A STUDY ON INCIDENCE OF MALIGNANCY IN THYROID NODULES

Dissertation submitted to

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Branch – 1

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DEPARTMENT OF GENERAL SURGERY

MAY 2020

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **A STUDY ON INCIDENCE OF MALIGNANCY IN THYROID NODULES** is a bonafide and genuine research work carried out by me under the guidance of **Dr. PREMKUMAR S** M.S., Professor and HOD of Department of General Surgery, PSG Institute of Medical Sciences, Coimbatore.

Date : Signature of the Candidate

Place: Name: Dr.A. Soundrapandiyan.,

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **A STUDY ON INCIDENCE OF MALIGNANCY IN THYROID NODULES** is a bonafide word done by Dr. A.SOUNDRAPANDIYAN in partial fulfilment of the requirement for the degree of M.S. in General Surgery under my guidance.

Date:

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Following points must be noted:

1. IHEC should be informed of the date of initiation of the study
2. Status report of the study should be submitted to the IHEC every 12 months
3. PI and other investigators should co-operate fully with IHEC, who will monitor the trial from time to time
4. At the time of PI's retirement/intention to leave the institute, study responsibility should be transferred to a colleague after obtaining clearance from HOD, Status report, including accounts details should be submitted to IHEC and extramural sponsors
5. In case of any new information or any SAE, which could affect any study, must be informed to IHEC and sponsors. The PI should report SAEs occurred for IHEC approved studies within 7 days of the occurrence of the SAE. If the SAE is 'Death', the IHEC Secretariat will receive the SAE reporting form within 24 hours of the occurrence
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   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
   b. Alteration in the budgetary status should be clearly indicated and the revised budget form should be submitted
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7. Final report along with summary of findings and presentations/publications if any on closure of the study should be submitted to IHEC

Kindly note this approval is subject to ratification in the forthcoming full board review meeting of the IHEC.

Thanking You,

Yours Sincerely,

Dr Sudha Ramalingam
Alternate Member - Secretary
Institutional Human Ethics Committee

PSG Institute of Medical Sciences & Research
Institutional Human Ethics Committee

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To
Dr Soundarapandiyan A
Postgraduate
Department of General Surgery
Guide/s: Dr S Prem Kumar
PSG IMS & R
Coimbatore

Ref: Project No. **17/373**

Date: December 29, 2017

Dear Dr Soundarapandiyan,

Institutional Human Ethics Committee, PSG IMS&R reviewed and discussed your application dated 06.12.2017 to conduct the research study entitled "*A study on incidence of malignancy in thyroid nodules*" during the IHEC meeting held on 29.12.2017.

.The following documents were reviewed and approved:

1. Project submission form
2. Study protocol (Version 1 dated 06.12.2017)
3. Application for waiver of consent
4. Confidentiality statement
5. Data collection tool (Version 1 dated 06.12.2017)
6. Permission letter from concerned Heads of Department
7. Current CVs of Principal investigator, Co-investigator
8. Budget

The following members of the Institutional Human Ethics Committee (IHEC) were present at the meeting held on 29.12.2017 at IHEC Secretariat, PSG IMS & R between 10.00 am and 11.00 am:

Sl. No.	Name of the Member of IHEC	Qualification	Area of Expertise	Gender	Affiliation to the Institution Yes/No	Present at the meeting Yes/No
1	Mr R Nandakumar (Chairperson, IHEC)	BA., BL	Legal Expert	Male	No	Yes
2	Dr D Vijaya (Member – Secretary, IHEC)	M Sc., Ph D	Basic Medical Sciences (Biochemistry)	Female	Yes	Yes
3	Dr S Shanthakumari	MD	Pathology, Ethicist	Female	Yes	Yes
4	Dr Sudha Ramalingam	MD	Epidemiologist, Ethicist Alt. member-Secretary	Female	Yes	Yes
5	Dr G Subhashini	MD	Epidemiologist	Female	Yes	Yes

The study is approved in its presented form. The decision was arrived at through consensus. Neither PI nor any of proposed study team members were present during the decision making of the IHEC. The IHEC functions in accordance with the ICH-GCP/ICMR/Schedule Y guidelines. The approval is valid until one year from the date

ENDORSEMENT BY THE HOD/DEAN/HEAD OF THE INSTITUTION

This is to certify that the dissertation entitiled"**A STUDY ON INCIDENCE OF MALIGNANCY IN THYROID NODULES"** is a bonafide work done by Dr. A.SOUNDRAPANDIYAN, under the guidance of Dr. S.PREMKUMAR , Professor,Head of Department of General Surgery, PSG Institute of Medical Science and Research, Coimbatore.

Signature of the HOD
Dr. S. Premkumar
Professor and Head of Department,
Department of General Surgery,
PSG Institute of Medical Sciences,
Coimbatore

Signature of the Dean
Dr.Ramalingam S
Dean,
PSG Institute of Medical Sciences,
Coimbatore

ACKNOWLEDGEMENT

I wish to thank our Dean for having permitted me to conduct this study in our hospital.

I would like to sincerely thank Dr. S. Premkumar, Head of department of general surgery for his guidance and motivation . His mentorship was of paramount value all through the study.

My thanks are also to my colleagues for the considerable help extended to me.

I wish to place on record my gratitude to all the patients who have been an integral part of this study.

Finally and importantly ,I would like to thank my family for their support , encouragement and unwavering love which has been the pillar of my strength.

PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled "A STUDY ON INCIDENCE OF MALIGNANCY IN THYROID NODULES" of the candidate DR.A.SOUNDRAPANDIYAN with registration number 221711502 for the awards of M.S in the branch of GENERAL SURGERY . I Personally verified the urkund .com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows 6 percentage of plagiarism in the dissertation .

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ABSTRACT

INTRODUCTION :

A thyroid nodule is a discrete and radiographically definable lesion within the thyroid. Many thyroid nodules are not palpable, and not all palpable thyroid lesions correspond to a distinct radiographically definable lesion. Only findings truly definable radiographically may be classified as a thyroid nodule.

Thyroid nodules are very common with an estimated prevalence of 1% to 5% for palpable nodules. This prevalence is higher when considering nodules detected on imaging. The incidence of thyroid malignancy is raising. Thyroid cancers occurs in 5%to 15% of thyroid nodules.[1]

Aim:

The aim of the study is to determine the incidence of thyroid nodules in relation to age and sex of the patient turning out to be malignancy

OBJECTIVES

PRIMARY OBJECTIVE: To find out the incidence of malignancy in benign thyroid disorders in patients who get admitted and operated in PSG Institute of medical sciences and research, Coimbatore

SECONDARY OBJECTIVE:

1. To find out the demographic difference in patients presenting with malignancy in benign thyroid disorders.
2. To find out % of recurrence in these patients in thestudy group
3. To find out the histological types of malignancy in the study group

MATERIALS AND METHODS:

- STUDY DESIGN : Observational study
- STUDY POPULATION : Individuals who got admitted in surgery ward with thyroid nodule (solitary thyroid nodule, MNG, Hashimotos and other types) and operated at PSG Institute of medical sciences and research ,Coimbatore.
- STUDY LOCALITY: PSG Institute of Medical Sciences and Research, Coimbatore.
- SAMPLE SIZE: 151

- **Retrospective analytical study** will be carried out from period of Jan 2014 to Dec 2017 by collecting old case files from MRD.
- Details of patients demographics ,clinical presentation and diagnosis, results of FNAC ,USG findings, gross features and biopsy results of the resected thyroid specimens are obtained from patients case files.
- H& E stained slides of the thyroidectomy specimens were analyzed by an independent pathologist. **Histopathological diagnosis will be considered as gold standard**.

Parameters for assessment

Clinical details (age,sex), gross and microscopic picture of all thyroid malignant tumors,will be discussed individually. The following statistical tests will be performed.

1.Chi sqare test

2.Ratio

3.Percentage

RESULTS

Out of 151 patients with benign thyroid nodule, 15 were found to develop malignancy (10%) , in which 14 had papillary carcinoma of thyroid and 1 had hurtle cell carcinoma.

There was statistically significant association between age and malignancy.

Out of 76 patient of solitary nodular goitre 10 patient found to be malignant and out of 75 multi nodular goitre 5 found to be malignant histopathologically.

CONCLUSION

From this study we have concluded that the incidence of thyroid malignancy in benign thyroid disorder is 10%.

Therefore Incidence of malignancy in solitary nodular goitre is higher compared to multinodular goitre.

INTRODUCTION

The thyroid an endocrine gland normally weighs around 20to 25 gmlocated anterior to trachea which comprises of two lobes and an isthmus that connects it, which normally cannot be palpated on physical examination. The thyroid uses iodine to secrete hormones that controls sympathetic system, basal metabolic rate

It consists of 25 to 40 follicles lined by cubical epithelium. majority of thyroid nodules are benign. It is estimated that 3% to 7% of population have a palpable nodule and prevalence increase to more than 70 to 75% if patients are screened by ultrasound. approximately 5% of detected thyroid nodules are malignant, with the exception of nodules discovered by PET scans, which have a 33% increased risk for malignancy(1).

Newly discovered thyroid nodules are clinically important, because need to exclude thyroid cancers. risk factors includes family history, lymphadenopathy, history of goiter, female sex, and history of radiation predominantly to the head and neck region. Thyroid cancers occurs more frequently in women than in men, at an approximate ratio of 3:1

Along with a thyroid nodule symptoms of thyroid cancer include a painless swelling in the front of the neck, difficulty in breathing, difficulty in swallowing change in voice/ voice hoarseness

The increase in the incidence of thyroid cancers may be due to widespread use of imaging studies .

Thyroid neoplasm broadly classified as benign and malignant . benign includes follicular adenoma that can be colloid which is commonest follicle-derived (thyroid epithelial) neoplasms, other epithelial tumours, non-epithelial tumours and secondary tumours based on pathological, clinical and genetic characteristics. These tumours can be benign, borderline or malignant, depending on their biological behaviour within. hyalinising trabecular tumour. encapsulated follicular-patterned thyroid tumours,

Malignant includes differentiated which includes papillary thyroid carcinoma (PTC), follicular thyroid carcinoma, Hurtle cell tumour and poorly differentiated thyroid carcinoma, anaplastic thyroid carcinoma and squalors cell carcinoma comprises major thyroid epithelial neoplasm's. Some of the other epithelial tumours found in the thyroid gland include medullar carcinoma, salivary gland-type tumours, mutinouscarcinoma thymic tumours, whilst tumours like paraganglioma, peripheral nerve sheath, vascular, smooth muscle, solitary fibrous and histiocytic tumours,

teratoma and lymphomafall under the non-epithelial tumours of the thyroid

Thyroglossal duct develops from median bud of the pharynx and its present at base of tongue which vestigial remnant is foramen cecum .

Parathyroid glands develop from the third and fourth pharyngeal pouches and thymus also develops from the third pharyngeal pouch and when it descends; it takes the associated parathyroid gland with it which explains why the inferior parathyroid nerve which arises from the third pharyngeal pouch normally lies inferior to the superior gland. The developing thyroid lobes fuse with the structures that arise in the fourth pharyngeal pouch, i.e. the superior parathyroid gland and the ultimobranchial body. Parafollicular cells (C cells) which arise from the neural crest reach the thyroid via the ultimobranchial body

Surgical Anatomy:

The normal thyroid gland weight is about 20 g–25 g and the functional unit is the lobule that is supplied by a single arteriole and composed of 24-40 follicles lined by cuboidal epithelium. The follicle contains colloid in which thyroglobulin is stored.

The arterial supply is rich, and extensive anastomoses occur between the main thyroid arteries and branches of the tracheal and

esophageal arteries. There is an extensive lymphatic network within the thyroid gland but some lymph channels pass directly to the deep cervical nodes, the subcapsular plexus drains mainly to the central compartment and paratracheal nodes and nodes on the superior and inferior thyroid veins (level 4 VI), and from there to the deep cervical (levels II, III, IV and V) and mediastinal groups of nodes (level VII)

Goitre

The normal thyroid gland is not palpable but generalized enlargement of the thyroid gland is known as goiter (from the Latin guttur = the throat). Thyroid nodules are found in 4%-7% of the people on neck palpation.(2) An isolated swelling in one lobe with no palpable abnormality elsewhere is termed a solitary nodule while swellings with evidence of abnormality elsewhere in the gland are termed dominant nodule. An increased incidence of thyroid cancer (usually follicular type) has been reported from endemic areas so dominant or rapidly growing nodules in long-standing goiters should always be subjected to aspiration cytology.

AIMS AND OBJECTIVES

PRIMARY OBJECTIVE: To find out the incidence of malignancy in benign thyroid disorders in patients who get admitted and operated in PSG Institute of medical sciences and research, Coimbatore

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Lymphatic Drainage(RG)

The chief afferent lymphatic pathways are superior, inferior and lateral; they follow the superior blood vessels, inferior thyroid arteries, and the inferior and the middle thyroid veins. The so-called central compartment nodes are the primary site of drainage whereas the nodes of the lateral neck (internal jugular, posterior triangle) constitute the zone of secondary drainage. This fact has a significant bearing on the tailored modifications of the neck surgery generally used in treating thyroid malignancies.[13] It is postulated that the metastases to the upper and the submandibular nodes occur in the later stages because of the lymphatic obstruction that occurs with increasing primary tumour size and also when the pretracheal and paratracheal have become obstructed by metastases. Lymphatic drainage of the thyroid gland.

Major

Middle jugular nodes: level III Lower jugular nodes: level IV Posterior triangle nodes: level V

Lesser

Pretracheal and paratracheal nodes: level VI Superior mediastinal nodes: level VI

Compartments Nerves Associated with the Thyroid gland

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

Itthenpassesposteriortothecarotidsheathandintothethyroidbed,there it is closer to and parallel to the tracheoesophageal groove than its counterpart on the other side of the neck. Recurrent nerve run behind the artery in 53% on right and 69% on left and run anterior to artery in 37% on right and 24% on left. It is easily susceptible to stretching when the thyroid lobe is retracted anteriorly near the berry ligament. Unusually the non-recurrent laryngeal nerve can arise directly from the vagus and pass directly into the thyroid this non-recurrent anatomy is found in 1-1.5% of patients. Even more infrequently, there may be recurrent and non-recurrent laryngeal nerves. These two nerves usually join in a position beneath the lower pole of the thyroid.

The superior laryngeal nerves arise from the vagus nerve at the base of the skull and descend towards the superior pole of the thyroid along

the internal carotid artery. The smaller external branch travels along the lateral surface of the inferior pharyngeal constrictor muscle and usually descends anteriorly and medially along with the superior thyroid artery. Within 1 cm of the superior thyroid artery's entrance into the thyroid, the nerve takes a medial course and enters into the cricothyroid muscle.

The nerve is not usually visualized during surgery as it has already entered the inferior pharyngeal muscle fascia. This nerve is at risk of severed or entrapped if the superior pole vessels are ligated too above the superior pole of the thyroid gland.

Epidemiology of Thyroid Malignancies

Thyroid cancer is less common in children than in adults but still accounts for 1.4% of childhood malignancies. The incidence of thyroid cancer in children younger than 15 years is approximately 0.5 per million per year, with a rapid rise occurring after the age of 5.(3) 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.

