Cancer Registry Program, and the NCRP has collected the data of more than 3,00,000 cancer patients between the periods 1984 and 1993. Among these patients, the NCRP noted 5614 cases of thyroid cancer, and this included 3617 females and 2007 males. The six centers involved in the studies were at Mumbai, Delhi, Thiruvananthapuram, Dibrugarh, Chandigarh, and Chennai. Among them, Thiruvananthapuram had the highest relative frequency of cases of thyroid cancer among all cancer cases enrolled in the hospital registry, 1.99% among males and 5.71% among females. The nation widerelative frequency of thyroid cancer among all the cancer cases was 0.1%–0.2%.

The age-adjusted incidence rates of thyroid cancer per 100,000 are about 1 for males and 1.8 for females as per the Mumbai Cancer Registry, which covered a population of 9.81 million subjects. The histological types of thyroid cancer were studied in a Hospital Cancer Registry of 1185 “new cases” of thyroid cancer. The commonest cancer type was papillary, followed by follicular cancer.

Thyroid cancer is less common in children than in adults but still accounts for 1.4% of childhood malignancies.20 The incidence of thyroid

cancer in children younger than 15 years is approximately 0.5 per million per year, with a rapid rise occurring after the age of 5. 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.Women are affected more than men the ratio is somewhere around 1:1.6 to 1:3.15 Even though the overall incidence of differentiated thyroid cancer is morecommon in women than in men, a nodule in a man is more likely to be malignant than in a woman.

ETIOLOGY

1. Radiation exposure:

Exposure to radiation is the only proved thyroid carcinogen.This was first recognized by Duffy and Fitzgerald in 1950. A 10 to 20 year postradiation 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. In contrast to external radiation, there is little evidence to suggest that internal radiation from I131 used for therapeutic or diagnostic medical purposes causes thyroid cancer in humans.

2. Hereditary factors:

Among the thyroid malignancies, the medullary carcinoma is familial in 10% to 30% of cases. Patients with familial version have medullary carcinoma as an autosomal dominant trait in one of the three distinct clinical syndromes.

i. Isolated familial medullary thyroid carcinoma (FMTC)

ii. Multiple endocrine neoplasia syndrome type 2A (MEN 2A)

iii. Multiple endocrine neoplasia syndrome type 2B (MEN 2B)

Patients with Cowden's syndrome and Gardner's syndrome have an increased risk of benign and malignant neoplasms of the thyroid. About 6% of the patients with differentiated thyroid cancers have familial non-medullary thyroid cancer. Papillary thyroid cancer accounts for 90% of familial non-medullary thyroid cancer.

3. Family History:

Thyroid cancer is a risk factor for the development of both medullary and nonmedullary thyroid cancer. Familial medullary thyroid cancer occurs in association with other tumours as part of multiple endocrine neoplasia 2 (MEN 2) syndromes. Non-medullary thyroid

cancer can occur in association with known familial cancer syndromes such as Cowden's syndrome, Werner's syndrome, Gardner's syndrome and FAP. Papillary thyroid cancer accounts for 90% of familial non medullary thyroid cancer**.**

4. Thyroid stimulating hormone elevation:

An increased risk of thyroid cancer is seen in patients with chronic elevation of TSH. Animal experiments indicate that prolonged TSH stimulation can cause thyroid cancer. Even though it is not clear in humans, increased TSH though not being sufficient to cause thyroid cancers may stimulate its growth once present.

5. Chronic Lymphocytic Thyroiditis:

Thyroid lymphoma most often occurs against a background of autoimmune lymphocytic thyroiditis (Hashimotos disease).

6. Solitary thyroid nodule:

Presence of solitary thyroid nodule is also a risk factor for malignancy. The incidence of malignancy with in a clinically apparent SNT is approximately 5-10%. If imaging investigations show the nodule to be truly solitary, then the likelihood of it being malignant increases to about 20%.

CLASSIFICATION OF THYROID MALIGNANCIES

PRIMARY

1. Follicular epithelial cells

Differentiated

Papillary carcinoma

Follicular carcinoma

Undifferentiated

Anaplastic carcinoma

2. Parafollicular cells

Medullary carcinoma

3. Lymphoid cells

Lymphoma

SECONDARY

1. Metastatic

2. Local infiltration

PATHOLOGY AND NATURAL HISTORY

PAPILLARY CANCER –THYROID

The typical PTC on physical examination is firm with an irregular border, has a white colour, and may contain micro calcifications. It can be classified as occult (less than 1.5 cm in greatest dimension), intrathyroidal (larger than 1.5 cm but confined to the gland), and extrathyroidal (extending beyond the capsule to involve the surrounding viscera). At the time of presentation, upto 80%-90% of the primary lesions are confined to the gland. Encapsulation of the tumour is seen in 10% of the cases. Tumour multicentricity is seen in 20% to 30% of cases in most of the studies. In 1971 Woolner described papillary cancer seen by light microscopy: “The typical histological picture is a mixture of papillary excrescences and neoplastic follicles containing varying degrees of colloid. The percentage of papillary and follicular elements is varied. The nucleus is hypodense with large areas that appear empty and are apparently devoid of chromatin. Consequently, the nucleus appear opaque and are given many names including “clear”, “watery”, “pale”, or the most imaginative

“Orphan Annie Eyes”. Consequently the diagnosis of PTC is based on a constellation of findings. In particular, papillae projecting into open

spaces, as well as clear nuclei with prominent nuclear grooves are all important features of the diagnosis. Another important feature is the presence of psammoma bodies (Greek: psammoma – sand) which are laminated calcific areas. They are seen in 50% of cases in most series. Although the etiology is unclear it is believed to represent the remains of the dead papillae and are quiet specific for PTC and are rarely seen in other thyroid lesions.

Morphological variants of papillary thyroid carcinoma

Variants with similar clinical behaviour

- Follicular
- Micropapillary
- Encapsulated Solid
- Solid/Trabecular

Variants with more aggressive behaviour

- Tall cell
- Diffuse sclerosing
- Columnar
- Oxyphil { hurthle cell }

The propensity for papillary cancer to spread in the lymphatics within and outside the gland is striking. 5-10% of patients present with distant metastases at some time in course of the disease. The natural prognosis of the metastatic cancer seems to be volume related. It is worse in patients with bone, lung and CNS metastases. The tall cell variant has a worse prognosis in all age groups.

Fig 7 :PAPILLARY CA THYROID --

GROSS

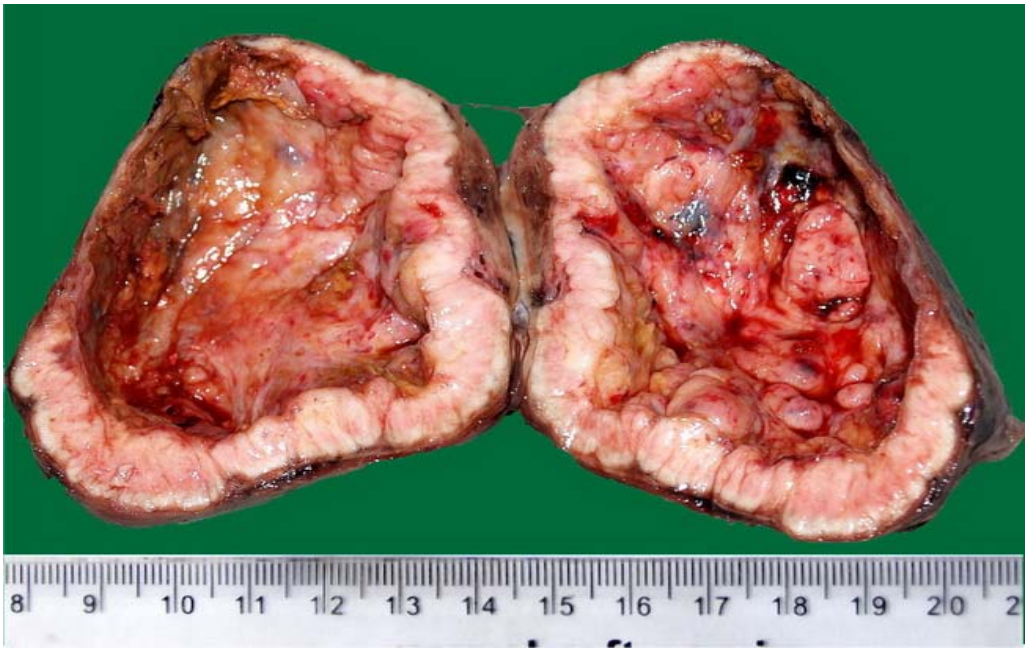
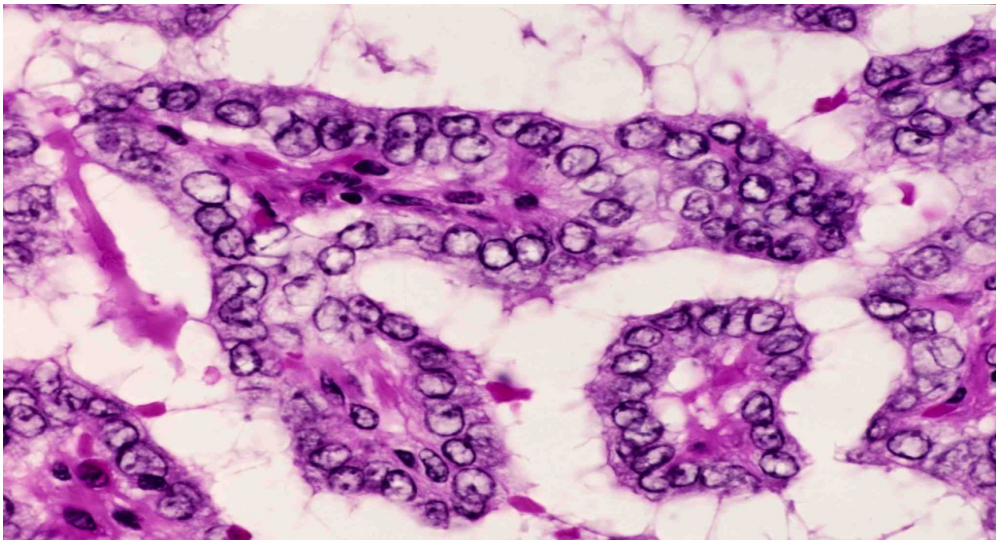


Fig 8: PAPILLARY CA THYROID -- MICROSCOPIC



FOLLICULAR CARCINOMA OF THYROID (FTC)

Follicular thyroid cancer accounts for approximately 10–15 % of thyroid malignancies. Follicular cancers are encapsulated lesions and are very difficult to differentiate from its benign counterpart follicular adenomas. They are characterized microscopically by large nuclei, frequent and/or atypical mitotic figures, vascular invasion, and distant metastases. In contrast to papillary carcinoma intrathyroidal multifocal disease rarely occurs in follicular cancers. Instead these lesions are usually solitary, encapsulated and have a microfollicular histologic pattern. The findings that constitute malignancy are not cytologic but instead are histological features like transcapsular invasion and microvascular invasion of the vessels along the thyroid capsule. Lymph node involvement is unusual and it occurs late in the course of the disease. Follicular cancers are divided into “minimally invasive” and “widely invasive”. The minimally invasive forms are grossly encapsulated and the diagnosis depends upon the presence of vascular or capsular invasion: The widely invasive form is characterized by widespread infiltration of the blood vessels or the adjacent thyroid tissue. Tumours that represent a mixed form of papillary and follicular features, showing signs of follicular differentiation and also signs of papillary

cancer should clinically regarded as papillary rather than follicular cancers

MORPHOLOGICAL VARIANTS OF FOLLICULAR THYROID CARCINOMA

- Hurthle cell variant (Oxyphil or Oncocyticcarcinoma)
- Insular cell variant

30% to 50% of Hurthle cell carcinomas are associate with lymph node metastases, compared with 5% to 10% of follicular cancers.The Hurthle cell variant, unlike other follicular cells does not take up radioactive iodine. This variant occurs particularly in adult women and is usually solid, well vascularised and well encapsulated. The insular tumours were so named because the clusters of cells within it contain small follicles that resemble the pancreatic islet cells. Insular thyroid cancer is a more aggressive malignancy and is perceived to behave less favourable than the papillary and follicular cancers.

FIG 9:FOLLICULAR CA THYROID{GROSS}

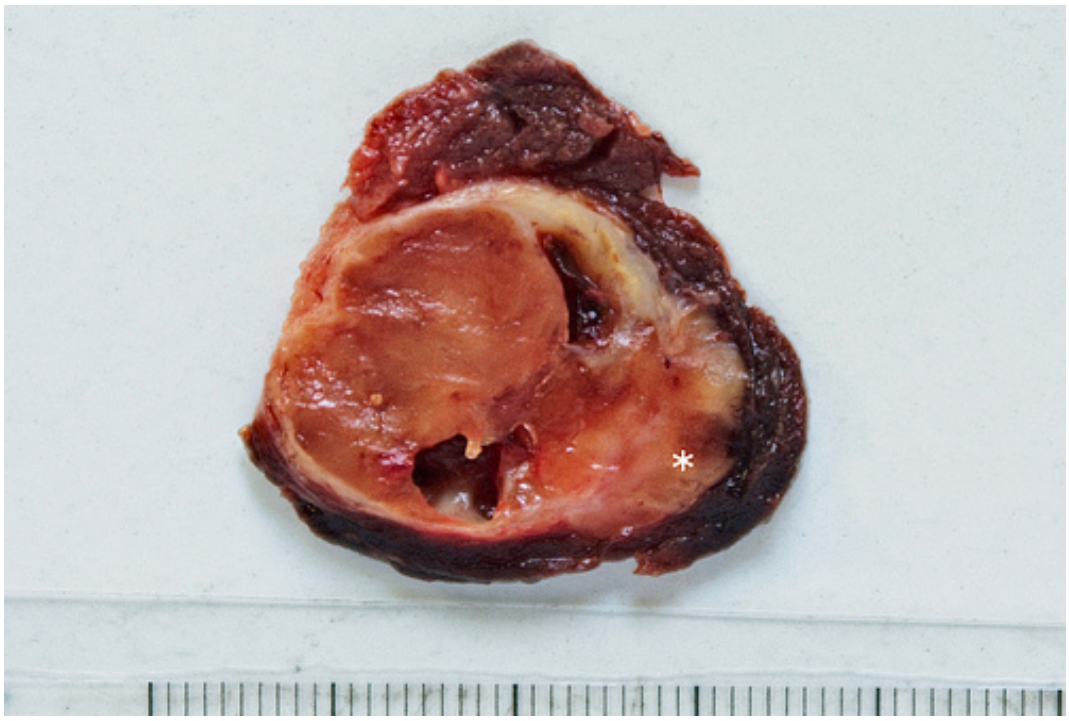
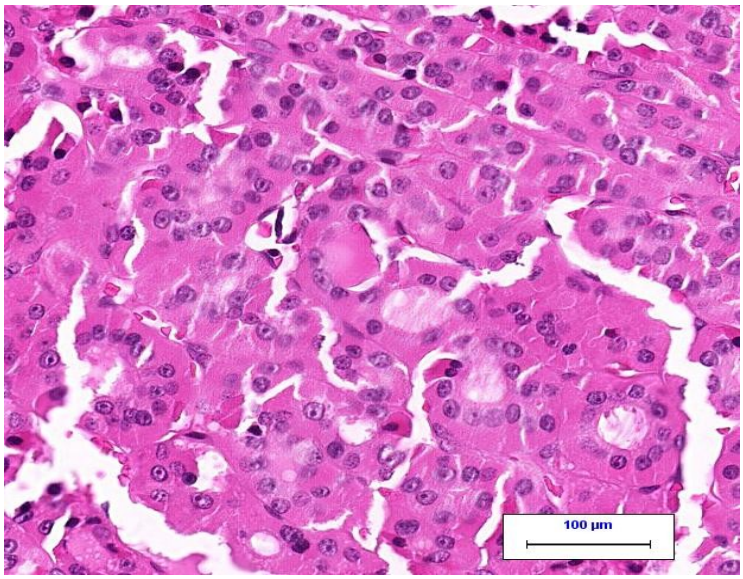


FIG 10 :FOLLICULAR CANCER THYROID { MICROSCOPIC}



ANAPLASTIC CARCINOMA OF THE THYROID (ATC)

Anaplastic carcinoma is a devastating disease that usually overcomes thehostin a matter of months, sometimes even weeks. They represent 5% to 14% of thyroid malignancies.The median age of onset of ATC is consistently in the seventh decade of life and the disease is characterized by female preponderance ranging from 55% to 77%. The anaplastic component is composed of varying proportions of spindle, polygonal and giant cells. In general, the lethality of anaplastic cancer should not be underestimated, even when minimal in size amid a background of predominately differentiated cancer. The natural history of this cancer is characterized by rapid and massive locoregional growth, dysphagia, Svsyndrome and finally asphyxiation or exsanguination.

