A CLINICOPATHOLOGICAL STUDY AND MANAGEMENT OF THYROID CARCINOMA

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The Tamilnadu Dr. M.G.R Medical University, Chennai.

In partial fulfillment of the requirements for the degree of

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Under the guidance of
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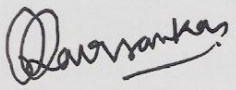
I hereby declare that this dissertation entitled "A CLINICOPATHOLOGICAL STUDY AND MANAGEMENT OF THYROID CARCINOMA" is a bonafide and genuine research work carried out by me in the Department of General Surgery, Madurai Medical College under the guidance of **PROF. SOUNDARARAJAN. M.S.**, Head of the Department of General Surgery, Madurai Medical College. This is submitted to **The Tamilnadu Dr. M.G.R. Medical University, Chennai,** in partial fulfillment of the regulations for the award of MS degree (Branch I) General Surgery course on April 2013.



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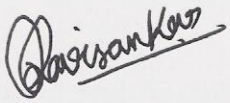

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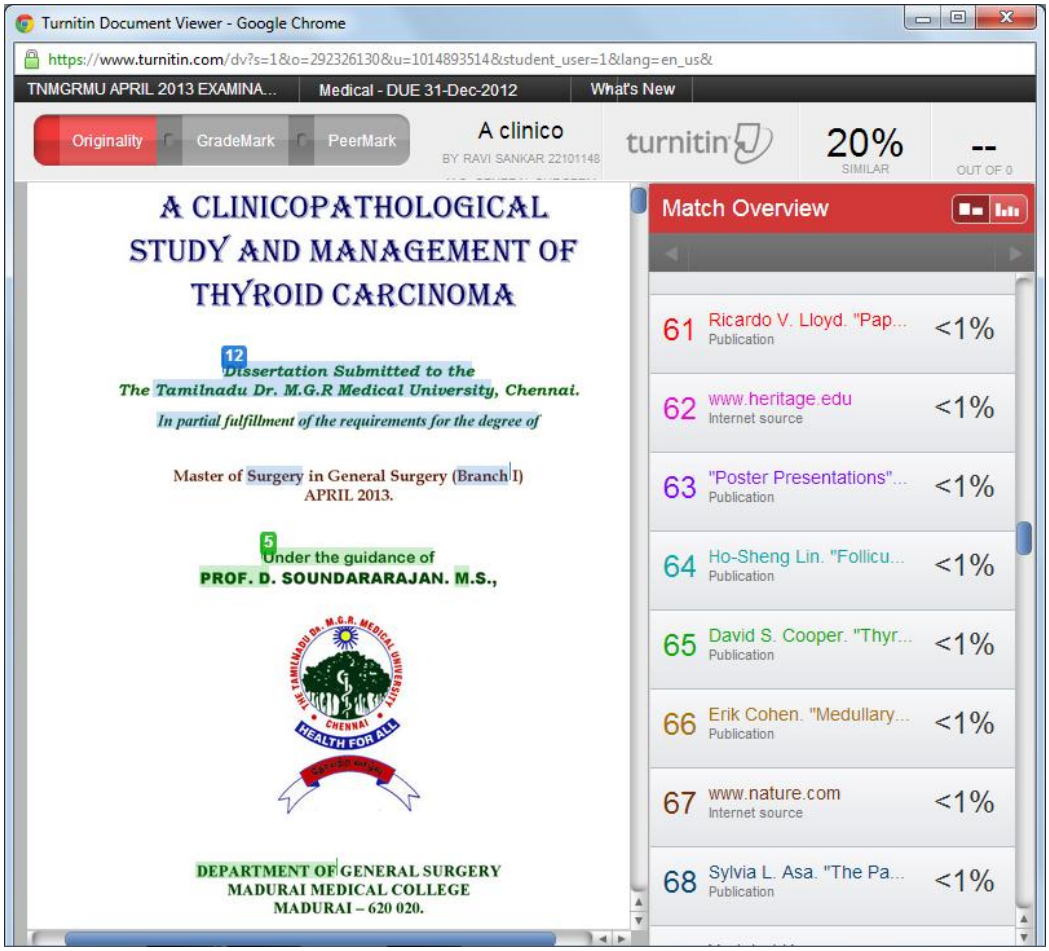

LIST OF ABBREVIATIONS

AGES	-	Age, grade of tumor, extent of tumor, 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

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INTRODUCTION

Thyroid cancer is the most common endocrine cancer and accounts for 1% of all the malignant cases. Thyroid malignancy is overwhelmingly the commonest type of endocrine malignancy and it accounts majority of the mortality of the cases due to the endocrine cancers. Patients with thyroid cancer have varied presentations and they usually present with a solitary thyroid nodule or multi-nodular goiter. Of all the thyroid nodules, the incidence of malignant lesions is 5%. The majority of the patients with carcinoma of the thyroid have differentiated cancer varying in history from a papillary carcinoma to a follicular carcinoma and also undifferentiated carcinoma such as anaplastic carcinoma. Differentiated carcinoma of the thyroid gland is most prevalent in young adults with female and male ratio of 3:1.

Cancer of the thyroid gland represents a spectrum of different histological entities with diverse clinical behavior. Generally there is a very low progression from differentiated carcinoma to anaplastic carcinoma in some cases. However, this transition takes decades to takes place in most instances. The evaluation of thyroid nodule is a problem that confronts the clinicians. The majority of thyroid nodules are benign, but any thyroid swelling might harbor malignancy demanding proper investigation to establish the diagnosis. The natural history of the thyroid carcinomas allows the surgeon to do thoughtful preoperative workup for the diagnosis.

The fine needle aspiration cytology (FNAC) is now the corner stone of investigation for many of these patients and evaluation. The clinical management of the well-differentiated thyroid carcinomas rests on the retrospective studies and individual clinical experience. The clinical management depends upon the low risk and high risk categories of the malignancy. The surgical management is the primary modality of the treatment in thyroid carcinoma. The surgical management ranges from hemithyroidectomy to total thyroidectomy and the neck node dissection range from the prophylactic neck node dissection to the functional neck dissection depending on the clinical presentation. The post operative management of the patients includes radioactive iodine therapy after the evaluation of the need for the therapy. The role of radiotherapy and chemotherapy are very limited in the management of the thyroid carcinoma.

REVIEW OF LITERATURE

Andres Vasalieus (1514-1564 A.D.), who is credited as the "Father of Anatomy" gave the first description of thyroid gland. Pathological swellings in the anterior surface of the neck have been recognized since ancient times. The Greeks were the first to allude to thyroid gland enlargements, referring to them as bronchoceles or hernias of the wind pipe. The close anatomical association of these glands with the larynx led to the name of thyroid (shaped like a shield) after the designation given by Galen to the thyroid cartilage.

Several successful extirpations were described after the year 1500. With the advent of general anesthesia in the mid 19th century, improvements in surgical techniques, judicious selection of cases; and the antiseptic era which was heralded in 1866, the intra and post operative complications of thyroidectomies were looked upon and controlled. This led to the beginning of the golden years of thyroidectomy in 1896 in the hands of such great surgeons as Billroth and Kocher in Europe, and William Halstead, Charles Mayo in united states, among many others. The surgeons perform thousands of thyroidectomies with a mortality which progressively reduced to less than 1% from the high mortality era.

Theodore Kocher is considered the greatest contributor to the field of thyroid surgery. His efforts were recognized and rewarded in 1909 by the Nobel Prize in medicine for his work. Butlin review in 1887 included 50 patients, 60% of them died soon after surgery. By 1901 mortality decreased by 34%. Two types of lesions with better prognosis, papillary carcinoma

and encapsulated carcinoma; were recognized. In 1920 Mayo clinic published a report with better surgical results. 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.[2] 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 Karoliska hospital defined the precise diagnostic criteria and determined the diagnostic accuracy.[10]

Surgical Anatomy of the Thyroid Gland

Thyroid is a highly vascular gland, weighing about 15 to 25 grams, and consists of two lobes, united in mid line by the isthmus, which overlies the second and third tracheal rings enclosed between the layers of the deep cervical fascia. There may also be a pyramidal lobe present in 50% of cases and is remnant of the thyroglossal tract.[11] Its surgical capsule is external to the true capsule and is only prominent posteriorly where it condenses to form the suspensory ligament of Berry to connect the lobes of the gland to the cricoid cartilage and the first two tracheal rings and this attachment causes the thyroid to move on swallowing. The lateral lobes lie between the great vessels of the neck and the tracheoesophageal structures and confined by their capsule.

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.[3] 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 and it divides at the superior pole of the gland to lie in the anterior and posterior surface of the lobe and it lies postero laterally and parallel to the external branch of the superior laryngeal nerve. The inferior thyroid arteries branch directly from the thyrocervical trunk and it usually gives off one or two branches, one directed cephalically to the superior parathyroid gland and another inferiorly to the inferior parathyroid gland and hence the inferior thyroid artery should be ligated beyond these take off sites.

Lymphatic Drainage

The so-called central compartment nodes are the primary site of drainage whereas the lymph nodes of the internal jugular, posterior triangle nodes that constitute the lateral neck nodes are the site of secondary drainage.[13] It is postulated that the metastases to the upper and the submandibular nodes occur in the later stages once the pretracheal and paratracheal have become obstructed by metastases.[14]

Nerves Associated with the thyroid gland

The thyroid gland is closely associated with two nerves namely the recurrent laryngeal and the external laryngeal nerves. Of the two nerves, the right recurrent laryngeal nerve branches from 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 branches from 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. Unusually the non-recurrent laryngeal nerve can branch directly from the vagus and pass directly to the thyroid and this non-recurrent nerve is found in 1-1.5% of patients.[15]

The superior laryngeal nerves branch from the vagus nerve at the level of base of the skull and descend towards the superior pole along with the internal carotid artery. The smaller external branches are related with the inferior pharyngeal constrictor muscle on its lateral surface and usually descend anteriorly and also medially with the superior thyroid artery. The nerve takes a medial course in the neck and enters into the cricothyroid muscle within 1 cm of the superior thyroid artery's entry into the thyroid. If severed or entrapped during surgery, the nerve is at the risk of injury if the superior pole vessels are ligated too above the superior pole of the thyroid.[9]

Epidemiology of Thyroid Malignancies

The incidence of thyroid cancer is increasing from 3.59 per 1, 00,000 persons in 1973 to 8.71 per 1, 00,000 persons in 2002 at 2.41 fold increase as per the U.S. Statistics. There is increase in incidence of papillary carcinoma during this period from 2.71 to 7.71 per 1, 00,000 persons, a 2.91 fold increase in the incidence.

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 less 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. In an autopsy study Fukunaga and Yatani reported data from multiple countries that there was an 11 % overall incidence of occult papillary thyroid cancer.[21] Female are affected more than males and the ratio is somewhere around 1:1.6 to 1:3.[15] Even though the overall incidence of differentiated thyroid cancer is more common among the females than in males, a nodule in a male is more likely to be malignant variety than in a females.[23]

Overall papillary cancer is more common than follicular, which is more common than medullary, is more common than anaplastic. B.B. Yeole, reported that incidence of thyroid carcinoma in Bombay and other parts of India is quiet low in the both the sexes in comparison with international experience and preponderance to Muslims has been reported.[24]

Etiology of Thyroid Malignancies

1. Radiation exposure : Exposure to radiation is the only proved thyroid carcinogen.[25] A 10 to 20 year post radiation latency period was reported earlier but this has not been noted in the pediatric thyroid cancer cases that have resulted from the Chernobyl nuclear disaster in the Ukraine in 1986, where there has been a dramatic increase in such cancers as early as 1989.[26] In contrast to external radiation, there is little evidence to suggest that internal radiation from I^{131} used for therapeutic or diagnostic medical purposes causes thyroid cancer in humans.[27]

2. Hereditary factors: Among the thyroid malignancies, the medullary carcinoma is familial in 10% to 30% of cases. Patients with familial variety have the medullary carcinoma as an autosomal dominant in one of the three clinical syndromic scenarios.

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, Werner's syndrome and FAP have an increased risk of benign and malignant neoplasms of the thyroid.[21] About 6% of the patients with differentiated thyroid cancers have familial thyroid cancer.[29] Papillary thyroid cancer accounts for 90% of familial non-medullary thyroid cancer.[30]

3. Family History: Thyroid cancer is one of the risk factors for the development of both medullary and well differentiated thyroid cancers. Familial medullary thyroid cancer occurs in association with other tumours as part of MEN2 syndromes.

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.[31] 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 (Hashimoto's 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	**Undifferentiated**
Papillary carcinoma	Anaplastic carcinoma
Follicular carcinoma	

2. Para follicular cells — Medullary carcinoma
3. Lymphoid cells — Lymphoma

SECONDARY

1. Metastatic
2. Local infiltration

Pathology and natural history of carcinomas

Papillary thyroid carcinoma

The typical PTC on physical examination is firm with an irregular border, has a white color, and may contain micro calcifications. It can be classified as occult or intra thyroidal and extra thyroidal. At the time of presentation, upto 80%-90% of the primary lesions are confined to the gland.[32] Encapsulation of the tumour is seen in 10% of the cases.[33] Tumour multi centricity 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.[34]

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.[35] 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.[36] They are seen in 50% of cases in most series.[37] 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.[38]

Several variants of papillary cancer exist, some behave like typical PTC whereas others have a more aggressive behavior.

Morphological variants of papillary thyroid carcinoma[39]

Variants with similar clinical behavior	Variants with more aggressive behavior
Follicular	Tall cell
Micro papillary	Diffuse sclerosing
Encapsulated Solid	Columnar
Solid/Trabecular	Oxyphil

The papillary cancer has a broad behavioral spectrum in general. There are evidence that small foci of PTC remain dormant for the duration of a person's life, and not infrequently regress or even disappear while metastatic sites of the same tumour continue to grow.[40] 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.[41] The natural prognosis of the metastatic cancer seems to be volume related. It is worse in patients with bone, lung and CNS metastases.[42] The tall cell variant has a worse prognosis in all age groups.

Follicular carcinoma of thyroid

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.[43] In contrast to papillary carcinoma intra thyroidal multifocal disease rarely occurs in follicular cancers. Instead these lesions are usually solitary, encapsulated and have a micro follicular histological pattern. The findings that constitute malignancy are not cytological but instead are histological features like transcapsular invasion and micro vascular 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".[44] 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.[45]

Morphological variants of follicular thyroid carcinoma

Hurthle cell variant (Oxyphil or Oncocytic carcinoma)

Insular cell variant

30% to 50% of Hurthle cell carcinomas are associated with lymph node metastases, compared with 5% to 10% of follicular cancers.[46] 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.[47] Insular thyroid cancer is a more aggressive malignancy and is perceived to behave less favorably than the papillary and follicular cancers.[48]

Anaplastic carcinoma of the thyroid

Anaplastic carcinoma is a devastating disease that usually overcomes the host in a matter of months, sometimes even weeks. They represent 5% to 14% of thyroid malignancies.[49] 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%.[50] The anaplastic component is composed of varying proportions of spindle, polygonal and giant cells.[51] 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 loco regional growth, dysphagia, SVC syndrome and finally asphyxiation or exsanguinations.

Medullary carcinoma of the thyroid

These malignancies are derived from the non epithelial para follicular or the C cells which have the ability to synthesize and secrete calcitonin. MTC typically arises from the upper portion of the thyroid where the C-cells are concentrated. These cells 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.[52] 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%.[53] 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 well demarcated 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.[54]

The natural history of this type of thyroid cancer depends upon whether the MTC is familial or sporadic and the syndromes associated with the cancer. The knowledge about the genetic makeup of the neoplasm impacts upon management as it allows for screening, early detection and prophylactic treatment.

Characteristics of the sporadic and familial forms of MTC[55]

	Sporadic	Familial		
		Non MEN	MEN 2A	MEN 2B
Age at diagnosis	42 – 45	43 – 45	24 – 27	15 – 20
Gender (F:M)	1 : 1	1 : 1	1 : 1	1 : 1
Associated diseases	None	None	Pheochromocytoma Hyperparathyroidism	Pheochromocytoma Marfanoid habitus Mucosal neuromas GIT Ganglioneuromas
Disease extent	Unilateral	Bilateral	Bilateral	Bilateral
Lymphnode metastasis	40 – 0%	10 –20%	14%	38%
Distant metastasis	12%	0%	0 – 3%	20%
Cured of MTC	14 – 30%	70 – 80%	56 – 100%	0%
Dead of MTC	30%	0%	0 – 17%	50%

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 intra lesion 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%.[56] 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.[57] 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.[58]

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 multinodular goiters with or without substernal extension can cause tracheal shift or impingement and alteration of the airway.[59] Local compressive symptoms are a rule in case of anaplastic carcinoma.

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.[60] They are found in more than 75% 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.[62]

The underlying mechanism is still to be clarified. Prostaglandins, Vasoactive 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 presentation of sporadic MTC in some cases.[63] 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 tests are not revealing in persons with most types of thyroid cancer. However the following blood tests may be helpful in some cases.

1. Thyroid function tests: The vast majority of thyroid cancers are clinically euthyroid. A malignant toxic thyroid nodule rarely causes hyperthyroidism.

2. Thyroglobulin: 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.[64] 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.[65] Serum thyroglobulin levels > 2 ng/ml after thyroidectomy indicates presence of metastatic disease and a rise in serum thyroglobulin in a patient with known metastases indicates progression of disease. Thyroglobulin levels of > 60 ng/ml suggest thyroid cancers.

3. Plasma calcitonin: Of all the blood products, the plasma calcitonin has the most direct diagnostic value in determining the nature of the thyroid mass.[66] Calcitonin levels are elevated in almost all patients with MTC. However in those patients who do have a normal baseline values, detections of micro lesions or C-cell hyperplasia associated with MEN2A or MEN2B can be accomplished with a pentagastrin or a calcium stimulation of calcitonin.[67] Normal calcitonin levels < 10 pg/ml. A stimulated value of < 30 pg/ml is considered normal and a value greater than 100pg/ml is abnormal.