Women are affected more than men the ratio is somewhere around 1:1.6 to 1:3. Even though the overall incidence of differentiated thyroid cancer is more common in women than in men, a nodule in a man is more likely to be malignant than in a woman. There are definite age patterns for individual cancers of the thyroid. In general, the incidence of papillary carcinoma peaks in the early adult life and then gradually decreases in frequency, whereas the incidence of follicular carcinoma tends to peak sometime later. Anaplastic cancer occurs later in life than differentiated cancers.Overall,papillary cancer is more common than follicular, which is more common than medullary, which is more common than anaplastic.

Etiology of Thyroid Malignancies

1. **Radiation exposure:** Exposure to radiation is the only proved thyroid carcinogen. this was first recognized by Duffy and Fitzgerald in 1950. A 10 to 20 yearpostradiation latency period was reported earlier but this has not been noted in the pediatric thyroid cancer cases that have resulted from the Chernobyl nuclear disaster in the Ukraine in 1986, where there has been a dramatic increase in such cancers as early as 1989. In contrast to external radiation, there is little evidence to suggest that internal radiation from I^{131} used for therapeutic or diagnostic medical purposes causes thyroid cancer inhumans(4).

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

a. Isolated familial medullary thyroid carcinoma(FMTC)
b. Multiple endocrine neoplasia syndrome type 2A (MEN2A)
c. Multiple endocrine neoplasia syndrome type 2B (MEN2B)

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

3. **Family History:** Thyroid cancer is a risk factor for the development of both medullar and nonmodularly thyroid cancer. Familial modularly thyroid cancer occurs in association with other tumours as part of multiple endocrineneoplasia2 (MEN 2) syndromes. Non-medullary thyroid cancer can occur in association with known familial cancer syndromes such as Cowden's syndrome, Werner's syndrome, Gardner's syndrome and FAP. Papillary thyroid cancer accounts for 90% of familial non medullary thyroid cancer.

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

5. **Chronic Lymphocytic Thyroiditis:** Thyroid lymphoma most often occurs against a background of autoimmune lymphocytic thyroiditis (Hashimotosdisease).

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 about20%.

Classification of Thyroid Malignancies

<table>
<tr><td colspan="2">PRIMARY</td></tr>
<tr><td colspan="2">1. Follicular epithelial cells</td></tr>
<tr><td>Differentiated

Papillary carcinoma Follicular

carcinoma</td><td>Undifferentiated Anaplastic

carcinoma</td></tr>
<tr><td>2.Parafollicularcells</td><td>Medullary carcinoma</td></tr>
<tr><td>3.Lymphoid cells</td><td>Lymphoma</td></tr>
<tr><td colspan="2">Secondary</td></tr>
<tr><td colspan="2">1. Metastatic 2. Local infiltration</td></tr>
</table>

Pathology and natural History of papillary carcinoma of thyroid

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 (less than 1.5 cm in greatest dimension), intrathyroidal (larger than 1.5 cm but confined to the gland), and extrathyroidal (extending beyond the capsule to involve the surrounding viscera). At the time of presentation, up to 80%-90% of the primary lesions are confined to the gland. Encapsulation of the tumour is seen in 10% of the cases. Tumour multicentricity is seen in 20% to 30% of cases in most of the studies. In 1971 Woolmer described papillary cancer seen by light microscopy: “The typical histological picture is a mixture of papillary excrescences and neoplasticfollicles containing varying degrees of colloid. The percentage of papillary and follicular elements is varied. The nucleus is hypodense with large areas that appear empty and are apparently devoid of chromatin. Consequently, the nucleus appear opaque and are given many names including “clear”, “watery”, “pale”, or the most imaginative “Orphan Annie Eyes”. Consequently the diagnosis of PTC is based on a constellation of findings. In particular, papillae projecting into open spaces, as well as clear nuclei with prominent nuclear grooves are all important features of the diagnosis. Another important feature is the presence of psammoma bodies (Greek:

psammoma – sand) which are laminated calcify areas. They are seen in 50% of cases in most series.Although the etiology is unclear it is believed to represent the remains of the dead papillae and are quiet specific for PTC and are rarely seen in other thyroid lesions.(5)

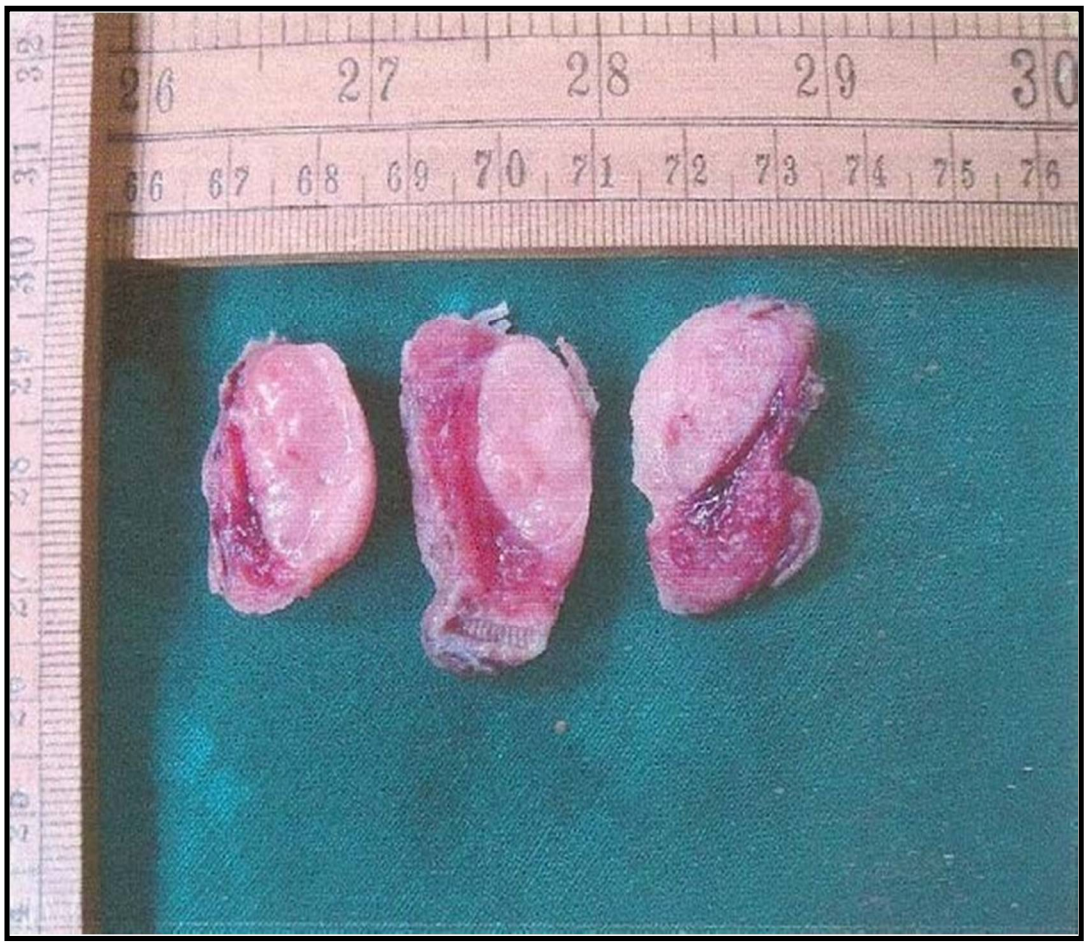
Several variants of papillary cancer exits, some behave like typical PTC whereas others have a more aggressive behaviour.

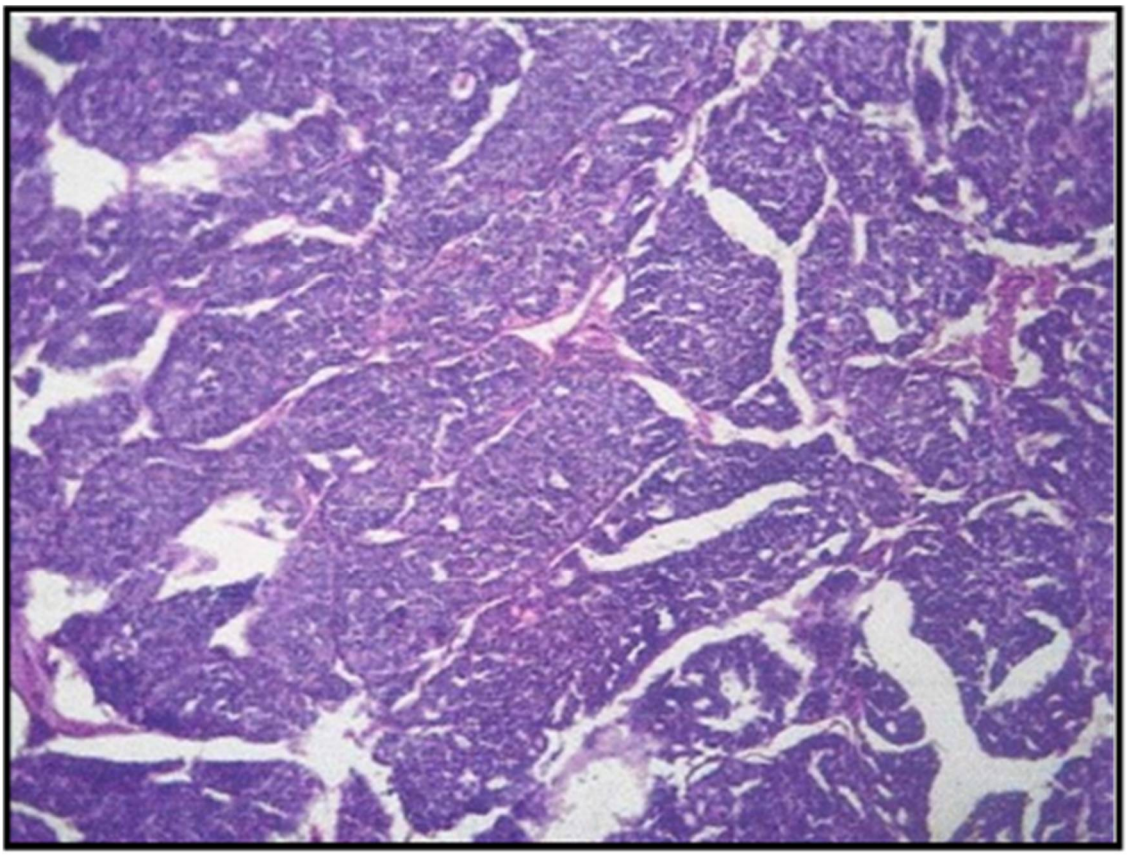
Morphological variants of papillary thyroid carcinoma

Variants with similar clinical behavior	**iants with more aggressive behavior**
Follicular	Tall cell
Micropapillary	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. The propensity for papillary cancer to spread inthelymphatics within and outside the gland is striking. 5-10% of patients present with distant metastases at some time in

course of the disease.The natural prognosis of the metastatic cancer seems to be volume related. It is worse in patients with bone, lung and CNS metastases.The tall cell variant has a worse prognosis in all age groups.





Follicular Carcinoma of Thyroid (FTC)

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

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. The Hurthle cell variant, unlike other follicularcells does not take up radio active iodine. This variant occurs particularly in adult women and is usually solid, well vascularised and well encapsulated. The insular tumours were so named because the clusters of cells within it contain small follicles that resemble the pancreatic islet cells. Insular thyroid cancer is a more aggressive malignancy and is perceived to behave less favorably than the papillary and follicularcancers.

Anaplastic Carcinoma of the Thyroid (ATC)

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. The median age of onset of ATC is consistently in the seventh decade of life and the disease is characterized by female preponderance ranging from 55% to 77%. The

anaplastic component is composed of varying proportions of spindle, polygonal and giant cells.In general, the lethality of anaplastic cancer should not be underestimated, even when minimal in size amid a background of predominately differentiated cancer. The natural history of this cancer is characterized by rapid and massive locoregional growth, dysphagia, SVC syndrome and finally asphyxiation or exsanguination.

Medullary Carcinoma of the Thyroid (MTC)

Medullary carcinoma of thyroid derived from parafollicular or the C cells which has non epithelial nature and have the ability to secrete calcitonin. parafollicular 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 neuroendocrine tumours such as carcinoid tumours, pancreatic islet cell tumours and pheochromocytomas.They occur in two basic forms, sporadic and familial. the familial form is 10% to 20% whereas sporadic type is upto 70 to 90%.(6). FNAC yields presumptive clues to the diagnosis of MTC. triangular cells or spindle shaped with dendritic extensions are highly suggestive of MTC. Although amyloid stromamay be presumptively identified in Papanicolau stains, it is confirmed by restaining with Congo red. a firm, solid, grayish, or pale brown well demarcated from the surrounding tissues seen on gross examination.

Polyhedral cells arranged in sheets with irregular trabeculae is typical appearance of medullary thyroid carcinoma microscopically.

Clinical Presentation of Thyroid Carcinomas

1. Thyroidswelling

Thyroid cancer most commonly presents as a single neck mass noted incidentally by the patient or the physician. A thyroid mass in a child no matter its size or consistency is highly suspicious of malignancy. Regardless of the sex, the mass in advanced years is likely to be malignant. Though many women develop thyroid cancer than in men, any given nodule in a man is more likely to be malignant. Although such words as hard with fixation can apply to a mass associated with thyroiditis, these features must be viewed with suspicion for malignancy. The opposite must not be assumed, however; soft masses with no fixation to the surrounding tissues are not necessarily benign. Rapid enlargement can be deceptive because of the tendency for intralesional hemorrhage. On the other hand, the relentless and rapid growth that can be seen in anaplastic carcinoma is so impressive that its ominous nature is quiet obvious. Cystic lesions are more likely benign, but cystic carcinomas do occur. Solid lesions have a 21% risk of malignancy, cystic 7% and mixed lesions had a risk of 12%.[56] 5% to 10% of multiple nodules and 10% to 20% of solitary nodules are malignant.(7)

2. Cervicallymphadenopathy

In case of papillary carcinoma which is known for its lymphatic spread the patient present with cervical lymphadenopathy alone in 20% of cases and a mass in the thyroid with cervical lymphadenopathy in 13% of cases. Children and young adults more often have palpable nodal metastases. Most studies report a 30% to 40% incidence of cervical nodal metastasis when therapeutic nodal dissections were performed. In medullary carcinoma metastases are mostly found in the neck and mediastinal lymph nodes, and may calcify. Sporadic cases of MTC are more prone for lymph nodal spread than the familial cases. In the presence of a seemingly normal thyroidgland, lateral neck mass with biopsy proven thyroid tissue was previously misconceived to represent an embryonic nest of thyroid tissue and erroneously termed "lateral aberrant thyroid". This presentation is now considered to be caused by metastatic well differentiated thyroid carcinoma from an occult primary within the gland until proved otherwise.

3. Symptoms related to the tumourgrowth

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. Local compressive symptoms are a rule in case of anaplastic carcinoma and can include stridor, dysphagia, dyspnoea, hoarseness, weight loss and even superior vena cavasyndrome.

