“SOLITARY NODULE THYROID- A DIAGNOSTIC DILEMMA”

A DISSERTATION SUBMITTED TO THE TAMILNADU

DR MGR MEDICAL UNIVERSITY

CHENNAI

In partial fulfillment of the requirement for the degree of

M.S. (GENERAL SURGERY)

BRANCH – I

Register No: 221711369

DEPARTMENT OF GENERAL SURGERY

TIRUNELVELI MEDICAL COLLEGE

TIRUNELVELI- 11

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DECLARATION

I solemnly declare that the dissertation entitled **"SOLITARY NODULE THYROID- A DIAGNOSTIC DILEMMA**" is done by me at Tirunelveli Medical College hospital, Tirunelveli. I also declare that this bonafide work or a part of this work was not submitted by me or any others for any award, degree, or diploma to any other University, Board, either in or abroad. The dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University towards the partial fulfilment of requirements for the award of M.S. Degree (Branch I) in General Surgery.

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PROTOCOL TITLE: SOLITARY NODULE THYROID – A DIAGNOSTIC DILEMMA
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DESIGNATION OF PRINCIPAL INVESTIGATOR: DR.THIRUPPATHI RAJA, G. MBBS.,
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Dear Dr.THIRUPPATHI RAJA.G, MBBS., The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during The IEC meeting Held on 01.09.2017.

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1.	TIREC Application Form	☐
2.	Study Protocol	☐
3.	Department Research Committee Approval	☐
4.	Patient Information Document and Consent Form in English and Vernacular Language	☐
5.	Investigator's Brochure	☐
6.	Proposed Methods for Patient Accrual Proposed	☐
7.	Curriculum Vitae of The Principal Investigator	☐
8.	Insurance /Compensation Policy	☐
9.	Investigator's Agreement with Sponsor	☐
10.	Investigator's Undertaking	☐
11.	DCGI/DGFT approval	☐
12.	Clinical Trial Agreement (CTA)	☐
13.	Memorandum of Understanding (MOU)/ Material Transfer Agreement (MTA)	☐
14.	Clinical Trials Registry-India (CTRI) Registration	☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 3weeks before for renewal / extension of The validity
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7. The PI should report to TIREC within 7 days of the occurrence of the SAE. If the SAE is Death, the Bioethics Cell should receive the SAE reporting form within 24 hours of the occurrence.
8. In the events of any protocol amendments, TIREC must be informed and the amendments should be highlighted in clear terms as follows:
   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in The original project. (Page no. Clause no. etc.)
   b. The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and The revised budget form should be submitted.
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   e. Approval for amendment changes must be obtained prior to implementation of changes.
   f. The amendment is unlikely to be approved by the IEC unless all the above information is provided.
   g. Any deviation/violation/waiver in The protocol must be informed.

STANDS APPROVED UNDER SEAL

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CERTIFICATE – II

This is certify that this dissertation work title **"SOLITARY NODULE THYROID - A DIAGNOSTIC DILEMMA"** of the candidate **Dr.THIRUPPATHI RAJA G** with registration Number **221711369** for the award of M.S. Degree in the branch of **GENEARL SURGERY (I)**. 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 page and result shows **5 percentage** of plagiarism in the dissertation.

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CONTENTS

INTRODUCTION

Any enlargement of the thyroid gland is called goiter. The solitary thyroid nodule may be defined as a discrete swelling in an otherwise impalpable gland. The incidence of solitary **nodule** in general population in South India is 9%.

Solitary nodule in thyroid has aroused interest since 1949, when Warren H Cole in his study concluded that incidence of malignancy is higher in solitary nodule when compared with Multi-nodular goiter (MNG).

Thyroid nodules are very common with estimated prevalence that ranges from 4% by palpation to 67% by ultrasonography. Autopsy studies reveal that 50% of adults had nodules, the majority of which are impalpable. Thyroid nodules are 4 times more common in females than in men.

A **solitary nodule** is a clinical diagnosis and not a pathological diagnosis. Almost all conditions of the thyroid may present clinically as a solitary nodule. Diagnostic possibilities in case of solitary nodules are adenoma, carcinoma, thyroid cyst and palpable nodule in an evolving multinodular colloid goiter. Other rare causes of solitary nodules include inflammatory thyroid lesions and developmental abnormalities such as dermoid cyst, teratoma etc.