4. Genetic testing: Genetic testing is available for family members at risk for developing medullary cancer. The ret proto-oncogene encodes a protein receptor, tyrosine kinase. Mutations of ret are associated in 95% of hereditary medullary thyroid cancers, MEN 2A, MEN 2B and FMTC.[68]

5. 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

Core needle biopsy has been used extensively in a few institutions in the United State and abroad but has failed to gain widespread acceptance. It is particularly helpful in diffuse diseases such as Hashimoto's thyroiditis and in forming the diagnosis of advanced malignant neoplasms. Most authors have been reluctant to use this technique in the evaluation of the single thyroid nodule because of the small but definitive risk of complication. FNAC has been instead, in matter of few years became an extremely popular technique for the evaluation of solitary thyroid nodules. Its approach is obvious, its quick and inexpensive, can be carried out in the office and risk of complications are minimal.[69] Furthermore the material is suitable for immunohistochemical evaluation. Most papillary carcinomas and

other types of malignancy other than follicular carcinoma can be identified with ease. 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.[70]
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 cytoarchitectural 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.[72] 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 infraction of the tumor with only a thin rim of tissue preserved at the periphery. This complication is particularly common with hurtle cell tumors and it may result in transient elevation of Tg. Another complication of the procedure when carried out in cystic lesions has been the development of transient thyrotoxicosis.[72]

Imaging in Carcinoma of Thyroid

1. 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. When calcifications are seen in the gland and 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 calcification can also be seen in metastatic MTC in the cervical nodes.[73]

2. Ultrasound: High frequency (7-13 MHz), small parts instruments have become widely available since mid 1980s and provide good spatial resolution and image quality. Intrathyroid nodules as small as 3 mm in

diameter and cystic nodules as small as 2 mm can be readily detected. Neck USG may confirm the presence of thyroid nodule when the findings on physical examination are equivocal. The diagrammatic representation of the neck showing the location or locations of any abnormal finding is a useful supplement to routine film images which serves as a reference for sonographer on follow up examinations.[74] In patients with known thyroid cancer sonography can be useful in evaluating the extent of disease, both preoperatively and postoperatively. In most instances, sonography is not performed routinely before thyroidectomy but can be useful in patients with large cervical masses for evaluation of nearby structures to exclude the possibility of direct invasion or encasement by tumor.

3. CT and MRI: CT scan and MRI of the neck and the thorax is helpful in assessing the extent and relationship of larger thyroid tumours, particularly the involvement of the larynx, trachea, esophagus and the major vessels. The presence of metastatic cervical and mediastinal adenopathy is usually obvious in the CT and MRI.

Abdominal CT is indicated when a pheochromocytoma is suspected. Advantage of MRI include multiplanar image acquisition, good soft tissue contrast and the fact that iodine containing contrast is not required, which can significantly hamper the postoperative radio nucleotide imaging.

4. Scintigraphy: The most important use of scintigraphic imaging of the thyroid tissue is to define areas of decreased or increased function (Cold or hot areas, respectively) relative to function of the remainder of the gland, provided that they are 1 cm in diameter. Almost all malignant nodules are hypo functioning; but more than 80% of benign nodules are nonfunctioning. Conversely, functioning nodules, particularly if they are more active than secondary tissue or the sole functioning tissue; are rarely malignant.

Thyroid body scanning is performed with I^{131} in the follow up of patients with papillary and follicular thyroid cancer. Uptake by the neoplastic tissue is always lower than in normal and may be found only after TSH stimulation. For this reason sufficiently high dose of I^{131} should be given; and scanning should be performed 2 to 3 days after the dose, when background blood activity is low and when contrast is optimal.

In a series of proved thyroid carcinomas that had been radioactively scanned 61% of the scans revealed cold nodules, 29% were normal scans and 10% showed hot spots at or near the malignant lesion. Malignancy has been shown to occur in 15% to 20% of cold nodules and in 5% to 9% of warm or hot nodules, mandating continued aggressive approach to clinically nodules even if they are not cold. In practice, if a thyroid nodule warrants removal on the basis of history or physical or cytological findings, a radioisotope study need not be done.

STAGING OF THYROID CANCER[117]

TNM Staging Primary tumour (T)

Tx Primary tumor cannot be assessed.

T0 No evidence of primary tumor

T1 Tumor 2 cm or less in greatest dimension and limited to the thyroid

T1a Tumor 1 cm or less and limited to the thyroid

T1b Tumor more than 1 cm but not more than 2 cm in greatest dimension and limited to the thyroid

T2 Tumor more than 2 cm but not more than 4 cm in greatest dimension and limited to the thyroid

T3 Tumor more than 4 cm in greatest dimension limited to the thyroid or any tumor with minimal extrathyroid extension (eg, extension to sternothyroid muscle or perithyroid soft tissues)

T4a Moderately advanced disease

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

T4b Very advanced disease

Tumor invades into the prevertebral fascia or encases carotid artery or mediastinal vessel.

All anaplastic carcinomas are considered T4 tumors.

T4a Intrathyroidal anaplastic carcinoma

T4b Anaplastic carcinoma with gross extrathyroid extension

Regional Lymph Nodes (N)

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

Nx Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Regional lymph node metastasis

N1a Metastasis to Level VI (Pretracheal, paratracheal, and prelaryngeal/ Delphian Lymph nodes)

N1b Metastasis to unilateral, bilateral, or contralateral cervical (Levels I, II, III, IV or V) or retropharyngeal or superior mediastinal lymph nodes (Level VII)

Distant Metastasis (M)

M0 No distant metastasis

M1 Distant metastasis

Stage Grouping

Separate stage grouping are recommended for papillary or follicular, medullary and anaplastic carcinoma.

Papillary or Follicular carcinoma

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

Under 45 years

Stage I	Any T	Any N	M0
Stage II	Any T	Any N	M1

45 years and older

Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1a	M0
	T2	N1a	M0
	T3	N1a	M0
Stage IV A	T4a	N0	M0
	T4a	N1a	M0
	T1	N1b	M0
	T2	N1b	M0
	T3	N1b	M0
	T4a	N1b	M0
Stage IV B	T4b	Any N	M0
Stage IV C	Any	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[112] (Age, Metastatic disease, Extrathyroidal extension, Size). A group from Canada added an assessment of the DNA content by flow cytometry to this which carries the acronym DAMES with the DNA content, and showed that the high-risk 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[76]

	Low Risk	**High Risk**
Age	Male <41, female <51	Male >40, female >50
Metastases 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%

Management of Thyroid Carcinoma

A. Management of differentiated carcinoma 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 1gm 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.

Arguments for and against conservative and radical surgeries in well-differentiated cancers of thyroid[81,82]

Issue	Conservative surgery	Radical surgery
Prognostic risk factors	An occasional low risk patients develop recurrence. Who have 20 year survival of 99% and 20 year DFS of >95%	An occasional low risk patient develops recurrence.
Safety of Surgery	No risks of permanent complications. Minimal complications such as hypocalcemia or recurrent laryngeal nerve injury with experienced surgeons.	Minimal complications with experience surgeons.
Postperative iodine	If necessary I^{131} ablation can be accomplished with no morbidity.	Thyroid ablation with I^{131} is complicated with pain and decreased efficacy with thyroid remnant.
Thyroglobulin Follow-up	Not possible	Possible and an accurate marker.
Multicentricity and Recurrence	Tumor multicentricity seems to have little prognostic significance.	Eliminates the contralateral cancers at the sites of recurrence.

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 I^{131} ablation increases the sensitivity of diagnostic I^{131} 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.

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 malignant lesions. 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.[84]

Lymph node dissection

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 I^{131}. 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[114,115]

The postoperative treatment of patients with well differentiated thyroid cancer, particularly relating to radiotherapy, is some what controversial. I^{131} 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.

Radioiodine therapy for locally advanced disease

High ablative dose ranging from 100-150 mCi should be used in older age group, high risk patients such as those after an incomplete resection; an invasive primary tumor or distant metastases. The dose should deliver no more than 200 cGy to the blood, with no more than 120 mCi retained at 48 hrs or 80 mCi in the presence of pulmonary metastases. 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 I^{131} therapy and the development of leukemia.

Radioiodine Therapy for Metastatic Disease

Metastatic follicular cell derived thyroid carcinoma may concentrate iodine in upto 80% of cases, and TSH can stimulate this uptake. Treatment with I^{131} is therefore used widely to treat distant metastases, whether they are present at the time of original diagnosis or appear at a later time. There is shrinkage of pulmonary and other distant metastases after effective I^{131} treatment because of the limited tissue penetration of the emitted beta particles. Prophylactic steroid administration may be helpful as the lesions tend to enlarge initially to form space occupying lesions. Bone metastases may require several modalities for adequate therapy. Surgery may be needed for orthopedic stabilization or palliation of pain.

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 in 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

1. I^{131} whole body scan: Whole body scan is most sensitive when there is minimal remnant thyroid tissue. 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 I^{131}, usually 1 to 3 mCi. These scans are repeated at regular intervals for duration depending on the risk of the patient.

2. Serum thyroglobulin: Thyroglobulin is detectable in the serum in 75% to 90% of healthy adults (normal levels-0 to30 ng/ml). After a total thyroidectomy, serum thyroglobulin is expected to be low or undetectable. 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.[104]

3. Ultrasound: Ultrasound 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. 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 I^{131} 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 F^{18}-Fluorodeoxyglucose than I^{131}. Hence the PET is found to be 50% to 85% sensitive in the localization of thyroid cancer that does not concentrate I^{131}. Identification of these metastatic sites by FDG scanning may lead to significant alteration in the management of these patients.

Postoperative thyrotropin suppression

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. Most investigators have reported an improved survival and lower recurrence rate in patients with TSH suppressive therapy.[79] 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.

B. Management of Anaplastic Carcinoma of the Thyroid

Treatment results of anaplastic carcinoma are discouraging. Even under the most favorable circumstances and despite the employment of various aggressive treatment strategies that consists of surgery, radiotherapy, chemotherapy or a combination of all the three, almost all patients with the disease die a cancer-related death. Pathologically even a

focus of poorly differentiated or undifferentiated thyroid cancer in a background of well-differentiated cancer is believed to carry a prognosis similar to that of anaplastic cancer. The median survival of anaplastic thyroid cancer is 4 to 5 months, and a few patients have survived for a long term. After the possibility of anaplastic carcinoma is entertained based on history and physical examination, large core cutting needle biopsy will establish the diagnosis in most of the patients.

The role of surgery is limited to the following: (a) open biopsy when needle biopsy fails to obtain enough tissue to differentiate anaplastic carcinoma from thyroid lymphoma and (b) securing the airway via tracheostomy. The most effective single cytotoxic drug is doxorubicin and in some patients this in combination with cisplatin has yielded a favorable response.[88]

C. Management of medullary carcinoma of the thyroid

The principal treatment advised for the patient with medullary carcinoma is surgery. Total thyroidectomy is the treatment appropriate for all cases irrespective of the primary tumour size. With improved early diagnosis by routine calcitonin measurement in nodular disease, occult medullary carcinoma of the thyroid has increasingly been observed. Considering the frequent involvement of central neck compartment in pT_1 carcinoma, an additional en bloc micro dissection central neck compartment is performed for accurate staging. In the presence of central lymph node metastases demonstrated by ultrasonography or demonstrated

intraoperatively, microdissection of both lateral compartments with curative intent is advocated because of frequent occurrence of lateral lymph node metastases in this setting.[89]

If lymph node metastases are suspected in the upper mediastinum then a trans-sternal four-compartment lymphadenectomy is performed.. Patients with distant metastases at presentation usually have an unfavorable course that does not warrant extended surgery apart from total thyroidectomy, central lymphadenectomy and selective removal of symptomatic lymph nodes or tumour infiltrates. Radiation therapy is used as an adjuvant for patients with extensive soft tissue invasion or those with significant extra capsular extension in positive nodes after removal of all gross disease.[90] It may also be considered for palliative control of inoperable disease.

LYMPHOMA OF THE THYROID

Thyroid lymphoma accounts for 1 % to 5% of all thyroid cancers and the incidence of lymphoma is 2% in patients undergoing surgery for thyroid malignancy.[94] Thyroid lymphoma is a relatively rare disease constituting less than 1% of all lymphomas and accounting for 2% of extra-nodal Non-Hodgkin's lymphoma.[95] Most thyroid lymphomas develop in patients with chronic lymphocytic thyroiditis. Chronic antigenic lymphocytic stimulation has been suggested to result in lymphoma transformation. The most common presentation is that of a slowly growing thyroid mass, although approximately one third of the patients present with a more rapidly growing tumour. Patients usually present with symptoms similar to those

of anaplastic carcinoma and also with Type B symptoms in 20% of patients. Similar to patients with Hashimoto's thyroiditis these patients may present in a euthyroid, hypothyroid and occasionally even in hyperthyroid state. Open surgical biopsy is also indicated for the definite diagnosis or classification of lymphomas where FNA or core biopsy cannot provide sufficient information.[92] Resection, chemotherapy and radiotherapy have an important role in the management depending on the stage of the disease.

Sarcoma of the thyroid gland[101]

Sarcoma of the thyroid gland is a rare neoplasm that may be confused pathologically with the spindle cell variant of anaplastic carcinoma of the thyroid.[94] The treatment of sarcomas of thyroid is primarily surgical and consists of total thyroidectomy with excision of any locally involved tissue along with neck dissection for involved cervical nodes followed by postoperative radiotherapy is advocated for aggressive disease.

Secondaries in the thyroid gland

Although rare, secondary metastasis to the thyroid gland does occur, and accounts for about 1 % to 2% of all thyroid malignancies. The vascularity of the gland is thought to give rise to this phenomenon and Renal cell carcinoma has been the most common primary malignancy clinically.[102] Other observed primary tumour sites include lung, breast, melanoma and head and neck tumors. Secondary metastases to the thyroid signify a very poor prognosis. Some patients present with occult primary tumour.

OBJECTIVES

The objectives of this study include the following:-

1. To study the age and gender incidence of Thyroid carcinoma.
2. To study the various clinical presentations of thyroid carcinoma in relation to the various pathological types of thyroid carcinoma.
3. To study the role of the Fine Needle Aspiration Cytology (FNAC) in the diagnosis of the thyroid carcinoma.
4. To study the clinical characteristics of the histological variants of the papillary and follicular thyroid carcinoma.
5. To study the role of the radiological investigations in the evaluation of the Thyroid carcinoma.
6. To study the correlation between the size of the thyroid carcinoma to the various morphological characteristics of the thyroid carcinoma
7. To study the surgical management in the Thyroid carcinoma.
8. To study the immediate post operative complications of thyroid surgeries in cases of Thyroid carcinoma.

METHODOLOGY

STUDY AREA:

This study was conducted in the Department of General surgery and Department of Surgical Oncology in Madurai Medical College and Government Rajaji Hospital, Madurai.

STUDY PERIOD:

It was two years duration and the data collected during the period from June 2010 to May 2012.

SOURCE OF DATA:

This is a retrospective study done in the Madurai Medical College and Government Rajaji Hospital, Madurai. The data was collected regarding Thyroid carcinoma from all the cases diagnosed and treated for Thyroid Carcinoma with histological evidence. The details after collecting from the Medical Records Department of Government Rajaji Hospital were entered and evaluated in the proforma (ANNEXURE -2). The institute ethical committee clearance was obtained for this study.

SAMPLE SIZE

The total number of cases that were included in the study was 60 in number as per the criteria.

INCLUSION CRITERIA:

1. Cases diagnosed as Thyroid Carcinoma with histological diagnosis from the case sheets diagnosed as Thyroid Carcinoma and admitted in the hospital, from the Medical Records Department of Madurai Government Rajaji Hospital with age 13 years and above during the period from June 2010 to May 2012.

2. Patients who were operated previously for benign conditions of thyroid and diagnosed as Carcinoma of thyroid at present in the study period

EXCLUSION CRITERIA:

1. Patients below 12 years of age.
2. Patients who were clinically diagnosed as Thyroid carcinoma and without any histological diagnosis on subsequent evaluation.
3. Patients diagnosed as Thyroid carcinoma clinically and post operative specimen turned out to be benign lesion.
4. Patients who were not willing for any treatment after the diagnosis were excluded from the study.
5. Patients who were operated previously for carcinoma of thyroid with recurrence in this study period excluded.
6. Patients who discontinued the treatment during the study period were excluded.

METHODS OF COLLECTION OF DATA:

- A Proforma for study of all the patients of carcinoma thyroid was used. The presentation, clinical findings, investigations and line of management were documented in the proforma.

All cases of thyroid carcinoma underwent pre operative ultrasonography of the thyroid and the lateral neck and were preceded for FNAC based on the sonographic features and the clinical features. The sonographic lesions found were solid nodules, mixed cystic-solid nodules, spongiform nodules, simple cyst. The sonographic features considered as suspicious for malignancy include hypo echoic lesions, micro calcifications, increased central vascularity, infiltrative margins and the lesions taller than wide in the transverse plane.

The sonographic features and clinical features suggesting malignancy of the thyroid lesions underwent FNAC for diagnosis in all the sonographic lesions except in simple cystic lesions.

- If FNAC report shows papillary carcinoma or features suggestive of papillary carcinoma were proceeded for total Thyroidectomy and prophylactic central compartment neck nodal dissection of Total Thyroidectomy with comprehensive neck dissection if nodes are palpable or suspicious nodes found in the ultrasound of the lateral neck.
- If FNAC report shows "Follicular of Hurthle cell neoplasms", Total

thyroidectomy was done in cases of invasive cancer and metastatic cancer or the patients preferring total thyroidectomy and in all other cases hemithyroidectomy was done initially and the post operative histopathology showing follicular carcinoma/Hurthle cell carcinoma, completion of the thyroidectomy was done and comprehensive neck dissection was done if the neck nodes were found clinically and radiologically.

- If FNAC report describes the lesion as, "Follicular lesion of undetermined significance, the lesions underwent repeat FNAC and was preceded for the surgery based on the cytology report, sonographic features and clinical features.
- If FNAC report shows Thyroid lymphoma, they were preceded accordingly.
- If FNAC report shows, "Insufficient biopsy, non diagnostic" and it is solid lesion by Sonography, they were succumbed to repeat FNAC and proceeded accordingly.