MEDULLARY CARCINOMA OF THE THYROID (MTC)

These malignancies are derived from the non epithelial parafollicular or the C cells which have the ability to synthesize and secrete calcitonin. MTC typically arise from the upper portion of the thyroid where the C-cells are concentrated. These cell are derived from the neural crest and are therefore of neuro ectodermal origin. Hence the medullary carcinomas have histological and cytological features typical of other neuro endocrine tumours such as carcinoid tumours, pancreatic

islet cell tumours and pheochromocytomas. They occur in two basic forms, sporadic and familial. The sporadic type make up 70% to 90% of the total and the familial 10% to 20%. FNAC yields presumptive clues to the diagnosis of MTC. Spindle shaped or triangular cells with dendritic extensions are highly suggestive of MTC. Although amyloid may be presumptively identified in Papanicolau stains, it is confirmed by restaining with Congo red. On gross examination it is firm, solid, grayish, or pale brown welldemarcated from the surrounding tissues Microscopically the typical appearance is that of polyhedral cells arranged in sheets or irregular trabeculae. In familial cases there are often microscopic foci of C cell hyperplasia, or microscopic medullary carcinoma in areas of normal parenchyma, thus demonstrating multicentric tumour origin.

PHENOTYPES RELATED TO MUTATION OF THE RET PROTO-ONCOGEN MEN 2A (60%)

Medullary thyroid carcinoma	100
Pheochromocytoma	10-60
Hyperparathyroidism	5-20

MEN 2B (5%)

Medullary thyroid carcinoma	100

Pheochromocytoma	50
Marfanoid habitus	100
Mucosal neuromas (gut) and ganglioneuromatosis	100

FMTC (35%)

Medullary thyroid carcinoma	100

{MEN 2A, multiple endocrine neoplasia type 2A; MEN 2B, multiple endocrine neoplasia type 2B; FMTC, familial medullary thyroid carcinoma. }

CLINICAL PRESENTATION OF THYROID CARCINOMAS

1. Thyroid swelling

Thyroid cancer most commonly presents as a single neck mass noted incidentally by the patient or the physician. A thyroid mass in a child no matter its size or consistency is highly suspicious of malignancy. Regardless of the sex, the mass in advanced years is likely to be malignant. Though many women develop thyroid cancer than in men, any given nodule in a man is more likely to be malignant. Although such

words as hard with fixation can apply to a mass associated with thyroiditis, these features must be viewed with suspicion for malignancy. The opposite must not be assumed, however; soft masses with no fixation to the surrounding tissues are not necessarily benign. Rapid enlargement can be deceptive because of the tendency for intralesional hemorrhage. On the other hand, the relentless and rapid growth that can be seen in anaplastic carcinoma is so impressive that its ominous nature is quiet obvious. Cystic lesions are more likely benign, but cystic carcinomas do occur. Solid lesions have a 21% risk of malignancy, cystic 7% and mixed lesions had a risk of 12%. 5% to 10% of multiple nodules and 10% to 20% of solitary nodules are malignant.

2. Cervical lymphadenopathy

In case of papillary carcinoma which is known for its lymphatic spread the patient present with cervical lymphadenopathy alone in 20% of cases and a mass in the thyroid with cervical lymphadenopathy in 13% of cases. Children and young adults more often have palpable nodal metastases. Most studies report a 30% to 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. Sporadic cases of MTC are

more prone for lymph nodal spread than the familial cases. In the presence of a seemingly normal thyroid gland, a lateral neck mass with biopsy proven thyroid tissue was previously misconceived to represent an embryonic nest of thyroid tissue and erroneously termed “lateral aberrant thyroid”. This presentation is now considered to be caused by metastatic well differentiated thyroid carcinoma from an occult primary within the gland until proved otherwise.

3. Symptoms related to the tumour growth

These symptoms may infrequently precede or occur simultaneously with the development of a nodule, include hoarseness, dyspnoea and dysphagia, reflecting local infiltration of the recurrent laryngeal nerve, the trachea and the esophagus respectively. Horner’s syndrome associated with a thyroid mass usually represents an ominous circumstance. Large multi nodular goiters with or without substernal extension can cause tracheal shift or impingement and alteration of the airway. Local compressive symptoms are a rule in case of anaplastic carcinoma and can include stridor, dysphagia, dyspnoea, hoarseness, weight loss and even superior vena cava syndrome.

4. Symptoms related to distant metastases

Among the thyroid malignancies anaplastic carcinomas are quiet likely to have a distant metastasis which are usually pulmonary but can also involve bone, brain and soft tissues. Distant foci of the tumour are seen in 20% to 50% of patients. Most distant metastases are found in the lung, liver and bone.They are found in more than75% who die from thyroid carcinoma and lung metastasis account for almost 50%tumour related deaths.

5. Symptoms related to hormonal derangement

Thyroid cancer can present with hyperthyroid features with the incidence currently at about 5% to 10% in patients with Grave's disease. Papillary carcinoma accounts for 75% of thyroid cancers associated with Grave's disease.61 Patients who present with clinical evidence of thyroid cancer and have Grave's disease have more aggressive tumours, whereas patients with occult thyroid cancers who are treated for Grave's disease have an excellent prognosis. Diarrhea has been reported in 20% to 30% of cases of sporadic MTC at presentation often in patients with extensive disease. The underlying mechanism is still to be clarified. Prostaglandins, Vaso active intestinal polypeptide, Calcitonin gene related peptide and Seratonin have all been suggested as mediators of this symptom.

Although rare, concomitant Cushing's syndrome is the most striking presentationof sporadic MTC in some cases. This unusual phenomenon is explained by the common precursor of ACTH and calcitonin. When cortisol production is excessive and the tumour burden is too large for resection, bilateral adrenalectomy is the last resort.

LABORATORY EVALUATION

BLOOD INVESTIGATIONS

Serum TSH

TSH levels can be measured accurately down to very low serum concentrations with an immune chemiluminometric assay. When the serum TSH level is in the normal range, measuring the T3 and T4 levels is redundant. Interpretation of deranged TSH levels, however, depends on knowledge of the T3 and T4 values . In the euthyroid state, T3, T4 and TSH levels will all be within the normal range. Florid thyroid failure results in depressed T3 and T4 levels, with gross elevation of the TSH. Incipient or developing thyroid failure is characterised by low normal values of T3 and T4 and elevation of TSH. In toxic states the TSH level is suppressed and undetectable.

Thyroxine (T4) and tri-iodothyronine (T3)

There are transported in plasma bound to specific proteins (TBG). Only a small fraction of the total (0.03% of T4 and 0.3% of T3) is free and physiologically active. Assays of total hormone for both are now obsolete because of the confounding effect of circulating protein concentrations, influenced by the level of circulating oestrogen and the nutritional state. Highly accurate radio immunoassays of free T3 and free T4 are now routine. T3 toxicity (with a normal T4) is a distinct entity and may only be diagnosed by measuring the serum T3, although a suppressed TSH level with a normal T4 may suggest the diagnosis. An appropriate combination to establish the functional thyroid status at initial assessment is measurement of serum TSH and assay of anti-thyroid antibodies, supplemented by free T4 and T3 evaluation when TSH is abnormal.

Thyroid auto antibodies

Serum levels of antibodies against thyroid peroxidase (TPO; previously referred to as thyroid microsomal antigen) and thyroglobulin are useful in determining the cause of thyroid dysfunction and swellings. Autoimmune thyroiditis may be associated with thyroid toxicity, failure or euthyroid goitre. Levels above 25 units ml–1 for TPO antibody and

titres of greater than 1:100 for anti-thyroglobulin are considered significant, although a proportion of patients with histological evidence of lymphocytic (autoimmune) thyroiditis are seronegative. The presence of antithyroglobulin antibody interferes with assays of serum thyroglobulin with implications for the follow-up of thyroid cancers.

Calcitonin

Of all the blood products, the plasma calcitonin has the most direct diagnostic value in determining the nature of the thyroid mass. This polypeptide is produced exclusively by the C-cells, and its measurement is sensitive, accurate and consistent to a degree that it is possible to diagnose C-cell hyperplasia or medullary cancers as small as 1 mm in diameter. Calcitonin levels are elevated in almost all patients with MTC. However in those patients who do have a normal baseline values, detections of microlesions or C-cell hyperplasia associated with MEN2A or MEN2B can be accomplished with a pentagastrin or a calcium stimulation of calcitonin. Normal calcitonin levels < 10 pg/ml. A stimulated value of < 30 pg/ml is considered normal and a value greater than 100 pg/ml is abnormal

Thyroglobulin

Serum thyroglobulin is reflective of three factors: the mass of thyroid tissue present, the presence of injury or inflammation of the gland, which allows leakage of Tg, and the degree of stimulation of the TSH receptor. Thyroglobulin is present in normal serum in concentrations of 20 to 40 ng/ml, but elevation above this offers no specific information. Thyroiditis and even hyperthyroidism may be responsible for an abnormal high thyroglobulin. It should be noted that, eventhough diagnostic sensitivity has not been described, a thyroglobulin level of more than 10 times the upper limit of normal is highly suggestive of cancer. Serum thyroglobulin levels > 2 ng/ml after thyroidectomy indicates presence of metastatic disease and a rise in S. thyroglobulin in a patient with known metastases indicates progression of disease. Thyroglobulin levels of > 60 ng/ml suggests thyroid cancers.

Genetic testing

Genetic testing is available for family members at risk for developing medullary cancer. The ret protooncogene encodes a protein receptor, tyrosine kinase. Mutations of ret are associated in 95% of hereditary medullary thyroid cancers, MEN 2A, MEN 2B and FMTC.

Other blood tests

Patients with MEN 2A and 2B have associated pheochromocytoma and hyperparathyroidism and hence those with family history or those with features of either of these must be investigated for these disorders also.

FINE NEEDLE ASPIRATION CYTOLOGY{ FNAC }

FNA has revolutionized the management of thyroid nodules, providing an extremely sensitive and cost-effective method of detecting thyroid malignancies. The impact this procedure has had on clinical practice is reflected by a reduction of the total number of thyroid surgical procedures performed, a greater proportion of malignancies removed at surgery, and an overall reduction in the cost of managing patients with thyroid nodules. The accuracy of cytologic diagnosis from FNA ranges from 70% to 97% and is highly dependent on both the skill of the individual performing the biopsy and the cytopathologist interpreting it. In most instances, the cytology report will be one of the following three:

1. **Probably benign nodule**, when the material is composed largely of colloid, histiocytes and few normal looking follicular cells. This will

be indication for a conservative approach unless the clinical data suggests otherwise.

2. **Follicular neoplasm**; when cellularity higher than that found in the usual hyper plastic nodule, but the nuclear features of papillary cancer are absent. The diagnosis of Hurthle cell neoplasm usually falls in the category.71 The presence of highly hyper chromatic nuclei, micro follicular or solid pattern, scanty colloid and necrotic debris suggest the prevalence of poorly differentiated cancer. The diagnosis of follicular neoplasm is an indication for removal of the nodule, unless this is contraindicated for medical reasons.

3. **Papillary cancer**, when the characteristic cyto architectural features of this tumor type are present, such as papillary fronds, psammomma bodies, nuclear pseudo inclusions, and nuclear grooves. It should be remembered that the ground glass nuclear feature is usually not apparent in cytological preparations; even when prominent in tissue sections. Concerning the follicular variant of papillary carcinoma, the nuclear change should be particularly well developed. In both the classic and the follicular variants of the tumor the colloid often exhibits a peculiar streaking and smearing that can be compared with that of a bubble gum. The cytological diagnosis of papillary cancer is obviously an

indication for therapeutic intervention, even if occasional surgical specimen may show only a papillary micro carcinoma. The performance of FNA may result in a partial or complete.

The malignant potential of follicular neoplasms can rarely be determined by cytologic evaluation; thus, the biopsies from such lesions are generally classified as suspicious or indeterminate, and most come to surgical resection. The cells from follicular adenomas and follicular carcinomas appear cytologically identical; only by identifying capsular or vascular invasion on histologic specimens can cancer be diagnosed. Specimens with predominantly Hurthle cells are treated in the same fashion; however, extensive hurthle cell changes can be seen in Hashimoto's thyroiditis. Malignancy is found in approximately 20% of follicular nodules that are classified as indeterminate on FNA.

A variety of molecular markers have been assessed in FNA specimens in an attempt to develop more discriminating cytologic sub classifications to improve the yield of malignancy found at surgery. These markers include telomerase activity, loss of heterozygosity, as well as various pattern of protein expression by immunocytochemistry. Although there is little doubt that molecular markers will prove useful in

the future, currently there is no single or group of markers that has been adopted in routine clinical practice.

THE BETHESDA SYSTEM FOR REPORTING THYROID CYTOPATHOLOGY:

Recommended Diagnostic Categories

I. Nondiagnostic or Unsatisfactory

- Cyst fluid only
- Virtually acellular specimen
- Other (obscuring blood, clotting artifact, etc)

II. Benign

- Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc)
- Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context
- Consistent with granulomatous (subacute) thyroiditis
- Other

III. Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance

IV. Follicular Neoplasm or Suspicious for a Follicular Neoplasm

Specify if Hürthle cell (oncocytic) type

V. Suspicious for Malignancy

- Suspicious for papillary carcinoma
- Suspicious for medullary carcinoma
- Suspicious for metastatic carcinoma
- Suspicious for lymphoma
- Other

VI. Malignant

- Papillary thyroid carcinoma
- Poorly differentiated carcinoma
- Medullary thyroid carcinoma
- Undifferentiated (anaplastic) carcinoma

- Squamous cell carcinoma
- Carcinoma with mixed features (specify)
- Metastatic carcinoma
- Non-Hodgkin lymphoma
- Other

THYROID IMAGING

ULTRASOUND

Ultrasound is helpful in assessing a thyroid nodule. Its advantages include portability, cost-effectiveness, and lack of ionizing radiation. It is extremely useful in patients who are being managed conservatively because it can easily determine whether a nodule has increased in size. Ultrasound is used routinely in the office setting and is also available for intraoperative evaluation. It has proved highly effective in determining the location and characteristics (cystic versus solid) of nodules but is unable to accurately predict the diagnosis of solid nodules . The finding of a cystic lesion may be reassuring, but such lesions represent a small minority of thyroid nodules (1%-5%). Additionally, well-differentiated thyroid cancers may have cystic components, although this is very

unusual.Ultrasound uses a high-frequency probe in the 7.5- to 12-MHz range. Ultrasound devices have become portable enough to allow use in the clinic and the operating room. B-mode ultrasonography can be used preoperatively or intraoperatively. It is increasingly being used to assist in FNA

Radioisotope Scanning

Whereas ultrasound allows anatomic evaluation, radionuclide scans allow assessment of thyroid function. Technetium pertechnetate (99mTc) is taken up rapidly by the normal activity of follicular cells. It is trapped by follicular cells, but not organified. 99mTc has a short half-life and low radiation dose. Its rapid absorption allows quick evaluation of increased uptake (so-called hot) or hypofunctioning (so-called cold) areas of the thyroid. Because screening with 99mTc shows uptake in the salivary glands and major vascular structures, interpretation of thyroid pathology requires a higher level of expertise. 123I and 131I iodine scintigraphy is also used to evaluate the functional status of the gland . Both are trapped by active follicular cells and organified. 123I has a shorter half-life (12-13 hours) and allows a quicker image. Advantages of scanning with 123I include a low dose of radiation (30 mrad) and short half-life. 123I is a

good choice for evaluating suspected lingual thyroids or substernal goiters.

131I has a longer half-life (8 days) and emits higher levels of β-radiation. 131I is optimal for imaging thyroid carcinoma. It is the screening modality of choice for the evaluation of distant metastasis. Radionuclide scanning demonstrates the function of thyroid nodules as hot (excess uptake) or cold (no uptake) in comparison to surrounding tissue. Malignancy has been shown to occur in 15% to 20% of cold nodules and, additionally, in 5% to 9% of nodules with uptake that is warm or hot, thus mandating a continued aggressive approach to clinically suspicious nodules, even if they are not cold.