Solitary nodule of the thyroid has aroused interest because of its varied etiology and diverse clinical presentations. Majority of the solitary nodules are benign and thyroid carcinoma is comparatively rare.

Clinically, solitary nodules fall into two categories. In the first, there is a certainty or grave suspicion of malignancy and in the second there is a smooth, firm, mobile nodule which is probably benign but carries a small but significant risk of being malignant.

The critical issue is to determine whether the nodule is benign or malignant.

Fine Needle Aspiration Cytology has become the mainstay in the initial evaluation of thyroid nodule.FNAC has got its own disadvantage because of false negatives & false positives reports & the same time the results have inter-observer variation . Even FNAC has got less specificity in identifying the micro-papillary projection & can't differentiate between follicular adenoma & carcinoma.

The uses of USG & radioisotope studies are often additive but not much of value in confirming the diagnosis particularly in malignancy.

Though exact incidence of nodular goitre is not available, World Health Organization in estimated that goitre was present in 7% of World's population. Solitary Nodular goiters are more common in women than in men and the nodularity increases with increasing age. Solitary Thyroid Nodule (STN) can become malignant but it is rare.

OBJECTIVE OF THE STUDY

- To estimate the proportion of malignancy in Solitary Nodule Thyroid

REVIEW OF LITERATURE

EMBRYOLOGY

Thyroid gland is developed from median endodermal thyroid diverticulum, which grows down in front of the neck from the floor of "primitive pharynx", just caudal to tuberculum impar. The lower end of the diverticulum enlarges to form the gland. The rest of the narrow part of the diverticulum is known as thyroglossal duct, of which disappears. The site of origin of diverticulum is seen as a depression called foramen caecum and the lower end often persists as pyramidal lobe. Thyroid is the earliest glandular structure to appear. It becomes functional during the third month of development of fetus.