The patients were referred for higher centre for the post operative radioiodine evaluation and the treatment.

STATISTICAL TESTS

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

RESULTS

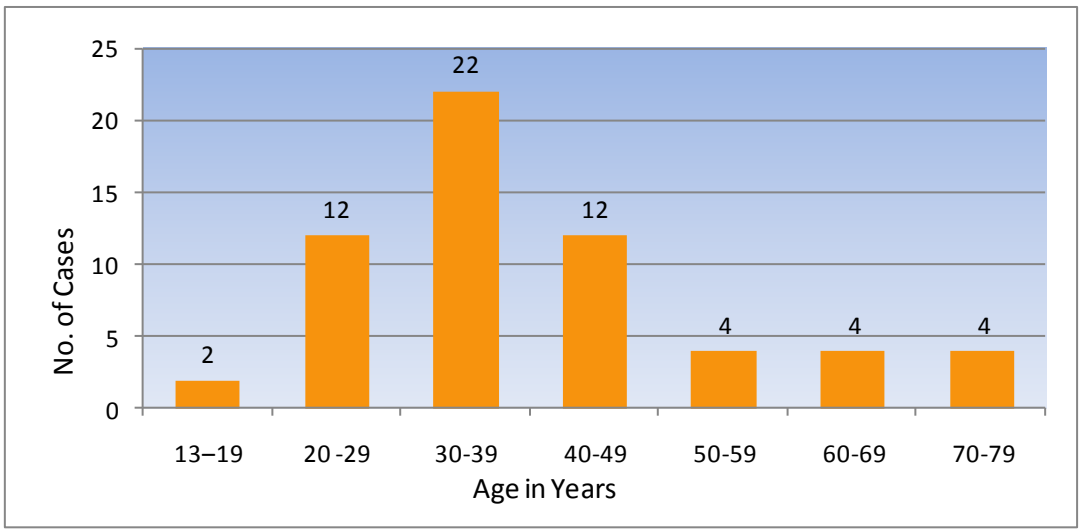
Age and gender incidence:

The incidences of thyroid carcinoma among the various age groups were calculated. (Table 1, Fig.1.). It was found that the commonest age group belongs to the fourth followed by fifth and second decades of life.

Table. 1: Age Incidence in Thyroid Malignancies in our study group of 6o patients.

Age in years	Total No. of Cases	Percentage (%)
13–19	2	3.3
20 -29	12	20
30-39	22	36.7
40-49	12	20
50-59	4	6.7
60-69	4	6.7
70-79	4	6.7
Total	**60**	**100**

Fig. 1: Age Incidence in thyroid carcinoma in our study group of 60 patients.

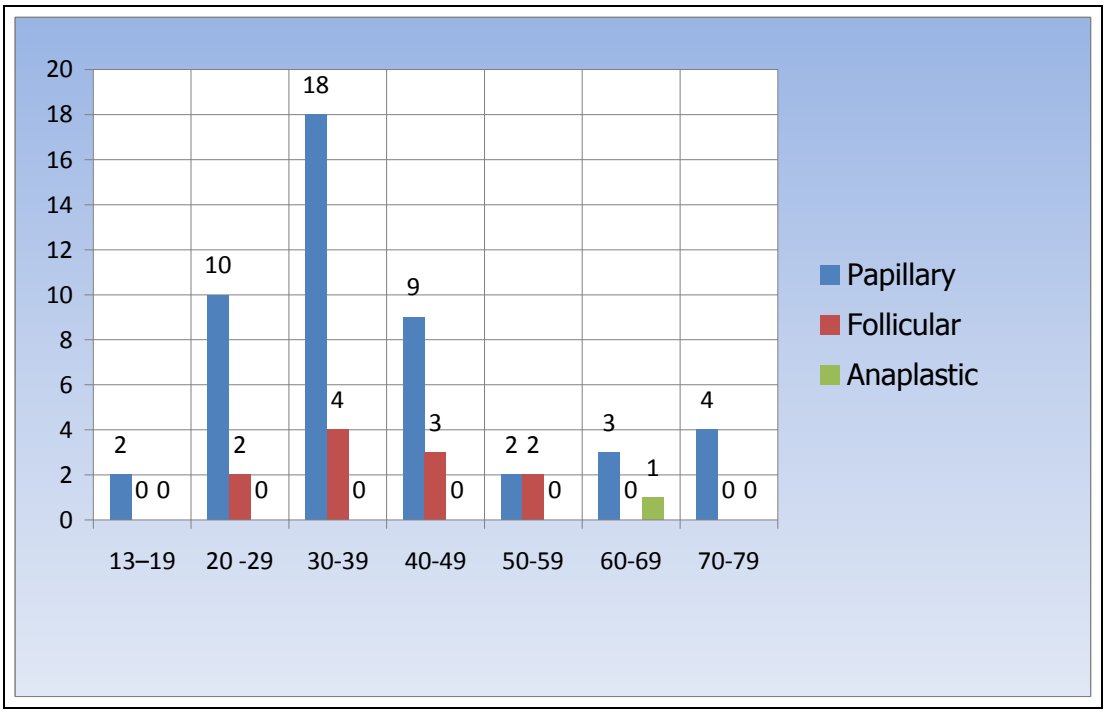


The histological variants of thyroid carcinoma in relation to the age distribution are depicted in Table 2 and Fig.2.

Table 2: Age distribution in relation to the histological variants of thyroid carcinoma

Age in years	Papillary	Follicular	Anaplastic
13–19	2	0	0
20 -29	10	2	0
30-39	18	4	0
40-49	9	3	0
50-59	2	2	0
60-69	3	0	1
70-79	4	0	0
Total	48	11	1

Fig. 2: Age distribution in relation to the histological variants of thyroid carcinoma.



The gender incidence in thyroid carcinoma in relation to the histological variants of Thyroid Carcinoma in our study is depicted in Table 3 and Fig. 3.

Table 3: Gender incidence in relation to the histological variant of Thyroid Carcinoma in the study.

Histological Variant	Females	Males	Total
Papillary Carcinoma	40	8	48 (80%)
Follicular Carcinoma	9	2	11 (18.33%)
Anaplastic Carcinoma	1	0	1 (1.67%)
Medullary Carcinoma	0	0	0
Lymphoma	0	0	0
Total	50	10	60

Fig. 3. Gender incidence in relation to the histological variant of Thyroid Carcinoma in the study.

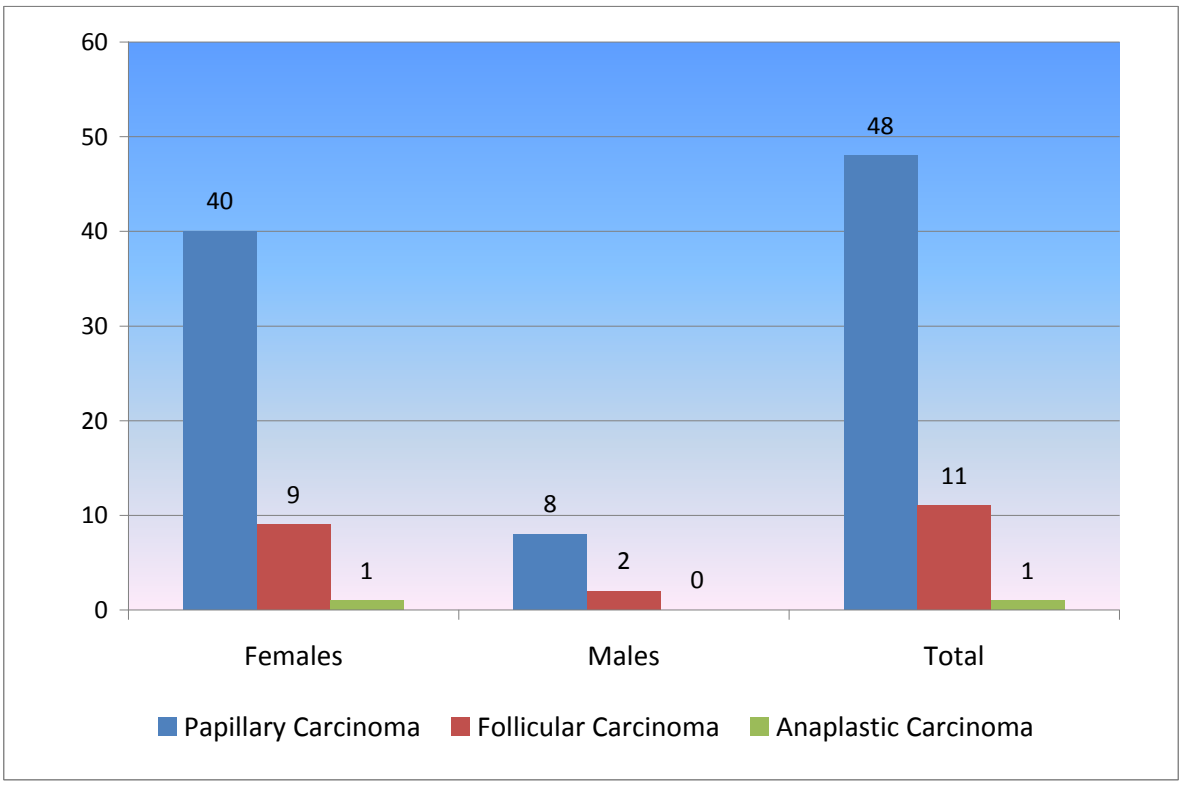
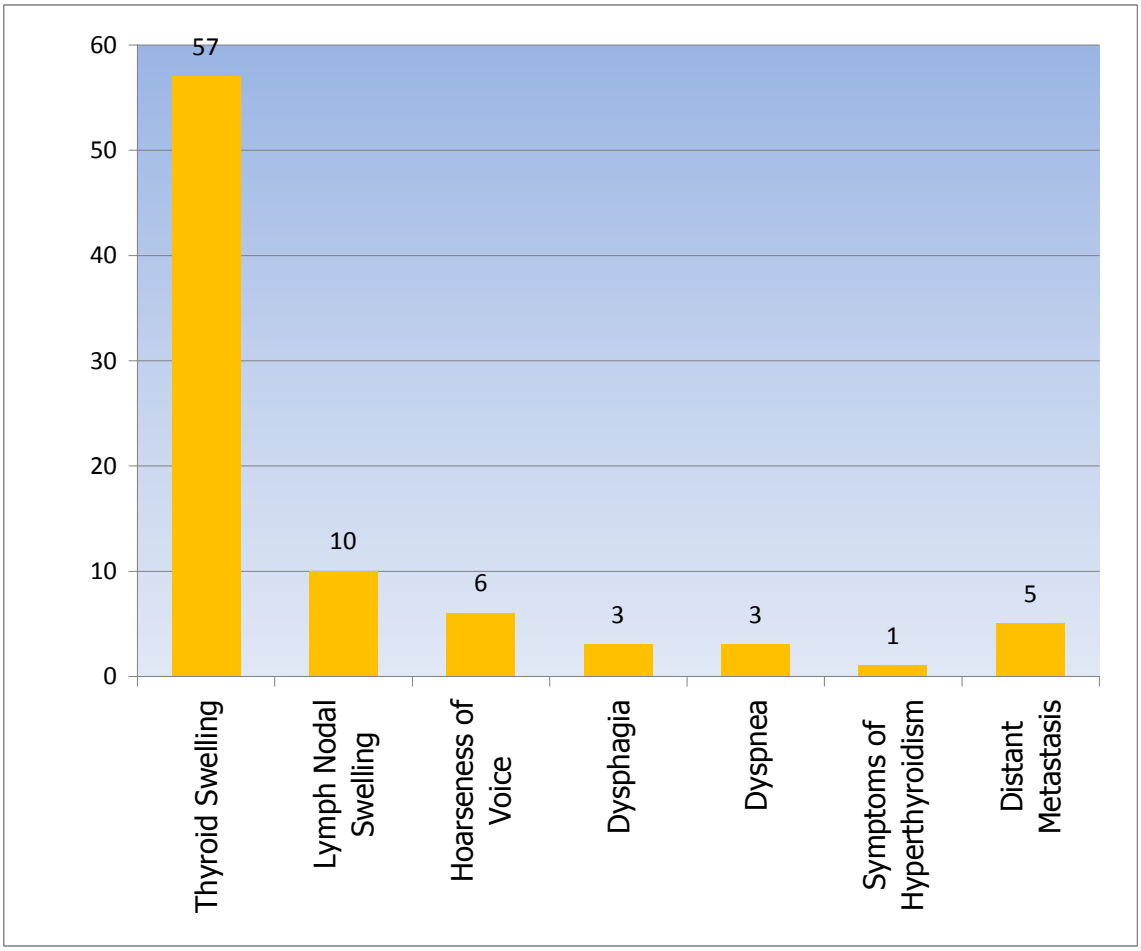


Table 4: Clinical symptoms found in this study group.

S. No.	Symptoms	No. of. cases	Percentage
1	Thyroid Swelling	57	95
2	Lymph Nodal Swelling	10	16.33
3	Hoarseness of Voice	6	10
4	Dysphagia	3	5
5	Dyspnea	3	5
6	Symptoms of Hyperthyroidism	1	1.33
7	Distant Metastasis	5	8.13

Fig 4: Clinical features found among the 60 cases in the study.



In our study group, it was found out to be that the patients predominantly presented with the enlargement of thyroid in 95% of the cases followed by the lymph nodal swelling in ten cases of which 3 cases had only lymph node swelling without any thyroid enlargement. The most common pressure effect found in our study group is hoarseness of voice in six patients clinically followed by dyspnea and dysphagia in three patients each. The results are depicted in Table 4 and Fig.4.

Thyroid Profile:

The thyroid profile done in all the patients which did not show any features of hypo or hyperthyroidism except one patient who had diagnosis of papillary carcinoma.

Indirect Laryngoscopy:

Indirect laryngoscopic examination was done preoperatively in all the patients revealed vocal cord palsy in eight of them of which six patients had hoarseness of voice clinically. Six patients were diagnosed to be of papillary carcinoma of thyroid and one case found out to be follicular carcinoma and the other being the case of anaplastic carcinoma.

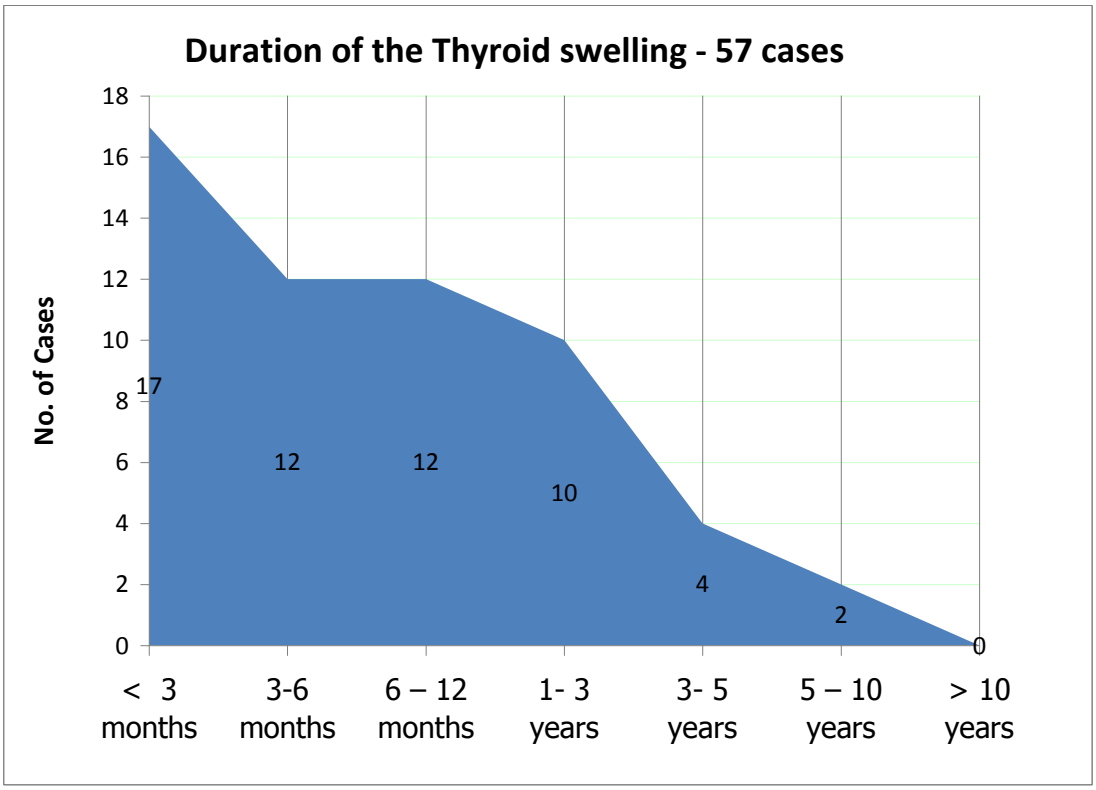
Duration of the thyroid swelling:

The duration of the swelling are depicted in the Table 5 and Fig.5. Predominantly they present with symptoms duration less than three months followed by duration between three to six months.

Table. 5: Duration of the Thyroid swelling in the 60 patients.