Positron emission tomography (PET) with 18F-fluorodeoxyglucose can be used to provide three-dimensional reconstruction images. There is increasing enthusiasm for its use in detecting primary and metastatic thyroid cancer. Interestingly, PET scans identify occasional so-called thyroid incidentalomas when evaluating other solid malignancies. The majority of these findings, however, are not malignant. The appropriateness of PET in the workup or follow-up of thyroid nodules remains to be firmly established or agreed on.

CT and MRI

It is fairly well agreed that CT and MRI do not add significantly to the workup of uncomplicated thyroid nodules. Either modality, however, may be of help in evaluating for local extension in more advanced stages of thyroid cancer. CT or MRI is particularly appropriate for a suspicious mass (or biopsy-proven cancer) with palpable cervical lymph nodes. Additionally, either can be used for postoperative follow-up, particularly for suspicion of recurrent disease. Preoperative CT or MRI is advisable for larger thyroid masses that show significant tracheal deviation suggestive of a substernalgoiter on chest radiographs.

CT and MRI are both equally sensitive and specific for the evaluation of thyroid masses. Consideration must be given to the use of IV contrast for CT evaluation of a possible cancer. The iodine load may interfere with postoperative plans for 131I scanning.

Radiograph:

Standard radiographs provide limited information in the evaluation of a thyroid mass, and with the exception of identification of metastatic lung disease, provide no specific information. The chest radiograph should include the lower neck that the position of the trachea is

visualized. This can also suggest substernal extension of a large goiter. When calcifications are seen in the glandand especially if they are bilateral bulky and near the junction of the upper two third and the lower one third, medullary cancer is suggested. Such calcifications can also be seen in metastatic MTC in the cervical nodes.

Fig11 Thyroid USG

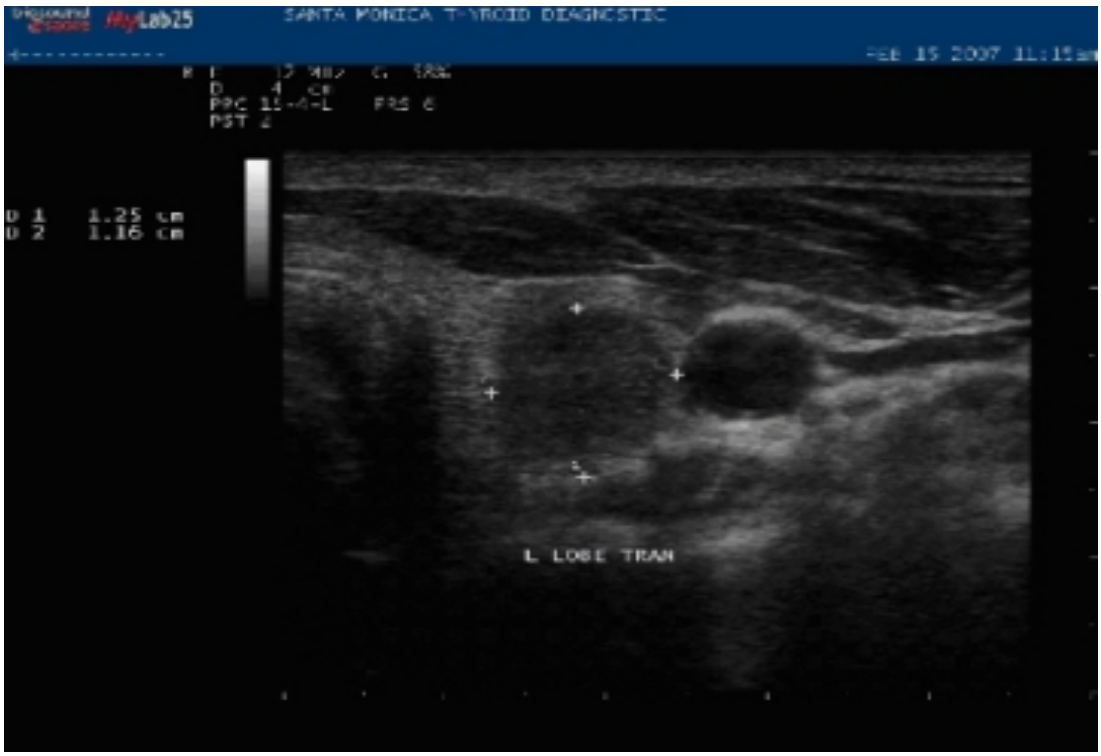
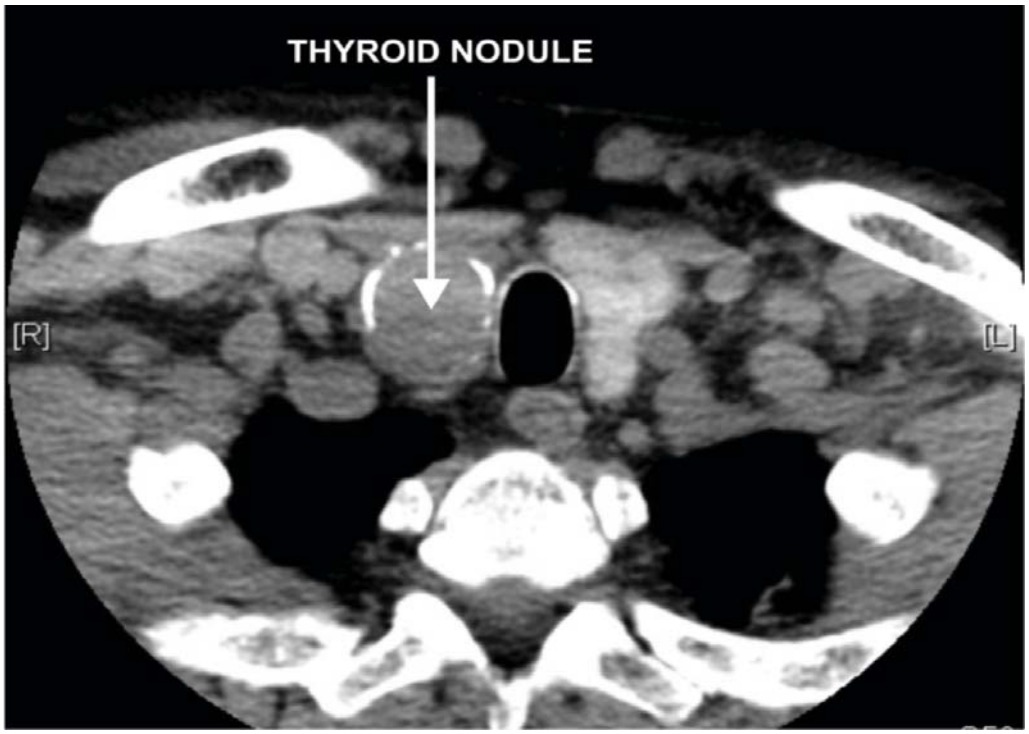


Fig 12 CT Scan Thyroid



STAGING OF THYROID CANCER

TNM Staging -- Primary tumour (T)

Tx - Primary tumour cannot be assessed.

T0 - No evidence of primary tumour.

T1 - Tumour 2 cm or less in greatest dimension limited to the thyroid.

T2 - Tumour more than 2 cm but not more than 4 cm in greatest dimension limited to the thyroid.

T3 - Tumour more than 4 cm in greatest dimension limited to the thyroid or any tumour with minimal extrathyroid extension.

T4a - Tumour of any size extending beyond the thyroid capsule to invade the subcutaneous soft tissues, larynx, trachea, esophagus or recurrent laryngeal nerve.

T4b - Tumour invades prevertebral fascia or encases the carotid artery or mediastinalvessels.

All Anaplastic carcinomas are T4 tumours.

T4a - Intrathyroidal anaplastic carcinoma - surgically resectable.

T4b - Extrathyroidal anaplastic carcinoma - surgically unresectable.

Regional lymph nodes (N)

Regional lymph nodes are the central compartment, lateral cervical, mediastinal lymph nodes.

Nx - Regional lymph nodes cannot be assessed.

N0 - No regional lymph node metastases.

Nl - Regional lymph node metastases.

N1a - Metastases to level 6 (pretracheal, paratracheal and prelaryngeal/Delphian lymph nodes).

N1b - Metastases to unilateral, bilateral or contralateral cervical or superior ediastinallymph nodes.

Distant metastases

Mx - Distant metastases cannot be assessed.

M0- No distant metastases.

M1- Distant metastases.

PAPILLARY OR FOLLICULAR CARCINOMA

Stage Grouping of Papillary / Follicular carcinomas (<45 years)

Stage 1	**Any T**	**Any N**	**M0**
Stage 2	**Any T**	**Any N**	**M1**

STAGE GROUPING OF PAPILLARY / FOLLICULAR CARCINOMAS (>45YEARS)

STAGE 1	**T 1**	**N 0**	**M0**
STAGE 2	**T 2**	**N0**	**M0**
STAGE 3	**T3** **T1** **T2** **T3**	**N0** **N1A** **N1A** **N1A**	**M0** **M0** **M0** **M0**
STAGE 4 A	**T4A** **T4A** **T1** **T2** **T3** **T4A**	**N0** **N1A** **N1B** **N1B** **N1B** **N1B**	**M0** **M0** **M0** **M0** **M0** **M0**
STAGE 4 B	**T4B**	**ANY N**	**M0**
STAGE 4 C	**ANY T**	**ANY N**	**M1**

MEDULLARY CARCINOMA --STAGE GROUPING OF

MEDULLARY CARCINOMAS

Stage 1	**T1**	**N0**	**MO**
Stage 2	**T2**	**N0**	**M0**
Stage 3	**T3** **T1** **T2** **T3**	**N0** **N1A** **N1A** **N1A**	**M0** **M0** **M0** **M0**
Stage 4a	**T4A** **T4A** **T1** **T2** **T3** **T4A**	**N0** **N1A** **N1B** **N1B** **N1B** **N1B**	**M0** **M0** **M0** **M0** **M0** **M0**
Stage 4b	**T4B**	**ANY N**	**M0**
Stage 4c	**ANY T**	**ANY N**	**M1**

ANAPLASTIC CARCINOMA

All anaplastic carcinomas are considered as stage IV.

Stage Grouping of Anaplastic carcinomas

STAGE 4A	**T4A**	**ANY N**	**MO**
STAGE 4B	**T4B**	**ANY N**	**M0**
STAGE 4C	**ANY T**	**ANY N**	**M1**

Survival and Prognostic Features

Overall survival in well differentiated carcinoma from various institutional series shows a better 10 year survival for papillary cancer, ranging between 74% and 93% as compared to follicular cancer, with a 10 year survival of 43% to 94%. Although many institutions have reported their data based on these histologic subcategories, a more meaningful system is to categorize patients according to definite risk factors more pertinent to generating prognostic information. The risk categorization scheme developed at the Lahey clinic, by Cady and group carries the acronym **AMES** (Age, Metastatic disease, Extrathyroidal extension, Size). A group from Canada added an assessment of the **DNA** content by flowcytometry to this which carries the acronym **DAMES** with the **DNA** content, and showed that the highrisk patients with aneuploid tumours have a poor long term survival. The initial system

developed at the Mayo clinic group in 1987 by Hay and associates carried the acronym **AGES** (Age, Grade of the tumour, Extent of tumour, Size). A mathematical formula to develop a PS with different weights on these factors was developed. A more recent modification of this system is seen in **MACIS** (Metastasis, Age, tumor extent divided into Completeness of the surgery, Invasion and tumor Size). The **MACIS** scale is a more sophisticated post operative system modified from **AGES** scale. In addition some studies have reported that incomplete resection of the gland, vascular invasion, male sex, lymph node metastases, certain morphologic variants of PTC and tumour multicentricity are significant prognostic factors.

Prognostic Risk Categorization Schemes

AMES categorization scheme

	LOW RISK	HIGH RISK
Age	Male <41, female <51	Male >40, female >50
Metastases	Absent	Present
Extent	Intrathyroidal papillary or follicular with minor capsular invasion	Extrathyroidal papillary or Follicular with major capsular invasion
Size	<5 cm	> 5 cm
Definition	A: Any low risk age group without metastases. B: High risk age without metastases and with low risk extent and size	A: Any patient with metastases. B. High risk age with either high risk extent or size.
Overall survival (OS)	98%	54%
Disease survival (DFS)	95%	55%

DAMES categorization scheme

LOW RISK	Low-risk AMES + euploid	DFS-92%
INTERMEDIATE RISK	Low-risk AMES + aneuploid	DFS-45%
HIGH RISK	High risk AMES + aneuploid	DFS-0%

AGES categorization scheme

PS= 0.05 x age in years (age < 40 yrs= 0),
+ 1 (grade 2) or + 3(grade 3-4),
+ 1 (if extrathyroidal) or + 3 (if distant metastases),
+ 0.2 x tumour size (in cms).

PS range= 0- 11.65, median=2.6

Risk categories:

0- 3.99 (DFS - 20 yrs - 99%);

4- 4.99 (DFS - 20 yrs - 80%);

5- 5.99 (DFS - 20 yrs - 33%);

> 6 (DFS - 20 yrs - 13%).

MACIS categorization system

PS= 3. I (age< 39 yrs) or 0.08 x age (if age > 40 yrs),

+0.3 x tumour size (in cms),

+ 1 (if incompletely resected),

+ 1 (if locally invasive),

+3 (if distant metastases are present).

Risk categories:

0-5.99 (DFS-20 yrs- 99%);

6-6.99 (DFS-20 yrs- 89%);

7-7.99 (DFS-20 yrs- 56%);

>8 (DFS-20 yrs- 24%).

DE GROOT CLASSIFICATION FOR PAPILLARY CARCINOMA

There are some other classification systems such as the DeGroot classification, SAG risk analysis system and the Mazzaferi staging system used in the risk categorization of papillary carcinomas of the thyroid.

CLASS	EXTENT DISEASE	RELATIVE RISK OF MORTALITY
I	INTRATHYROIDAL	1
II	CERVICAL METASTASIS	1
III	EXTRATHYROIDAL INVASION	5.8
IV	DISTANT METASTASIS	47

MANAGEMENT OF THYROID MALIGNANCIES

Management of differentiated carcinomas of the thyroid

1. **Surgery:**

The key decision in the surgical management of thyroid nodules or cancers is whom to operate on and how extensive a resection to perform.

Extent of thyroidectomy

A long standing controversy among endocrine surgeons has existed regarding the extent of surgical resection for well differentiated thyroid cancer. Technical contributions of surgeons such as Kocher, Lahey, Crile, Perzik, Attie, Thompson and others has established thyroidectomy safe and effective and it is the primary treatment for patients with well

differentiated carcinomas of the thyroid. However, for low risk patients, conflicting views by experts persist. For patients in the high-risk category, there is much less disagreement regarding the extent of the surgery, although there are still some proponents of less than total or near total thyroidectomy.

Acceptable surgical procedures to remove thyroid neoplasm include:

(i) ***Hemithyroidectomy*** (total removal of one lobe and the isthmus).

(ii) ***Sub-total thyroidectomy*** (total lobectomy leaving a rim of 2 to 4 gm of tissue in the upper lateral portion of the contralateral lobe)

(iii) ***Near-total thyroidectomy*** (total lobectomy and subtotal resection on the contralateral side to leave less than 19m of thyroid tissue). (**Hartley-Dunhill procedure)**

(iv) ***Total thyroidectomy***.

The difference between a total thyroidectomy and a near total thyroidectomy usually depends on the particular anatomy of the thyroid in any given patient. There may be a small ledge of thyroid tissue, called the tubercle of Zuckerkandl, at the ligament of Berry that may limit safe resection of the thyroid gland.

Setting apart all the controversies, total thyroidectomy is the treatment of choice for virtually all patients with PTC when postoperative radioiodine therapy is being considered. This basically includes all patients except those with occult PTC < 1 cm). Even in patients with low risk PTC, total or near-total thyroidectomy is associated with lower rates of recurrence and mortality. When a total thyroidectomy cannot be performed without injury to the recurrent laryngeal nerve or parathyroid glands, a near total thyroidectomy is performed and the small amount of thyroid tissue left behind can subsequently be ablated with radioactive iodine. This controversy also exists with follicular carcinomas, with conservative surgeons advocating less aggressive procedures for small tumours < l cm. However in most centers a total thyroidectomy with postoperative radioiodine ablation is performed for all tumours beyond stage I. A combination of total or near-total thyroidectomy and I131 ablation increases the sensitivity of diagnostic I131 total body imaging in the search of metastases and allows the destruction of residual microscopic disease. The removal of normal thyroid tissue is also a prerequisite for postoperative measurements of serum thyroglobulin, a tumour marker used to detect recurrent disease.