4. Symptoms related to distantmetastases

Among the thyroid malignancies anaplastic carcinomas are quiet likely to have a distant metastasis which are usually pulmonary but can also involve bone, brain and soft tissues. Distant foci of the tumour are seen in 20% to 50% of patients. Most distant metastases are found in the lung, liver and bone. They are found in more than 75% who die from thyroid carcinoma and lung metastasis account for almost 50% tumour related deaths.(8)

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. Patients who present with clinical evidence of thyroid cancer and have Grave's disease have more aggressive tumours, whereas patients with occult thyroid cancers who are treated for Grave's disease

have an excellent prognosis. Diarrhea has been reported in 20% to 30% of cases of sporadic MTC at presentation often in patients with extensive disease. The underlying mechanism is still to be clarified. Prostaglandins, Vasoactive intestinal polypeptide, Calcitonin gene related peptide and Seratoninnave all been suggested as mediators of this symptom.(9) Although rare, concomitant Cushing's syndrome is the most striking presentation of sporadic MTC in some cases. This unusual phenomenon is explained by the common precursor of ACTH and calcitonin. When cortisol production is excessive and the tumour burden is too large for resection, bilateral adrenalectomy is the last resort.

Laboratory Evaluation

Blood 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. It should be noted that,

even though diagnostic sensitivity has not been described, a thyroglobulin level of more than 10 times the upper limit of normal is highly suggestive of cancer. Serum thyroglobulin levels > 2 ng/ml after thyroidectomy indicates presence of metastatic disease and a riseinS. thyroglobulin in a patient with known metastases indicates progression of disease. Thyroglobulin levels of > 60 ng/ml suggests thyroidcancers.

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

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

Needle Biopsy and 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 this particularly helpful in diffuse diseases such as Hashimoto's thyroiditis and in conforming 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 minima1.Furthermore the material is suitable for immune histochemical evaluation. Published results claim a sensitivity and specificity of over

90%, leading some authors to recommend FNA as initial test in the evaluation of any thyroid nodule. 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 ind**icati**on for a conservative approach unless the clinical data suggests otherwise.

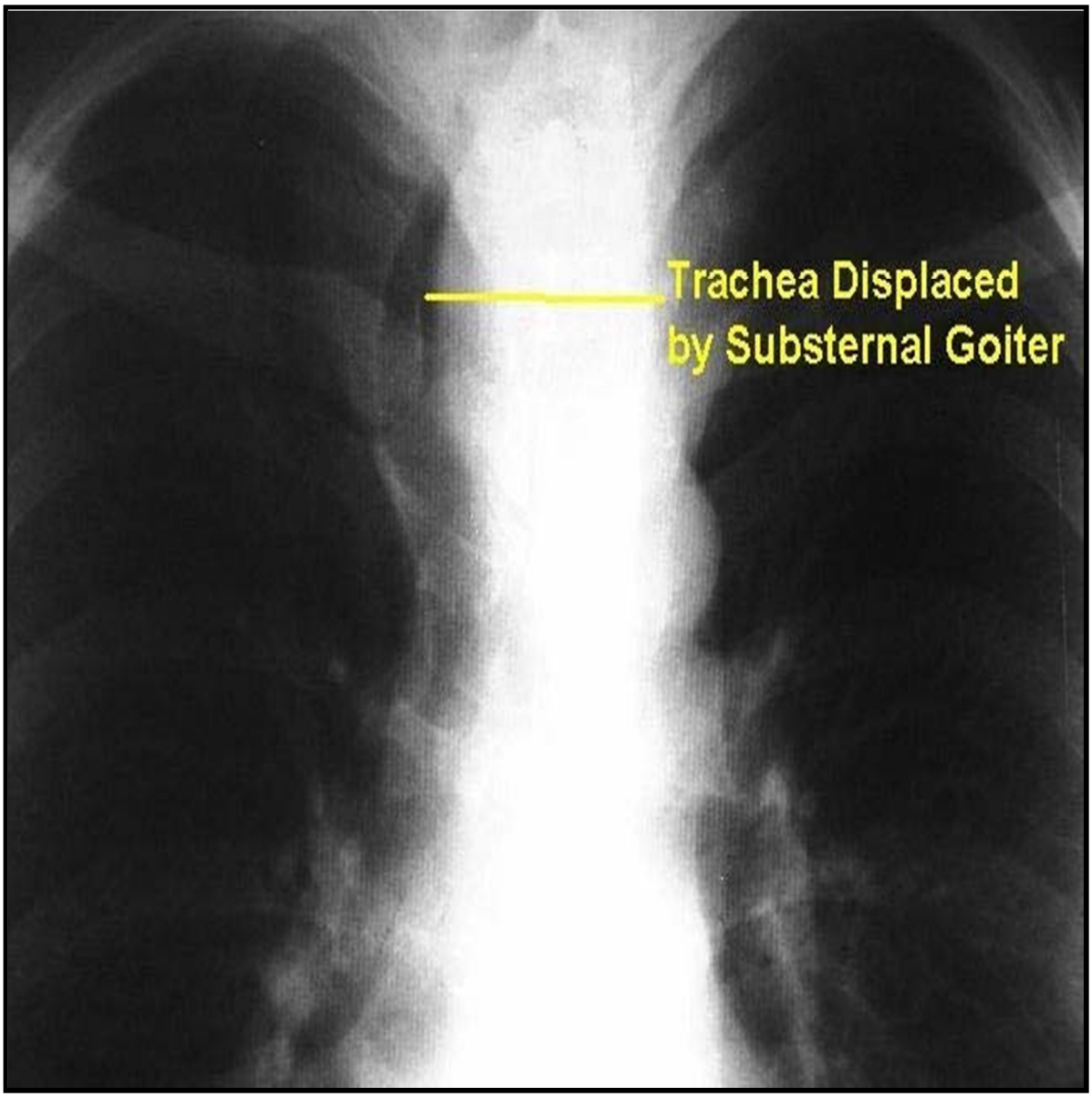
2. Follicular neoplasm; when cellularity higher than that found in the usual hyper plastic nodule, but the nuclear features of papillary cancer are absent. The diagnosis of Hurthlecell neoplasm usually falls in the category. The presence of highly hyper chromatic nuclei, micro follicular or solid pattern, 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. 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 microcarcinoma.

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.

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. This can also suggest substernal extension of a large goiter. 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 calcifications

Can also be seen in metastatic MTC in the cervical nodes.



Substernal goitre – Displacing trachea

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; with serves as a reference for sonographer on follow up examinations. In patients with known thyroid cancer sonography can be useful in evaluating the extent of decease, both preoperatively and postoperatively. In most instances, sonography is notperformed 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.

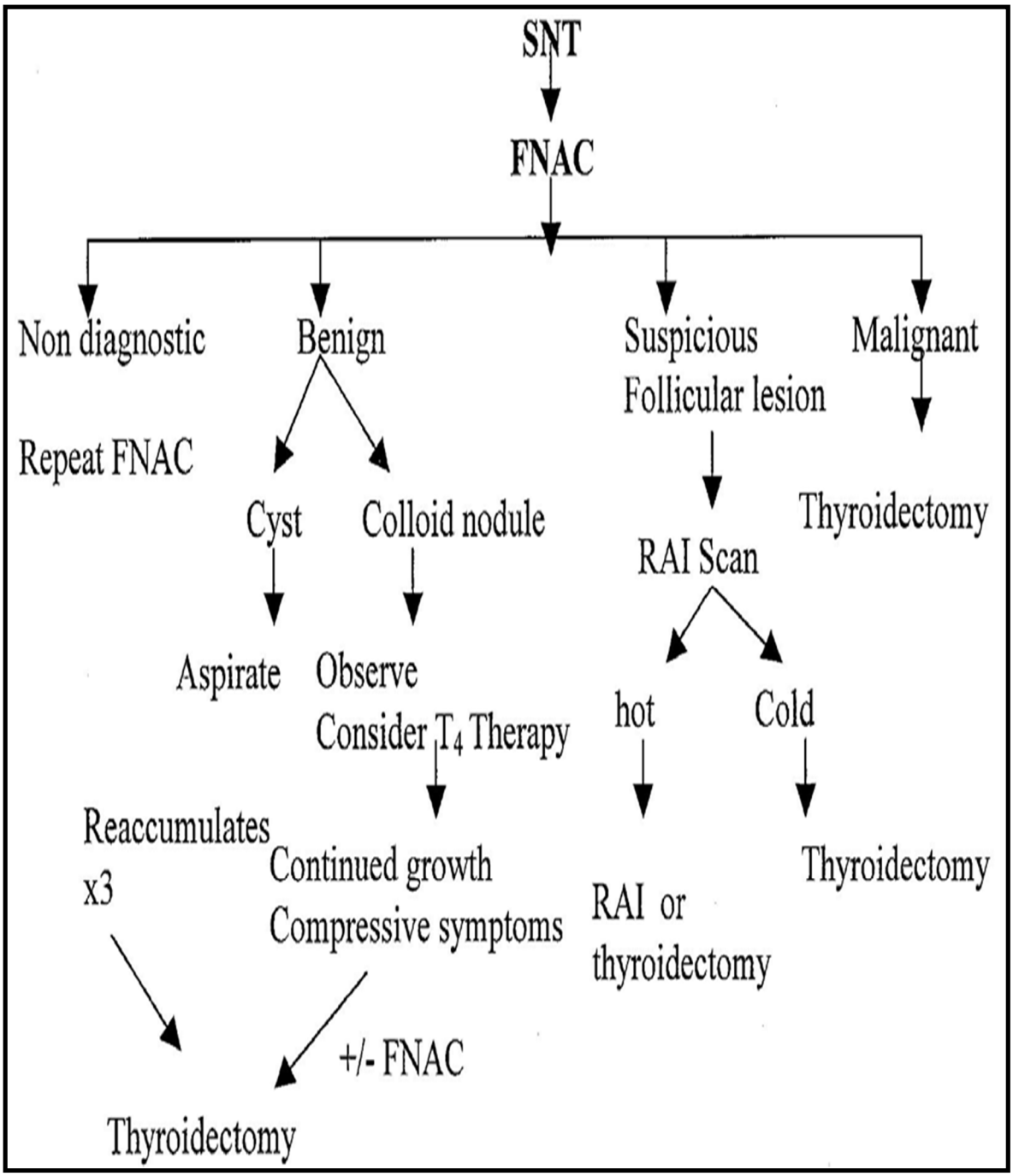
3. **CT and MRI:** CT scan and MRI of the neck and the thorax is helpful in assessing the extent and relationship of larger thyroid tumours, particularly the involvement of the larynx, trachea, esophagus and the major vessels. The presence of metastatic cervical and mediastinal adenopathy is usually 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. The radioisotopes of iodine have been used in thyroid imaging. I^{131} was commonly used in the past and still useful when functioning metastasis of thyroid cancer are being sought; however I^{131} is a beta emitter, its physical half life is 8.1 days, and the energy of its y rays is high, so poorly adapted. I^{123} is, in many respects ideal but is expensive. By energy of its rays is adapted for its detection by cameras. Its short half life is 0.55 days and the absence of beta radiation result in radiation dose to thyroid that is about 1% of that delivered by a comparable activity of I^{131}. 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.(13) True functioning nodules using I^{123} are unlikely to be malignant. 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 cytologic findings, a radioisotope study need not be done. Other radiopharmaceuticals can be used in the investigation and treatment of thyroid tumours. I^{123} MIBG (metaiodobenzylguanidine) is taken up by the tumours of the neural crest origin such as pheochromocytoma and some cases of MTC. It is therefore useful in suspected cases of MEN. Gallium scanning with Gallium citrate is useful in detecting lymphoma, and may be used in long standing patients with Hashimoto's thyroiditis who develop a thyroidnodule.(10)

Evaluation of solitary nodule thyroid



STAGING OF THYROID CANCER

TNM Staging Primary tumour(T)

T_x - Primary tumour cannot be assessed. T0 - No evidence of primarytumour.

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

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

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

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

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

All Anaplastic carcinomas are T4 tumours.

T4a - Intrathyroidal anaplastic carcinoma -surgically resectable.

T4b - Extrathyroidal anaplastic carcinoma - surgically unresectable.

Regional lymph nodes (N)

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

Nx - Regional lymph nodes cannot be assessed. N0 - No regional lymph node metastases.

Nl - Regional lymph node metastases.

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

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

Distant metastases

Mx - Distant metastases cannot be assessed. M0- No distant metastases.

M1- Distant metastases.

Stage Grouping

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

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	Ml

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

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 IVA	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

Medullary carcinoma

Stage Grouping of Medullary carcinomas[113]

Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	Nla	M0
	T2	Nla	M0
	T3	Nla	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 T	Any N	M1

Anaplastic carcinoma

All anaplastic carcinomas are considered as stage IV.

Stage Grouping of Anaplastic carcinomas

Stage IV A Stage IVB Stage IVC	T4a T4b Any T	Any N AnyN AnyN	M0 M0 M1

Survival and Prognostic Features

Overall survival in well differentiated carcinoma shows a better 10 year survival for papillary cancer, ranging between 75% ato 93% as compared to follicular cancer, with a 10 year survival of 43% to94%.(11) Although many institutions have reported their data based on these histologic subcategories, meaningful system is to categorize patients according to definite risk factors more pertinent to generating the prognostic information.

Risk categorization scheme developed at the Lahey clinic, by Cady and group carries the acronym **AMES** (Age, Metastatic disease, Extra thyroidal extension, Size). Canada group added an assessment of the DNA content by flowcytometry to this which carries the acronym DAMES with the DNA content, and showed that the high- risk patients with aneuploid tumours which have a very 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, tumour extent , Size).

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 prognosticfactors.

Prognostic Risk Categorization Schemes AMES categorization scheme

AMES categorization scheme

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

DAME's categorization scheme

Low risk	Low-risk AMES + euploid	DFS-92%
Intermediate risk	Low-risk AMES + aneuploid	DFS-45%
High risk	High risk AMES + aneuploid	DFS-0%

AGE's categorization scheme

PS= 0.05 x age in years (age < 40 yrs= 0),

+ 1 (grade 2) or + 3(grade 3-4),

+ 1 (if extrathyroidal) or + 3 (if distant metastases),

+ 0.2 x tumour size (in cms).

PS range= 0- 11.65, median=2.6

Risk categories: 0- 3.99 (DFS - 20 yrs -99%);

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

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

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

MACIS categorization system

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

+0.3 x tumour size (in cms),

+ 1 (if incompletely resected),

+ 1 (if locally invasive),

+3 (if distant metastases are present).

Risk categories: 0-5.99 (DFS-20 yrs-99%);6-6.99 (DFS-20 yrs-89%);7-7.99 (DFS-20 yrs-56%);>8 (DFS-20 yrs- 24%).

De Groot classification for carcinoma thyroid

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

De Groot classification for carcinoma thyroid

Class	Extent of the disease	Relativerisk of mortality
I	Intrathyroidal	1
II	Loco regional Cervical node metastases	1
III	Extrathyroidal invasion	5.8
IV	Distant spread	47

Management of Thyroid Carcinoma

A. Management of differentiated carcinomas of the thyroid

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

Extent of thyroidectomy

A long standing controversy among endocrine surgeons has existed regarding the extent of surgical resection for well differentiated thyroid cancer. Technical contributions of surgeons such as Kocher, Crile, Attie, perzik Lahey and Thompson and others has established thyroidectomy is 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.(14) Acceptable surgical procedures to remove thyroid neoplasm include:

(i) Hemithyroidectomy (along with removal of one lobe and entire isthmus is removed).