Duration of the swelling	Number of the Cases	Percentage
< 3 months	17	28.33%
3-6 months	12	20 %
6 – 12 months	12	20%
1- 3 years	10	16.33%
3- 5 years	4	6.67%
5 – 10 years	2	3.33%
> 10 years	0	0

Fig. 5: Duration of the Thyroid Swelling in the study group



Results of the FNAC diagnosis:

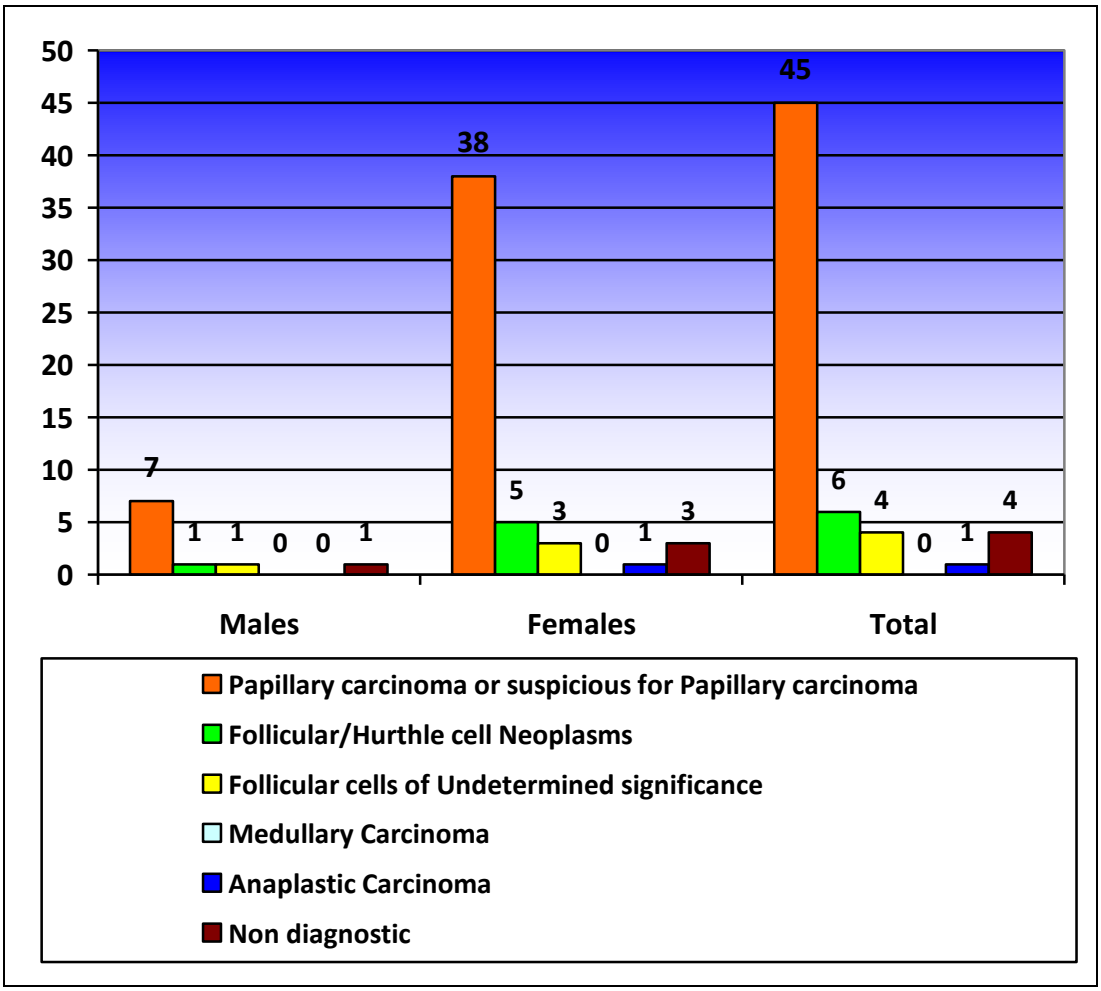
The results of the FNAC showing papillary carcinoma or suspicious for papillary carcinoma in 45 cases, Follicular/Hurthle cell neoplasms in 6 cases, Follicular cells of undetermined significance in 4 cases, anaplastic carcinoma in a case and non diagnostic in 4 cases. Eight cases which revealed cytological report as "Follicular cells of undetermined significance" and "Non diagnostic" were subjected to sonographic guided FNAC of which three cases showed diagnosis of papillary carcinoma and preceded accordingly and three cases showed follicular/Hurthle cells and were preceded accordingly, whereas two cases did not have any cytological diagnosis even after repeat FNAC and were subjected to hemithyroidectomy in a case and total thyroidectomy in the other case based on the clinical and sonographic features.

Table 6: Reports of the FNAC in this study:

FNAC diagnosis	Males	Females	Total
Papillary carcinoma or suspicious for Papillary carcinoma	7	38	45
Follicular/Hurthle cell Neoplasms	1	5	6
Follicular cells of Undetermined significance	1	3	4
Medullary Carcinoma	0	0	0
Anaplastic Carcinoma	0	1	1
Non diagnostic	1	3	4
Total	10	50	60

Of the Four cases which showed diagnosis of Follicular/Hurthle cell neoplasms, two cases were subjected to total thyroidectomy based on sonographic features of invasion and two cases subjected to hemithyroidectomy and diagnosed as follicular carcinoma and were subjected to the completion of thyroidectomy. The results are depicted in Table 6 and Fig.6.

Fig.6. Reports of the Fine needle aspiration cytology in this study.



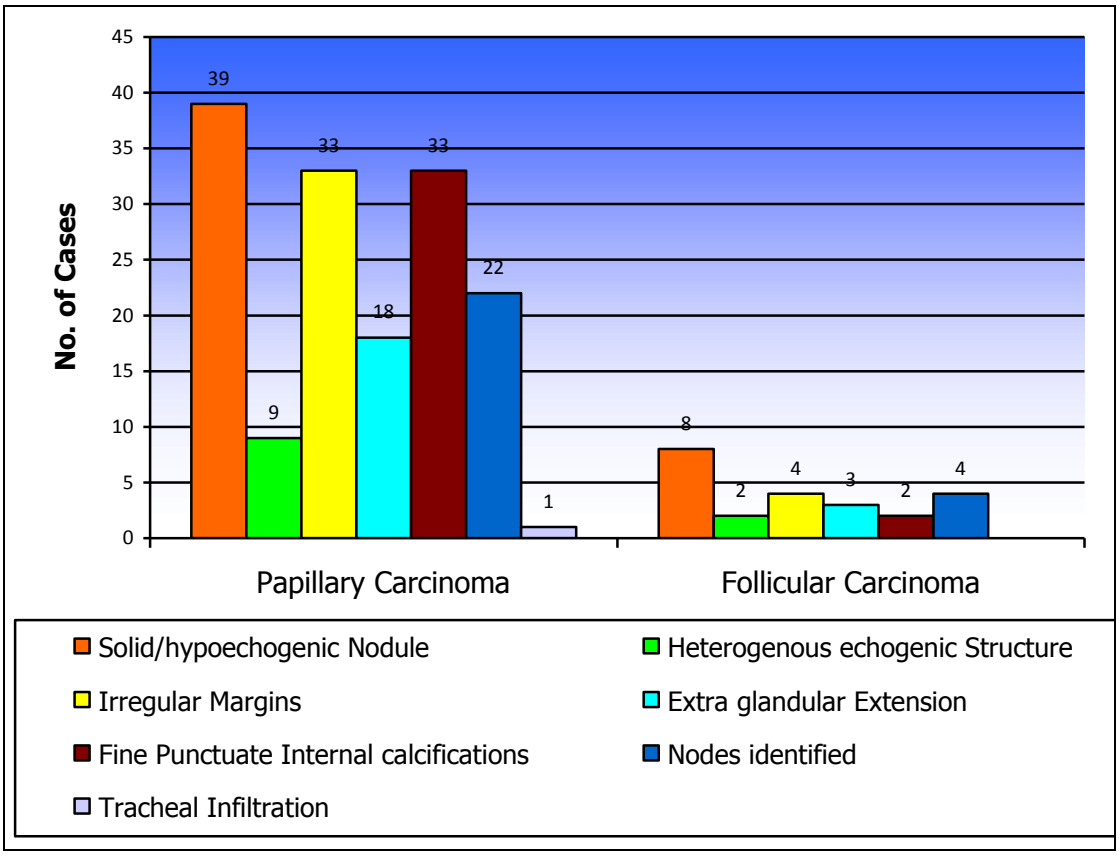
Ultrasonographic findings:

Sonography was done in all the patients and the findings suggestive of the malignancy in the ultrasonography was found and compared in Table 7 and Fig.7. There were hypoechogenic nodules found in 47 cases in total, irregular margins in 37 cases and fine punctuate internal calcifications found in 35 cases and the features in total were compared. Also sonogram identified nodes in 13 cases which were not palpable clinically. And CT of the neck was done in the cases with bulky tumours, or tumours with retrosternal extension, but not routinely done in all cases. Invasion of the tumour was found in 21 cases in total and of those 18 cases were papillary carcinoma and 3 cases were of follicular carcinoma in this study.

Table 7: Ultrasonographic findings found preoperatively in the cases of thyroid carcinoma in this study.

Findings on Ultrasonogram	Papillary Carcinoma	Follicular Carcinoma
Solid/hypoechogenic nodule	39	8
Heterogenous echogenic structure	9	2
Irregular margins	33	4
Extraglandular extension	18	3
Fine punctuate internal calcifications	33	2
Suspicious nodes	22	4
Tracheal infiltration	1	-

Figure 7: Ultrasonographic findings found pre operatively in the cases of Thyroid carcinoma in this study.



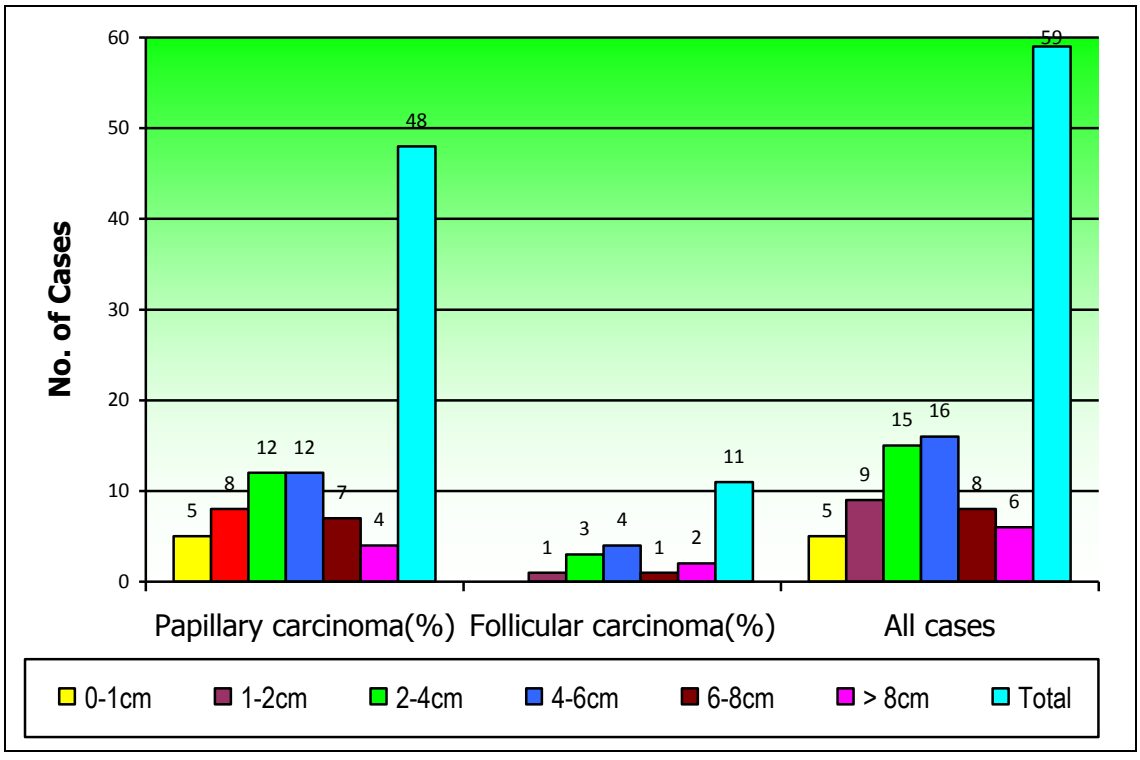
Size of the thyroid swelling:

The clinical and radiological size of the thyroid nodule suspicious of malignancy was found and they were correlated with the incidence of lymph node metastasis, as we know that the diameter of the tumour is an independent prognostic factor and the association between them is found. We found out that cases predominantly were present between 2-6 cm in diameter and the details are depicted in the Table 8 and Fig.8.

Table 8: Diameter of the tumour in relation to the histological variants found in this study.

Diameter of the tumour	No. of cases of Papillary carcinoma(%)	No. of cases of follicular carcinoma(%)	Total. No. of cases
0-1cm	5	0	5
1-2cm	8	1	9
2-4cm	12	3	15
4-6cm	12	4	16
6-8cm	7	1	8
> 8cm	4	2	6
Total	48	11	59

Fig. 8: Diameter of the tumour in the histological variants found in this study.



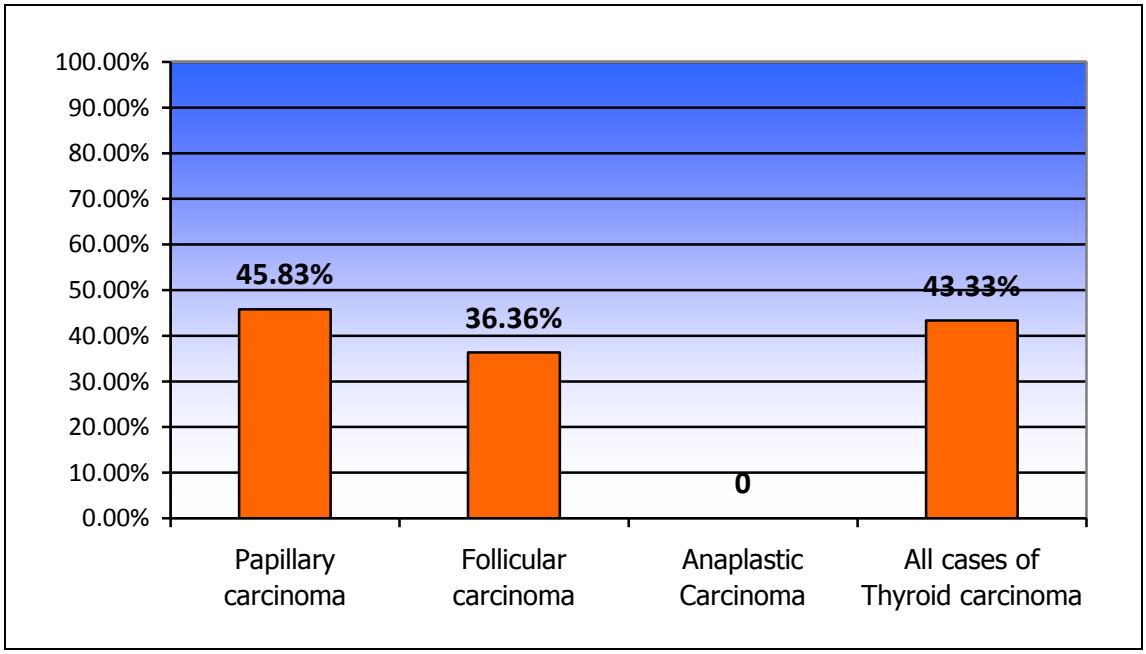
Lymph Node metastasis found among the histological variants of the thyroid carcinoma in the study.

The incidence of lymph node metastasis between the histological variants of thyroid carcinoma was found and analyzed in Table 9 and Fig.9. In total 26 cases of lymph node metastasis was found clinically and of those, 22 cases had papillary carcinoma as the histological variants and 4 cases had follicular carcinoma.

Table 9: No. of cases of the lymph node metastasis found among the histological variants of thyroid carcinoma.

Histological variant	No. of cases	No. of. Cases with nodal metastasis	Percentage of nodal metastasis
Papillary carcinoma	48	22	45.83%
Follicular carcinoma	11	4	36.36%
Anaplastic Carcinoma	1	0	0
Total	60	26	43.33%

Fig. 9: No. of cases of the lymph node metastasis found among the histological variants of thyroid carcinoma.



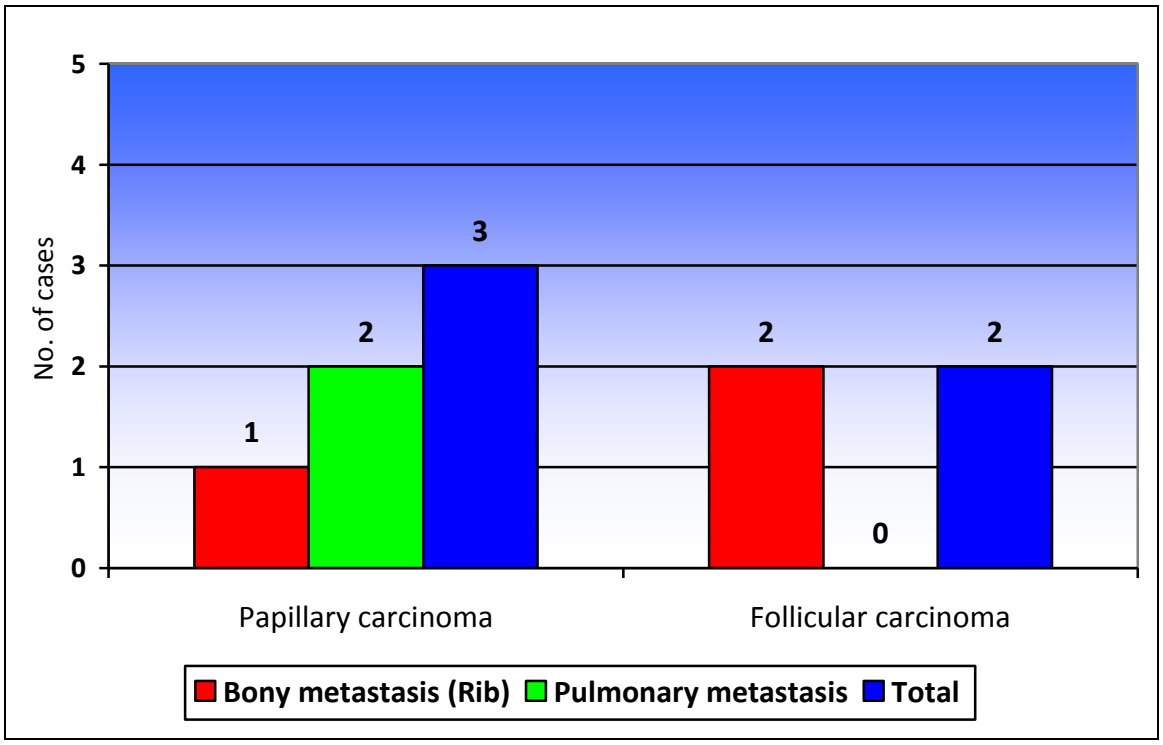
Distant metastases found among the histological variants of the thyroid carcinoma:

There were five cases of thyroid carcinoma with the distant metastasis in the study. Of the five cases, three cases belong to the papillary carcinoma and two cases belong to the follicular carcinoma and are depicted in Table 10 and Fig.10.