ARGUMENTS FOR AND AGAINST CONSERVATIVE AND RADICAL SURGERIES IN WELL-DIFFERENTIATED CANCERS OF THYROID

ISSUE	CONSERVATIVE SURGERY	RADICAL SURGERY
Prognostic risk factors	Systems to define risk can accurately identify patients developing recurrence.	An occasional low risk patient develops recurrence.
Safety of surgery	No risks of permanent Minimal complications with hypocalcemia or recurrent laryngeal nerve injury	Minimal complications with experience surgeons.
Postoperative iodine	If necessary I131 ablation can be accomplished with no morbidity.	Thyroid ablation with I131 is complicated with pain and decreased efficacy with thyroid remnant.
Anaplastic cancer	Local recurrence able to be managed: risk of anaplastic cancer <1%.	Potential for local recurrence with possible dedifferentitation to a more aggressive tumour.
Thyroglobulin Follow-up	Not possible.	
Multicentricity and Recurrence	Tumor multicentricity seems to have little prognostic significance.	Possible and an accurate marker. Eliminates the contralateral cancers at the sites of recurrence

Role of frozen section

There have been few careful reviews of the value of frozen section examination in the management of thyroid cancer. Frozen section is unnecessary when a FNAC diagnosis is either benign or malignant. In case of suspect findings it would be of value and hence it is recommended that frozen section be reserved for lesions with persistently non-diagnostic results on FNA, for confirmation of lymph node metastases and for thyroid nodules diagnosed during surgery and not previously sampled.76 Although the sensitivity of frozen section was only 62.5%, 58.3%, and 75% in benign, suspect and inadequate FNA cases respectively, the technique did permit the identification of some unrecognized malignant lesions at the time of surgery and influenced the extent of resection. The patients are undoubtedly spared of the second surgery to complete a total thyroidectomy when a malignant diagnosis is confirmed. Hence intraoperative frozen section for the thyroid nodular disease can be of value when FNA results are reported as benign, suspect or inadequate, although there are some limitations regarding its sensitivity. When FNA is reported as malignant, frozen section is unnecessary.

TOTAL THYROIDECTOMY – OPERATIVE PROCEDURE

Positioning of the patient

The patient is placed in the supine position with the arms tucked close to the side. A rolled towel is placed vertically between the scapula and beneath the vertebral column so that the shoulders can fall away from the operative field, thus exposing the neck and the upper chest.

Skin incision, exposure of the thyroid

The skin incision is made approximately two finger-breaths above the sternal notch. The lateral borders of the incision can approach the medial borders of the sternocleidomastiod muscle but can be lengthened if the lateral neck is to be investigated. It ordinarily extends laterally to the jugular veins; however it might be necessary to extend the incision depending upon the size of the thyroid gland and the presence of enlarged lymph nodes lateral to the gland. Subplatysmal skin flaps are raised, superior flap extending till the thyroid cartilage and the inferior flap till the sternal notch. Self-retaining retractors are then placed. The strap muscles are separated in the midline for full extent of the operative field. The side of the neck on which the thyroid mass is located should be explored first. If the thyroid mass is invading the strap muscle or is tightly adherent to the muscle the strap muscles can be excised. For adequate

exposure, it is necessary to elevate the thyroid lobe and retract it medially. As the lobe is elevated the adjoining strap muscles are swept away from the gland and retracted laterally. At this point the recurrent laryngeal nerve is identified. It is also important to identify the parathyroids as one prepares to resect the lobe containing the thyroid mass. The lower pair is situated within or immediately adjacent to the thyrothymic ligament and the upper pair is located on the posterior surface of the midportion of the gland surrounded by a lobule of fat close to the point at which the inferior thyroid artery enters the thyroid parenchyma

Resection of the thyroid lobe

The thyroid lobe is retracted medially and arteriorly and the lateral tissues are swept posterolaterally using a peanut sponge. The middle thyroid veins are ligated and divided. The fascia just cephalad to the isthmus is divided. The superior thyroid pole is identified by retracting the thyroid inferiorly and medially, and then the upper pole is mobilised caudally and laterally. The dissection place is kept as close to the thyroid as possible and the superior pole vessels are individually identified, skeletonized, ligated, and divided low on the thyroid gland, to avoid injury to the external branch of the superior laryngeal nerve. The

recurrent laryngeal nerve then should be identified within 1 cm of the crossing of the inferior thyroid artery and the RLN. The lower pole of the thyroid gland should be mobilised by gently sweeping all tissue dorsally. The inferior thyroid vessels are dissected, skeletonized, ligated divided as close to the surface of the thyroid gland as possible, minimize devascularisation of the para thyroids or injury to the RLN. Once the Berry ligament is divided, the thyroid can be separated from the underlying trachea by sharp dissection. If a lobectomy is to be performed the isthmus divided flush with the trachea on the contralateral side and suture ligated. The procedure is repeated on the opposite side for a total thyroidectomy. During the course of total thyroidectomy, every effort should be made to identify the parathyroid glands and if their blood supply cannot be preserved they should be resected and placed in iced saline. These glands are very hard and are viable for hours in this state. If at the completion of the thyroidectomy, it is necessary to remove all four glands, one or more of them should be auto grafted into a muscle bed, most often in the sternocleidomastoid. After ensuring that there is no bleeding in the bed, the strap muscles are then approximated. The platysma is closed with interrupted sutures and then subcuticular suturing is done.

Lymph node dissection

The surgical management of lymph node metastases from well differentiated thyroid cancer is no longer controversial. Gross cervical metastatic disease is treated by modified radical neck dissection, which results in excellent local control and minimal morbidity. Even though 80% of patients with PTC have occult cervical lymph node metastases most of these metastases can be ablated with radioiodine treatment postoperatively, and some does not appear to grow. Central compartment (medial to the carotid sheath) lymph nodes are frequent in word in patients with papillary, medullary and Hurthle cell carcinomas, and should be removed at the time of thyroidectomy, preserving the recurrent laryngeal nerves and parathyroid glands. Central Neck dissection is particularly important in patients with medullary and Hurthle cell carcinoma because of the high frequency of microscopic tumor spread and because these tumors cannot be abalated with I131. An ipsilateral modified radical neck dissection is indicated in the presence of palpable cervical lymph nodes or prophylactically in patients with medullary carcinoma when the thyroid lesion is larger than 1.5 cm. Because contralateral lymph node metastases are uncommon (about 10%) a contralateral neck dissection is performed only when gross evidence of lymph node metastases is found.

RADIOIODINE THERAPY

The postoperative treatment of patients with well differentiated thyroid cancer, particularly relating to radiotherapy, is some what controversial. All patients who have undergone a total or near total thyroidectomy for papillary or follicular Carcinoma larger than 1 to 1.5 cm should be considered candidates for radio iodine ablation. I131 ablation decreases tumor recurrence, development of distant metastases, and cancer death. Some studies have failed to detect an enhanced survival with the use of radio iodine ablation, particularly in low risk patients as defined by AMES criteria The majority of follicular cell derived differentiated thyroid carcinomas (75% or more) retain the capacity to take up and concentrate iodine, although frequently rather less efficiently than normal thyroid tissue.

Mode of action:

Administered orally, iodine isotopes are absorbed rapidly and reliably from the upper gastrointestinal tract, circulate in the bloodstream and concentrated in the tissues that express a functional sodium iodine transporter (NIS). These tissues include normal and cancerous thyroid tissue, salivary gland, breast, stomach and the colon. This NIS is also

expressed in the kidney, which transports and filters iodine arid circulating iodine is excreted rapidly through the urine and stool.

The uptake of iodine into both normal and cancerous thyroid tissue is dependant on TSH and hence a hypothyroid state has to be created when I131 uptake is needed. The treatment of thyroid carcinoma with radioiodine depends upon the emission of β-particles emitted by the decay of radioiodine. These moderate and high-energy β-particles travel only short distances, on an average around 0.5 cm. They result in ionization and generation of superoxide radicals, which cause DNA damage. As the cancer cells lack efficient mechanisms to repair double strand breaks in the DNA the thyroid cancer cells are more susceptible to the effects of P radiation. The serum TSH levels, amount of residual normal thyroid tissue, degree of differentiation of the PTC and the patient's age all affect the amount of radioactive iodine uptake

Complications of High dose Therapy with I131

The most common side effects from radio iodine therapy include sialadenitis, nausea, and temporary bone marrow suppression. Testicular function and spermatogenesis are transiently impaired but appear to recover with time. There is a dose dependent in relationship between I131 therapy and the development of leukemia. A higher incidence of bladder

carcinoma has been seen in patients who have received high cumulative doses of radio iodine. Pulmonary side effects include pneumonitis and pulmonary fibrosis.

External radiation therapy

Conventional radiation therapy may be detrimental to the success of radioiodine therapy in thyroid adenocarcinoma and should not precede therapeutic efforts with radio iodine. External radiation therapy is the management of thyroid cancer has been preserved for anaplastic carcinoma and lymphoma and differentiated cancer that does not concentrate radioiodine. Beneficial results with 35 to 70 Gy have been reported in the treatment of local recurrence in some differentiated cancers that did not take up radio iodine. In older patients with invasive papillary cancer and positive lymph nodes, 50-60 Gy external radiation significantly reduced the 10 year recurrence rate.

Postoperative follow up

The follow up of patients with differentiated thyroid carcinoma include physical examination, monitoring of thyroglobulin levels, I131 whole body scanning, radiographic imaging and functional nuclear imaging.

1. I131 whole body scan:

Whole body scan is most sensitive when there is minimal remnant thyroid tissue. Significant amounts of thyroid tissue may result in failure to detect metastatic disease. Tumours that are poorly differentiated, tumours in older patients and particularly Hurthle cell carcinoma may not concentrate iodine; this limits the usefulness of whole body thyroid scan. Patients stop using thyroid hormone 3 to 6 weeks before scanning to induce hypothyroidism. They are then administered tracer doses of I131, usually 1 to 5 mCi. There occurs a stunning effect of doses above approximately 3 mCi, which results in reduced intake of subsequent doses of I131. Consequently for whole body scanning, doses of 3 mCi are nowadays used. These scans are repeated at regular intervals for duration depending on the risk of the patient.

2. Serum thyroglobulin:

Thyroglobulin is a large glycoprotein that is synthesized by the follicular cells and secreted and stored in the colloid lumen, where it is iodinated. Later it is reabsorbed by the follicular cells, hydrolyzed and released as thyroid hormone. It is detectable in the serum in 75% to 90% of healthy adults (normal levels- 0 to 30 ng/ml). After a total thyroidectomy, serum thyroglobulin is expected to be low or

undetectable. Detectable TSH indicates either residual thyroid tissue or recurrent differentiated thyroid cancer. The magnitude of thyroglobulin levels may be related to the tumour mass, degree of differentiation and the location of the metastases. A thyroglobulin level of 2 ng/ml or more in euthyroid patients and above 10 ng/ml in hypothyroid patients usually indicates recurrent differentiated thyroid carcinoma.

3. Ultrasound:

Ultrasound (USG) is commonly used in the postoperative management of thyroid carcinoma to detect local or regional disease recurrence. Advantages include the ability to detect non-palpable recurrent disease and the ability to perform a simultaneous USG-guided FNA for diagnosis. USG does not use ionizing radiation, does not require thyroxin withdrawal and it may detect recurrent disease in approximately 10% of cases in whom serum thyroglobulin in false negative. It may be useful in patients in whom thyroglobulin measurement is not reliable.

4. Magnetic resonance imaging (MRI):

MRI is sometimes used in the follow up of patients with differentiated thyroid carcinoma to detect the local or regional recurrence

when serum thyroglobulin is elevated, and other testing like I131 whole body scan fail to localize disease recurrence.

5. Positron emission tomography (PET):

It is now clear that poorly differentiated carcinomas are much more likely to concentrate F18-Fluorodeoxyglucose than I131. Hence the PET is found to be 50% to 85% sensitive in the localization of thyroid cancer that does not concentrate I131 but whose presence is known secondary to elevated levels of thyroglobulin. Identification of these metastatic sites by FDG scanning may lead to significant alteration in the management of these patients.

Postoperative thyrotropin suppression

Thyroid stimulating hormone (TSH) acts as a potential growth factor on any thyroid tissue remaining after surgical or radioactive iodine treatment. Therefore suppression of TSH levels should be achieved with comparatively high doses of oral T4 continued for life, with attention to the potential thyrotoxic effects such as atrial fibrillation and cardiac compensation. Even though TSH controls the thyroid gland function, its role in the tumourigenesis is unclear. But most investigators have reported an improved survival and lower recurrence rate in patients with

TSH suppressive therapy. The standard dose prescribed after a total thyroidectomy is 0.1 to 0.2 mg daily. Failure of TSH suppression to a level <0.1 mU/.L indicate an inadequate dose of thyroxine. Suppressive dose of thyroxine is probably not of value in follicular carcinoma and is unlikely to be of benefit in low-risk patients treated with lobectomy.

METHODOLOGY

Source of data

Cases admitted as inpatients in various surgical wards in Madras Medical College and RGGGH with signs and symptoms of carcinoma thyroid, who are clinically evaluated and confirmed by FNAC were chosen for study.

Methods of collection of data:

- A Performa for study of all consecutive patients of carcinoma thyroid was used. The presentation, clinical findings, investigations and line of management were documented.

- Between JULY 2012 – DECEMBER 2012 , 30 cases of carcinoma thyroid were selected on the basis of simple random sampling technique and clinically evaluated.

- The patients confirmed by FNAC were subjected to surgery .

- The patients were followed up a month after surgery and underwent thorough clinical examination, investigative procedures like chest X-ray, thyroglobulin assay, radioiodine scan for locoregional recurrence or distant metastasis.

Inclusion criteria

The patients presenting with symptoms and signs of carcinoma thyroid and diagnosed by FNAC in various surgical wards in MMC & RGGGH were selected.

Exclusion criteria

1. Patients with benign thyroid disorders

2. Patient who refused any mode of treatment.

3. Patients less than 12 years of age.

4. Patients who have previously been treated surgically for any thyroid ailments.

Mode of selection

All patients admitted to Madras Medical College & RGGGH during the course of study, who have positively diagnosed as having thyroid malignancies by investigations have been selected. The study required certain investigations to be conducted on the patient viz. routine blood investigations, thyroid function tests when needed, x-ray chest and neck, fine needle aspiration and cytological diagnosis. Indirect laryngoscopy was done in all patients to determine the status of the vocal

cords specifically their movements. The study also required certain intervention to be conducted on patients like biopsy for diagnosis as in case of lymphoma or anaplastic carcinomas. All the investigations and interventions were done only after the proper consent from the patients.

Statistical tests

The statistical tests used in this study are the test of proportion and percentage.

Fig 13 ANAPLASTIC CA THYROID

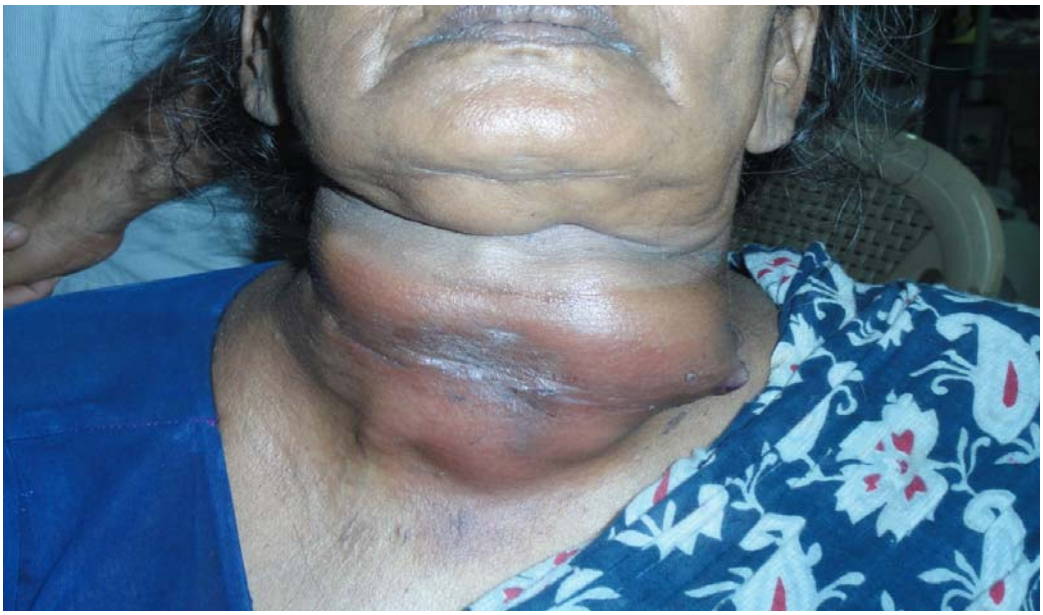


Fig 14 FOLLICULAR CA THYROID

RESULTS

The study consists 30 cases of proven thyroid carcinoma who were admitted in various surgical wards during the period July 2012 to December 2012 in MMC & RGGGH, CHENNAI.