(ii) Sub-total thyroidectomy (total lobectomy leaving about rim of 2 to 8 gm of tissue in upper lateral portion of opposite side lobe is removed)

(iii) Near-total thyroidectomy (both lobes except lower pole which is very close to recurrent laryngeal nerve and parathyroid removed leaving less than 2gms of thyroid tissue)

(iv) Hartley Dunhill procedure is removal of one entire lobe with isthmus and partial removal of opposite lobe

(v) Totalthyroidectomy.

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

Issue	Conservative surgery	Radical surgery
Prognostic risk factors	Systems to define risk can An occasional low risk patient accurately identify patients develops recurrence. Who have	An occasional low risk patient develops recurrence.
Safety of surgery	20 year survival of 99% and 20 year DFS of 95% No risks of permanent Minimal complications	Minimal complications with experience surgeons.
Postoperative iodine	with hypocalcemia or recurrent experienced surgeons laryngeal nerve injury.	Thyroid ablation with I^{131} is
Anaplastic cancer	If necessary I^{131} ablation can be accomplished with no morbidity.	complicated with pain and decreased efficacy with thyroid remnant.
Thyroglobulin Follow-up	Local recurrence able to be managed; risk of anaplastic cancer1%.	Potential for local recurrence with possible dedifferentitation to a more aggressive tumour.
Multicentricity and Recurrence	Not possible. Tumor multicentricity seems to have little prognostic significance.	Possible and an accurate marker. Eliminates the contralateral cancers at the sites of recurrence.

Total thyroidectomy is the treatment of choice for virtually all patients with Papillary thyroid cancer 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 laryngealnerve or parathyroid lands, 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.(15)

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

Frozen section is not necessary when 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 non-diagnostic results on FNAC Sensitivity of frozen section varies from 50 to 65%. patients are undoubtedly spared of the second surgery to complete a total thyroidectomy when a malignant diagnosis is confirmed intra operative frozen section for the thyroid may helpful .(17) When FNAC is reported as malignant, frozen section is unnecessary.

Total thyroidectomy – Operative procedure Positioning of the patient

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

Skin incision, exposure of the thyroid

The skin incision is made approximately two finger-breaths above the sternal notch. The lateral borders of the incision can approach the medial borders of the sternocleidomastiod muscle but can be lengthened if the lateral neck is to be investigated. It ordinarily extends laterally to the jugular veins; however it might be necessary to extend the incision depending upon the size of the thyroid gland and the presence of enlarged lymph nodes lateral to the gland. Subplatysmal skin flaps are raised,

superior flap extending till the thyroid cartilage and the inferior flap till the sternal notch. Self-retaining retractors are then placed. The strap muscles are separated in the midline for full extent of the operative field. The side of the neck on which the thyroid mass is located should be explored first. If the thyroid mass is invading the strap muscle or is tightly adherent to the muscle the strap muscles can be excised. For adequate exposure, it is necessary to elevate the thyroid lobe and retract it medially.

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

The thyroid lobe is retracted medially and arterially and the lateral tissues are swept poster laterally using a peanut sponge. The middle thyroid veins are legated and divided. The fascia just cephalic to the isthmus is divided. The superior thyroid pole is identified by retracting the thyroid inferiorly and medially, and then the upper pole is mobilized caudally and laterally.

The dissection place is kept as close to the thyroid as possible and the superior pole vessels are individually identified, skeleton zed, legated, and divided low on the thyroid gland, to avoid injury to the external branch of the superior laryngeal nerve. The recurrent laryngeal nerve then should be identified within 1 cm of the crossing of the inferior thyroid artery and the RLN. The lower pole of the thyroid gland should be mobilized by gently sweeping all tissue dorsally. The inferior thyroid vessels are dissected, skeletonized, ligated divided as close to the surface of the thyroid gland as possible, minimize revascularization of the para thyroids or injury to the RLN. Once the Berry ligament is divided, the thyroid can be separated from the underlying trachea by sharp dissection. If a lobotomy is to be performed the isthmus divided flush with the trachea on the contra lateral side and suture legated. The procedure is repeated on the opposite side for a total thyroidectomy. During the course of total thyroidectomy, every effort should be made to identify the parathyroid glands and if their blood supply cannot be preserved they should be rejected and placed in iced saline. These glands are very hard and are viable for hours in this state. If at the completion of the thyroidectomy, it is necessary to remove all four glands, one or more of them should be auto grafted into a muscle bed, most often in the sternocleidomastoid.

After ensuring that there is no bleeding in the bed, the strap muscles are then approximated. The platysma is closed with interrupted sutures and then subcuticular suturing is done.

Lymph node dissection

The surgical management of lymph node metastases from well differentiated thyroid cancer is no longer controversial. Gross cervical metastatic disease is treated by modified radical neck dissection, which results in excellent local control and minimal morbidity. Even though 80% of patients with PTC have occult cervical lymph node metastases most of these metastases can be ablated with radioiodine treatment postoperatively, and some does not appear to grow.(18) 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.(19). 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 areuncommon (about 10%)

a contralateral neck dissection is performed only when gross evidence of lymph node metastases is found.(20)

Functional neck dissection- operative procedure

When the surgeon decides to perform a functional neck dissection, either because of obvious lymph node involvement or because the primary tumour is large and microscopic nodes are suspected, it may be necessary to extend the incision laterally and superiorly. It is unnecessary to sacrifice the sternocleidomastoid, jugular vein or the XI cranial nerve. As one extends the superior flap, care must be taken not to damage the mandible branch of the facial nerve, which can be identified as it crosses over the external maxillary artery and the anterior facial vein. This nerve innervates the lower lip and produces an unsightly droop if injured. The inferior flap is extended to expose the upper border of the clavicle. The tendinous and the muscular insertions of the sternocleidomastoid into the sternum and the clavicle are then divided and the muscle is retracted superiorly. Beginning at the superior most extension of the field near the angle of the mandible, the lymph nodes and the associated adventitia are swept inferiorly. During this process it is necessary to remove the omohyoid muscle. With this exposure it is possible to remove all the soft tissue anterior and adjacent to the carotid artery, internal jugular vein, and the vagus nerve. Additionally the lymph nodes and the soft tissue in the anterior and posterior triangles are removed. At the end of the dissection

the space between the vascular bundle in the lateral neck and the esophagus and the trachea is evident. Also the muscles bordering the anterior and the posterior triangles are exposed. At the end a suction drain is left in the lateral neck, and the sternocleidomastoid is sutured to its sternal and clavicles origins. The procedure may also be performed without division of the muscle by retracting it alone. Finally the strap muscles are approximated and the platysma is closed with interrupted sutures and subcuticular stitch is put.

REVIEW OF LITERATURE

The modern name of thyroid gland was introduced in 1656 when Thomas Wharton called it the thyroid gland, after the Greek for "shield shaped" because of the configuration of the nearby thyroid cartilage.

Study conducted by Htwe et al[1] on incidence of thyroid malignancies among goitrous thyroid lesions the incidence of cancer was highest for the age group of >60 years. They had also found that though the presence of goitre was high in women, cancer incidence was more among men. Also, because of the aggressive nature of thyroid malignancy in men they emphasized on early detection of thyroid cancers in them.

Duffy BJ and Fitzgerald PJ[2] in 1950 studied thyroid malignancies in children which showed papillary carcinoma to be the predominant type. Out of 28 cases of thyroid malignancies 10 patients had received irradiation for enlarged thymus between the fourth and sixteenth month of life.

In 1977,E.Williams et al[3] studied on comparison between thyroid carcinoma among iodine rich and normal iodine intake areas. This study revealed increased incidence of papillary carcinoma in iodine rich area and that of follicular carcinoma in endemic goiter areas. Malignant lymphoma and lymphocytic thyroiditis were high in iodine deficient areas. This suggests different histological types of malignancy are influenced by different etiological factors.

Similar type of study conducted in Goa, by Raman Arora et al[4]showed a decrease in papillary to follicular carcinoma ratio in iodine deficient area.

Selzer[5] at 1977 et al studied 254 cases of carcinoma of thyroid. In that M:F was 3.5:1.In the study 68 cases were pure papillary,66 cases mixed papillary and follicular,78 cases follicular 66 cases mixed papillary and follicular and 9 cases of medullary carcinoma. Ground glass nuclei were present in 55.5% and psammoma bodies in 45.6% of papillary carcinoma.

In a study conducted by Othman NH et al[6] thyroid malignancy had a peak in the age group of 30-49 years. Majority were papillary carcinoma with F:M ratio 5.2:1.Histopathology showed more than 50% of papillary cancers arising from previous nodular hyperplasia.

Another study conducted by Cacangiu ML et al[7], of 241 cases of papillary cancers of thyroid M:F was 1:2.6 and 16 patients had previous neck irradiation.55.7% showed pure papillary growth. Tumor margins were infiltrating in 66.7% of cases. Fibrosis was detected in 56.2% of cases and squamous metaplasia was found in 18.7% and psammoma bodies in 51.6% of cases.

Study conducted by Desai SS et al[8] on medullary thyroid cancers they found that medullary thyroid cancers twice as common in men as in women and for some reasons it occurred earlier in women. In histological

study it revealed some interesting features like presence of apoptosis in more than 50% of tumors and the adjacent thyroid in about 19% of cases showed optically clear nuclei in the follicles that were close to the tumor cells. These features were similar to that seen in papillary cancers.

In a study of 130 patients with minimally invasive follicular carcinoma diagnosed in Armed forces institute of pathology,95 patients were confirmed to have micro invasive follicular carcinoma based on authors criteria of small to medium vessel invasion, capsular invasion of upto full thickness, absent parenchymal tumor extension and absent tumor necrosis.

MATERIALS AND METHODS:

- STUDY DESIGN : Observational study
- STUDY POPULATION : Individuals who got admitted in surgery ward with thyroid nodule (solitary thyroid nodule, MNG, Hashimotos and other types) and operated at PSG Institute of medical sciences and research ,Coimbatore.
- STUDY LOCALITY: PSG Institute of Medical Sciences and Research, Coimbatore.
- SAMPLE SIZE: 151

INCLUSION CRITERIA :

- All patients with clinically palpable thyroid swelling who admitted in surgery ward..
- Patients with long standing benign thyroid diseases now suspecting /proven to be malignant.

EXCLUSION CRITERIA :

- Patients with known thyroid malignancy since the initial presentation
- **Retrospective analytical study** will be carried out from period of Jan 2014 to Dec 2017 by collecting old case files from MRD.
- Details of patients demographics ,clinical presentation and diagnosis, results of FNAC ,USG findings, gross features and biopsy results of the resected thyroid specimens are obtained from patients case files.

- H& E stained slides of the thyroidectomy specimens were analyzed by an independent pathologist. **Histopathological diagnosis will be considered as gold standard**.

Parameters for assessment

Clinical details(age, sex), gross and microscopic picture of all thyroid malignant tumors, will be discussed individually. The following statistical tests will be performed.

1.Chi sqare test

2.Ratio

3.Percentage

RESULTS

Table 1 and shows distribution of study subjects as per their sex. Majority were Females i.e. 88.7% and males constituted only 11.3% of benign thyroid nodule.

Table 1: Distribution of study subjects as per their sex

S.No.	Sex	Frequency	Percentage
1.	Male	17	11.3
2.	Female	134	88.7
	Total	151	100

Figure 1: Distribution of study subjects as per their sex

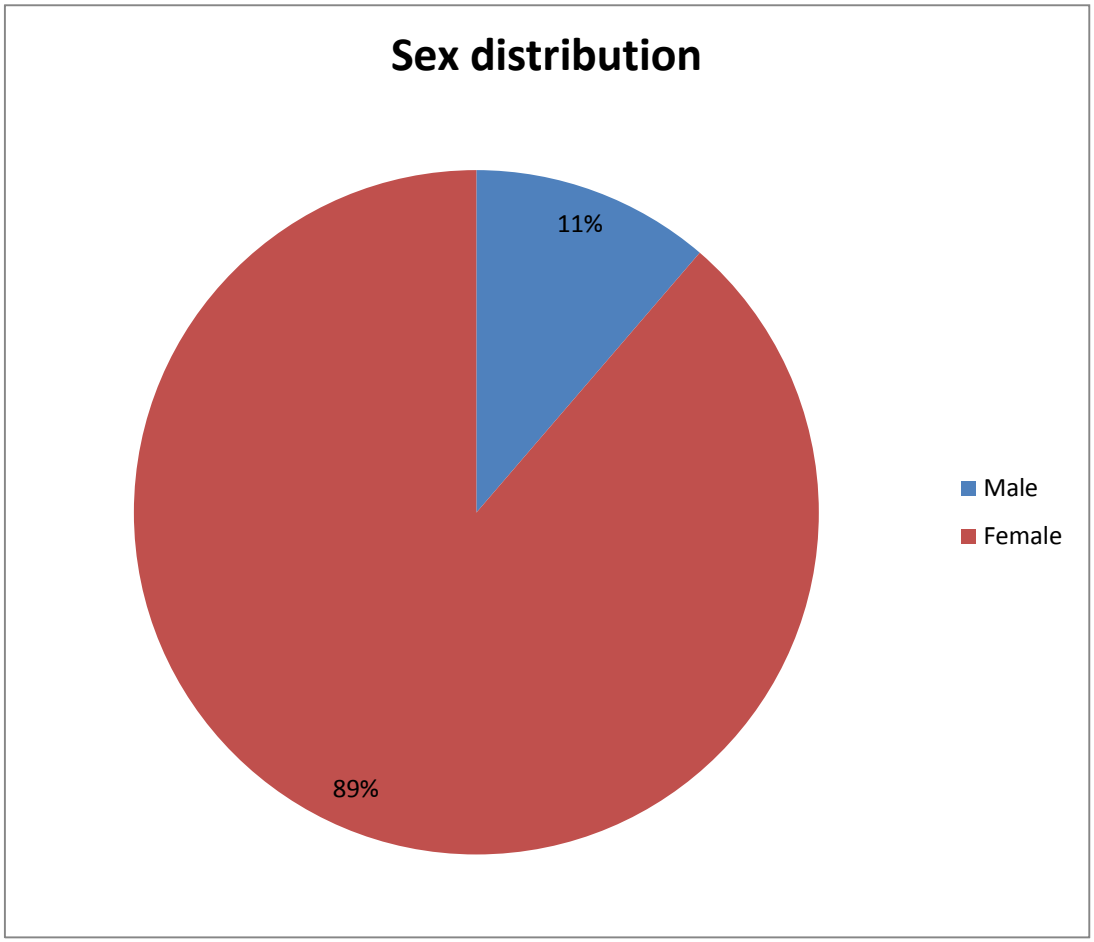


Table 3: Distribution of thyroid nodule among the study subjects

Variable	Minimum	Maximum	Mean	SD
Age	11	82	47.28	13.179

Table 2 shows the mean age of study subjects which is 47.28, with minimum age of 11years and maximum age of 8 years.