Table 10: No. of cases of distant metastases in relation to the histology of the thyroid carcinoma in this study.

Site of Metastasis	Papillary carcinoma	Follicular carcinoma
Bony metastasis (Rib)	1	-
Bony metastasis (Mandible)	-	1
Multiple Bony metastasis to rib, mandible, skull	-	1
Pulmonary metastasis	2	-
Total	3	2
Incidence of distant metastasis in percentage	**6.25%**	**18.2%**

Fig.10: No. of cases of distant metastases in relation to the histology of the thyroid carcinoma in this study.



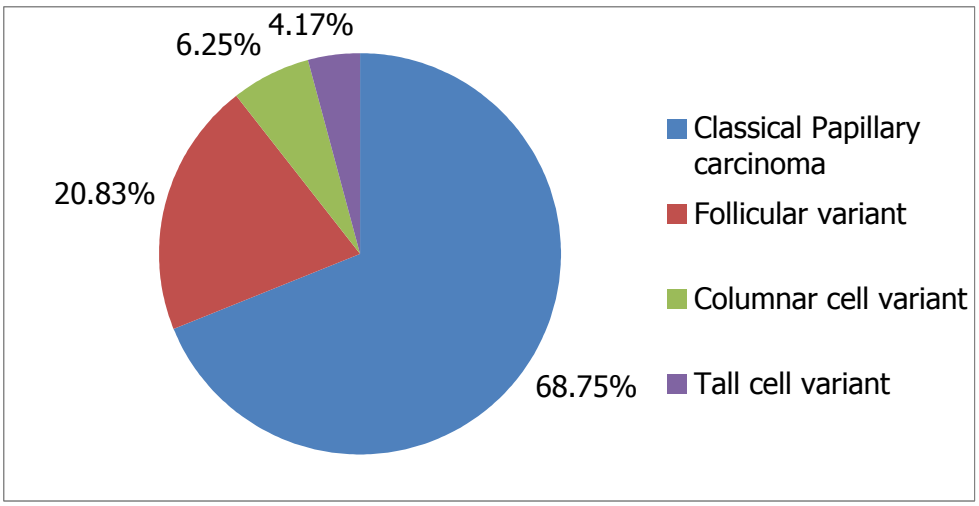
Papillary carcinoma and its variants:

Out of 48 cases of papillary carcinoma in our study, 33 cases were found out to be of classical papillary carcinoma, 10 cases were follicular variant of papillary carcinoma, 3 cases were columnar cell variant of papillary carcinoma and two cases were tall cell variant of papillary carcinoma and are depicted in Table 11 and Fig.11.

Table 11: Papillary carcinoma and the histological variants found in the study.

Histological variants	Number of the cases	Percentage
Classical Papillary carcinoma	33	68.75%
Follicular variant	10	20.83%
Columnar cell variant	3	6.25%
Tall cell variant	2	4.17%
Total	**48**	**100%**

Fig.11. Papillary carcinoma and the histological variants found in the study.



Age, Gender and clinical features of the individual histological variants of the papillary carcinoma of the thyroid.

The various individual histological variants of the papillary carcinoma were compared and analyzed in Table 12.

Table 12: Comparison of the age, gender and clinical features of the individual histological variants of the papillary carcinoma of the thyroid.

	Classical Variant	Follicular variant	Columnar variant	Tall cell variant
No. of. cases	33	10	3	2
Mean age	37	33	46	53
Female : Male	6:1	9:1	2:1	1:1
Lymph node metastases	17	3	2	2
Distant Metastases	2	1	-	-

The classical papillary carcinoma shows mean age at diagnosis of 37 years whereas the follicular variant of papillary carcinoma showed mean age at diagnosis of 33 years, followed by columnar variant of 46 years of age and the tall cell variant of 53 years of age. There was also significant difference in the gender incidence and clinical features of the individual variants which are depicted in Table 12. Also there is relatively decreased incidence of the lymph node metastases found in the Follicular variant of papillary carcinoma in this study.

Comparison of the diameter of the tumour with the various morphological parameters in our study.

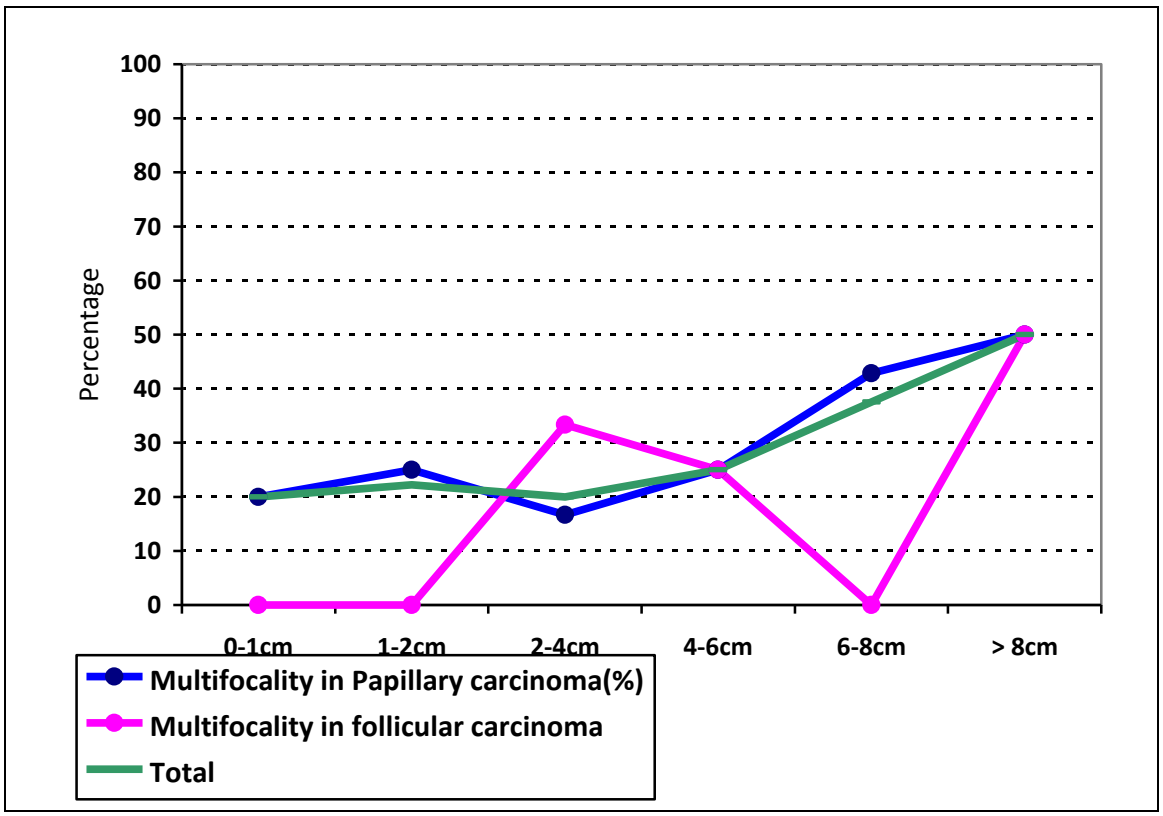
We compared the diameter of the tumour and the histological variants with the various morphological parameters viz., the multifocality, the invasion of the tumour, the risk of the lymph node metastases, and the risk of the distant metastases and statistically correlated. The results are depicted in the table 13, 14, 15, 16, 17 and were statistically analyzed.

Table. 13: Comparison between the diameter of the tumour and the multifocality of the tumour.

Diameter of the tumour	Papillary Carcinoma			Follicular Carcinoma			All cases of Thyroid Carcinoma		
	No. of cases	Multifocality	%age	No. of cases	Multifocality	%age	No. of Cases	Multifocality	%age
0-1cm	5	1	20.00	0	-	0	5	1	20.00
1-2cm	8	2	25.00	1	-	0.00	9	2	22.22
2-4cm	12	2	16.67	3	-	33.33	15	2	20.00
4-6cm	12	4	33.33	4	1	25.00	16	5	31.25
6-8cm	7	2	28.57	1	1	0.00	8	3	25.00
> 8cm	4	2	50.00	2	1	50.00	6	3	50.00
Total	**48**	**13**	**27.08**	**11**	**3**	**27.27**	**59**	**16**	**27.12**

There were 13 cases of papillary carcinoma with multifocal carcinoma and three cases of follicular carcinoma with multifocality as depicted in the Table 13 and Fig.12. Follicular carcinoma has increased incidence of multifocality surprisingly as the tumour size increases over 4 cm but the statistical correlation could not be found due to less number of cases in follicular carcinoma. There was weak statistical correlation between multifocality in papillary carcinoma and the diameter of the tumour once the diameter of the tumour increases above 4 cm. ("P" value- 0.03). One case which had only nodal metastases and on total thyroidectomy specimen showed multifocality without any clinical evidence of thyromegaly.

Fig. 12: Comparison between the diameter of the tumour and the occurrence of the multifocality of the tumour.

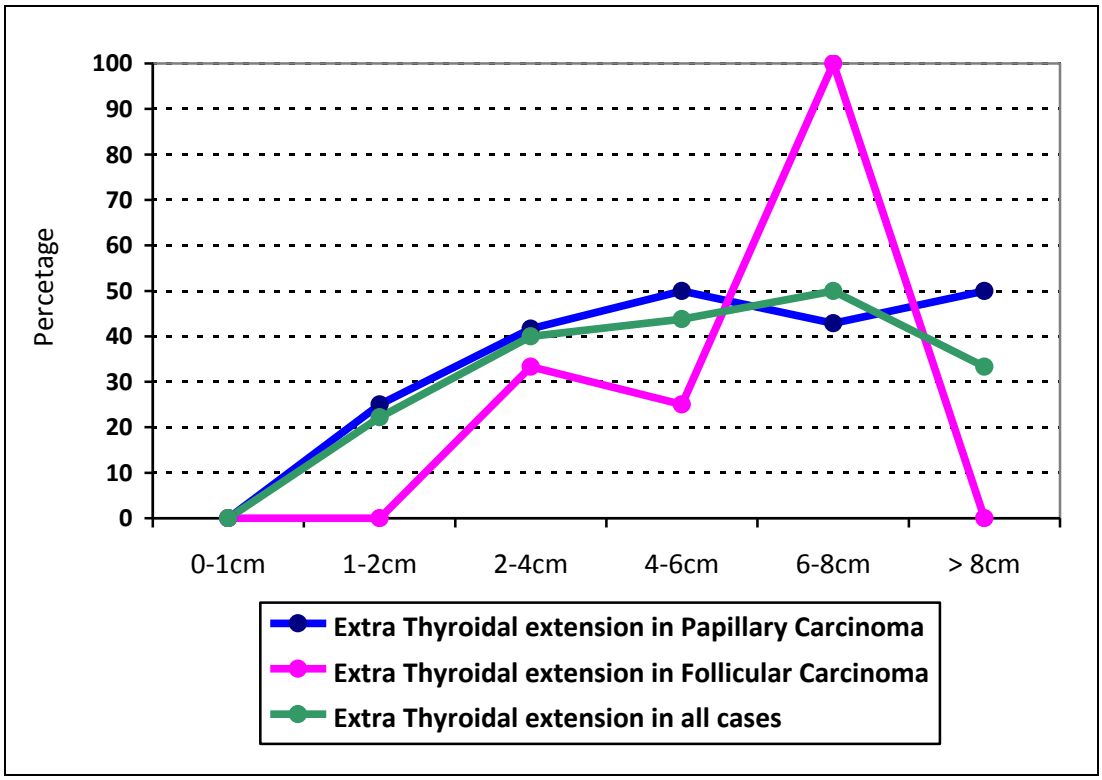


The diameter of the tumour and the incidence of extra thyroidal extension among the histological variants of the thyroid carcinoma in this study was compared and analyzed in Table.14 and Fig.13. There was statistically correlation found between the diameter of the tumour and extra thyroidal extension in cases of papillary carcinoma as the diameter of the tumour increases. But there was no clear cut statistical association found in the follicular carcinoma between diameter of the tumour and the extra thyroidal extension.

Table 14: Comparison between the diameter of the tumour and the occurrence of the extra thyroidal extension.

Diameter of the tumour	Papillary Carcinoma			Follicular Carcinoma			All cases of Thyroid Carcinoma		
	No. of cases	Extra Thyroidal extension	%age	No. of cases	Extra Thyroidal extension	%age	No. of Case	Extra Thyroidal extension	%age
0-1cm	5	0	0.00	0	0	0.00	5	0	0.00
1-2cm	8	2	25.00	1	0	0.00	9	2	22.22
2-4cm	12	5	41.67	3	1	33.33	15	6	40.00
4-6cm	12	6	50.00	4	1	25.00	16	7	43.75
6-8cm	7	3	42.86	1	1	100.00	8	4	50.00
> 8cm	4	2	50.00	2	0	0.00	6	2	33.33
Total	**48**	**18**	**37.50**	**11**	**3**	**27.27**	**59**	**21**	**35.59**

Fig. 13: Comparison between the diameter of the tumour and the occurrence of the extra thyroidal extension.



The lymph node metastasis was correlated with diameter of the tumour in relation to the histological variants of the thyroid carcinoma and is depicted in Table 15 and Fig.14. There were three cases of isolated lymph node metastases without any thyromegaly. There was strong statistical correlation found between the diameter of the tumour and the incidence of the lymph node metastases above 2 cm in papillary carcinoma and above 4 cm in follicular carcinoma as the diameter of the tumour increases. The correlation between the diameter of the tumour and the distant metastases is depicted in Table 16 and Fig.15 but there was no statistical correlation found between the two parameters in this study.

Table 15: Comparison between the diameter of the tumour and the occurrence of the lymph node metastasis.

Diameter of the tumour	Papillary Carcinoma			Follicular Carcinoma			All cases of Thyroid Carcinoma		
	No. of cases	Lymph node metastases	%age	No. of cases	Lymph node metastases	%age	No. of Case	Lymph Node Metastases	%age
0-1cm	5	3	60.00	0	0	0	5	3	60.00
1-2cm	8	1	12.5	1	0	0	9	1	11.11
2-4cm	12	4	33.33	3	0	0	15	4	26.67
4-6cm	12	8	66.67	4	2	50	16	10	62.5
6-8cm	7	4	57.14	1	1	100	8	5	62.5
> 8cm	4	2	50.00	2	1	50	6	3	50.00
Total	48	22	45.83	11	4	36.36	59	26	44.07

Fig 14: Comparison between the diameter of the tumour and the occurrence of the lymph node metastases in this study.

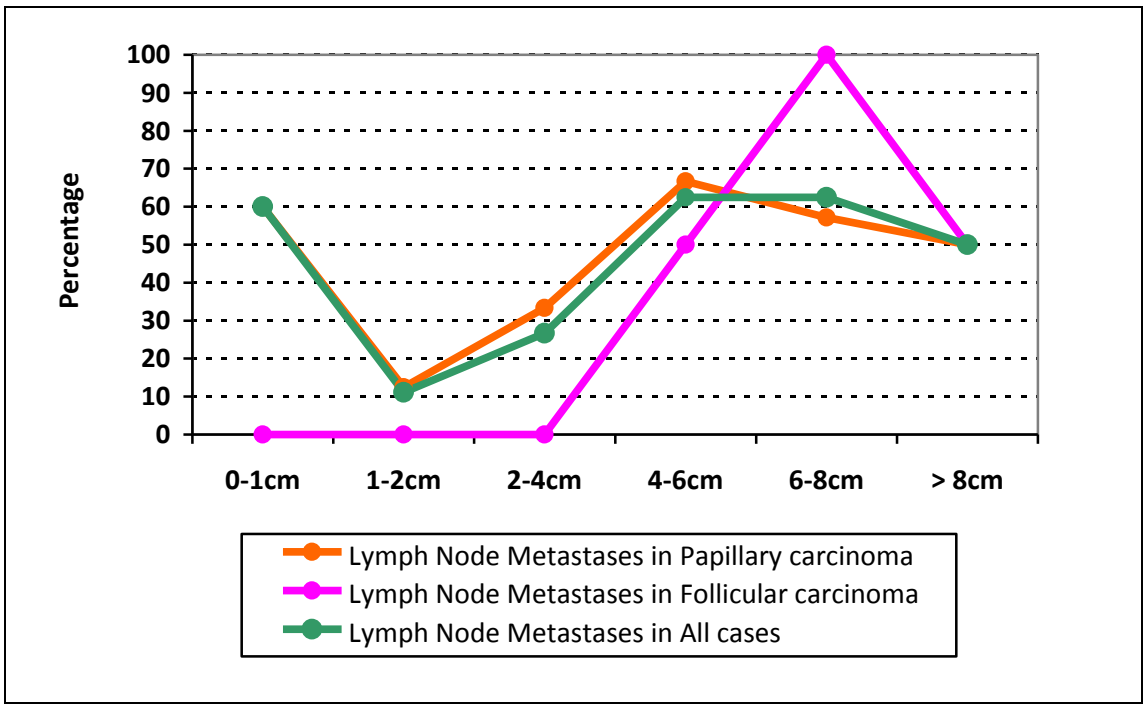


Table 16: Comparison between the diameter of the tumour and the occurrence of the distant metastasis in this study.

Size of the tumour	Papillary Carcinoma			Follicular Carcinoma			All cases of Thyroid Carcinoma		
	No. of cases	Distant Metastases	%age	No. of cases	Distant Metastases	%age	No. of Case	Distant Metastases	%age
0-1cm	5	-	0.00	0	-	0.00	5	-	0.00
1-2cm	8	-	0.00	1	-	0.00	9	-	0.00
2-4cm	12	1	8.33	3	-	0.00	15	1	6.67
4-6cm	12	1	8.33	4	1	25.00	16	2	12.50
6-8cm	7	-	0.00	1	1	100.00	8	1	12.50
> 8cm	4	1	25.00	2	-	0.00	6	1	16.67
Total	**48**	**3**	**6.25**	**11**	**2**	**18.18**	**59**	**5**	**8.47**

Fig. 15: Comparison between the diameter of the tumour and the distant metastasis in this study.