INCIDENCE OF THYROID CARCINOMA

In the study period; 1965 patients were admitted in MMC & RGGGH with different types of malignant diseases (Medical Records Division, MMC & RGGGH, CHENNAI) of which thyroid cancer constitutes 1.53% (30 out of 1965).

AGE INCIDENCE

Table 1: Age incidence in thyroid malignancies

Age (in years)	No of cases	Percentage
0-9	0	0
10-19	1	3
20-29	6	20
30-39	11	36
40-49	6	20
50-59	2	7
60-69	2	7
70-79	2	7
80-89	0	0
90-99	0	0

Figure 15 : Age incidence

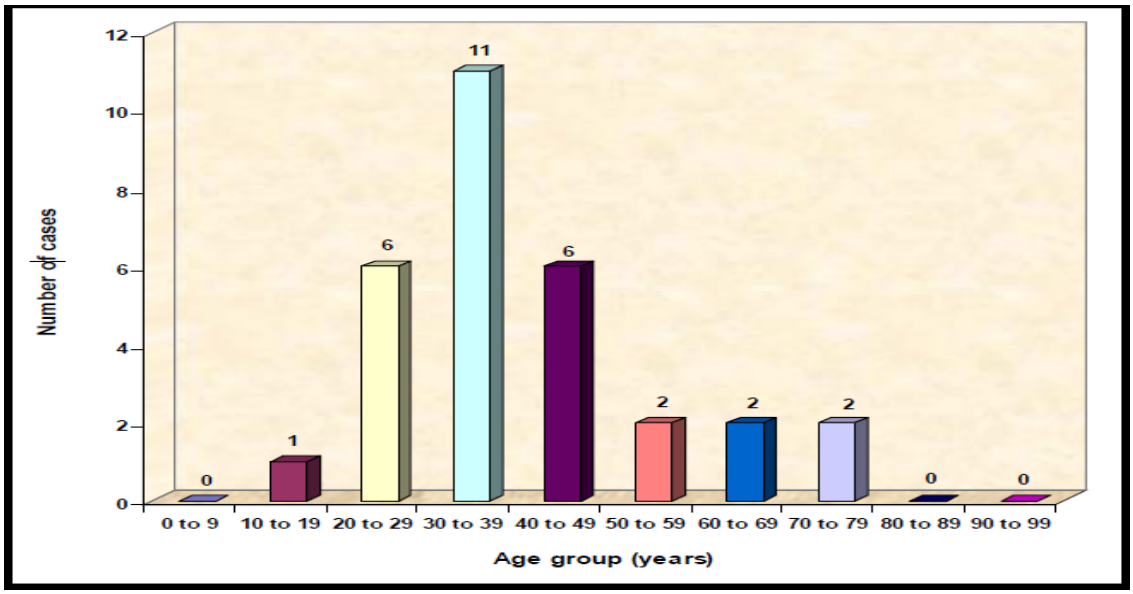


Table 2: Age incidence in different thyroid malignancies

Age(yrs)	Papillary	Follicular	Medullary	Anaplastic	Lymphoma
0-9	0	0	0	0	0
10-19	1	0	0	0	0
20-29	5	1	0	0	0
30-39	8	3	0	0	0
40-49	4	2	0	0	0
50-59	1	1	0	0	1
60-69	1	0	0	1	0
70-79	1	0	0	0	1
80-89	0	0	0	0	0
90-99	0	0	0	0	0

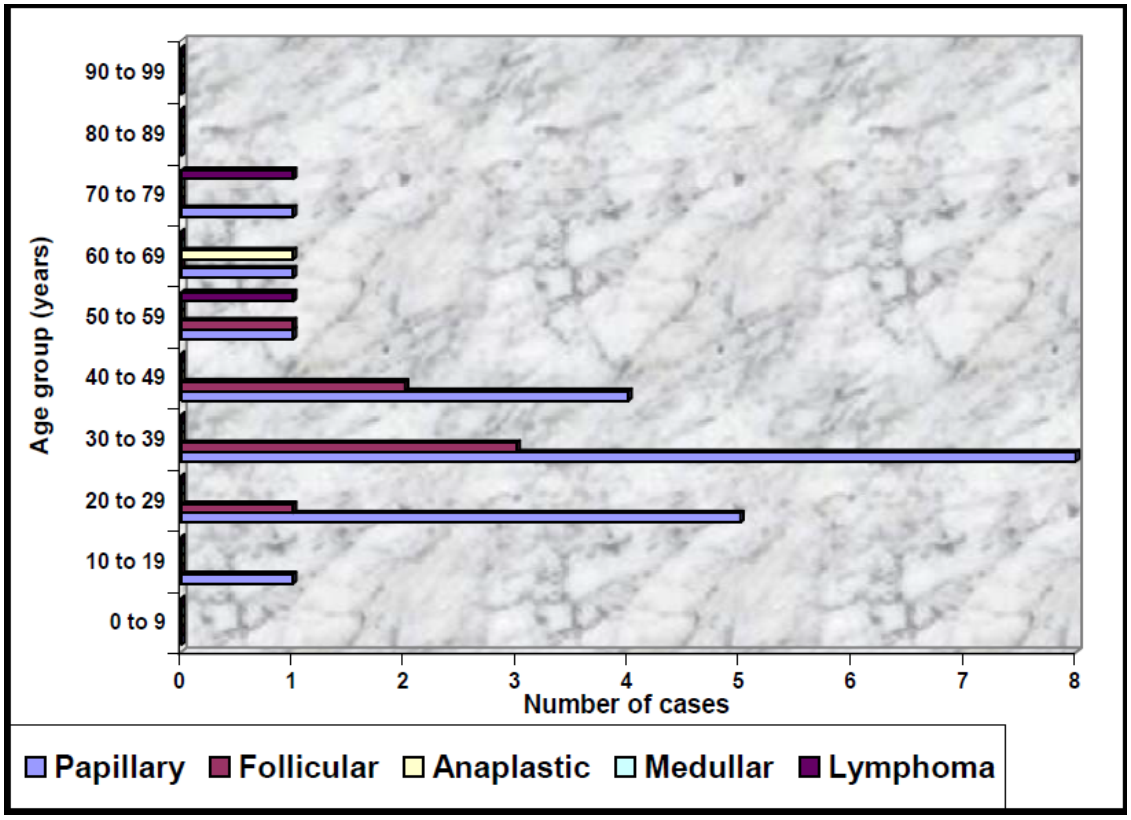


Fig 16 : Age Incidence In Thyroid Malignancies

In this series, it was found that thyroid carcinoma is commonly seen in the age group of 30-39 and the common type of malignancy seen is the papillary thyroid carcinoma. The most commonest histological type (i.e. papillary carcinoma) is also common in fourth decade.

Sex incidence:

1. Number of female patients – 25

2. Number of male patients – 5

Table 3: Sex incidence in relation to type of malignancy

TYPE	FEMALE	MALE	PERCENTAGE
PAPILLARY	17	4	21(70%)
FOLLICULAR	6	1	7 (23%)
ANAPLASTIC	1	0	1(3%)
MEDULLARY	0	0	0
LYMPHOMA	1	0	1(3%)
TOTAL	25	5	30

Male to female ratio was 5:1 in the study.

FIG 17 Sex incidence in thyroid malignancies

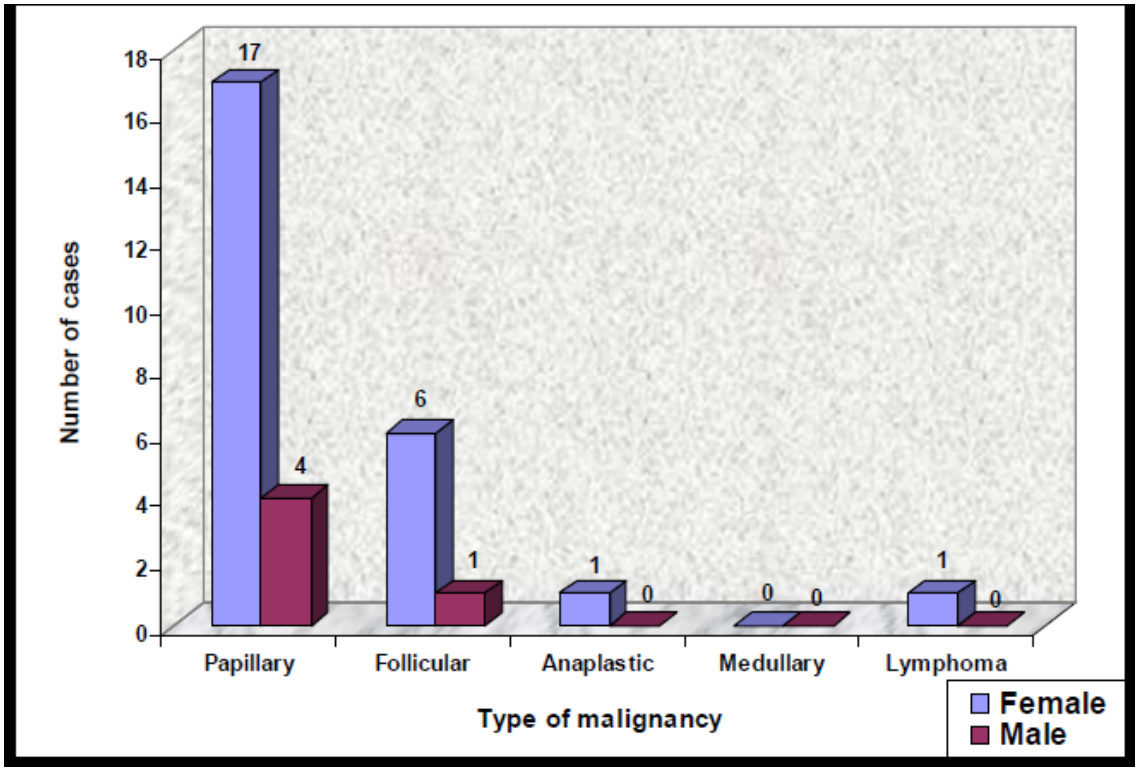
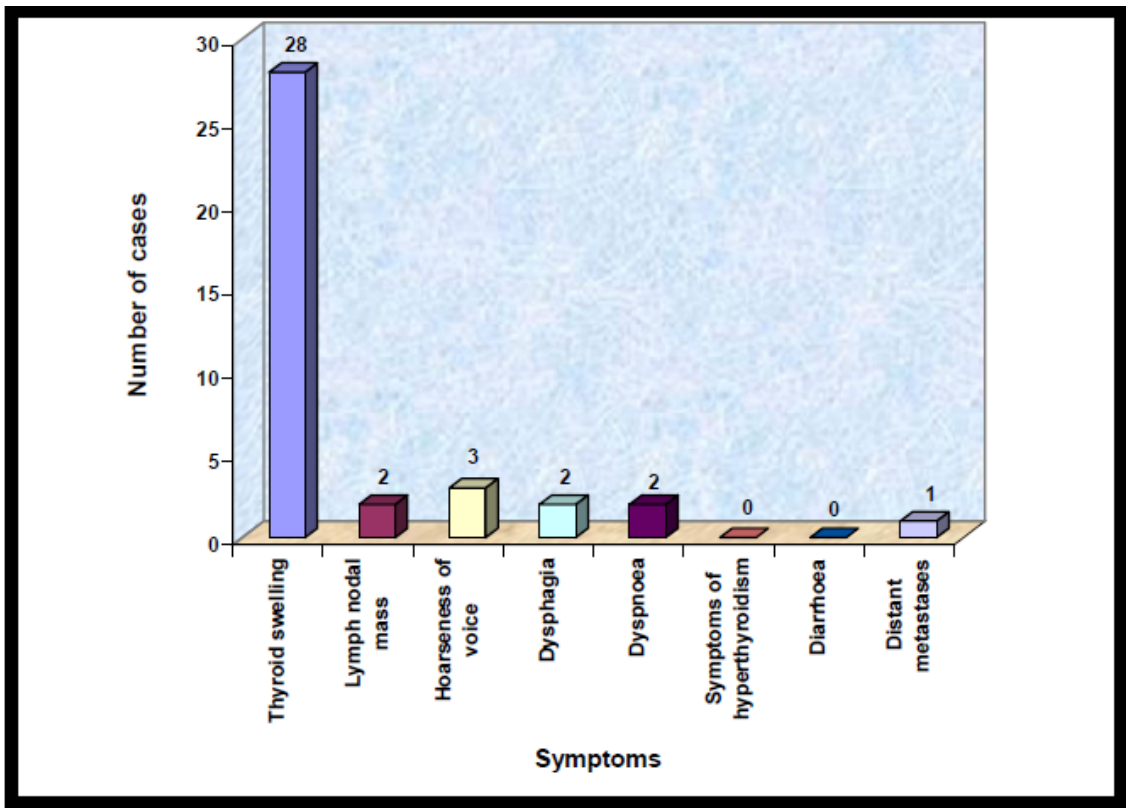


TABLE 4: Clinical features in thyroid malignancies

SYMPTOMS	NO OF CASES	PERCENTAGE
THYROID SWELLING	28	93
LYMPH NODE MASS	2	7
HOARSENESS	3	10
DYSPNEA	2	6
DYSPHAGIA	2	6
HYPERTHYROIDISM	0	0
DIARRHOEA	0	0
DISTANT METASTASIS	1	3

FIGURE 18 : Clinical features of thyroid malignancy



In study, patients predominantly presented with swelling of the thyroid (93%), followed by hoarseness of voice (10%). Most common pressure effect is hoarseness of voice, which was present in 10% of the patients. Only 6% of patients in study had symptoms of dyspnoea and dysphagia, and 3% had presented with distant metastases.

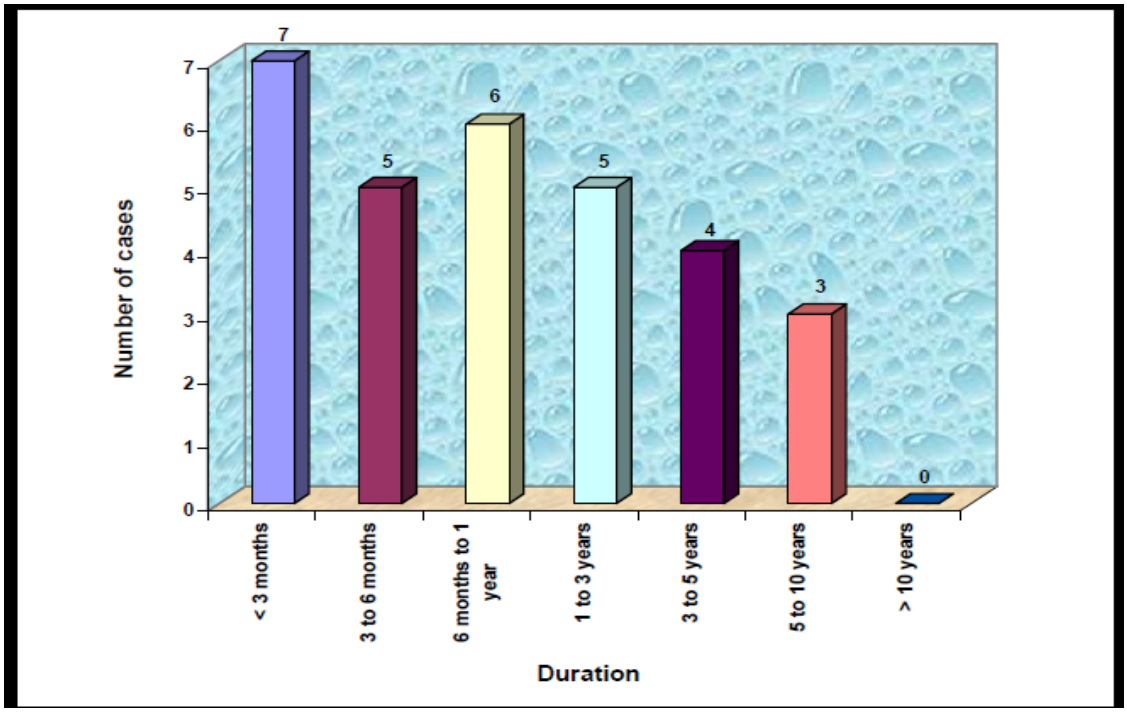
Duration of Thyroid Swelling

Of the 30 patients who presented with thyroid swelling most of the patients noticed the swelling in a period less than 3 months (23%). Sixty percent of the patients presented with swelling of less than one year duration.