S.No.	Clinical Diagnosis	Frequency	Percentage
1.	Solitary Nodular Goitre	75	49.7
2.	Multinodular Goitre	75	49.7
3.	Hashimotos thyroiditis	1	0.6
	Total	151	100

Figure 2: Distribution of thyroid nodule among the study subjects based on clinical diagnosis

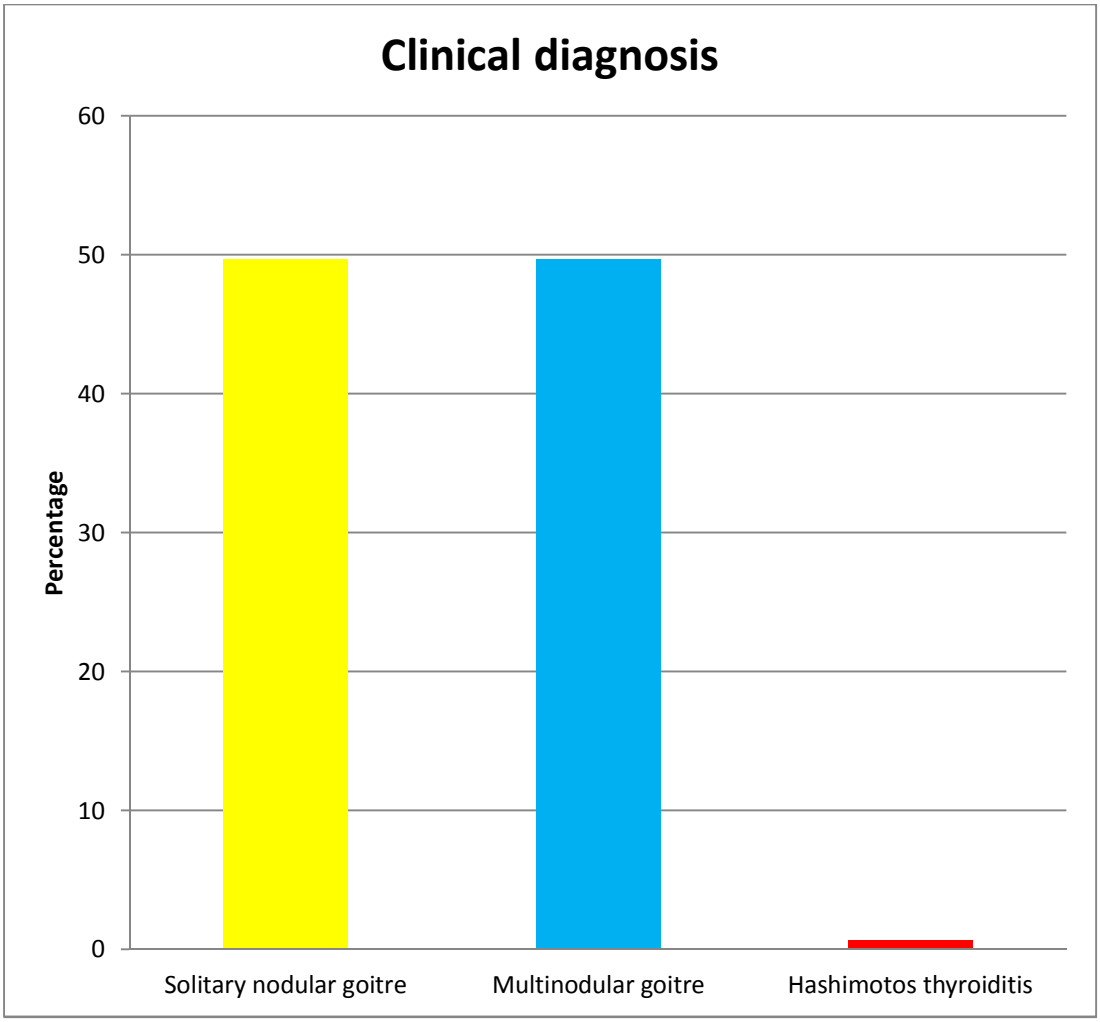


Table 3 and Figure 2 shows the distribution of thyroid nodule among study subjects. 49.7% had solitary nodular goiter , 49.7% had multinodular goiter and 0.6% had hashimotos thyroiditis.

Table 4: Distribution of study subjects as per the histologically proven malignancy

S.No.	Malignant status	Frequency	Percentage
1.	No	136	90.1
2.	Yes	15	9.9
	Total	151	100

Figure 3: Distribution of study subjects as per the histologically proven malignancy

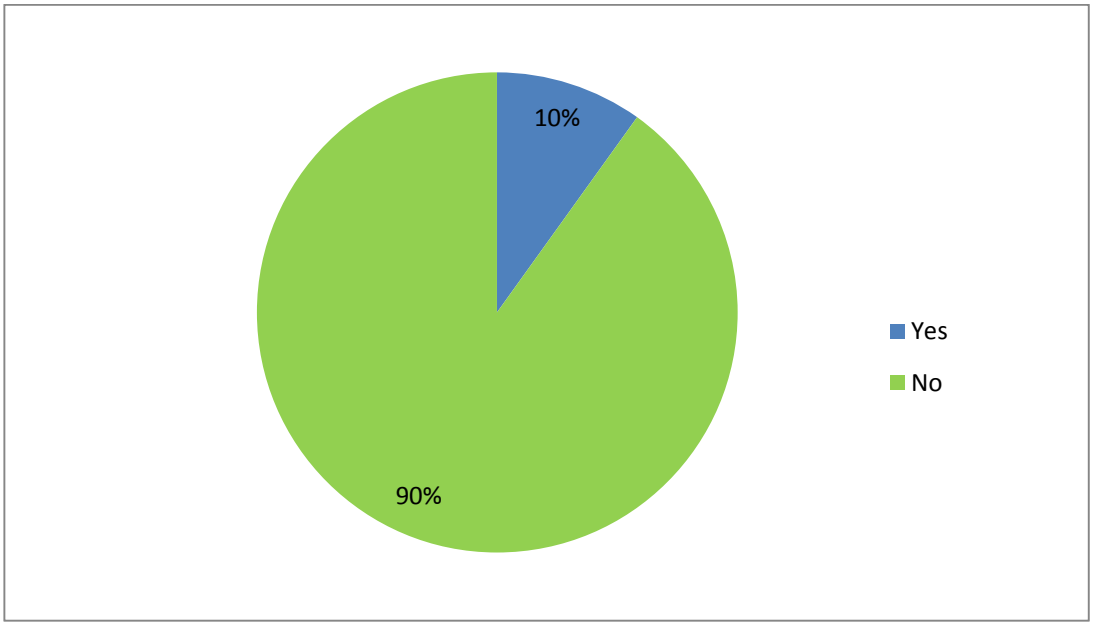


Table 4 and figure 3 shows the incidence of malignancy in benign thyroid disorders proven histologically, in patients who got admitted and operated in PSG IMS&R is 10%, Out of them 14 (93.3%) have Papillary carcinoma of thyroid and 1 (6.7%) have Hurtle cell carcinoma (Figure 4).

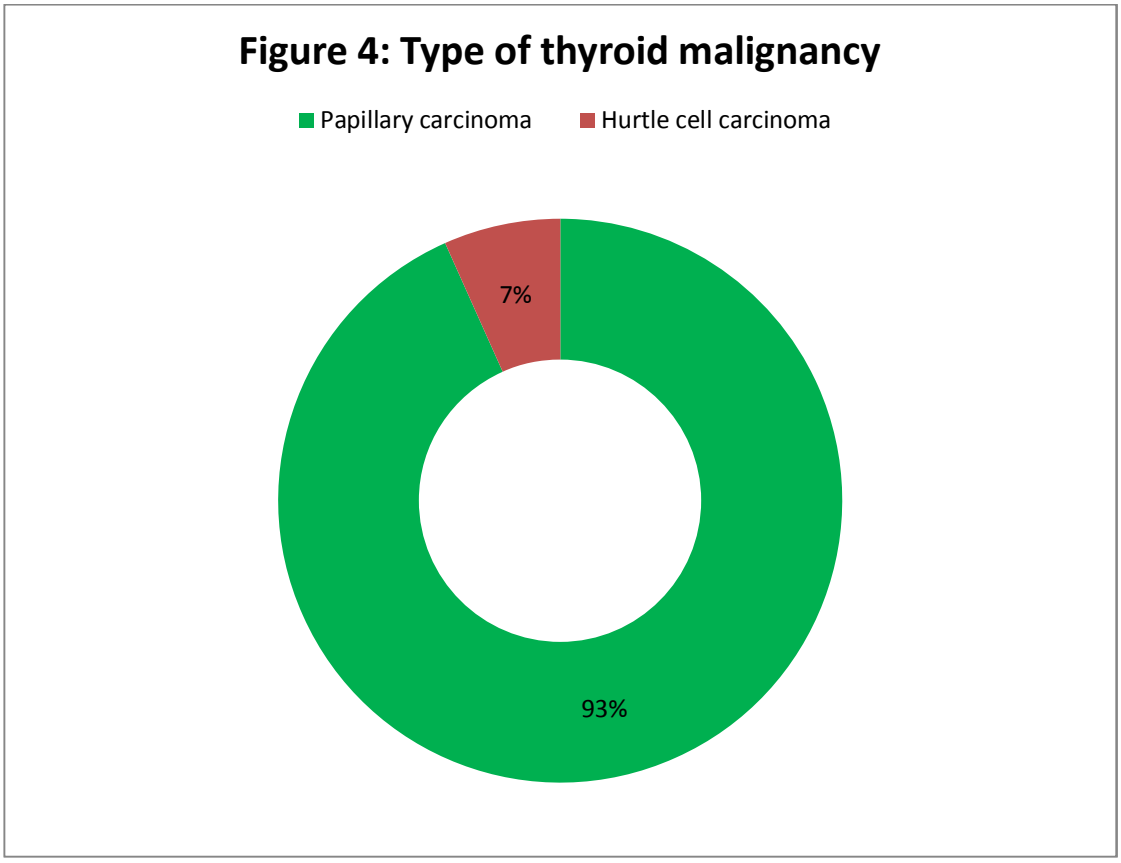
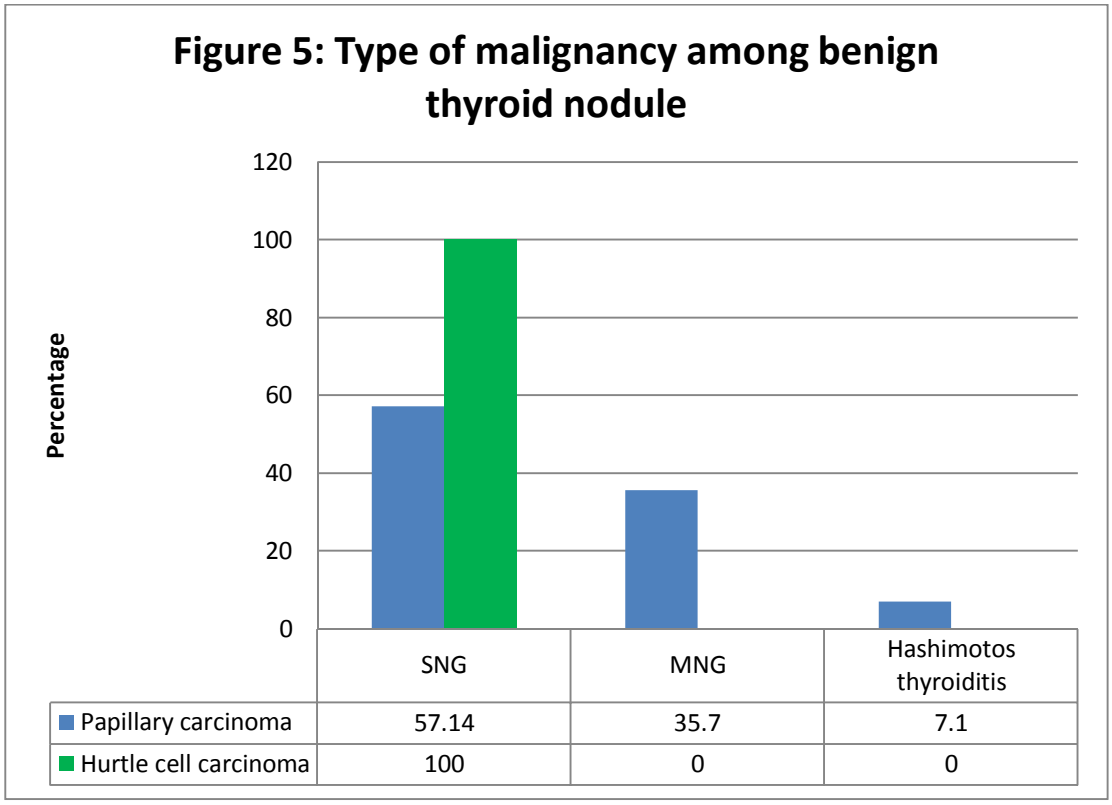


Figure 5 shows among those who had papillary carcinoma (14) of thyroid 1 was diagnosed with hashimotos thyroiditis (7.1%) , 8 were diagnosed with solitary nodular goiter (57.14%), 5 were diagnosed as Multinodular goiter (35.7%).



Among those who had papillary carcinoma (14) of thyroid the FNAC findings are as follows 2 were diagnosed with hashimotos thyroiditis , 1 had non colloid goiter, 5 had colloid goiter and cystic changes 1 had follicular adenoma, 3 had follicular neoplasm, 1 had papillary carcinoma, 1 had adenomatous changes in nodule. One Solitary nodular goiter developed into hurtle cell carcinoma.