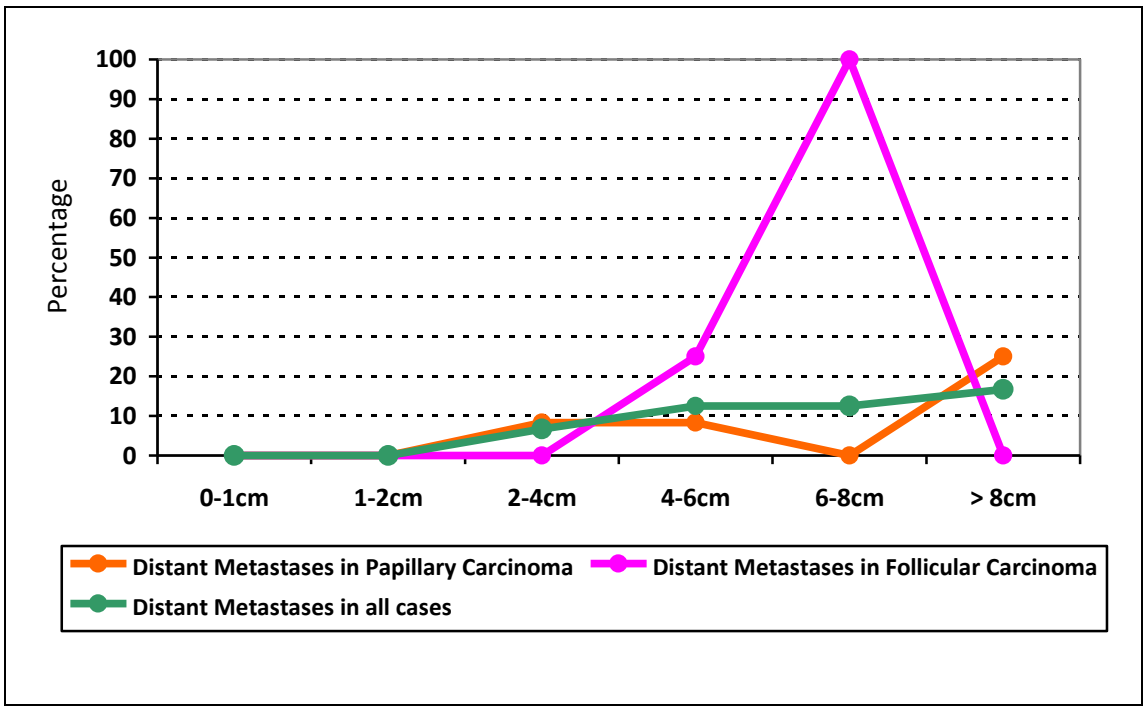


Table 17: Statistical correlation comparing the various morphological parameters comparing the diameter of the tumour in the papillary and follicular carcinomas in our study group.

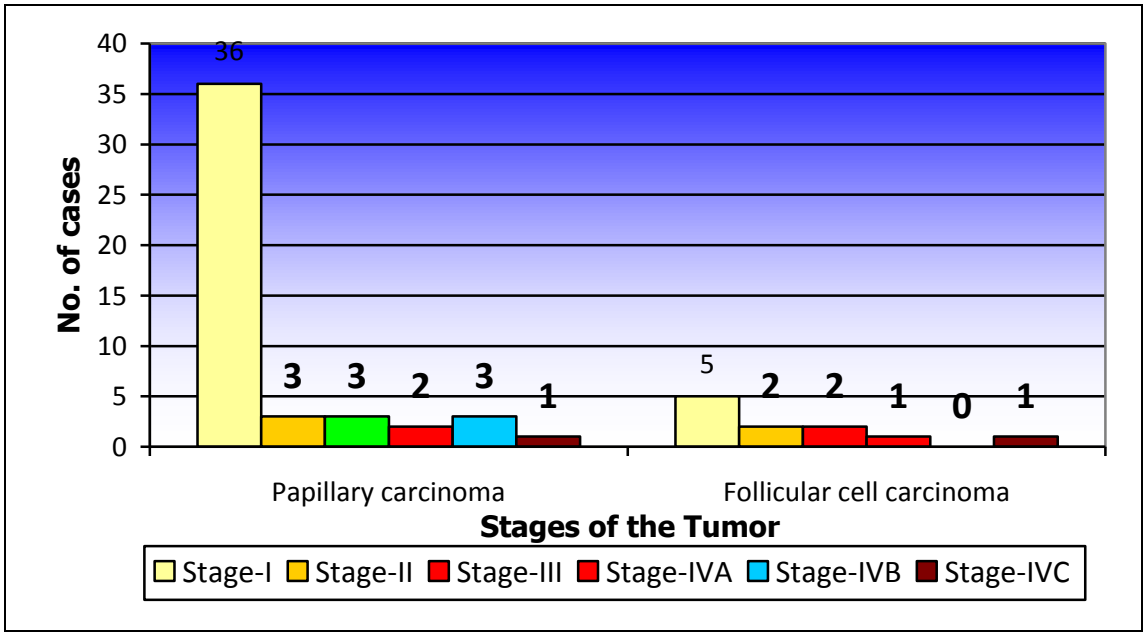
S.No.	Parameters	'P' Value	
		Papillary carcinoma	Follicular carcinoma
1.	Comparison between the diameter of the tumour and the multifocality	**0.02**	**0.3**
2.	Comparison between the diameter of the tumour and the extra thyroidal extension	**.01**	**0.001**
3.	Comparison between the diameter of the tumour and the lymph node metastasis	**<0.0001**	**0.001**
4.	Comparison between the diameter of the tumour and the distant metastasis	**0.26**	**0.35**

The statistical correlation was found between the diameter of the tumour and the multifocality, extra thyroidal extension and lymph node metastasis in papillary carcinoma and the 'P' value found to be 0.02, 0.01 and <0.0001 respectively and in cases of follicular carcinoma there was statistical correlation found between the diameter of the tumour and the extra thyroidal extension and 'P' value found to be 0.001 in both the cases. There was no statistical correlation found between the diameter of the tumour and the distant metastases and the results are depicted in the Table 17 mentioned above.

Table 18: AJCC TNM- 2010 staging of thyroid malignancies in the study group of 60 patients.

Staging	Papillary carcinoma	Percentage	Follicular cell carcinoma	Percentage
Stage I	36	75.0%	5	45.4%
Stage II	3	6.3%	2	18.2%
Stage III	3	6.3%	2	18.2%
Stage IVA	2	4.1%	1	9.1%
Stage IVB	3	6.3%	--	0.0%
Stage IVC	1	2.0%	1	9.1%
Total	**48**	**100%**	**11**	**100%**

Fig. 16: AJCC TNM 2010 staging of thyroid malignancies in the study group of 60 patients.

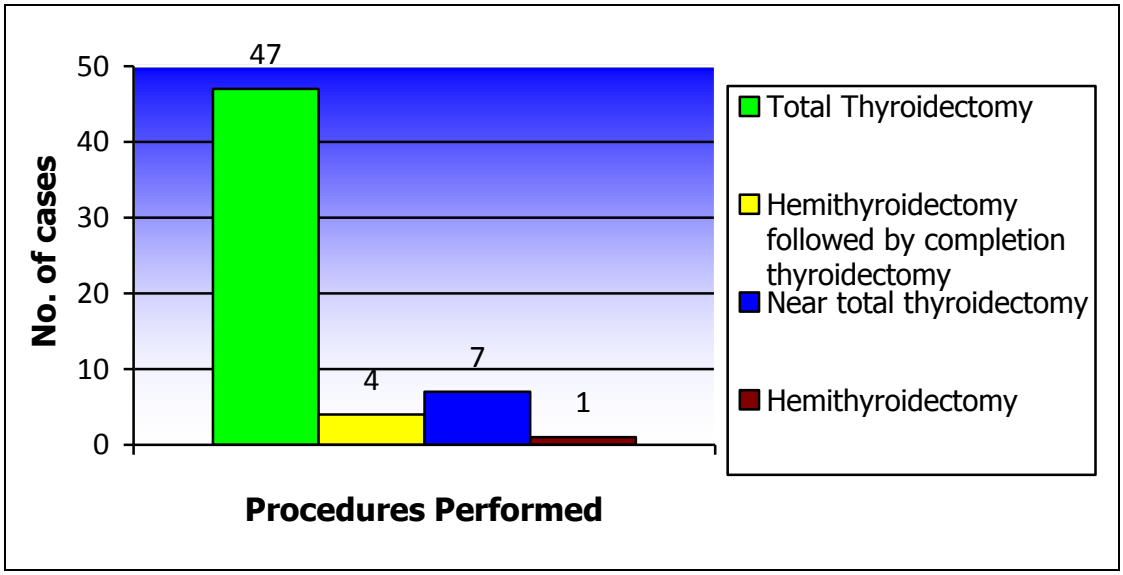


Most of the cases of the papillary carcinoma found to be Stage I (75%) and 45% of cases in the follicular carcinoma and are depicted in the Table 18 and Fig.16.

Table 19: Details of the surgery performed for the primary disease in this study.

Surgery	No. of Cases
Total Thyroidectomy	47
Hemithyroidectomy followed by completion thyroidectomy	4
Near total thyroidectomy	7
Hemithyroidectomy	1

Figure 17: Details of the surgery performed for the primary disease.



The most commonly performed surgery in the study was total thyroidectomy. Forty seven patients underwent total thyroidectomy. The four patients, whose cytology turned out to be follicular/Hurthle cells and with a solitary nodule underwent hemithyroidectomy and later a completion

thyroidectomy after the histopathological report had turned out to be follicular carcinoma. Five patients whose cytology showed, " Follicular cells of undetermined significance" and clinically showing multi nodular goiter and solitary nodular goiter with radiological findings suggestive of high possibility of malignancy underwent total thyroidectomy as the surgery for the primary procedure. Eight of the patients in the study had infiltration of the recurrent laryngeal nerve by the tumour and seven patients underwent a near-total thyroidectomy leaving minimal thyroid tissue adjoining the recurrent laryngeal nerve and other patient being anaplastic carcinoma was treated with external beam radiotherapy.

Surgery for Nodal Secondaries:

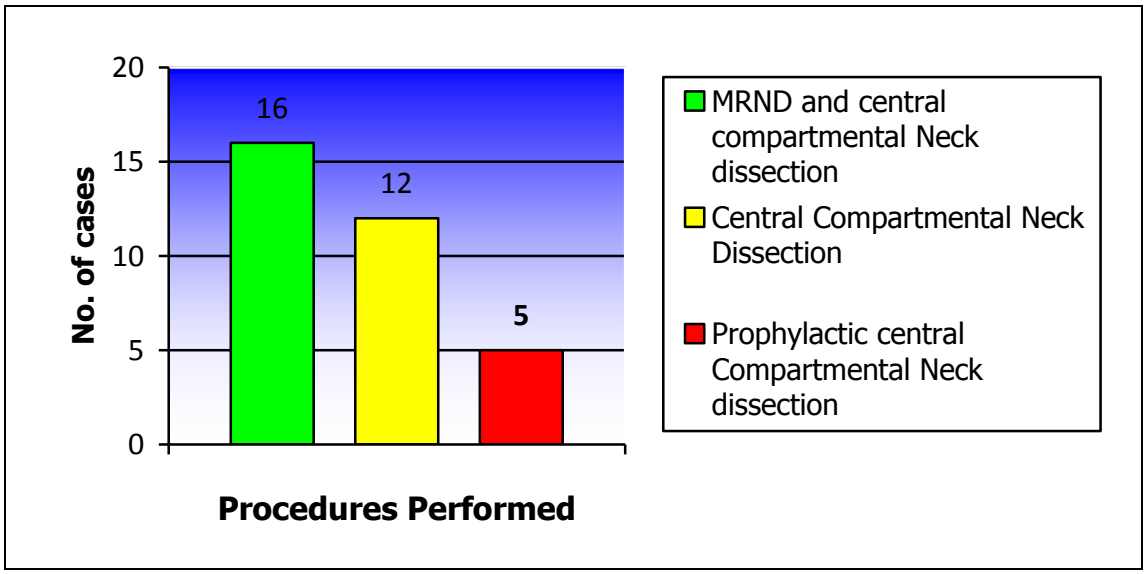
12 patients who had Level VI nodes clinically and radiologically were succumbed to central compartmental neck dissection and 16 patients who had cervical lymphadenopathy clinically and radiologically suspicious of malignancy in the Level II-V group of lymph nodes were subjected to functional neck dissection for level II, III and IV group of cervical lymph nodes and are depicted in Table 20 and Fig.18. The case with anaplastic carcinoma was subjected to External Beam Radiotherapy. One case which had a small lesion less than 1 cm underwent only hemithyroidectomy and did not undergo any neck dissection. Five cases without any nodal secondaries but with high risk features were subjected to Prophylactic central compartment neck dissection in addition to total thyroidectomy. The central compartment neck dissection included removal of pre tracheal, para tracheal and pre laryngeal nodal tissues. Other cases without any nodal secondaries and also with low risk features were

not subjected to any prophylactic central compartment neck dissection and were referred for radioactive iodine scanning for the residual disease. In total 33 cases were subjected to either central compartmental/lateral neck dissection in addition to the total thyroidectomy.

Table 20: Details of the patients who underwent neck dissection in this study.

Type of Neck Dissection	No. of cases
MRND and central compartmental Neck dissection	16
Central Compartmental Neck Dissection	12
Prophylactic central Compartmental Neck dissection	5
Total	**33**

Figure 18: Number of patients underwent neck dissection in this study.



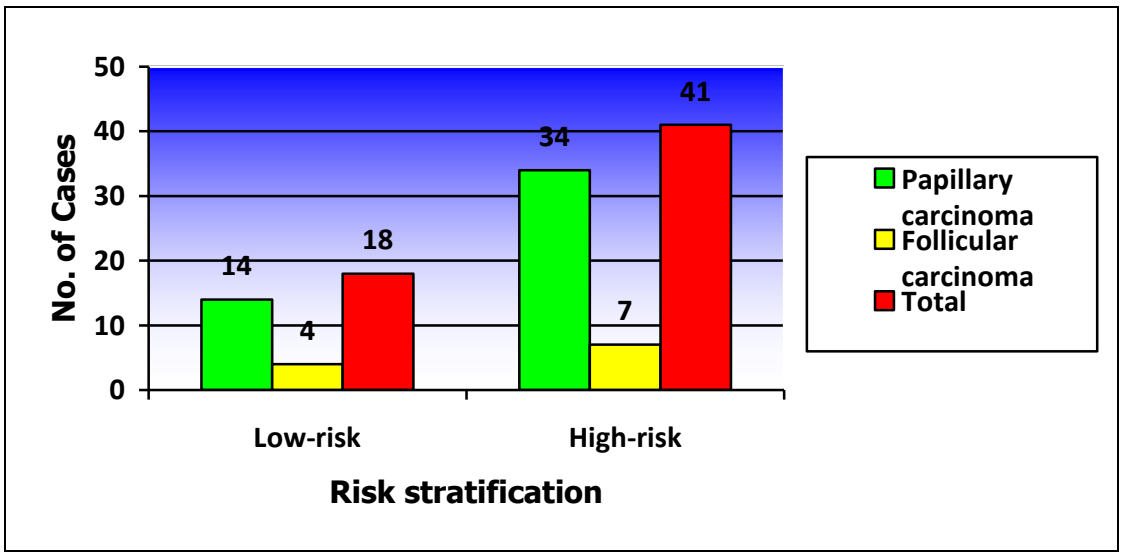
Risk Categorization

Among the 60 patients the study 59 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 21: AMES categorization scheme for well-differentiated Carcinomas in this study.

Type	Low-risk	High-risk
Papillary carcinoma	14	34
Follicular carcinoma	4	7
Total	18	41

Fig. 19: AMES categorization scheme for well-differentiated Carcinomas



When all patients with well-differentiated thyroid carcinomas were considered 30% of the patients were of the "low-risk" category and 70% were of the "high-risk" category. If patients with papillary thyroid carcinomas are alone considered 84% are of "high risk" and 20% are of "low 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 carpo pedal spasm by occlusion of the arm with a blood pressure cuff for 3 minutes) was positive.

Table 22: Complications of surgery found in this study after operated for thyroid carcinoma.

Complication	Number of cases
Transient hypo parathyroidism	7
Recurrent laryngeal nerve palsy	2

All symptomatic hypocalcaemia 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. Two patients out of 52 patients who had normal vocal cord status preoperatively suffered recurrent

laryngeal nerve palsy postoperatively and the remaining 8 patients who underwent near total thyroidectomy since they had pre operative unilateral vocal cord palsy did not have any additional vocal cord palsy. None of the patients had wound infection.

Among the patients who came for regular follow up none of the patients developed hypocalcaemia on a long term.

Postoperative Advice

All the patients with differentiated thyroid carcinomas were referred to higher centers for radioiodine therapy and follow up. One patient who had anaplastic carcinoma was advised to undergo external beam radiotherapy. All patients were started on the thyroxine suppressive therapy postoperatively.

DISCUSSION

Dave RI et al. (1983) and Basali 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[105, 106]. In our study, cases in the 4th decade & 5th decade of life followed by third decade are commonly affected. As we know, age at diagnosis is one of the important parameters that affect the prognosis. The mean age at the diagnosis is 49 years in the western studies and in our study group it was found to be 38 years.

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.[22] In the present study the sex ratio of thyroid malignancies is found to be 5:1. Even though females have an increased incidence of thyroid cancer, males demonstrate a poorer prognosis after diagnosis of the disease. The presence of large (greater than 5 cm) tumors doubles in the males. Males have high propensity to metastasize, both to regional nodes and distally. Mitchell et al. found that males were more likely to have advanced stage tumors at diagnosis. These factors, combined with the age at which men develop thyroid cancer, contribute to higher mortality rates among the male gender (7.1%) compared to women (3.5%). In our study we didn't find any significant difference between genders in the stage specific incidence between the groups which can be due to the less number of cases in the male gender.