TABLE 5: Duration of thyroid swelling in thyroid malignancies

Duration	Number of cases	Percentage
< 3 months	7	23
3 to 6 months	5	17
6 months to 1 year	6	20
1 to 3 years	5	17
3 to 5 years	4	13
5 to 10 years	3	10
> 10 years	0	0

FIGURE 19 : Duration of thyroid swelling in thyroid malignancies



Indirect Laryngoscopy

Indirect laryngoscopy done in the patients under study revealed vocal cord palsy in four of the patients. Three had papillary carcinomas and all of them underwent near-total thyroidectomy and the other was follicular variant of papillary carcinoma thyroid.

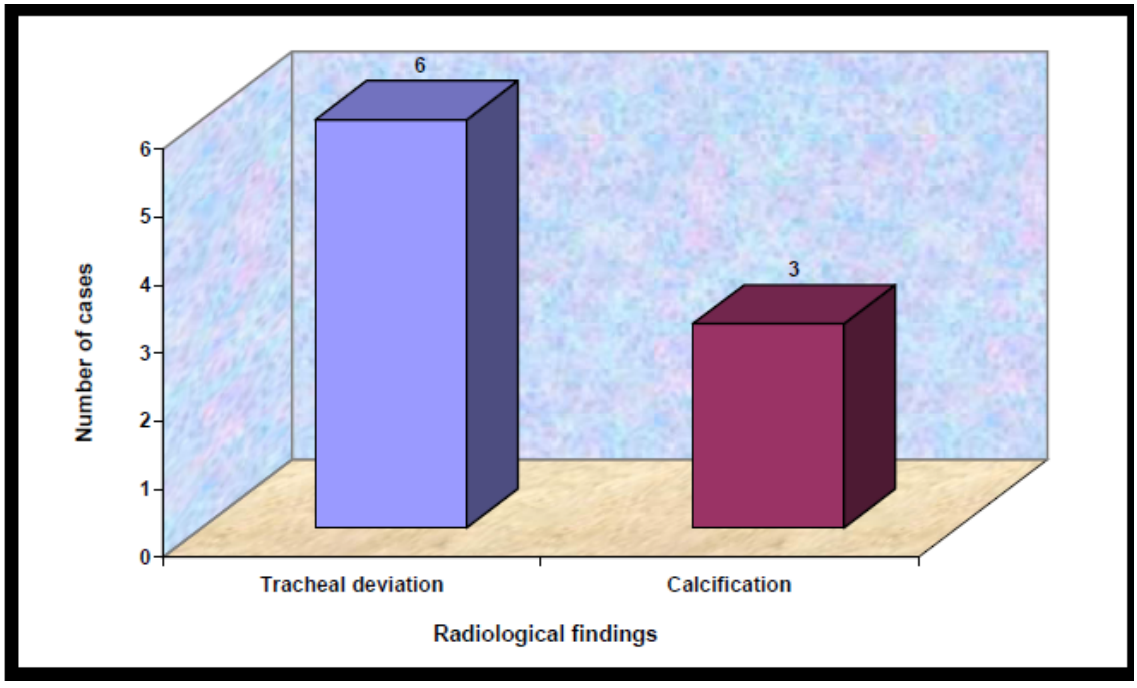
Radiological findings

Radiograph of the neck is made in the antero-posterior and the lateral views. The radiograph in 6 of the patients showed tracheal deviation and it showed calcifications in 3 of the patients. The rest of the patients showed normal radiograph of the neck.

TABLE 6 : Radiological findings

Radiological findings	Number of cases	Percentage
Tracheal deviation	6	20
Calcification	3	10

FIGURE 20: Radiological findings



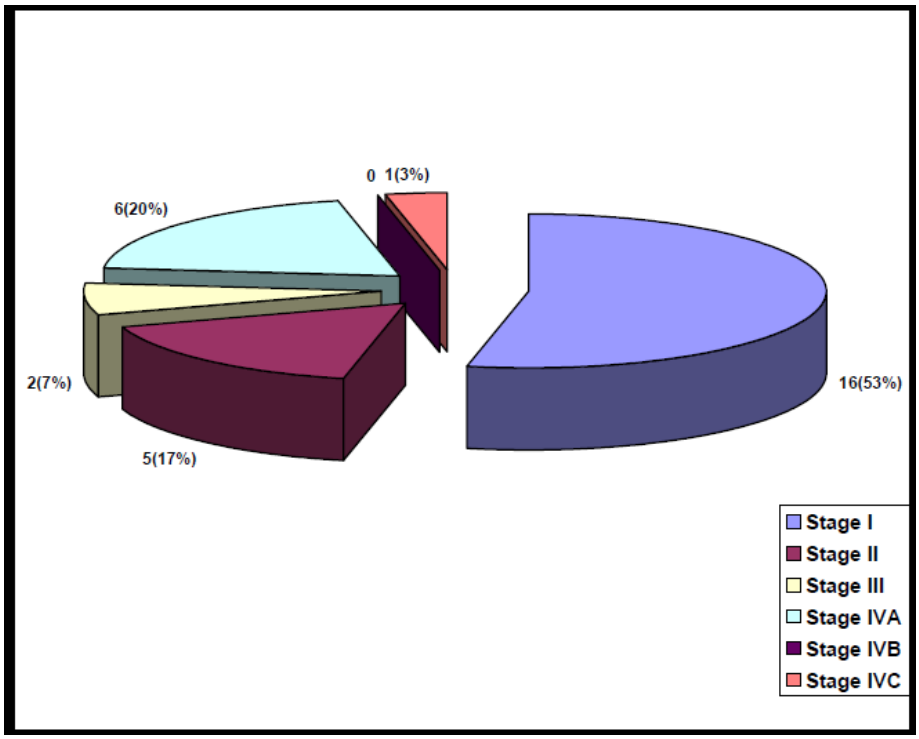
Staging

The patients were staged based on the AJCC 2002 staging system and the results are as follows

TABLE 7 Staging Of Thyroid Malignancies

Staging	Number of cases	Percentage
Stage I	16	53
Stage II	5	17
Stage III	2	7
Stage IVA	6	20
Stage IVB	0	0
Stage IVC	1	3

FIG 21 Staging Of Thyroid Malignancies



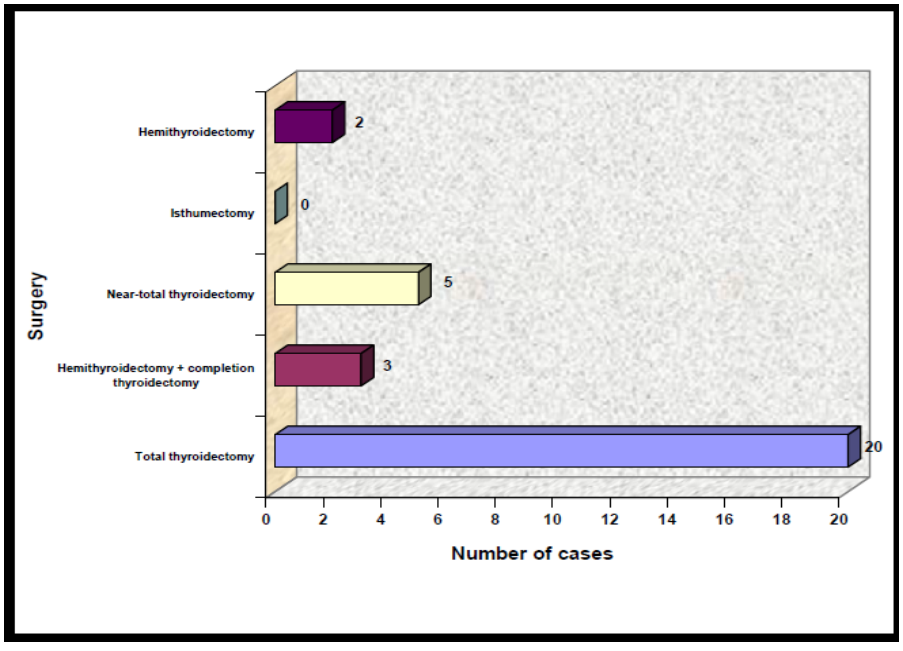
Most of cases after investigations and pathological reporting were found to be Stage I (53%) as most of patients in the study had differentiated thyroid carcinomas and most of them were below 45 years of age. Stage IVA was the next commonly seen stage of the disease and the patients constituted 20% of the patients in the study.

SURGICAL TREATMENT

TABLE 8: Surgery for the primary disease

Surgery	Number of cases	Percentage
Total thyroidectomy	20	67
Hemithyroidectomy + completion thyroidectomy	3	10
Near-total thyroidectomy	5	17
Isthumectomy	0	0
Hemithyroidectomy	2	6

Fig 22 Surgery For Primary Disease



The most commonly performed surgery in the study was total thyroidectomy. Twenty 20 patients (67%) underwent total thyroidectomy. Most of these patients were proven papillary carcinoma on cytology or suspicious of malignancy during surgical procedure. The patients 3 in number (10%), whose cytology turned out to be follicular neoplasm, and with a solitary nodule, initially underwent hemithyroidectomy, and later a completion thyroidectomy after the histopathological report. Five of the patients in the study had infiltration of the recurrent laryngeal nerve by the tumour and these patients underwent a near-total thyroidectomy leaving minimal thyroid tissue adjoining the recurrent laryngeal nerve. Two of the patients with follicular neoplasm underwent initially a hemithyroidectomy and their histological report was follicular carcinoma. However in view of their low-risk status and the associated poor medical condition the patient was advised follow-up.

Surgery for Nodal Secondaries

Three of the patients who presented with cervical lymphadenopathy underwent functional neck dissection for level II, III and IV group of cervical lymph nodes.

PATHOLOGY

FNAC Results

Both FNAC and biopsy were done in 475 cases during the study. The results are as follow

TABLE 9 FNAC RESULTS

FNA diagnosis	Histological diagnosis		Total
	Carcinoma	Benign	
Inadequate	0	15	15
Benign	8	370	378
Follicular neoplasm	0	54	54
Papillary carcinoma	21	5	26
Medullar carcinoma	0	0	0
Anaplastic carcinoma	1	0	1
Lymphoma	1	0	1
Total	31	444	475

FIG 23 FNAC RESULTS

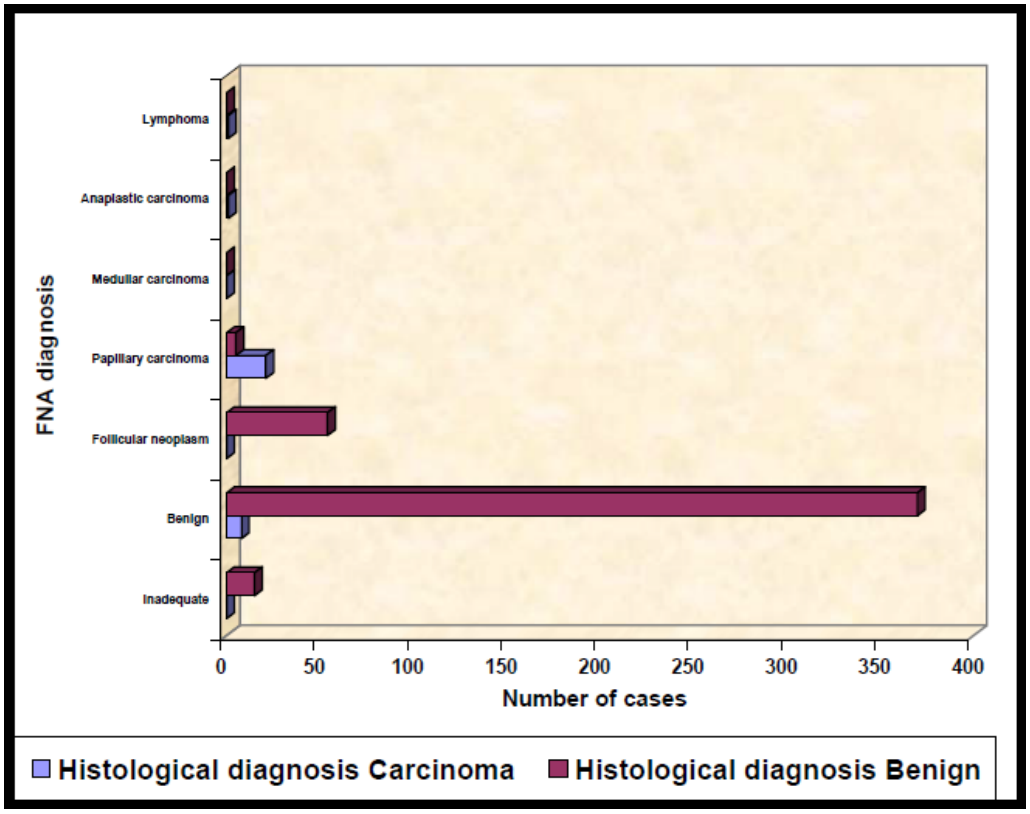


Table 10: Statistical methods

Test evaluated	Histology	
	Carcinoma	Benign
FNA positive	True positive 21 cases	False positive 5 cases
FNA negative	False negative 8 cases	True negative 370 cases

Reporting of follicular neoplasm is taken as inconclusive and excluded from the statistics. Total of 475 cases underwent both FNAC and biopsy. Out of this, 19 FNA were reported as inadequate material. In another 54 cases the FNAC report was follicular neoplasm. All of them turned out benign, either follicular adenoma or other benign lesion.

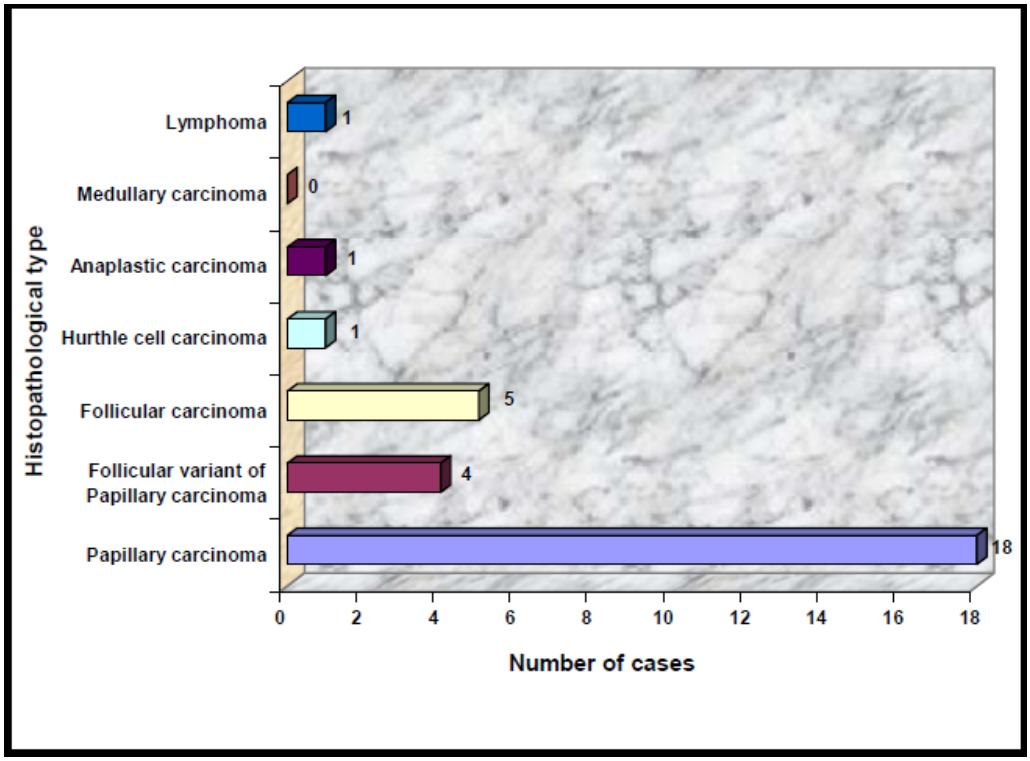
Histopathological Results

Four of the patients with papillary carcinoma had the histology of follicular cell variant type. The predominant variety is papillary carcinoma (61%) and the next common type in the study is follicular carcinoma. None of the other variants of papillary and follicular carcinomas were found in the histopathological study.