Figure 6: Distribution of study subjects as per the type of surgery done

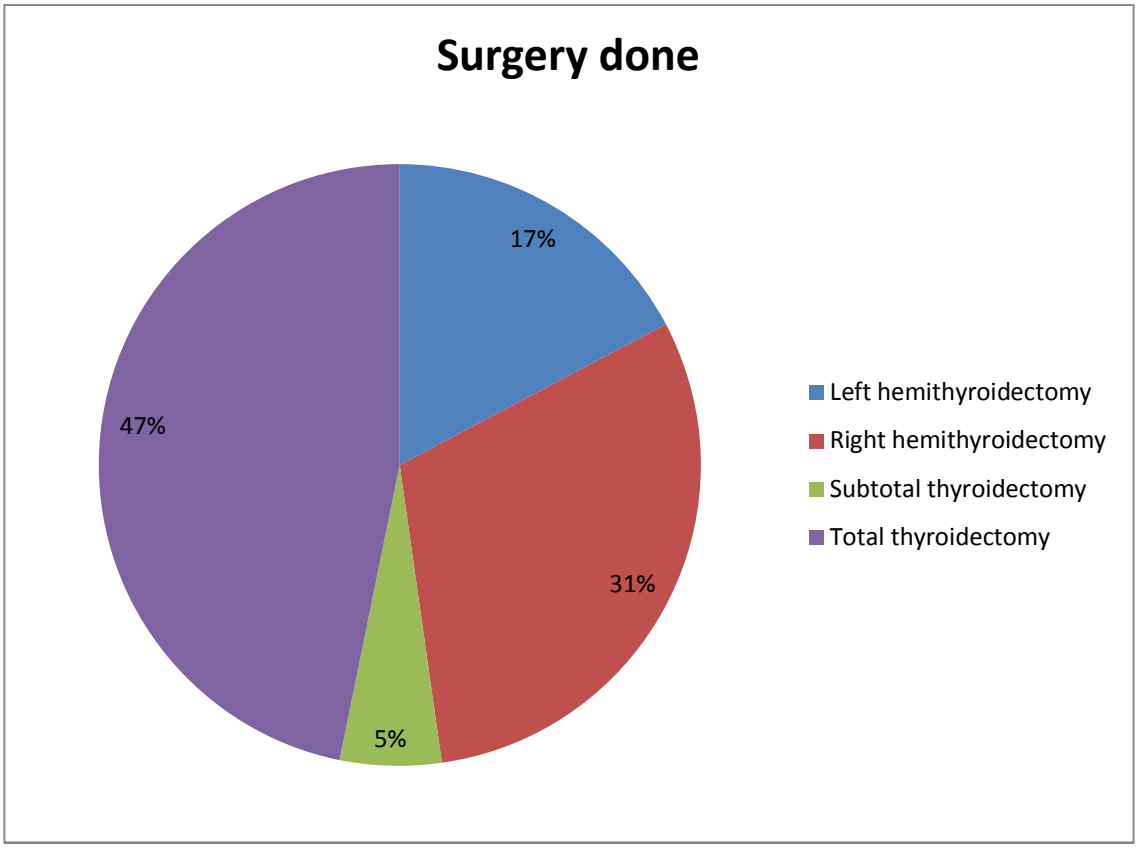


Figure 6 shows the distribution of study subjects as per the type of surgery done. 47% underwent total thyroidectomy followed by right hemithyroidectomy 31%, followed by left hemithyroidectomy 17% and subtotal thyroidectomy 5%

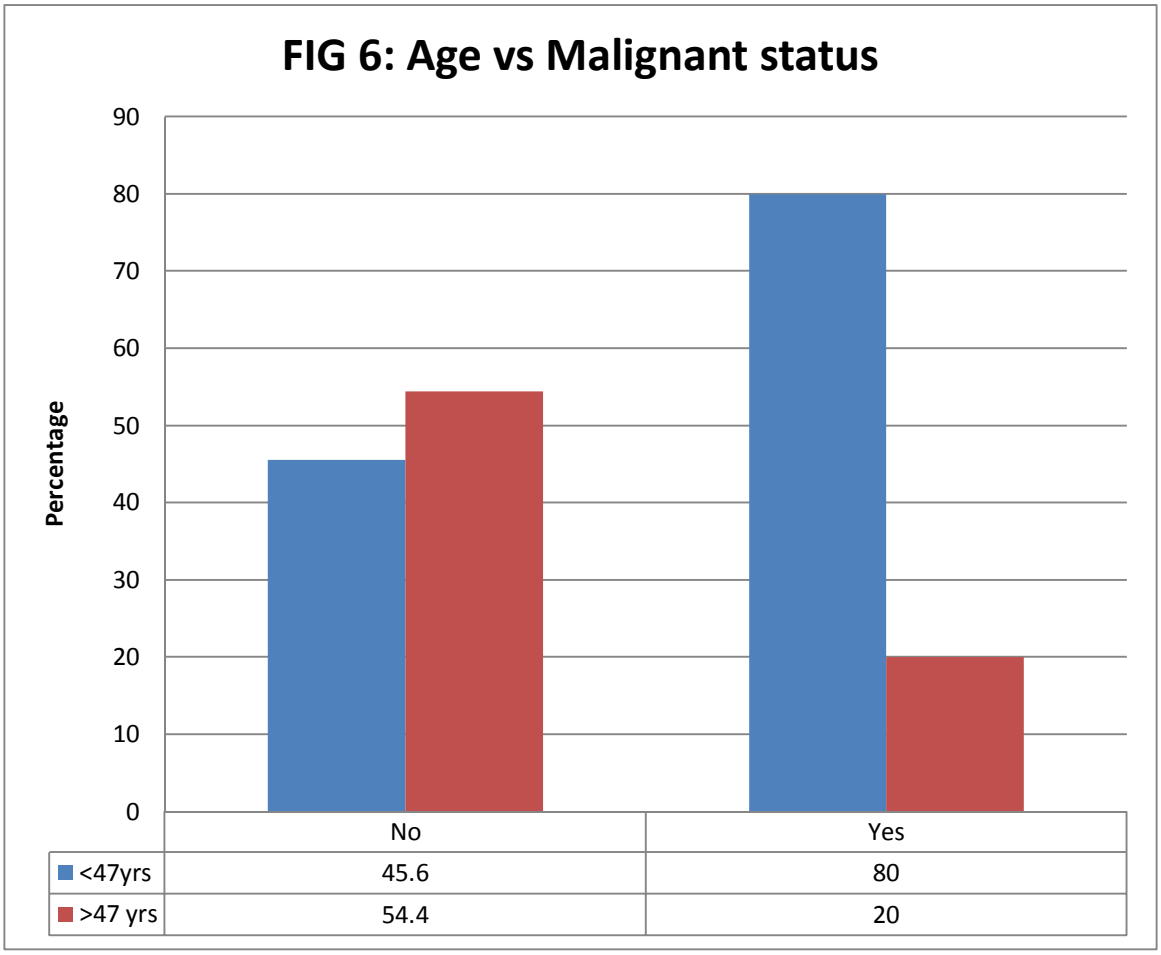
Table 5 : Association of age, sex and benign category with the malignant status

S.No.	Variable		Malignant status		P value
			No (136)	Yes (15)	
1.	Age	<47yrs	62 (45.6%)	12 (80%)	**0.011**
		≥47 yrs	74 (54.4%)	3 (20%)	
2.	Sex	Male	14 (10.3%)	3 (20%)	0.259
		Female	122 (89.7%)	134 (88.7%)	
3.	Benign Category	Solitary nodular goiter and hashimotos thyroiditis	66 (48.5%)	10 (66.7%)	0.182
		Multinodular goiter	70 (51.5%)	5(33.3%)	

Table 5 and Fig 6,7,8 shows the age , sex and benign category distribution among the malignant status of study population. Among those malignant thyroid disorder 80% belonged to less than 47 years, 88.7% were females and 66.7% were clinically diagnosed of having solitary thyroid nodule.

There is Statistically significant association between Age and Malignant status ($p < 0.05$). There is no statistically significant

association between sex and malignant status, and benign category and malignant status.



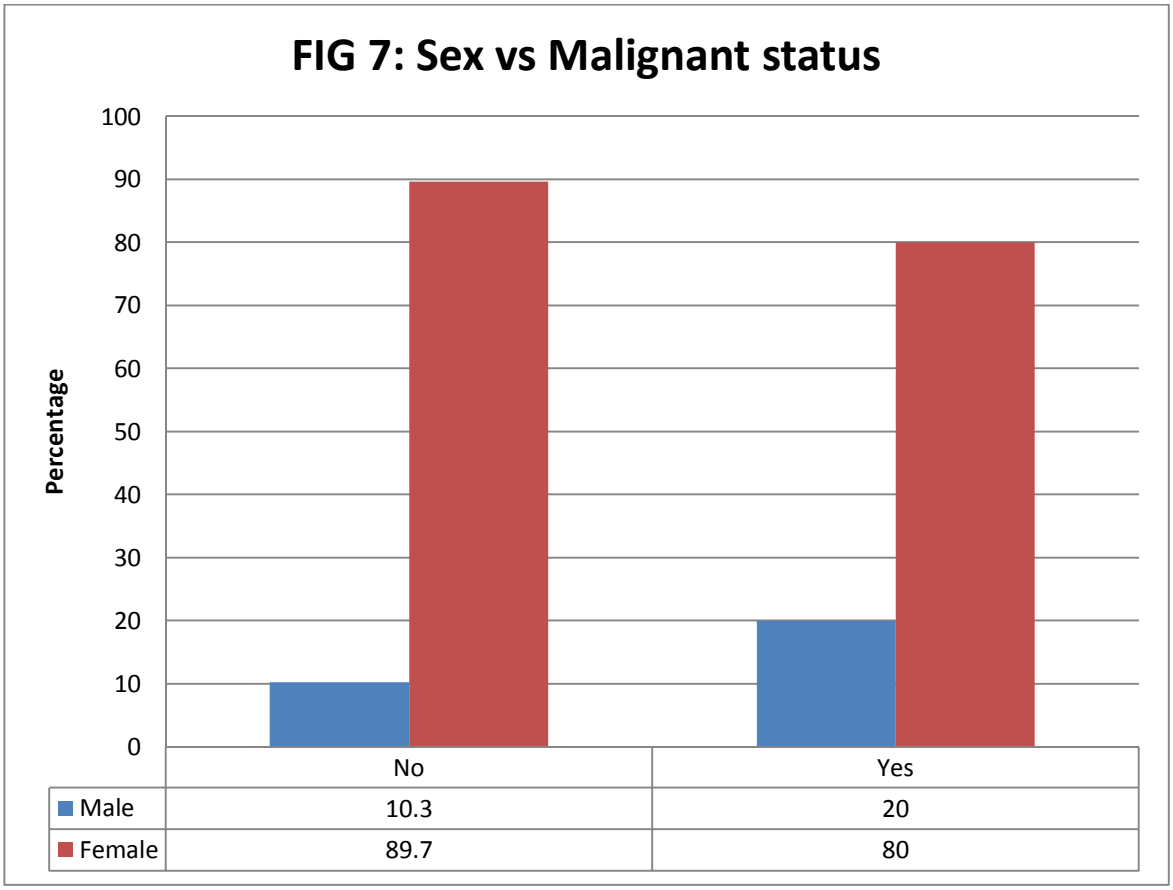


FIG 7: Sex vs Malignant status
Percentage
100
90
80
70
60
50
40
30
20
10
0
No
Yes
Male
10.3
20
Female
89.7
80

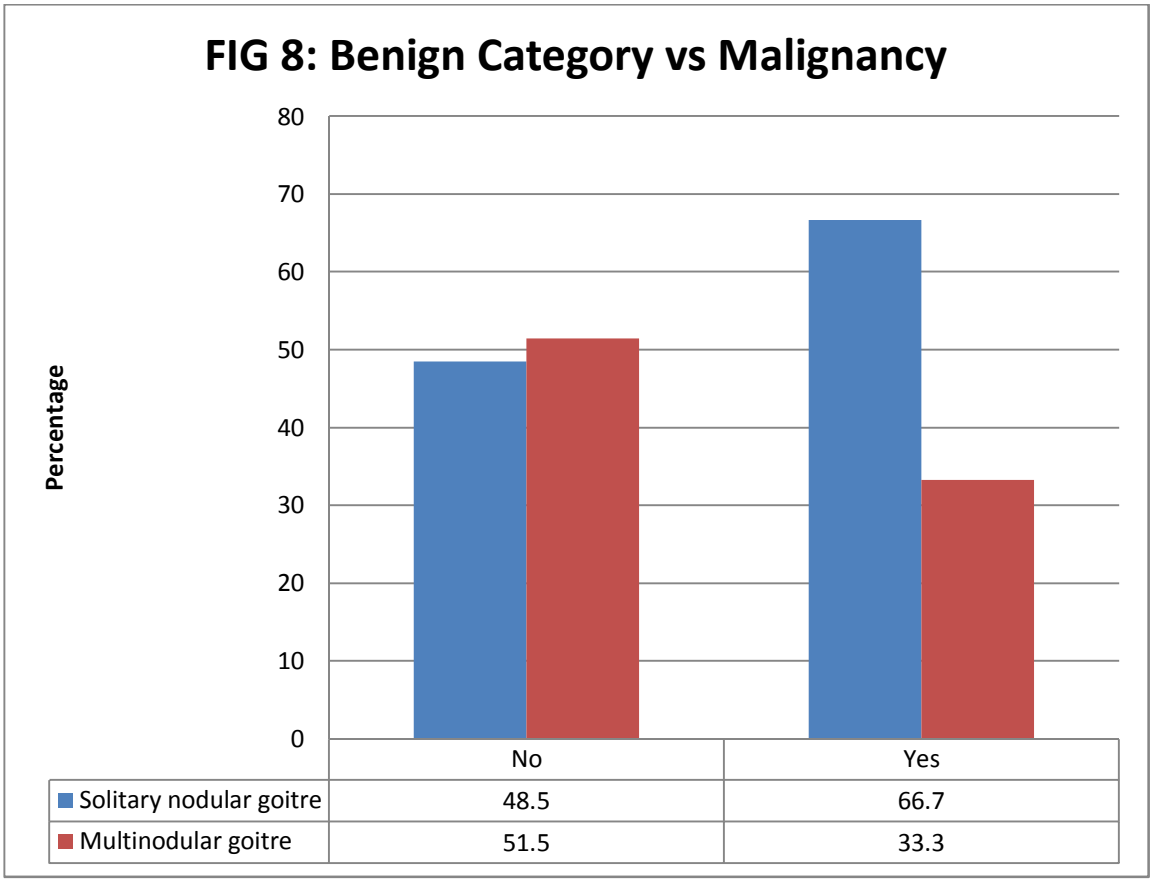


FIG 8: Benign Category vs Malignancy
Percentage
80
70
60
50
40
30
20
10
0
No
Yes
Solitary nodular goitre
48.5
66.7
Multinodular goitre
51.5
33.3

DISCUSSION

Clinical history and examination continue to be corner stone of diagnosis of thyroid neoplasm. Following initial assessment the next step is ultrasound and FNAC. Indeterminate or malignant lesions should be investigated with FNAC. Indications for radio iodine uptake scan are thyrotoxicosis. It allows assessment of function of nodule. Hot nodules shows rarely malignant and cold nodules will require assesmement for all other thyroid neoplasm.

The mean age of study subjects which is 47.28, with minimum age of 11years and maximum age of 82 years. Among those 80% belonged to less than 47 years, 88.7% were females and 66.7% were clinically diagnosed of having solitary thyroid nodule 47% underwent total thyroidectomy followed by right hemi thyroidectomy 31%, followed by left hemithyroidectomy 17% and subtotal thyroidectomy 5%the incidence of malignancy in benign thyroid disorders proven histologically, in patients who got admitted and operated in PSG IMS & R is 10%, Out of them 14 were found to have Papillary carcinoma of thyroid.. FNAC findings of 14 patients are as follows2 were diagnosed with hashimotos thyroidits 1 had non colloid goitre 5 had colloid goitre with cystic changes and 1 had adenomatous changes in nodule and only one diagnosed as papillary carcinoma. and 1 solitary nodular goitre in fnac

found to have hurthle cell carcinoma which is a variant of follicular carcinoma of thyroid . completion thyroidectomy done for patients whom biopsy reported as papillary carcinoma of thyroid who underwent hemithyroidectomy for solitary nodular goitre

Htwe T T hamdi et al in his study total of 820 thyroid case of these 677 females (82.6%) and males 143(17.4%) highest prevalence occur in age group of 41 to 60 years and incidence of malignacy is 6.7% papillary thyroid carcinoma is more of about 33% followed by follicular thyroid cancer 14%

selzar et al in his study of 254 malignant tumors of thyroid gland diagnosed in capetown university 83.5% were differentaited of which papillary with mixed papillary variant found to be more number (134) followed by follicular (78) and medullary (9)

Highest frequency occurs between ages of 20 and 50 years and females outnumbered males in the ratio of 3.2 to 3.7: 1

CONCLUSION

From this study we have concluded that the incidence of thyroid malignancy in benign thyroid disorder is 10%. Thus benign thyroid disorders should not be neglected since they may become malignant. So further studies with large sample size are needed to find out the exact incidence of malignancy in benign thyroid disorder among the general population.