The most plausible theory for the cause of the gender distinctions, however, is the hypothesis that the female sex hormones, primarily estrogen, play a role in the pathology of thyroid carcinoma and consequent to the finding, estrogen has become a major target for new therapy research in thyroid cancer. The supportive evidence for the estrogen theory is the decrease in incidence for females after menopause. In future, the molecular therapy targeting the estrogen receptor could become a new mode of treatment and possibly prophylaxis for thyroid carcinoma in high risk familial cases, but extensive studies looking at into these molecular issues are needed. Also we found difference in the mean age of incidence between the histological variants of the papillary carcinoma.

Table 23: Gender incidence of thyroid malignancies – Comparison.

Gender	Dos Santos Silva et al.[22]	Our study
Female:Male ratio	3:1 (74.1:25.9)	5:1

Clinical features that give rise to suspicion of malignancy include nodules at the extremes of age, male gender, hard consistency, fixation to the surrounding structures, and size of the tumour greater than 4 cm, rapid growth and a solitary nodule, a history of exposure to radiation in childhood. The most important finding suggestive of malignancy is implied by the presence of cervical lymphadenopathy.

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.[106] in 1996 in Germany and published in 2000; which was also the predominant symptom in Kannan RR[108] study of 670 Cases of carcinoma thyroid from 1956 to 1996 in cancer institute, Madras.

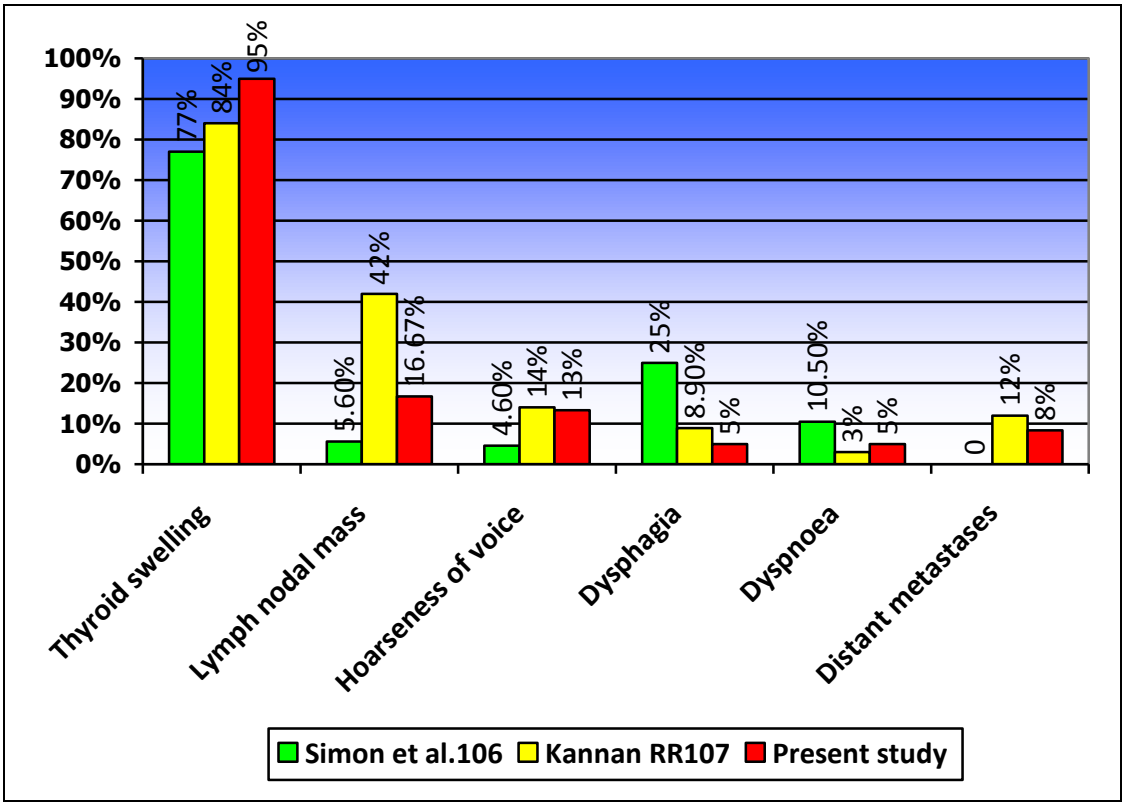
Thyroid carcinoma is known for its variability in the presentation ranging from the solitary thyroid nodule, multi nodular thyroid and also the isolated lymph node metastases without any thyroid swelling. The distant metastases found in our study were five out sixty patients. The hoarseness of voice in this study was due to the recurrent laryngeal nerve involvement which was found in eight of the patients and all were unilateral. The documentation of the vocal cord status using indirect laryngoscopic examination preoperatively is mandatory and all cases of thyroid carcinoma need to be carefully looked up even if they are not symptomatic. Vocal cord palsy was higher among the locally invasive tumours particularly anaplastic carcinoma and papillary carcinoma.

The percentage of patients presenting with dysphagia and dyspnea are very much less (6% each) compared to the study by Simon et al.[106] (25% and 10.5%). 8.33% of patients presented with distant metastases compare to 12% in Kannan RR[107] study.

Table 24: Clinical features of thyroid malignancies – Comparison between the studies.

Symptoms	Simon et al.[106]	Kannan RR[107]	Present study
Thyroid swelling	77%	84%	95%
Lymph nodal mass	5.6%	42%	16.67%
Hoarseness of voice	4.6%	14%	13.33%
Dysphagia	25%	8.9%	5%
Dyspnoea	10.5%	3%	5%
Distant metastases	0	12%	8.33%

Figure 20: Clinical features of thyroid malignancies – Comparison between the studies.



Thyroid carcinoma patients do not present with thyroid dysfunction commonly as numerous studies show hyperthyroidism in 1-2% of patients and in our study only one patient had features of hyperthyroidism that had solitary thyroid nodule and was managed accordingly.

As we know the course of the thyroid carcinoma can vary from the indolent course to slow growing tumour and to aggressive growth depending upon the type of the histological variants, and the type of malignancy and also depends upon the gender and the mode of presentation of the tumour. In our study, 70% of the cases present in the duration less than one year and 30% of cases have more than 12 months of history of the thyroid swelling which depicts the slow growing nature of thyroid carcinoma. Three of the cases who had only lymph node metastasis have varied duration of the history. Many patients have the tendency to present later to the physician owing to the low socio economic status, ignorance of the disease.

Cytological examinations by FNAC play an important role in the diagnosis of thyroid carcinoma in Solitary thyroid nodules. As per the NCI's state of the science conference held in 2007, FNA diagnosis from the FNA specimen is typically categorized into six types as described earlier. Although FNAC is sensitive, false negative results are common and FNAC needs to be repeated if concerning features found in the clinical features and/or sonographic features. Molecular diagnosis of mutations in BRAF, RET, or RAS patterns in the FNAC

samples that are indeterminate (Follicular/Hurthle cells of follicular cells of undetermined significance) but it is not commonly done due to the unavailability of the molecular tests in routine clinical practice. In our study, FNAC was found to be useful in diagnosis of thyroid carcinoma. FNAC was repeated in cases where the initial FNAC report which came as non diagnostic or follicular cells of undetermined significance. FNAC could not differentiate benign and malignant follicular lesions. The sensitivity of FNAC could not be found out in this study.

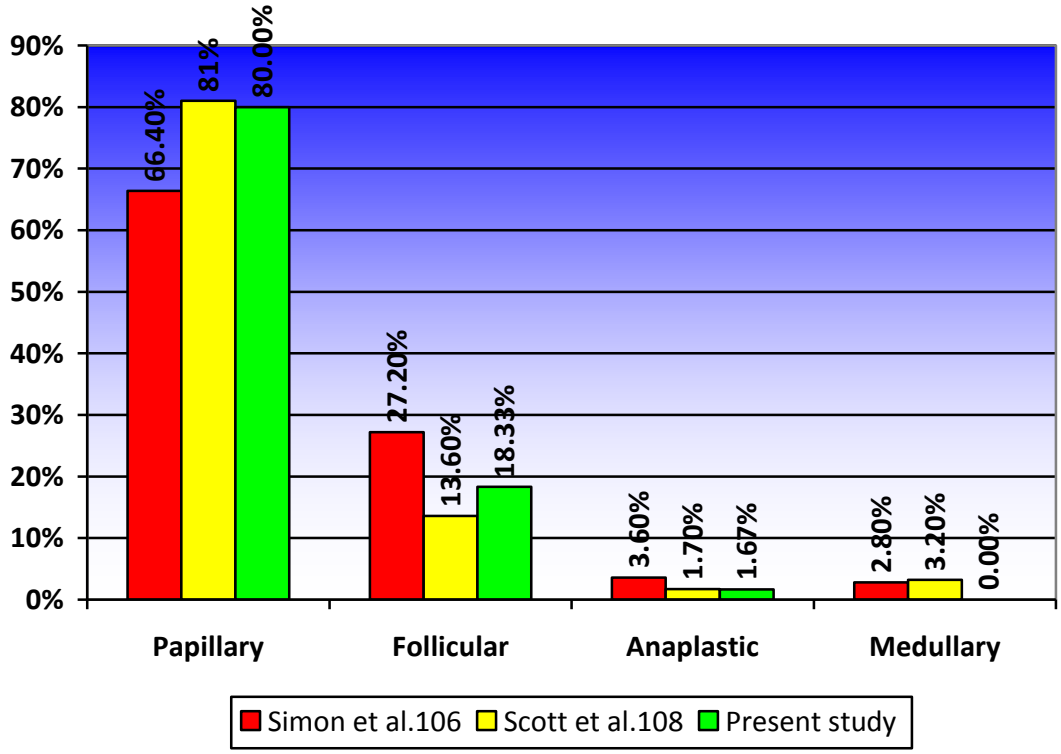
In the present study the papillary carcinoma was the most common type of thyroid malignancy seen in the hospital accounting for about 80 percent of the cases. In the study conducted by Simon et al.,[106] papillary thyroid carcinoma formed about 66.4% of the study. The proportions of different types of thyroid malignancies in the present study are similar to those in the study conducted by Simon et al.[106].

Among the follicular cell carcinoma, Hurthle cell carcinoma occurred in three cases and they have high metastatic potential than the follicular cell carcinoma and hence they are considered as the separate entity in the treatment guidelines different from the follicular cell carcinoma. In our study we found three cases of Hurthle cell carcinoma which had high incidence of lymph node and the distant metastasis than the follicular cell carcinoma.

Table 25: Various types of thyroid malignancies in different studies – Comparison

Type	Simon et al.[106]	Scott et al.[108]	Present study
Papillary	66.4%	81%	80%
Follicular	27.2%	13.6%	18.33%
Anaplastic	3.6%	1.7%	1.67%
Medullary	2.8%	3.2%	0

Figure 21: Various types of thyroid malignancies in different studies - Comparison



There are numerous histo pathologic variants of Papillary carcinoma of thyroid and each variant shows a combination of specific growth patterns, cell types and stromal changes histologically and the criteria used to define these subtypes are not rigorously defined which leads to inter observer variations.

In our study we found 30% incidence of lymph node metastases in the follicular variant slightly lesser than that of the classical papillary carcinoma cases and also the mean age of presentation was 33 years in comparison to the classical papillary carcinoma cases who had 37 years of age as the incidence. And also FVPTC showed less incidence of extra thyroidal invasion than the classical papillary carcinoma and also less calcifications in Sonography.

The frequency of prevalence of columnar cell variant, another ominous subtype of papillary carcinoma in the present study was 6.25%, the mean age being 46 years of age. They have less female incidence in relation to the other histological variants of the papillary thyroid carcinoma. The clinical presentation of these was evidently an indicator of their aggressive clinical behavior. In our study we found high incidence of lymph node metastases in comparable to the classical papillary carcinoma. The morphologic heterogeneity is found commonly in columnar cell variant carcinomas than other variants.

The tall cell variant of papillary thyroid carcinoma is not a common pathologic entity with the prevalence ranged from 4% to 17% of cases. The pathologists have proposed diagnostic criteria which include a composition of more than fifty percent tall cells, with a tall cell height of at least twice the width, cytoplasm eosinophilic and the nuclear features characteristic of papillary thyroid carcinoma. This variant is known for its rarity. In our study we found the prevalence of 4.17% in total number of the patients of papillary thyroid carcinoma (2 cases) and both of them had lymph node metastases

and they occurred in the fifth and sixth decade of life. Also they had equal gender incidence. There were no distant metastases found in our study in respect to the tall cell variant. Tall cell variant is high risk histological behavior which needs clinical suspicion and evaluation for the invasion and the metastases.

The other types of histological variants include the oncocytic variant, encapsulated variant, clear cell and oxyphilic variant, papillary carcinoma with lipomatous stroma, Warthin's-like tumor or with nodular fasciitis-like stroma and cribriform papillary carcinoma have been reported in the literature and each variants vary in the prevalence, gender difference and also the clinico pathological features and they also need to be considered in the cytological examination.

Thyroid calcifications within a mass are an important sonographic finding, and a malignant nodule may show both coarse calcifications and micro calcifications. Calcifications within a solitary mass can be considered an indicator of malignancy. Even though the coarse dystrophic calcifications within the thyroid tissue are considered to be of no diagnostic value, some articles have suggested that they would seem to have an association with carcinoma. Pathologically, thyroid calcifications are divided into psammoma bodies and dystrophic calcifications. Psammoma bodies are described as laminated, basophilic, spherical concretions and are a characteristic finding of papillary carcinoma. Most micro calcifications on Sonography represent psammoma bodies, suggesting cancerous changes.

In our study, as per the NCCN guidelines for the suspicious sonographic features, it was found out that the hypoechogenic nodules were found in 39 cases out of 48 cases of papillary carcinoma, while 8 cases out of 11 cases of Follicular carcinoma exhibit the same finding which explains the importance of sonographic examination in the diagnosis of thyroid carcinoma and the most malignant nodules present as Hypoechogenic structures and henceforth the value of suspicious sonographic features are established.

We found micro calcifications in 33 cases of papillary carcinoma but surprisingly only in 2 cases of follicular carcinoma which establishes the high incidence of micro calcifications in the papillary carcinoma. Sonographic examination is also useful in establishing the extent of the tumour and the nodes in the neck. Also Sonography is useful for image guided FNAC to increase the sensitivity of the cytological diagnosis. Although computed tomography examination is more sensitive in establishing the extent of the tumour but it is avoided usually in the fear of delayed radioactive iodine studies after surgery, and hence CT is done only for large bulky and tumours extending substernally.

In our study more than 70% of cases belong to the AJCC-TNM Stage I disease in cases of papillary carcinoma and 44% of cases follicular carcinoma cases belong to the same. This implies the large number of cases in the study with good prognosis. In a study conducted by Simon et al.[107] in 2000 the differentiated thyroid carcinomas were staged and their percentages were calculated. Various studies have described the incidence based on AJCC 5^{th} and 6^{th} edition of TNM staging of thyroid carcinoma and hence the results may not be able to be compared to the other

studies. The study which based on the AJCC TNM staging 7th edition is compared and our study showed high percentage of Stage IV disease. Simon et al showed higher incidence of Stage I disease.

In a Meta analysis, it was found that nodal metastasis was found in 36% of the papillary carcinoma cases and 17% of the patients with follicular carcinoma and 80% in children. Even though the lymph node metastases play an important role as prognosis in follicular carcinoma, the importance in papillary carcinoma is less. In our study, we found high incidence of lymph node metastases in papillary carcinoma (45.83% of cases) and 36.36% of follicular cell carcinoma cases. In all the cases of thyroid carcinoma, it was found to be 43.33% of cases with lymph node metastasis which is higher than many of the cases which showed a lymph node metastasis of 28-37% of cases in various studies. This can be presumed due to the long duration of the thyroid swelling presented in many of the cases and the sensitivity of the ultrasound of the lateral and central neck in detecting the suspicious nodes in the thyroid carcinoma.

In our study group, we found out that lymph nodes were clinically palpable in 10 of which three cases did not have any clinically evident thyroid swelling or nodules. Ultrasonographic evaluation showed suspicious nodes in 26 cases of which 22 cases where papillary carcinoma of thyroid and 4 cases were follicular cell carcinoma. The lymph node metastasis is related to the histological variants of both papillary and follicular carcinoma. Lymph node metastases was found high in tall cell, columnar cell variant and less in follicular variant of the papillary carcinoma of thyroid.

The thyroid carcinoma has low incidence of distant metastases compared to many of the other malignancies found in the body. In our study, we found distant metastasis found in five cases of which three cases had papillary carcinoma. Although the papillary carcinoma has high propensity for lymph node metastases, the incidence of haemetaogenous spread is less in compared to the follicular carcinoma, and in our study it was found to be 18.2% of cases. Papillary carcinoma of thyroid has high propensity for pulmonary metastases which is usually detected by radiographic examination, CT while the high sensitivity tool being the PET-CT. The follicular carcinoma of thyroid has avidity toward the bony metastasis due to the genetic alterations and the nature of the tumour.

In our study we found a clear relation between the primary tumor diameter and the development of more advanced disease. When tumor diameter is taken into consideration, Follicular carcinoma of the thyroid showed a more indolent clinical course than the papillary carcinoma of thyroid as the duration of the swelling taken into the consideration in contrary to some of the other studies which showed more indolent course in cases of papillary carcinoma of thyroid.

The tumor size adjusted risk of multifocal carcinoma was statistically significant in papillary carcinoma of thyroid ('P" value - 0.02) with the multifocality found in 20% of cases with tumour diameter less than 4 cm and 34% of cases of lesions above 4cm in diameter and there was cumulative risk of multifocality with increased size and the need for aggressive therapy in papillary

carcinoma. And multifocality was found only in tumours above 4cm in cases of follicular carcinoma of thyroid but the statistical correlation was not found due to the less number of cases in the study.

The identification of primary tumor size as a risk factor in itself is not new. Many prognostic scoring systems have embraced this parameter. The findings from the present study are largely in agreement with those of Machens *et al.* However, Machens *et al* – regardless of histological entity – found an increased risk of distant metastases for tumors larger than 20 mm comparable to 20 mm in the present study.