TABLE 11: Histopathological types of thyroid carcinoma

Histopathological type	Number of cases	Percentage
Papillary carcinoma	18	61
Follicular variant of Papillary carcinoma	4	13
Follicular carcinoma	5	17
Hurthle cell carcinoma	1	3
Anaplastic carcinoma	1	3
Medullary carcinoma	0	0
Lymphoma	1	3
Total	30	100

FIG 24 Histopathological types of thyroid malignancies



Lymph Node Involvement

Two patients with papillary carcinoma thyroid had lateral cervical group lymphadenopathy (lever III and IV).

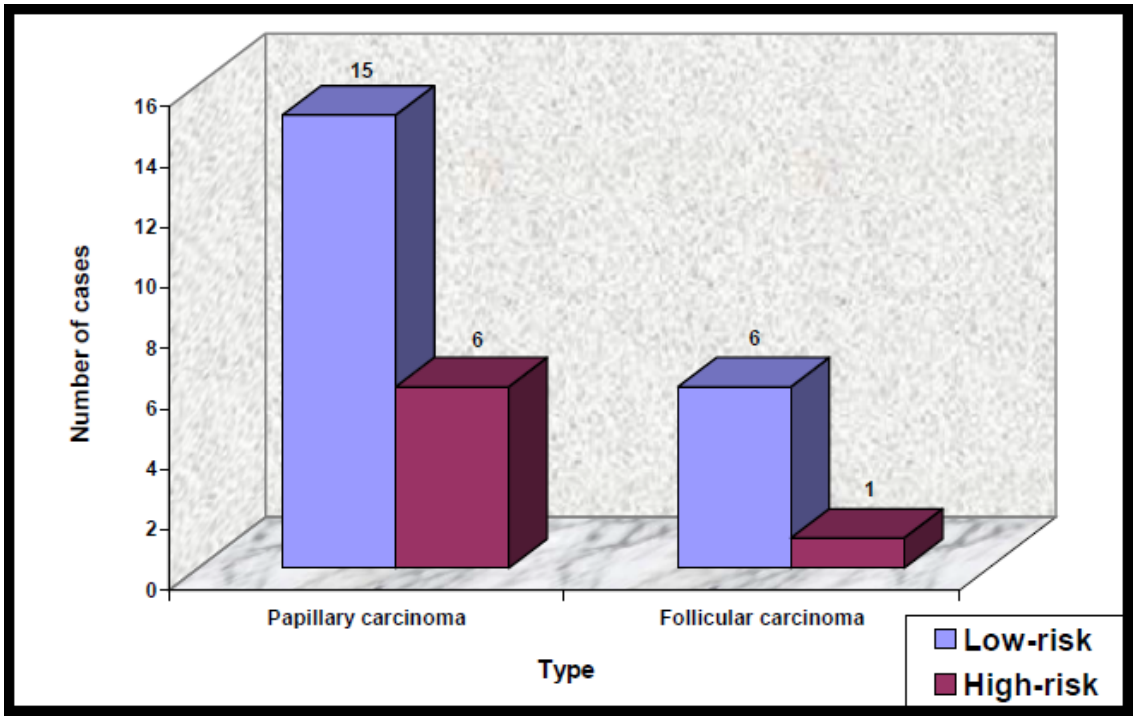
Risk Categorization

Among the 30 patients III the study 28 patients had well differentiated carcinomas of follicular cell origin. These patients were categorized into low and high risk groups based on the AMES categorization scheme.

TABLE 12 AMES categorization scheme for well-differentiate carcinomas

Type	Low-risk	High-risk
Papillary carcinoma	15 (71%)	6 (29%)
Follicular carcinoma	6 (86%)	1 (14%)
Total	21 (75%)	7 (25%)

FIG 25 AMES categorization scheme for well-differentiated carcinomas



When all patients with well-differentiated thyroid carcinomas were considered 75% of the patients were of the "low-risk" category and 25% were of the "high-risk" category. If patients with papillary thyroid carcinomas are alone considered 71% are of "low-risk" and 29% are of "high-risk" categories. 86% and 14% of follicular carcinoma patients were of "low" and "high" risk categories.

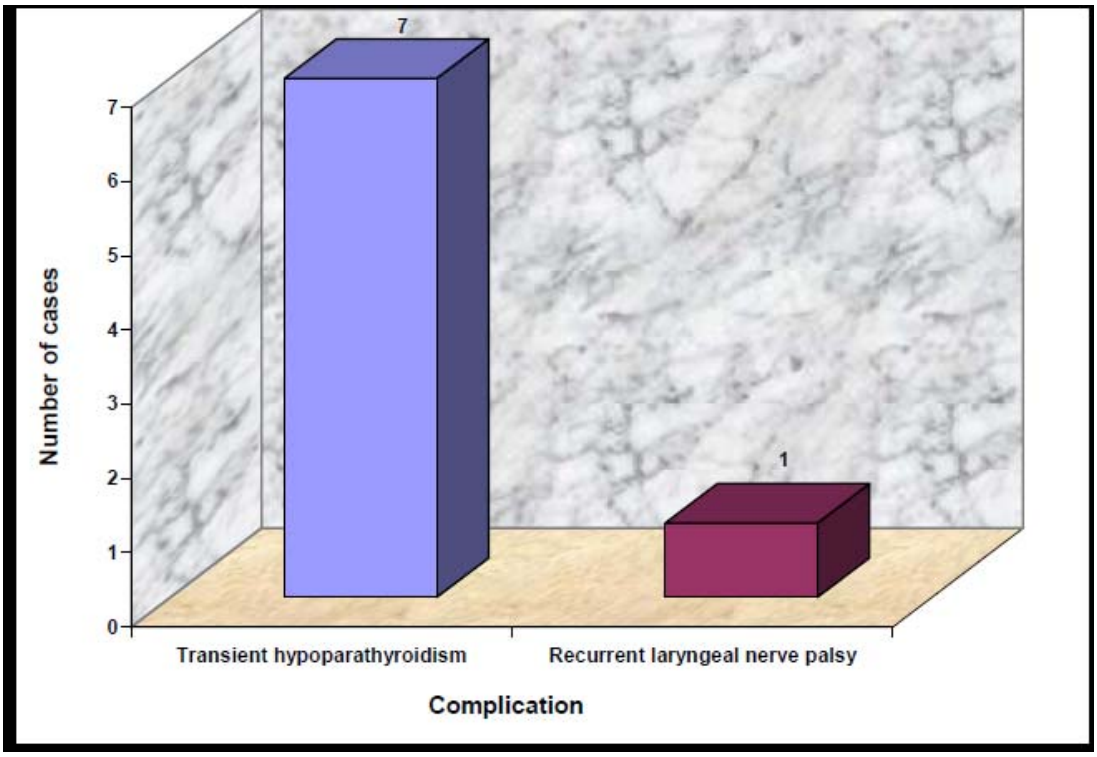
Complications of Surgery

All the patients were observed in the immediate post-operative period. The patients underwent indirect laryngoscopy in case they complain of hoarseness of voice, and the serum calcium was estimated if the Trousseau's sign (inducing carpopedal spasm by occlusion of the arm with a blood pressure cuff for 3 minutes) was positive.

TABLE 13 Complications of surgery

Complication	Number of cases	Percentage
Transient hypoparathyroidism	7	27
Recurrent laryngeal nerve palsy	1	3

FIG 26 Complications of surgery



All symptomatic hypocalcemic patients were treated with 10 ml of 10% calcium gluconate slow i.v. Less severe cases were treated with oral calcium supplements along with vitamin D. All the patients recovered in the immediate postoperative period. One patient suffered recurrent laryngeal nerve palsy postoperatively. None of the patients had wound infection. Among the patients who came for regular follow up none of the patients developed hypocalcemia on a long term.

POST OPERATIVE ADVICE

One patient who had anaplastic carcinoma was advised to undergo external beam radiotherapy. One patient who had lymphoma (NHL) was advised to undergo combined chemotherapy and external radiotherapy. All patients were started on the thyroxine therapy postoperatively.

DISCUSSION

INCIDENCE

In the TATA MEMORIAL HOSPITAL, MUMBAI, thyroid malignancies constituted 1.5% of all malignancies admitted in the year 1999. In the present Study thyroid malignancies accounted for 1.53% of all the malignancies admitted in MMC & RGGGH. In study conducted at ADYAR CANCER AND RESEARCH INSTITUTE, CHENNAI(2006 – 2008), thyroid malignancies formed about 2.16 % of all cases of malignancies.

TABLE 14: Incidence of thyroid malignancies – comparison

THYROID MALIGNANCIES	TATA MEMORIAL HOSPITAL	PRESENT STUDY	ADYAR CANCER INSTITUTE
PERCENTAGE OF TOTAL MALIGNANCIES	1.5 %	1.53%	2.16%

AGE INCIDENCE

Dave RI et al. (1983) and Bansali et al. (1979) have studied the age incidence of thyroid carcinoma and have reported that the commonest age group affected is the 5th and the 6th decade respectively. In the present

study the 4th decade is commonly affected. This may be due to the increased awareness among the people in recent days.

SEX INCIDENCE

The study conducted in England and Wales in 1993 to know the sex ratio of hormone dependant cancers by Dos Santos Silva and Swerdlow showed that thyroid cancer is predominantly seen in women in a ratio of 3:1. In the present study the sex ratio of thyroid malignancies is found to be 5:1.

CLINICAL FEATURES

The predominant symptom in the present study was thyroid mass which was also the predominant symptom in the study conducted by Simon Holzer et al. in 1996 in Germany and published in 2000; which was also the predominant symptom in Kannan RR study of 670 Cases of carcinoma thyroid from 1956 to 1996 in cancer institute, Madras.

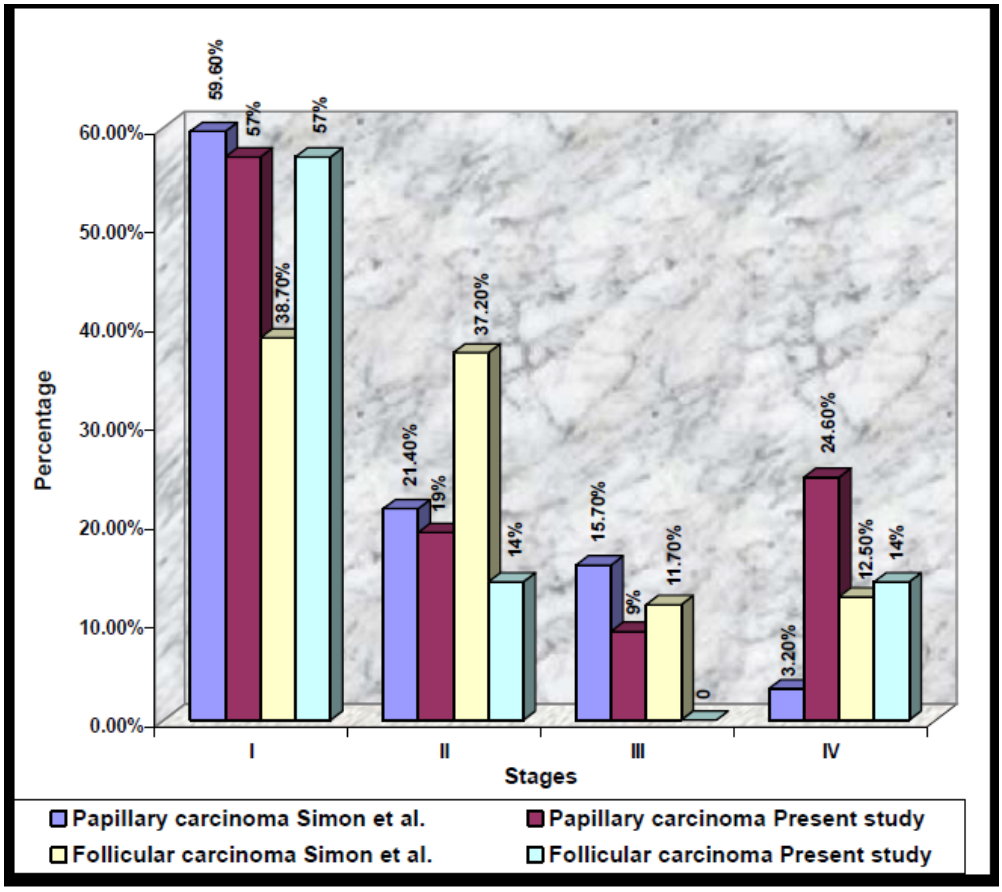
TABLE 15: Clinical features of thyroid malignancies – Comparison

Symptoms	Simon et al.[106]	Kannan RR[107]	Present study
Thyroid swelling	77%	84%	93%
Lymph nodal mass	5.6%	42%	7%
Hoarseness of voice	4.6%	14%	10%
Dysphagia	25%	8.9%	6%
Dyspnoea	10.5%	3%	6%
Distant metastases	0	12%	3%

STAGE OF THYROID CARCINOMA

In a study conducted by Simon et al. in 2000 the differentiated thyroid carcinomas were staged and their percentages were calculated. The table shows that percentage of Stage I and Stage II were almost similar in case of papillary carcinoma in two studies. But the incidence of stage IV disease was more in present study. In case of follicular carcinoma the present study showed predominant stage I disease which formed 57% of follicular carcinoma. In the present study, one patient of follicular carcinoma presented with stage IV. This difference may not be significant as only 7 cases of follicular carcinoma were reported.

FIG 27 Stages of thyroid carcinomas in different studies



PATHOLOGICAL DISTRIBUTION

In the present study the papillary carcinoma was the most common type of thyroid malignancy seen in the hospital accounting for about 70 of the cases. In the study conducted by Simon et al., papillary thyroid carcinoma formed about 66.4% of the study. The proportions of deferent types of thyroid malignancies in the present study are similar to dose in the study conducted by Simon et al. The reason for the increased

incidence of anaplastic carcinoma could be the long term negligence of the thyroid swelling, which would have gone for dedifferentiation.