SUMMARY

An observational study was done to find the incidence of thyroid malignancy among patients with benign thyroid disorders attending PSG IMS&R. 151 individuals who got admitted in surgery ward with benign thyroid nodule (solitary thyroid nodule, MNG, Hashimotos and other types) and operated at PSG Institute of medical sciences and research , Coimbatore were included in the study. Those with already existing thyroid malignancy were excluded. Out of 151 patients with benign thyroid nodule, 15 were found to develop malignancy (10%) , in which 14 had papillary carcinoma of thyroid and 1 had hurtle cell carcinoma. The FNAC findings of the patients who developed malignancy were hashimotos thyroiditis , non colloid goiter, colloid goiter and cystic changes , follicular adenoma, follicular neoplasm, papillary carcinoma and adenomatous changes in nodule. One Solitary nodular goiter developed into hurtle cell carcinoma. There was statistically significant association between age and malignancy.

Out of 76 patient of solitary nodular goitre 10 patient found to be malignant and out of 75 multi nodular goitre 5 found to be malignant histopathologically.

Therefore Incidence of malignancy in solitary nodular goitre is higher compared to multinodular goitre.

BIBLIOGRAPHY

1. Htwe TT, Hamdi MM, Swethadri GK, Wong JOL, Soe MM, Abdullah MS.Incidence of thyroid malignancy among goitrous thyroid lesions from the Sarwak General Hospital 2000-2004.*Singapore Med J*2009;50(7):724-728.
2. Duffy BJ, Fitz GPJ.Thyroid cancer in childhood and adolescents.*Cancer*1977;3:1018.
3. Williams ED,DoniachI,BjarnasonO,MichieW.Thyroid cancer in iodine rich area.A histopathological study.*Cancer*1977;39:215-22.
4. Arora R,DiasA.Iodine and thyroid cancer in Goa.*OJHAS Vol 5 Issue 4(3).*
5. Selzer G, Kahn LB,AlbertynL.Primary malignant tumors of the thyroid gland. Aclinicopathological study of 254 cases.*Cancer* 1977;40:1501-10
6. Othman NH, Omar E, Naing NN.Spectrum of Thyroid Lesions in Hospital University Sains-Malaysia Over 11-Years and A Review of Thyroid Cancers in Malaysia.*Asian Pacific J Cancer Prev*,2009;10:87-90.
7. CacangiuML,ZampiG.PupiA.Castagnoli A Rosai J. Papillary carcinoma of thyroid. A clinicopathological study of 241 cases.*Cancer*1985;55:805-28.
8. Desai SS, Sarkar S, Borges AM.A study of histopathological features of Medullary carcinoma of the thyroid:Cases from a single institute in

India.*Indian J of Cancer* 2005;42:25-29.

9. RosaiJ.Poorly differentiated thyroid carcinomas:introduction to the issue,itslandmarks,and clinical impact.*Endor Pathol*.2004;15:293-296.
10. Scopa CD.Histopathology of Thyroid Tumors.An Overview. *HORMONES* 2004,3(2):100-110.
11. Devita VT, Hellman S, Rosenberg SA. CANCER Principles and practice of Oncology, 7th ed.Philadelphia:LWW;2005;34(2):1502.

12.`Thompson LDR, Wieneke JA, Paal E, Frommelt RA, Adair CF, Heffess CS. A clinicopathologic study of minimally invasive follicular carcinoma of thethyroid gland with review of English literature. *Cancer* 2001;91:505-24.

13.Miller JM. Evaluation of thyroid nodule. Med Clinic of North Am. 1985;69:1063.

14. Ananthakrishnan N, Madhava Rao M, Narasimhan R, Veliath AJ. The single thyroid nodule.503 pts. Indian Journal of Surgery. 1993;55(10):487-92.

15. Fenn AS. Solitary nodule of thyroid. Ind J Surg. 1980;42:175-1.

16. Psarras, Papadopaoulous SN, Livadas D, Koutras DA. Single thyroid nodule. Br Surg 1972;59:545-8.

17. Bhansali SK. Solitary thyroid nodule 600 cases. Ind J Surg. 1982;44:547-61.

18. Kapur MM, Sarin R, Karmarkar MG, Sarda AK, Solitary thyroid nodule. Indian J Surg. 1982;44:1749.

19. Messaries G, Kyriakou K, Vasilopolous P, Tountas C. Single thyroid nodule & C A BMJ Surg. 1974;61:943-4.

20. Lindsay S, Dailey ME, Friedlander J, Yee G, Soley MH. Chronic thyroiditis. Clinical and pathological study of 354 patient's J Clin Endocrinol Metab. 1952;12:1578-600.

21. Enrico Papini, Rinaldo Guglielmi, Antonio Bianchini, Anna Crescenzi et al. Risk of Malignancy in Nonpalpable Thyroid Nodules: Predictive Value of Ultrasound and ColorDoppler Features, The Journal of Clinical Endocrinology and Metabolism. May 1 2002; 87(5):1941−46. https://doi. org/10.1210/jc.87.5.1941.

22. Hamberger B, Gharib H, Melton LJ III, Goellner JR, Zinsmeister AR. Fine needle aspiration cytology of thyroid.

23.Harrison BJ, Maddox PR, Smith DM. Disorders of thyroid gland. In: Cuschieri A, Steele RJ, Moossa AR, editors. Essential Surgical Practice. 4th ed. London: Arnold; 2002. p. 95−110.

24. DorairajanN,Jayashree N. Solitary nodule of the thyroid and the role of fine needle aspiration cytology in diagnosis, J. Indian Med. Assoc. 1996; 94:50−2,61.

25. Belfiore A, La Rosa GL. Fine-needle aspiration biopsy of the thyroid, Endocrinol Metab. Clin. North Am. 2001; 30:361−400. https://doi.org/10.1016/S08898529(05)70191-2.

26. Shyam Prasad Keshri. Clinico-Pathological Study of Solitary Thyroid Nodule with Special Reference to Fine Needle Aspiration Cytology, IJSR. 2017; 6(2):789−94.

27. Christensen SB, Bondeson L, Ericsson UB, Lindholm K. Prediction of malignancy in the solitary thyroid nodule by physical examination, thyroid scan, fine-needle biopsy and serum thyroglobulin. A prospective study of 100 surgically treated patients.

28. McCoy KL, Jabbour N, Ogilvie JB, Ohori NP, Carty SE, Yim JH. The incidence of cancer and rate of false-negative cytology in thyroid nodules greater than or equal to 4 cm in size, Surgery. 2007 Dec 31; 142(6):837−44. https://doi. org/10.1016/j.surg.2007.08.012. PMid: 18063065.

29. Moon WJ, Jung SL, Lee JH, Na DG, Baek JH, Lee YH, et al. Benign and malignant thyroid nodules: US differentiation− multicenter

retrospective study, Radiology. June 2008; 247:762−70. https://doi.org/10.1148/radiol.2473070944. PMid: 18403624.

30. Takashima S, Fukuda H, Nomura N, Kishimoto H, Kim T, Kobayashi T. Thyroid nodules: Reevaluation with ultrasound, J. Clin. Ultrasound. 1995; 23(3):179−84. https:// doi.org/10.1002/jcu.1870230306. PMid: 7730464.

ABBREVIATIONS

SNG	-	Solitary Nodular Goitre
MNG	-	Multinodular Goitre
FNAC	-	Fine Needle Aspiration Cytology
HPE	-	Histopathological Examiation
PTC	-	Papillary thyroid carcinoma

S.NO	IP NO	AGE	SEX	CLINICAL DIAGNOSIS	FNAC	SURGERY DONE	HPE
1	I14000145	38	f	SOLITARY NODULAR GOITRE	SNG	LEFT HEMI	adenomatous hyperplastic nodular colloid goitre
2	I 14000559	41	f	SOLITARY NODULAR GOITRE	Hashimotos thyroiditis	RIGHT	pappillary carcinoma
3	i14001927	38	f	MULTINODULAR GOITRE	multinodular Goitre	TOTAL	nodular colloid goitre
4	I14010844	57	F	SOLITARY NODULAR GOITRE	NODULAR COLLOID GOITRE	RIGHT	adenomatous hyperplastic nodular colloid goitre
5	I14004390	64	F	SOLITARY NODULAR GOITRE	COLLOID GOITRE	LEFT HEMI	Nodular colloid goitre
6	I14004599	29	F	MULTINODULAR GOITRE	colloid goitre with cystic changes	LEFT HEMI	adenomatous hyperplastic nodular colloid goitre
7	I14005389	44	F	SOLITARY NODULAR GOITRE	SNG	TOTAL THYROIDECTOMY	HURTHLE CELL CARCINOMA
8	I14005835	77	F	SOLITARY NODULAR GOITRE	COLLOID GOITRE	LEFT HEMI	COLLOID NODULAR GOITRE
9	I14007233	42	F	SOLITARY NODULAR GOITRE	Hashimotos thyroiditis	RIGHT HEMI	FOLLLICULAR ADENOMA
10	I14008869	37	F	SOLITARY NODULAR GOITRE	PAPILLARY CA	TOTAL THYROIDECTOMY	adenomatous hyperplastic nodular colloid goitre
11	I14009961	68	F	SOLITARY NODULAR GOITRE	nodulAR COLLOID GOITRE	right hemi	adenomatous hyperplastic nodular colloid goitre
12	I14016730	42	F	SOLITARY NODULAR GOITRE	SNG	right hemi	adenomatous hyperplastic nodular colloid goitre
13	I14012827	62	F	SOLITARY NODULAR GOITRE	colloid goitre with cystic changes	right hemi	adenomatous hyperplastic nodular colloid goitre
14	I1403182	60	F	SOLITARY NODULAR GOITRE	SNG	right hemi	adenomatous hyperplastic nodular colloid goitre

S.NO	IP NO	AGE	SEX	CLINICAL DIAGNOSIS	FNAC	SURGERY DONE	HPE
15	I14013677	43	F	SOLITARY NODULAR GOITRE	colloid goitre	left hemi	adenomatous hyperplastic nodular colloid goitre
16	I14014966	64	F	SOLITARY NODULAR GOITRE	colloid goitre with cystic changes right hemi	right hemi	adenomatous hyperplastic nodular colloid goitre
17	I14016230	68	F	SOLITARY NODULAR GOITRE	cystic degenerative changes	right hemi	adenomatous hyperplastic nodular colloid goitre
18	I14016397	48	F	SOLITARY NODULAR GOITRE	SNG	right hemi	nodular colloid goitre
19	i14016572	47	f	SOLITARY NODULAR GOITRE	non colloid goitre	right hemi	follicular variant of papiilary carcinoma
20	i14017445	38	F	SOLITARY NODULAR GOITRE	adenomatous changes in nodule	left hemi	hashimotos thyroiditis
21	I14017862	49	F	SOLITARY NODULAR GOITRE	large multilobulated lesion colloid	left hemi	adenomatous hyperplastic nodular colloid goitre
22	I14021433	30	F	SOLITARY NODULAR GOITRE	follicular neoplasm	LEFT HEMI	follicular adenoma
23	i14021678	43	F	SOLITARY NODULAR GOITRE	PAPILLARY CA	RIGHT HEMI	colloid goitre with hashimotos
24	I14024268	42	F	SOLITARY NODULAR GOITRE	colloid goitre	RIGHT HEMI	nodular colloid goitre
25	I14026481	39	F	SOLITARY NODULAR GOITRE	follicular neoplasm	LEFT HEMI	Pappilary carcinoma
26	I14027217	31	F	SOLITARY NODULAR GOITRE	colloid nodule	RIGHT HEMI	adenomatous hyperplastic nodular colloid goitre
27	I14027791	52	F	SOLITARY NODULAR GOITRE	adenomatous changes in nodule left hemi	LEFT HEMI	adenomatous hyperplastic nodular colloid goitre
28	I14028578	49	F	SOLITARY NODULAR GOITRE	only blood	RIGHT HEMI	adenomatous hyperplastic nodular colloid goitre

S.NO	IP NO	AGE	SEX	CLINICAL DIAGNOSIS	FNAC	SURGERY DONE	HPE
29	I15011810	63	F	MULTINODULAR GOITRE	NODULAR COLLOID GOITRE	SUBTOTAL	adenomatous hyperplastic nodular colloid goitre
30	I1503173	64	M	SOLITARY NODULAR GOITRE	colloid goitre	LEFT HEMI	pappilary carcinoma of thyroid
31	I15014508	35	F	SOLITARY NODULAR GOITRE	colloid goitre	RIGHT HEMI	follicular adenoma
32	I15017986	38	F	SOLITARY NODULAR GOITRE	follicular neoplasm	RIGHT HEMI	follicular adenoma
33	I15023769	22	F	SOLITARY NODULAR GOITRE	adenomatous changes in nodular colloid goitre	RIGHT HEMI	follicular adenoma
34	i15033194	70	F	SOLITARY NODULAR GOITRE	colloid goitre with cystic changes left hemi	LEFT HEMI	colloid goitre
35	I15034338	31	F	SOLITARY NODULAR GOITRE	cystic degenerative changes	RIGHT HEMI	colloid goitre
36	I15034694	57	F	SOLITARY NODULAR GOITRE	hurthle cell	TOTAL	adenomatous hyperplastic nodular colloid goitre
37	I15035183	35	M	SOLITARY NODULAR GOITRE	cellular And pleomorphic adenoma RIGHT HEMI	RIGHT HEMI	adenomatous hyperplastic nodular colloid goitre
38	I15035565	41	M	SOLITARY NODULAR GOITRE	colloid noduar goitre with hyperplastic thyroid	RIGHT HEMI	adenomatous hyperplastic nodular colloid goitre
39	I15036628	41	F	SOLITARY NODULAR GOITRE	cellular And pleomorphic adenoma RIGHT HEMI	RIGHT HEMI	adenomatous hyperplastic nodular colloid goitre
40	I16000402	41	F	SOLITARY NODULAR GOITRE	follicular neoplasm	LEFT HEMI	follicular variant of papiilary carcinoma
41	i16005702	51	F	SOLITARY NODULAR GOITRE	adenomatous changes in nodular colloid goitre	LEFT HEMI	follicular adenoma with colloid goitre
42	I16017256	28	F	SOLITARY NODULAR GOITRE	hyperplastic nodular colloid goitre LEFT HEMI	LEFT HEMI	nodular colloid goitre