Machens *et al* suggest pursuing aggressive diagnostic and therapeutic measures to rule out malignancy in any nodule exceeding 20 mm in diameter; these constitute about one-third of all thyroid nodules. Pursuing this strategy in all nodules over 10 mm would involve a far greater part of the population, and would therefore incur much greater costs. The present results, however, indicate that from a diameter of about 1 cm onwards, thyroid nodules deserve appropriate specialist evaluation in order to detect carcinomas in a curable stage. This is also advocated in the 2006 European consensus on the management of thyroid nodules.

An important criterion for classifying tumors is risk. Risk, however, is a wide-ranging concept and can be specified for many parameters. As patients with differentiated thyroid carcinoma (especially the ones with lower tumor stages) have a long-term survival of > 95%, 14 additional parameters for defining risk are useful to assist in determining the classification of tumors. The occurrence of distant metastases, which is generally considered to be a severe adverse event in the course of disease progression, can be such a criterion.

An interesting observation in the present study is the non-trivial percentage of FTC patients who develop lymph node metastases particularly above the diameter of tumour of 4 cm compared to papillary carcinoma of thyroid where lymph node metastases occur in all diameters of the tumour but increased risk found statistically above 4cm. (Table 15/Fig 15). This is somewhat contradictory to the supposedly primarily hematogenic spread of FTC. However, these lymph node metastases are almost exclusively caused by carcinomas with extra-thyroidal growth. It is conceivable that tumor cells that spread outside the thyroid can also be transported via the lymphatic pathways.

FTC patients with extra-thyroidal tumor growth should probably undergo a central compartment neck dissection in order to ascertain their lymph node status. As can be seen from the curves of tumor size adjusted cumulative risks, some tumors start metastasizing at considerably smaller diameters than others. Should one want to make a more accurate analysis of the risk of metastases (whether in addition to, or as a replacement of existing morphologic classification) genetic analysis is unavoidable.

The surgery for papillary carcinoma range from hemithyroidectomy to total thyroidectomy and also neck node dissection based on the clinical and radiological findings. Indications for total thyroidectomy in our study include age younger than 15 years or older than 45 years, radiation history, known distant metastases, bilateral nodularity, extra thyroidal extension, tumour greater than 4 cm in diameter, or aggressive variants which include the tall cell variant, columnar cell, or poorly differentiated and also for the patients who preferred total thyroidectomy and patients who tend to lose follow up protocol for

recurrence and metastasize. The controversy between the conservative surgery to aggressive surgery has less role in experienced surgeons hands and total thyroidectomy should be preferred for all cases of thyroid carcinoma particularly due to the risk of multifocality of well differentiated tumours.

The role of prophylactic central compartment node dissection in medullary carcinoma of thyroid is well known. Studies have shown the importance of prophylactic central compartment neck node dissection in high risk patients who have high chances of micrometastasis to the central compartmental neck nodes. In our study, when lymph nodes are not enlarged, the prophylactic central compartmental dissection was done in seven cases based on the size of the tumour, high risk variants, and involvement of surrounding structures.

The limitations of the study are that it is a retrospective study of the thyroid carcinoma where as other disorders of thyroid was not studied for the comparisons. Also the sensitivity of the FNA and other modalities in establishing the diagnosis of the thyroid carcinoma preoperatively could not be observed.

CONCLUSION

We found the incidence of thyroid cancer was higher in female gender with ratio of 5:1 and the incidence of thyroid cancers predominantly occur in the fourth decade of life. The most common mode of clinical presentation was thyroid swelling which was higher than those in comparative studies and the Ultrasonographic features play an vital role in finding the nodules suspicious for malignancy. Fine needle aspiration cytology is an inexpensive accurate and practical investigation for evaluation of thyroid carcinomas and the molecular studies may play an important role in establishing the diagnosis and evaluation in future era. The histological variants of papillary and follicular cell carcinoma have different clinical behavior and they need to be evaluated for the different incidence of metastases to node and distant areas. The size of the tumour is an individual parameter that helps to find out the risk for multifocality, invasion and the nodal metastases in both the papillary and follicular carcinoma of thyroid. The extent of surgery needs to be on the extent of the lesion, nodal metastases and the risk category.

SUMMARY

In summary, a total number of 60 patients with thyroid cancer were evaluated in the study period from June 2010 to May 2012 at Madurai Medical College retrospectively. The occurrence of thyroid cancer was maximum in the 4^{th} decade of life followed by the 5^{th} decade of the life. Female gender outnumbered males with a ratio of 5: 1 in this study, the commonest symptom of thyroid malignancy was a painless swelling in the front of the neck (95% of the patients) and the duration of symptoms varied greatly; with 70% of the patients presenting with a duration of less than 1 year. FNAC was helpful in establishing the diagnosis in 80% of cases. Ultrasonography of the neck was found to be very sensitive tool in thyroid carcinoma to find out the features suspicious of the malignancy and the impalpable nodal metastases.

The most common histopathological type was papillary carcinoma thyroid (80%); followed by follicular carcinoma thyroid (18.33%) and one case of the anaplastic carcinoma. The age of presentation, gender incidence and the clinical presentations varied between the histological variants of papillary and follicular carcinoma of thyroid. The diameter of the tumour was found to be an independent parameter and statistically correlates with the morphological parameters of the thyroid carcinoma that include the multifocality, extra thyroidal invasion, lymph node and distant metastases and were statistically correlated. Large number of the patients in this study belonged to the high risk category as per AMES Categorization criteria and also to the Stage I disease by AJCC (2010) TNM classification system. Total thyroidectomy was the common

procedure required for the treatment for the thyroid malignancies and the extent of the lymph node dissection depends on the level of lymph node involvement and the prophylactic lymph node dissection in well differentiated thyroid cancers are needed in high risk patients. The common complications commonly found in the study were vocal cord palsy and the transient hypoparathyroidism.

ANNEXURE-I

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ANNEXURE - II

PROFORMA

Unit	:		I.P. No.	:		Sl. No.	:	
Name	:		Age	:		Sex	:	
DOA	:		DOO	:		DOD	:	

I.	Chief Complaints			:	
II.	History of Present Illness				
	1.	Swelling in the Neck		:	
		a.	Onset	:	
		b.	Duration	:	
		c.	Rate of growth	:	
		d.	Associated with pain	:	
	2.	Pain			
		a.	Duration	:	
		b.	Character	:	
		c.	Radiation	:	
	3.	Pressure effect			
		a.	Dyspnoea	:	
		b.	Dysphagia	:	
		c.	Hoarseness of voice	:	
	4.	Symptoms of Thyrotoxicosis		:	
	5.	Symptoms of Hypothyroidism		:	
III.	Past History			:	

IV.	Local Examination				
	1.	Swelling in anterior aspect of Neck		:	
		a.	Size	:	
		b.	Surface	:	
		c.	Movement with deglutition	:	
		d.	Edge	:	
		e.	Lower Borders	:	
		f.	Other Swellings	:	
		g.	Dilatation of veins	:	
		h.	Congestion of face on raising the hand	:	
		i.	Consistency	:	
		j.	Plane	:	
		k.	Mobility	:	
		l.	Cervical Lymph nodes	:	
V.	Ultrasonographic findings				
	1.	Solid/ Hypoechogenic structure		:	
	2.	Heterogeneous echogenic structure		:	
	3.	Irregular margins		:	
	4.	Extra-glandular extension		:	
	5.	Fine punctuate internal calcifications.		:	
	6.	Tracheal infiltration		:	
	7.	Nodes if found		:	
		a.	Suspicious	:	
		b.	Insignificant	:	
VI.	Vocal cord status			:	
VII.	Thyroid function tests			:	

VIII.	Metastatic work up		:	
IX.	FNAC Report			
	1.	Papillary Lesions of suspicious of papillary carcinoma.	:	
	2.	Follicular/Hurthle cell neoplasms	:	
	3.	Follicular cells of undetermined significance	:	
	4.	Medullary carcinoma	:	
	5.	Insufficient biopsy, non diagnostic	:	
	6.	Lymphoma	:	
	7.	Anaplastic carcinoma	:	
X.	Repeat FNAC finding if it was done		:	
XI.	Procedure performed		:	
	1.	Total Thyroidectomy	:	
	2.	Hemithyroidectomy followed by completion thyroidectomy	:	
	3.	Near total thyroidectomy	:	
	4.	Hemithyroidectomy	:	
XII.	Lymph node dissection			
	1.	MRND and central compartmental Neck dissection	:	
	2.	Central Compartmental Neck Dissection	:	
	3.	Therapeutic central Compartmental Neck dissection	:	
XIII.	Intra operative findings		:	
XIV.	Post operative biopsy report			
	1.	Histological variant	:	
	2.	Type of histological variant	:	
	3.	Multifocality	:	
	4.	Extrathyroidal extension	:	
XV.	Radio Therapy		:	
XVI.	Complications		:	
XVII.	Treatment of Complication		:	

ANNEXURE – III

MASTER CHART

Key to Master Chart

Sl.No. - Serial number

Age - Age of the patient

Gender

- M - Male
- F - Female

Variants

- F - Follicular cell carcinoma
- P - Papillary cell carcinoma

Thyroid profile

- H - Hyperthyroidism
- N - Normal

Vocal cord Status

- U - Unilateral Vocal Cord Palsy
- No - No Vocal Cord Palsy

FNAC finding

- P - Papillary carcinoma or features of papillary carcinoma
- FCN - Follicular/Hurthle cell Neoplasms
- FCUS - Follicular cells of undermined significance
- A - Anaplastic carcinoma
- N Non diagnostic

Histological variant

- CL - Classical Papillary carcinoma
- FV - Folicular variant of Papillary carcinoma
- C - Columnar variant
- T - Tall cell variant
- H - Hurthle cell variant
- F - Follicular carcinoma
- A - Anaplastic carcinoma

AMES

LR	-	Low Risk
HR	-	High Risk

Primary Surgery

TT	-	Total Thyroidectomy
NT	-	Near Total Thyroidectomy
HT	-	Hemi Thyroidectomy
HTCT	-	Hemi Thyroidectomy followed by completion Thyroidectomy
NA	-	Not Applicable

Neck Dissection

No	-	No Neck Dissection
FND	-	Functional Neck Dissection
CLND	-	Central compartment Lymph Node Dissection
PCLND	-	Prophylactic Central compartment Lymph Node Dissection

Complications

T	-	Transient Hypoparathyroidism
P	-	Vocal Cord Palsy
NO	-	No complications
NA	-	NA

MASTER CHART

Sl.No.	Age	Gender	Variants	Thyroid Profile	Vocal cord status	Size of the swelling (in cm.)	FNAC	Invasion	Multifocality	Lymph Node Metastases	Distant Metastases	Histological variant	TNM - Stage	AMES	Primary surgery	Neck dissection	Complications
1.	17	F	P	N	No	1-2	P	No	No	No	No	CL	I	LR	TT	No	No
2.	16	F	P	N	No	2-4	P	No	No	No	No	CL	I	LR	TT	No	No
3.	23	F	P	N	No	4-6	P	No	No	Yes	No	CL	I	HR	TT	CLND	No
4.	27	F	P	N	No	0-1	P	No	No	No	No	CL	I	LR	HT	No	No
5.	26	F	P	N	No	2-4	P	Yes	No	Yes	No	CL	I	HR	TT	FND	No
6.	29	F	P	N	No	1-2	P	No	No	No	No	FV	I	LR	TT	No	No
7.	21	F	P	N	No	6-8	P	No	No	Yes	No	CL	I	HR	TT	CLND	T
8.	27	F	P	N	No	4-6	P	Yes	Yes	Yes	No	CL	I	HR	TT	FND	No
9.	25	F	P	N	U	>8	P	Yes	Yes	Yes	No	CL	I	HR	NT	FND	No
10.	26	F	P	H	No	2-4	P	No	No	No	No	CL	I	LR	TT	No	No
11.	28	F	P	N	No	6-8	P	Yes	Yes	Yes	No	CL	I	HR	TT	FND	P
12.	34	F	P	N	No	4-6	N	Yes	Yes	Yes	No	CL	I	HR	TT	FND	No
13.	36	F	P	N	No	1-2	P	No	No	No	No	FV	I	LR	TT	No	No
14.	39	F	P	N	No	4-6	P	No	No	No	No	CL	I	HR	TT	No	No
15.	34	F	P	N	No	0-1	P	No	Yes	Yes	No	FV	I	HR	TT	CLND	No
16.	33	F	P	N	No	2-4	P	No	No	No	No	CL	I	LR	TT	No	No
17.	39	F	P	N	U	6-8	P	Yes	No	Yes	No	CL	I	HR	NT	CLND	T
18.	38	F	P	N	No	4-6	P	Yes	No	No	No	CL	I	HR	TT	PCLND	No
19.	34	F	P	N	No	>8	P	No	No	No	No	FV	I	HR	TT	PCLND	No
20.	33	F	P	N	No	2-4	P	No	No	No	No	CL	I	LR	TT	No	No

Sl.No.	Age	Gender	Variants	Thyroid Profile	Vocal cord status	Size of the swelling (in cm.)	FNAC	Invasion	Multifocality	Lymph Node Metastases	Distant Metastases	Histological variant	TNM - Stage	AMES	Primary surgery	Neck dissection	Complications
21.	36	F	P	N	No	4-6	P	Yes	Yes	Yes	No	FV	I	HR	TT	CLND	T
22.	35	F	P	N	No	1-2	P	No	No	No	No	CL	I	LR	TT	No	No
23.	31	F	P	N	No	6-8	P	No	No	No	No	CL	I	HR	TT	No	No
24.	36	F	P	N	No	0-1	P	No	No	No	No	FV	I	LR	TT	No	No
25.	32	F	P	N	No	6-8	P	No	No	No	No	C	I	HR	TT	No	No
26.	33	F	P	N	No	2-4	P	Yes	Yes	Yes	Yes	CL	II	HR	TT	FND	No
27.	30	F	P	N	No	6-8	P	No	No	No	No	FV	I	HR	TT	No	No
28.	44	F	P	N	No	4-6	P	No	No	Yes	No	CL	I	HR	TT	CLND	No
29.	40	F	P	N	No	1-2	P	No	No	No	No	CL	I	LR	TT	No	No
30.	41	F	P	N	No	0-1	P	No	No	Yes	No	C	I	HR	TT	CLND	No
31.	44	F	P	N	No	2-4	P	No	No	No	No	CL	I	LR	TT	No	No
32.	43	F	P	N	No	>8	P	No	No	No	No	CL	I	HR	TT	No	No
33.	42	F	P	N	No	2-4	P	No	No	No	No	FV	I	LR	TT	No	No
34.	41	F	P	N	No	2-4	P	Yes	No	Yes	No	CL	I	HR	TT	CLND	No
35.	41	F	P	N	No	2-4	P	Yes	Yes	Yes	Yes	CL	I	HR	TT	FND	No
36.	53	F	P	N	No	2-4	FCUS	No	No	Yes	No	CL	I	HR	TT	CLND	No
37.	67	F	P	N	U	4-6	P	No	No	No	No	FV	IVA	HR	NT	CLND	No
38.	62	F	P	N	No	2-4	P	No	No	No	No	CL	II	HR	TT	No	No
39.	71	F	P	N	No	4-6	P	Yes	Yes	Yes	No	T	IVB	HR	TT	FND	No
40.	78	F	P	N	U	6-8	P	Yes	Yes	Yes	No	CL	IVB	HR	NT	FND	T

Sl.No.	Age	Gender	Variants	Thyroid Profile	Vocal cord status	Size of the swelling (in cm.)	FNAC	Invasion	Multifocality	Lymph Node Metastases	Distant Metastases	Histological variant	TNM - Stage	AMES	Primary surgery	Neck dissection	Complications
41.	34	M	P	N	No	2-4	P	Yes	Yes	Yes	No	T	IVA	HR	TT	FND	No
42.	34	M	P	N	No	4-6	P	Yes	No	Yes	No	CL	IVB	HR	TT	FND	P
43.	38	M	P	N	No	1-2	P	Yes	Yes	No	No	CL	III	HR	TT	CLND	No
44.	43	M	P	N	No	4-6	P	No	No	No	No	CL	III	HR	TT	PCLND	No
45.	52	M	P	N	U	>8	P	Yes	Yes	Yes	Yes	FV	IVC	HR	NT	FND	No
46.	61	M	P	N	No	4-6	N	Yes	No	No	No	CL	III	HR	TT	PCLND	No
47.	72	M	P	N	No	4-6	P	No	No	Yes	No	C	I	HR	TT	CLND	No
48.	77	M	P	N	No	1-2	P	No	No	No	No	CL	II	LR	TT	No	No
49.	24	F	F	N	No	4-6	FCN	No	No	No	No	F	I	HR	HTCT	No	No
50.	27	F	F	N	No	2-4	FCUS	Yes	No	No	No	F	I	HR	TT	PCLND	No
51.	33	F	F	N	No	1-2	N	No	No	No	No	F	I	LR	HTCT	No	No
52.	38	F	F	N	No	6	FCN	No	No	No	No	F	I	HR	TT	No	T
53.	30	F	F	N	U	4-6	FCN	Yes	Yes	Yes	Yes	H	II	HR	NT	FND	No
54.	41	F	F	N	No	2-4	FCN	No	No	No	No	F	I	LR	HTCT	No	No
55.	49	F	F	N	No	>8	N	No	Yes	Yes	No	H	IVA	HR	TT	FND	T
56.	46	F	F	N	No	4-6	FCN	No	No	Yes	No	F	III	HR	TT	FND	No
57.	51	F	F	N	No	2-4	FCUS	No	No	No	No	F	II	LR	HTCT	No	No
58.	37	M	F	N	U	6-8	FCN	Yes	Yes	Yes	Yes	H	IVC	HR	NT	FND	T
59.	55	M	F	N	No	4-6	FCUS	No	No	No	No	F	III	LR	TT	No	No
60.	67	F	A	N	U	4-6	A	Yes	No	No	No	A	IVA	HR	NA	NA	No