FIG 28 Various types of thyroid malignancies – Comparison

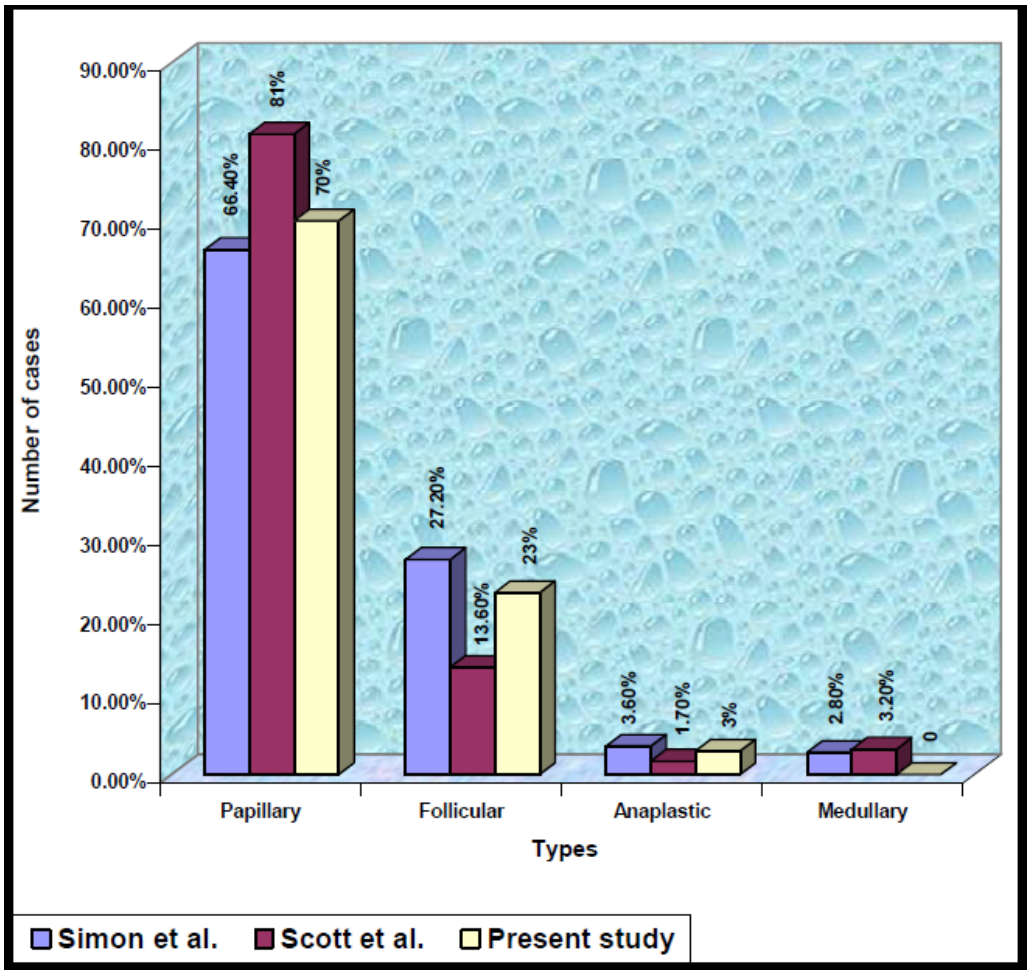
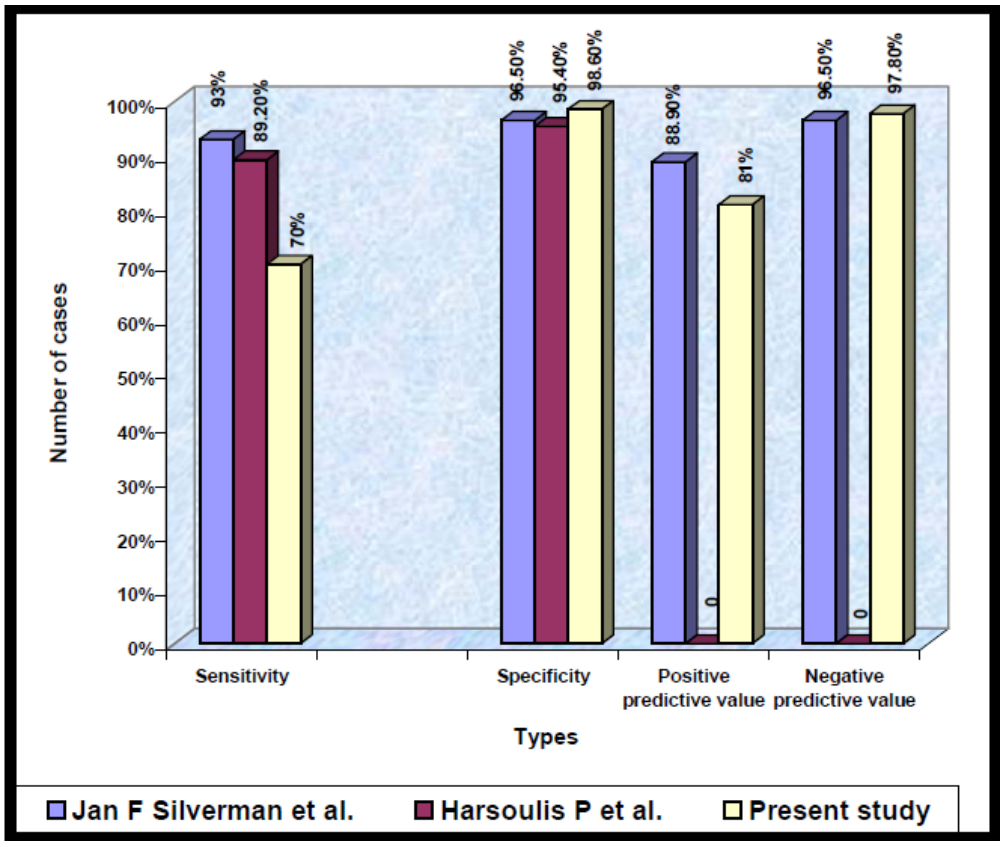


TABLE 16 Correlation of FNAC with Histopathology – Comparison

	Jan F Silverman et al.[109]	Harsoulis P et al.[110]	Present study
Sensitivity	93%	89.2%	70%
Specificity	96.5%	95.4%	98.6%
Positive predictive value	88.9%	0	81%
Negative predictive value	96.5%	0	97.8%

FIG 29 Correlation of FNAC with Histopathology – Comparison



The specificity in the present study is 98.6% which is comparable to the specificity in the studies conducted by Jan F Silver man et al. and Harsoulis P et al. Sensitivity of the present study is 70% which is lower than the other two studies. The low sensitivity in the present study could be due to sampling error. The positive and negative predictive value of the present study are similar to the results in the other two studies. A study at Ankara Oncology Education and Research Hospital, Ankara, Turkey, where 650 patients underwent thyroid surgeries and their cytological and

FNAC reports were correlated.

- Sensitivity - 90%
- Specificity - 79%
- False negative - 2%

Surgery for Thyroid Carcinoma

Total thyroidectomy remained as the most commonly done surgery either primarily or as a completion procedure in the present study. Gulliamondegui et al. (1983) reported that total thyroidectomy was the most commonly performed surgery for thyroid carcinoma.

Lymph Node Involvement

In the study done by Simon et al.106 cervical lymph node involvement was found in 6.6% of papillary carcinomas and 3.3% of follicular carcinomas. In the present study none of the patients with follicular carcinomas had cervical lymph nodal involvement, and all the patients who had such involvement had papillary carcinomas

TABLE 17 Incidence of lymph node metastases in various types of thyroid carcinoma

	Papillary carcinoma		Follicular carcinoma	
	Simon et al.[106]	Present study	Simon et al.[106]	Present study
LN metastases	6.6%	7%	3.3%	0

CONCLUSION

1. The incidence of thyroid malignancy in the present study is 1.53% comparable to incidence in other parts of India.

2. The incidence of thyroid cancer is higher in female when compared to those reported in the literature.

3. The most common mode of clinical presentation was thyroid swelling which was higher than those in comparative study.

4. FNAC is an inexpensive accurate and practical investigation for evaluation of thyroid carcinomas.

5. The accuracy of FNAC to diagnosing thyroid cancer was similar to that reported in literature. The low sensitivity may be due to sampling error.

6. The proportion of different histopathological types of thyroid cancer were similar to those reported in literature.

7. The most common complication was transient hypoparathyroidism which resolve with calcium supplementation.

SUMMARY

A total number of 30 patients with thyroid cancer were evaluated in the study period from JULY 2012 to DECEMBER 2012 IN MMC & RGGGH. A brief introduction and historical review of thyroid cancer has been presented with a detailed review on surgical anatomy, pathology, clinical evaluation, investigations including FNAC and management.

The findings of the study are as follows:

1. Thyroid malignancies constitute **1.53% to 2%** of all malignancies.
2. The occurrence of thyroid cancer was maximum in the **4th decade of life**.
3. Female patients outnumbered males with a ratio **of 5: 1.**
4. Commonest symptom of thyroid malignancy was **a painless swelling** in the front of the neck (93% of the patients).
5. Most common clinical presentation with thyroid swelling was **MNG**.
6. Duration of symptoms varied greatly; with 60% of the patients presenting with a **duration of less than 1 year.**
7. A large number of patients belonged to **AJCC (2002) Stage I disease (53%).**

8. Most common histopathological type was **papillary carcinoma thyroid (70%);** followed by follicular carcinoma thyroid (23%).

9. Most of the patients (73%) of well differentiated types of thyroid carcinoma belonged to **the low risk category** according to the AMES categorization scheme.

10. Most common surgery performed was **total thyroidectomy in 70%** of cases with minimal postoperative complications.

11. Overall **diagnostic accuracy of FNAC is 97%** in this study.

PROFORMA

Unit: IPNo.: S1. No.:

Name: Age: Sex:

Religion: Occupation: Address

DOA: DOO: DOD:

I. Chief Complaints

II. History of Present Illness

1. Swelling in the Neck:
   Onset
   Duration:
   Rate of growth
   Associated with pain

2. Pain:
   Duration
   Character
   Radiation

3. Pressure effect:
   Dyspnoea
   Dysphagia
   Hoarseness of voice

4. Symptoms of Thyrotoxicosis
   Loss of weight
   Preference of cold
   Intolerance to Heat
   Excessive sweating
   Insomnia
   Tremor of hands
   Palpitation
   Chest Pain
   Diplopia

5. Symptoms of Hypothyroidism
   Increase in weight
   Intolerance to cold weather
   Facial swelling
   Constipation
   Somnolence

III. Past History

Drug Intake:

IV. Personal History

Diet:

V. Menstrual History

VI. Family History

VII. General Examination

1. Built & Nourishment
2. Facies
3. Mental state & intelligence
4. Pulse
5. Sleeping pulse rate
6. Temperature
7. Respiratory rate
8. Blood pressure
9. Eye signs
   Lid retraction
   Exophthalmos
   Ophthalmoplegia
   Chemosis

10. Tremor

11. Skin

VIII. Local Examination

Inspection

Swelling in anterior aspect of Neck
Size
Surface
Movement with deglutition
Movement with tongue protrusion
Edge
Lower Borders
Other Swellings
Dilatation of veins
Congestion of face on raising the hand

Palpation:

Swelling
Size
Shape
Extent
Surface
Edge
Consistency
Plane
Mobility
Kocher’s test
Thrill
Bruit
Cervical Lymph nodes:
Carotid pulsation - Right
- Left

IX. Examination of other systems

Cardiovascular system
Respiratory system
Nervous system
Abdomen

X. Investigation

1. Haematological Hb
   TC
   DC
   ESR
2. Urine Examination Albumin
   Sugar
   Micro

3. Blood sugar
4. Urea
5. Serum Creatinine
6. Thyroid function test T3 T4 TSH
7. Radiograph of Neck AP and Lat
8. Radiograph of chest PA
9. Ultrasonography of the neck
10. FNAC

XI. Premedication and anaesthesia

XII. Operative details

XIII. Post operative management

Antibiotics
IV fluids

Analgesics
Eltroxin
Blood transfusion
Other drugs

Oral fluids
Removal of drain
Features of Hypoparathyroidism

XIV. Histopathological Report

XV. Complications

XVI. Treatment of Complication

XVII. Condition at time of discharge

XVIII. Follow up

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MASTER CHART

S.No.	Patient characteristics				Clinical features										Investigations						
	Name	Age (Years)	Sex	IP No.	Thyroids Swellings	Duration of swellings	Dysphagia	Dyspnea	Hoarseness of voice	Cervical lymphaden	Thyrotoxic symptoms	Diarrhoea	Metastasis	Nodularity	Thyroid profile	FNAC	IDL	Xray findings	Stage	AMES	Surgery
1.	**Bhagya**	**41**	**F**	**109874**	+	**5m**	-	-	-	-	-	-	-	**SN**	**EU**	**NG**	**N**	**N**	**I**	**LR**	**TT**
2.	**Prabha**	**21**	**F**	**98765**	+	**6m**	-	-	-	-	-	-	-	**SN**	**EU**	**PC**	**N**	**N**	**I**	**LR**	**TT**
3.	**Muniamma**	**37**	**F**	**99874**	+	**2y**	-	-	-	-	-	-	-	**MN**	**EU**	**PC**	**N**	**N**	**I**	**LR**	**TT**
4.	**Radha**	**51**	**F**	**89743**	+	**6m**	-	-	-	-	-	-	-	**MN**	**EU**	**PC**	**N**	**N**	**II**	**HR**	**TT**
5.	**Krishnan**	**46**	**M**	**88975**	+	**6y**	-	-	+	-	-	-	-	**SN**	**EU**	**FN**	**N**	**TD**	**I**	**LR**	**HT+CT**
6.	**Kamala**	**23**	**F**	**78654**	+	**3m**	-	-	-	-	-	-	-	**SN**	**EU**	**NG**	**V-R**	**CA**	**I**	**LR**	**HT**
7.	**Lakshma**	**64**	**F**	**109777**	+	**1m**	--	-	-	**RII& IV**	-	-	-	**SN**	**EU**	**NG**	**N**	**N**	**I**	**LR**	**HT**
8.	**Nagamma**	**34**	**F**	**78954**	+	**1y**	+	-	-	-	-	-	-	**MN**	**EU**	**PC**	**N**	**N**	**IVA**	**LR**	**NTT+ FND**
9.	**Munusamy**	**48**	**M**	**98765**	+	-	-	-	-	-	-	-	-	-	**EU**	**PC**	**N**	**N**	**I**	**HR**	**TT**
10.	**Kalaiselvi**	**23**	**F**	**97865**	+	**2y**	-	-	-	-	-	-	+	**MN**	**EU**	**NG**	**N**	**TD**	**II**	**HR**	**TT**
11.	**Pappamal**	**62**	**F**	**93765**	_	**2m**	-	-	-	-	-	-	-	**MN**	**EU**	**NG**	**N**	**N**	**IV A**	**LR**	**NTT+ FND**
12.	**Divya**	**18**	**F**	**87654**	+	**6m**	-	-	-	-	-	-	-	-	**EU**	**FC**	**N**	**N**	**III**	**LR**	**TT**
13.	**Sridevi**	**32**	**F**	**78694**	+	**7m**	-	-	-	-	-	-	-	**SN**	**EU**	**PC**	**V-R**	**TD**	**I**	**LR**	**TT**
14.	**Rajappan**	**65**	**M**	**90387**	_	**8m**	+	-	-	-	-	-	-	**MN**	**EU**	**PC**	**N**	**N**	**I**	**HR**	**TT**
15.	**Gayathri**	**49**	**F**	**109876**	+	**5y**	-	-	-	-	-	-	-	**SN**	**EU**	**PC**	**N**	**CA**	**II**	**LR**	**TT**
16.	**Ramani**	**56**	**F**	**76589**	+	**3y**	-	+	+	-	-	-	-	**MN**	**EU**	**PC**	**N**	**N**	**I**	**LR**	**TT**
17.	**Amulu**	**34**	**F**	**71234**	+	**6m**	-	-	-	**LI& III**	-	-	-	**SN**	**EU**	**FN**	**N**	**N**	**I**	**LR**	**NTT**
18.	**Veni**	**29**	**F**	**87123**	+	**8m**	-	-	-	-	-	-	-	**MN**	**EU**	**FN**	**V-L**	**N**	**I**	**HR**	**NTT**
19.	**Ramayee**	**56**	**F**	**89444**	+	**7m**	-	-	-	--	-	-	-	**MN**	**EU**	**PC**	**V-R**	**TD**	**I**	**LR**	**TT**

S.No.	Patient characteristics				Clinical features										Investigations						
	Name	Age (Years)	Sex	IP No.	Thyroids Swellings	Duration of swellings	Dysphagia	Dyspnea	Hoarseness of voice	Cervical lymphaden	Thyrotoxic symptoms	Diarrhoea	Metastasis	Nodularity	Thyroid profile	FNAC	IDL	Xray findings	Stage	AMES	Surgery
20.	**Geetha**	**31**	**F**	**111908**	+	1y	-	-	-	-	-	-	-	MN	EU	NG	N	CA	II	LR	TT
21.	**Shubha**	**32**	**F**	**119834**	+	7m	-	-	-	-	-	-	-	SN	EU	NG	N	N	IV C	HR	NTT
22.	**Shoba**	**34**	**F**	**56784**	+	2y	-	-	-	-	-	-	-	SN	EU	FN	N	N	I	LR	L-HT+CT
23.	**Mahesh**	**36**	**M**	**87692**	+	8y	-	-	--	-	-	-	-	SN	EU	PC	N	N	II	HR	TT
24.	**Raagavi**	**70**	**F**	**95810**	+	8y	-	+	-	-	-	-	-	MN	EU	PC	N	N	I	HR	TT
25.	**Naga**	**34**	**M**	**109111**	+	10m	-	-	-	-	-	-	-	MN	EU	PC	N	TD	I	LR	TT
26.	**Mangalam**	**44**	**F**	**76578**	+	15m	-	-	-	-	-	-	-	MN	EU	FN	N	N	III	LR	TT
27.	**Mariya**	**33**	**F**	**83245**	+	6y	-	-	+	-	-	-	-	MN	EU	NG	N	N	I	LR	TT
28.	**Parimala**	**56**	**F**	**98640**	+	2y	-	-	-	--	-	-	-	SN	EU	PC	N	N	IV	LR	TT
29.	**Chitra**	**34**	**F**	**81287**	+	1y	-	-	-	-	-	-	-	MN	EU	FN	N	N	I	HR	HT+CT
30.	**Bhuvaneshwari**	**44**	**F**	**101111**	+	4m	-	-	-	-	-	-	-	MN	EU	PC	N	CA	I	LR	TT+L+FND

-