S.NO	IP NO	AGE	SEX	CLINICAL DIAGNOSIS	FNAC	SURGERY DONE	HPE
43	I16018688	48	F	SOLITARY NODULAR GOITRE	follicular neoplasm	RIGHT HEMI	nodular colloid goitre
44	I16021048	36	F	SOLITARY NODULAR GOITRE	SNG	right hemi	adenomatous hyperplastic nodular colloid goitre
45	I16021307	62	M	SOLITARY NODULAR GOITRE	cellular smear	RIGHT HEMI	nodular goitre with cystic degeneration
46	I16022997	35	F	SOLITARY NODULAR GOITRE	acute suppurative inflammation	LEFT HEMI	colloid goitre
47	i16024980	23	F	SOLITARY NODULAR GOITRE	colloid goitre with cystic degeneration	RIGHT HEMI	nodular colloid goitre
48	i16026491	47	f	SOLITARY NODULAR GOITRE	colloid goitre with cystic degenerationRIGHT HEMI	RIGHT HEMI	colloid goitre
49	I16028557	47	F	SOLITARY NODULAR GOITRE	papillary carcinoms thyroid	RIGHT HEMI	no evidence of papillary carcinoma
50	i16028906	82	f	SOLITARY NODULAR GOITRE	follicular epithelial celss	LEFT HEMI	cystic degeneration and hemorrhage
51	I16035262	64	M	SOLITARY NODULAR GOITRE	follicular epithelial celss	LEFT HEMI	nodular colloid goitre
52	i17002207	55	F	SOLITARY NODULAR GOITRE	multinodular Goitre	TOTAL	cystic degeneration with colloid goitre
53	I1702323	48	M	SOLITARY NODULAR GOITRE	multinodular Goitre	TOTAL	colloid nodule with cystic changes
54	I17004203	63	F	SOLITARY NODULAR GOITRE	follicular epithelial cels	LEFT HEMI	nodular colloid goitre
55	I17012049	33	F	SOLITARY NODULAR GOITRE	follicular epithelial cels	RIGHT HEMI	nodular colloid goitre with adenomatous changes
56	i17013685	38	F	SOLITARY NODULAR GOITRE	follicular epithelial cels	RIGHT HEMI	adenomatous changes in nodular collod goitre

S.NO	IP NO	AGE	SEX	CLINICAL DIAGNOSIS	FNAC	SURGERY DONE	HPE
57	I17014167	50	F	SOLITARY NODULAR GOITRE	nodular colloid goitre	RIGHT HEMI	nodular colloid goitre with adenomatous changes
58	I17015191	46	F	SOLITARY NODULAR GOITRE	SNG	right hemi	adenomatous changes in nodular collod goitre
59	I17017945	19	F	SOLITARY NODULAR GOITRE	hurthle cell	LEFT HEMI	nodular colloid goitre with adenomatous changes
60	I17017998	38	F	SOLITARY NODULAR GOITRE	cystic colloid goitre	RIGHT HEMI	Nodular colloid goitre with Cystic changes
61	I17033490	51	F	SOLITARY NODULAR GOITRE	cystic colloid goitre	RIGHT HEMI	nodular colloid goitre with extensive degenerated changes
62	I17034187	52	F	SOLITARY NODULAR GOITRE	cystic colloid goitre	RIGHT HEMI	hurthle cell adenoma
63	I17038005	40	F	MULTINODULAR GOITRE	cystic lesion	LEFT HEMI	papillary carcinoma thyroid
64	I17039637	52	M	SOLITARY NODULAR GOITRE	hurthle cell	LEFT HEMI	hurthle cell adenoma
65	I17040361	52	F	SOLITARY NODULAR GOITRE	cystic colloid goitre	RIGHT HEMI	nodular collod goitre with cystic changes
66	I17043275	47	F	SOLITARY NODULAR GOITRE	cystic colloid goitre	RIGHT HEMI	hashimotos thyroiditos
67	i17043806	42	F	SOLITARY NODULAR GOITRE	adenomatous changes in nodule	RIGHT HEMI	adenomatous changes in nodular collod goitre
68	I17043841	46	F	HASHIMOTOS THYROIDITIS	Hashimotos thyroiditis	TOTAL	papillary carcinoma thyroid
69	I17048137	31	M	SOLITARY NODULAR GOITRE	papillary carcinoms thyroid	TOTAL	papillary carcinoma thyroid
70	I17052714	34	M	MULTINODULAR GOITRE	multinodular Goitre	TOTAL	nodular colloid goitre

S.NO	IP NO	AGE	SEX	CLINICAL DIAGNOSIS	FNAC	SURGERY DONE	HPE
71	i18000057	48	F	SOLITARY NODULAR GOITRE	Hashimotos thyroiditis	RIGHT HEMI	nodular colloid goitre asssociated with hashimotos
72	I18004314	11	F	SOLITARY NODULAR GOITRE	adenomatous changes in nodule	TOTAL	papillary carcinoma thyroid
73	I14000500	49	F	MULTINODULAR GOITRE	NODULAR COLLOID GOITRE	TOTAL	multi nodular
74	I14001422	46	F	MULTINODULAR GOITRE	multinodular Goitre	TOTAL	papillary carcinoma thyroid
75	I14002479	42	F	MULTINODULAR GOITRE	multinodular Goitre	TOTAL	multi nodular
76	I14003528	39	F	MULTINODULAR GOITRE	cystic lesion of thyroid	SUBTOTAL	nodular colloid goitre with degenerative changes
77	I14003885	58	F	MULTINODULAR GOITRE	Hashimotos thyroiditis	TOTAL	hashimotos thyroiditos
78	I14004528	60	F	MULTINODULAR GOITRE	multinodular Goitre	SUBTOTAL	multi nodular
79	I14004602	40	F	MULTINODULAR GOITRE	colloid goitre with cystic changes	TOTAL	diffuse hyperplastic thyroid
80	I14004982	28	F	MULTINODULAR GOITRE	colloid goitre with cystic changes	TOTAL	multi nodular
81	i14005471	64	m	SOLITARY NODULAR GOITRE	colloid goitre	left hemi	nodular goitre with cystic changes
82	I14006399	58	F	MULTINODULAR GOITRE	colloid goitre	left hemi	multi nodular
83	i14007141	41	f	MULTINODULAR GOITRE	multinodular Goitre	TOTAL	papillary micro carcinoma left lobe
84	i14007841	66	F	MULTINODULAR GOITRE	colloid goitre with cystic changes	TOTAL	nodular goitre with cystic changes

S.NO	IP NO	AGE	SEX	CLINICAL DIAGNOSIS	FNAC	SURGERY DONE	HPE
85	i14009697	52	m	SOLITARY NODULAR GOITRE	colloid goitre	RIGHT HEMI	right nodular goitre
86	i14010387	52	f	MULTINODULAR GOITRE	multinodular Goitre	TOTAL	nodular goitre
87	i14010473	52	f	MULTINODULAR GOITRE	cystic lesion of thyroid	TOTAL	hashimotos thyroiditos
88	i14010963	58	f	MULTINODULAR GOITRE	multinodular Goitre	TOTAL	nodular colloid goitre
89	i14012511	33	f	MULTINODULAR GOITRE	multinodular Goitre	TOTAL	hashimotos thyroiditos
90	i14013470	42	f	MULTINODULAR GOITRE	multinodular Goitre	TOTAL	multi nodular
91	i14014129	45	f	MULTINODULAR GOITRE	multinodu	TOTAL	hashimotos thyroiditos
92	i140020045	53	f	MULTINODULAR GOITRE	colloid goitre with cystic changes	near total	papillary carcinoma thyroid
93	i14020618	69	f	MULTINODULAR GOITRE	multinodular Goitre	total	adenomatous changes in nodular collod goitre
94	i14023353	41	f	MULTINODULAR GOITRE	Hashimotos thyroiditis	total	hashimotos thyroiditos
95	i14023548	64	f	MULTINODULAR GOITRE	colloid goitre	subtotal	multi nodular
96	i14024461	33	f	MULTINODULAR GOITRE	multinodular Goitre	total	hashimotos thyroiditos
97	i14024810	67	f	MULTINODULAR GOITRE	multinodular Goitre	total	multi nodular
98	i14026321	54	f	MULTINODULAR GOITRE	multinodular Goitre	total	colloid goitre

S.NO	IP NO	AGE	SEX	CLINICAL DIAGNOSIS	FNAC	SURGERY DONE	HPE
99	i14026969	39	f	MULTINODULAR GOITRE	Hashimotos thyroiditis	total	hashimotos thyroiditos
100	i14027811	59	f	MULTINODULAR GOITRE	adenomatous changes in nodule	total	multinodular goitre with hyperplastic oxyphil cells
101	i14030177	50	f	MULTINODULAR GOITRE	adenomatous changes in nodule	total	adenomatous changes in nodular collod goitre
102	i14030200	68	f	MULTINODULAR GOITRE	multinodular Goitre	total	adenomatous changes in nodular collod goitre
103	i14031098	52	f	MULTINODULAR GOITRE	adenomatous changes in nodule	total	hashimotos thyroiditos
104	i14031944	40	f	SOLITARY NODULAR GOITRE	1.follicular neoplasm 2. adenomatous changes in nodular colloid goitre	near total	papillary carcinoma thyroid
105	i15000431	24	m	MULTINODULAR GOITRE	follicular adenoma	total	papillary microcarcinoma
106	I15005345	39	F	MULTINODULAR GOITRE	NODULAR COLLOID GOITRE	right hemi	hashimotos thyroiditos
107	i15005525	40	f	MULTINODULAR GOITRE	multinodular Goitre	subtotal	adenomatous changes in nodular collod goitre
108	i15006671	61	m	MULTINODULAR GOITRE	multinodular Goitre	total	multi nodular
109	i15007441	36	f	MULTINODULAR GOITRE	multinodular Goitre	total	multi nodular
110	i15011396	62	f	MULTINODULAR GOITRE	multinodular Goitre	left	multi nodular
111	i15012633	64	f	MULTINODULAR GOITRE	multinodular Goitre	total	multi nodular
112	i15014038	39	m	thyrotoxicosis toxic nodular goitre	multinodular Goitre	total	hashimotos thyroiditos

S.NO	IP NO	AGE	SEX	CLINICAL DIAGNOSIS	FNAC	SURGERY DONE	HPE
113	i15014328	53	f	MULTINODULAR GOITRE	multinodular Goitre	total	multi nodular goiter
114	i15016128	66	f	MULTINODULAR GOITRE	multinodular Goitre	total	multi nodular goiter with adenomatous changes
115	i15017347	48	f	SOLITARY NODULAR GOITRE	NODULAR COLLOID GOITRE	right hemi	adenomatous changes in nodular collod goitre
116	i15017377	46	f	toxic multinodular goitre	multinodular Goitre	total	multi nodular goitre with secondary changes
117	i15017444	50	f	MULTINODULAR GOITRE	acellular smear	total	multi nodular goiter
118	i15017999	59	f	MULTINODULAR GOITRE	colloid with cystic macrophages total	total	multi nodular goitre
119	i15022207	47	f	MULTINODULAR GOITRE	colloid goitre with cystic changes	total	multi nodular goitre with cystic degeneration
120	i15022315	54	f	MULTINODULAR GOITRE	adenomatous changes in nodule	total	multi nodular goitre with cystic degeneration
121	i15022476	43	m	MULTINODULAR GOITRE	NODULAR COLLOID GOITRE	total	multi nodular goitte
122	i15023058	28	f	MULTINODULAR GOITRE	follicular neoplasm	total	hashimotos thyroiditos
123	i15024125	53	f	MULTINODULAR GOITRE	NODULAR COLLOID GOITRE	total	multi nodular goitre with cystic degeneration
124	i15029543	35	f	MULTINODULAR GOITRE	multinodular Goitre	total	nodular hashimotos thyroiditis
125	i15029679	24	f	MULTINODULAR GOITRE	NODULAR COLLOID GOITRE	total	
126	I15020709	47	F	MULTINODULAR GOITRE	NODULAR COLLOID GOITRE	total	multi nodular goitre

S.NO	IP NO	AGE	SEX	CLINICAL DIAGNOSIS	FNAC	SURGERY DONE	HPE
127	i15030222	43	f	MULTINODULAR GOITRE	NODULAR COLLOID GOITRE	total	nodular colloid goitre
128	i15031864	43	m	MULTINODULAR GOITRE	multinodular Goitre	total	multi nodular goitre
129	i15035716	72	f	MULTINODULAR GOITRE	multinodular Goitre	total	adenomatous changes in nodular colloid goitre
130	i15037228	42	f	MULTINODULAR GOITRE	multinodular Goitre	total	nodular colloid goitre with extensive degenerative changes
131	i15037828	41	f	MULTINODULAR GOITRE	multinodular Goitre	total	multi nodular goitre with cystic changes
132	i16009305	51	f	MULTINODULAR GOITRE	NODULAR COLLOID GOITRE	total	nodular colloid goitre wiith adenomatous changes
133	i16010223	34	f	SOLITARY NODULAR GOITRE	dominant nodule in nodular colloid goitre	left hemi	nodular colloid goitre with adenomatous changes
134	i16017533	18	f	MULTINODULAR GOITRE	multinodular Goitre	total	nodular colloid goitre with adenomatous changes
135	i16018268	43	f	MULTINODULAR GOITRE	Hashimotos thyroiditis	total	nodular hashimotos
136	i16018273	52	f	MULTINODULAR GOITRE	hashimotos thyroiditis	right hemi	hashimoto thyroiditis
137	i16019357	34	f	MULTINODULAR GOITRE	multinodular Goitre	TOTAL	multi nodular goitre with degenerative changes
138	i16019496	72	f	MULTINODULAR GOITRE	multinodular Goitre	total	multi nodular goitre
139	i16033173	58	f	MULTINODULAR GOITRE	multinodular Goitre	total	nodular colloid goitre with cystic changes
140	i16036439	53	f	MULTINODULAR GOITRE	NODULAR COLLOID GOITRE	TOTAL	nodular colloid goitre

S.NO	IP NO	AGE	SEX	CLINICAL DIAGNOSIS	FNAC	SURGERY DONE	HPE
141	i16037378	63	f	SOLITARY NODULAR GOITRE	benign follicular epithelial cells	right hemi	hurthle cell adenoma
142	i16038366	39	f	MULTINODULAR GOITRE	NODULAR COLLOID GOITRE	total	multi nodular goitre
143	i16038442	62	f	MULTINODULAR GOITRE	NODULAR COLLOID GOITRE	tOTAL	multi nodular goitre
144	i16038980	40	f	MULTINODULAR GOITRE	colloid goitre with cystic changes	tOTAL	multi nodular goitre
145	i16039000	29	f	MULTINODULAR GOITRE	colloid goitre with cystic changes	total	nodular colloid goitre
146	i16039088	64	f	SOLITARY NODULAR GOITRE	adenomatous changes in nodule	right hemi	multinodular goitre with adenomatous changes
147	i16040546	29	f	MULTINODULAR GOITRE	adenomatous changes in nodule	SUBTOTAL	multinodular goitre with adenomatous changes
148	i17002361	34	f	MULTINODULAR GOITRE	colloid goitre	left hemi	nodular colloid goitre with infarcted noule
149	i17003517	55	f	SOLITARY NODULAR GOITRE	adenomatous changes in nodule	right hemi	nodular goitre with cystic changes
150	i17011072	67	m	SOLITARY NODULAR GOITRE	colloid goit	left hemi	nodular colloid goitre with secondary degenerative changes and hashimotos thyroiditis
151	i17013096	70	f	MULTINODULAR GOITRE	NODULAR COLLOID GOITRE	total	nodular colloid goitre with degenerative changes