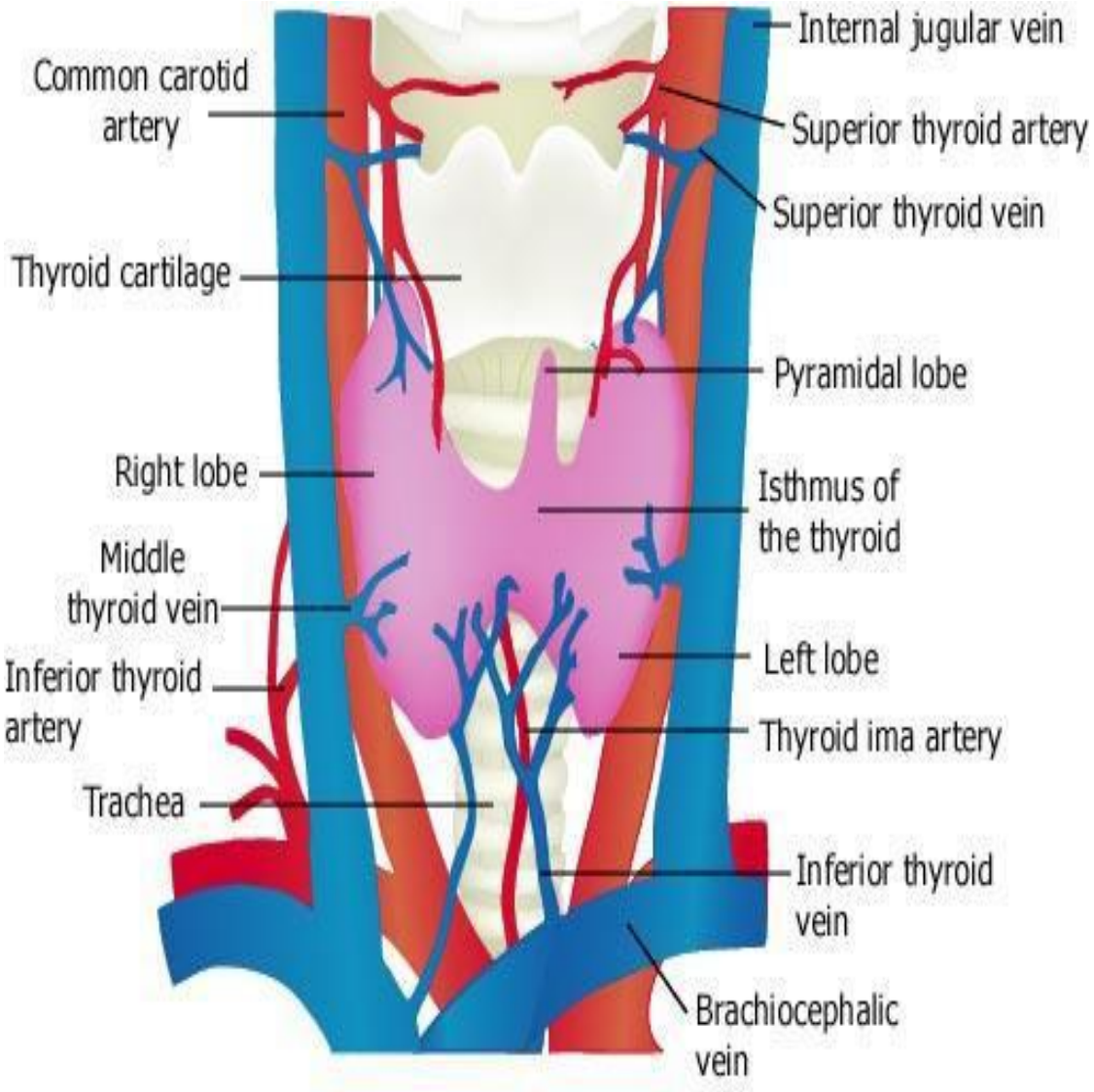

Fig 1:Thyroid gland- Anterior View

SURGICAL ANATOMY OF THYROID GLAND

The thyroid gland is composed of two lobes connected by an isthmus and appears as butterfly shape. The lobular extension is from the middle of thyroid cartilage to the sixth ring of trachea. The gland lies against 5th, 6th, 7th cervical and 1st thoracic vertebrae and the isthmus covers 2nd, 3rd and 4th tracheal rings. Rarely, aberrant and ectopic thyroids are found in stomach and ovaries.

Weight and Dimensions:

Thyroid gland averagely weighs 20-25 grams. It is larger in females than in males and increases further during pregnancy and menstruation. Each lobe measures 2x1x1 inches and isthmus 1x1 inch.

Thyroid capsules:

Two capsules surround the gland namely true and false capsule. Peripheral condensation of connective tissues of the gland is the true capsule and false capsule is derived from pretracheal layer of deep cervical fascia. These two capsules are pierced by blood vessels of the thyroid and ramify to form dense plexus immediately beneath the true capsule. Arterial and venous trunks traverse the space between the two capsules. So during surgery of the gland, these main vessels are secured between the two capsules, taking care not to damage true capsule, so the thyroid gland is removed with its true capsule.

Anatomical relations of thyroid gland

Each thyroid is conical in shape with an apex, base, two borders – anterior and posterior, three surfaces – superficial, medial and posterolateral. Apex is directed laterally and upwards and is limited by the attachment of sternothyroid on thyroid cartilage. Base is at the level of 5th or 6th tracheal rings; anterior border is thin and is related to branches of superior thyroid artery.

Posterior border is thick and rounded and is related to the inferior thyroid artery, parathyroid gland and thoracic duct on the left side. Superficial surface is covered by sternothyroid, sternohyoid and superior belly of omohyoid and anterior border of sternomastoid overlapping it inferiorly.

The surface is convex. Two tubes, trachea and oesophagus, two muscles, inferior constrictor and cricothyroid and two nerves, External laryngeal and Recurrent laryngeal nerves are related to the medial surface of thyroid gland. Posterior surface is related to carotid sheath and overlaps the common carotid artery.

The isthmus has two surfaces and two borders. Occasionally it may be absent. Anterior surface of isthmus is covered by sternothyroid, sternohyoid muscles and anterior jugular vein.

The upper border is related to the anastomotic branches of the two superior thyroid arteries. At the lower border inferior thyroid vein leaves the gland. A small portion of the gland substance often projects upwards from the isthmus, generally to the left of the midline, as the pyramidal lobe. Separate masses of thyroid tissue called accessory thyroid gland are often found near the hyoid bone, in the tongue, in the superior mediastinum, or anywhere along the path of descent of the thyroglossal duct.

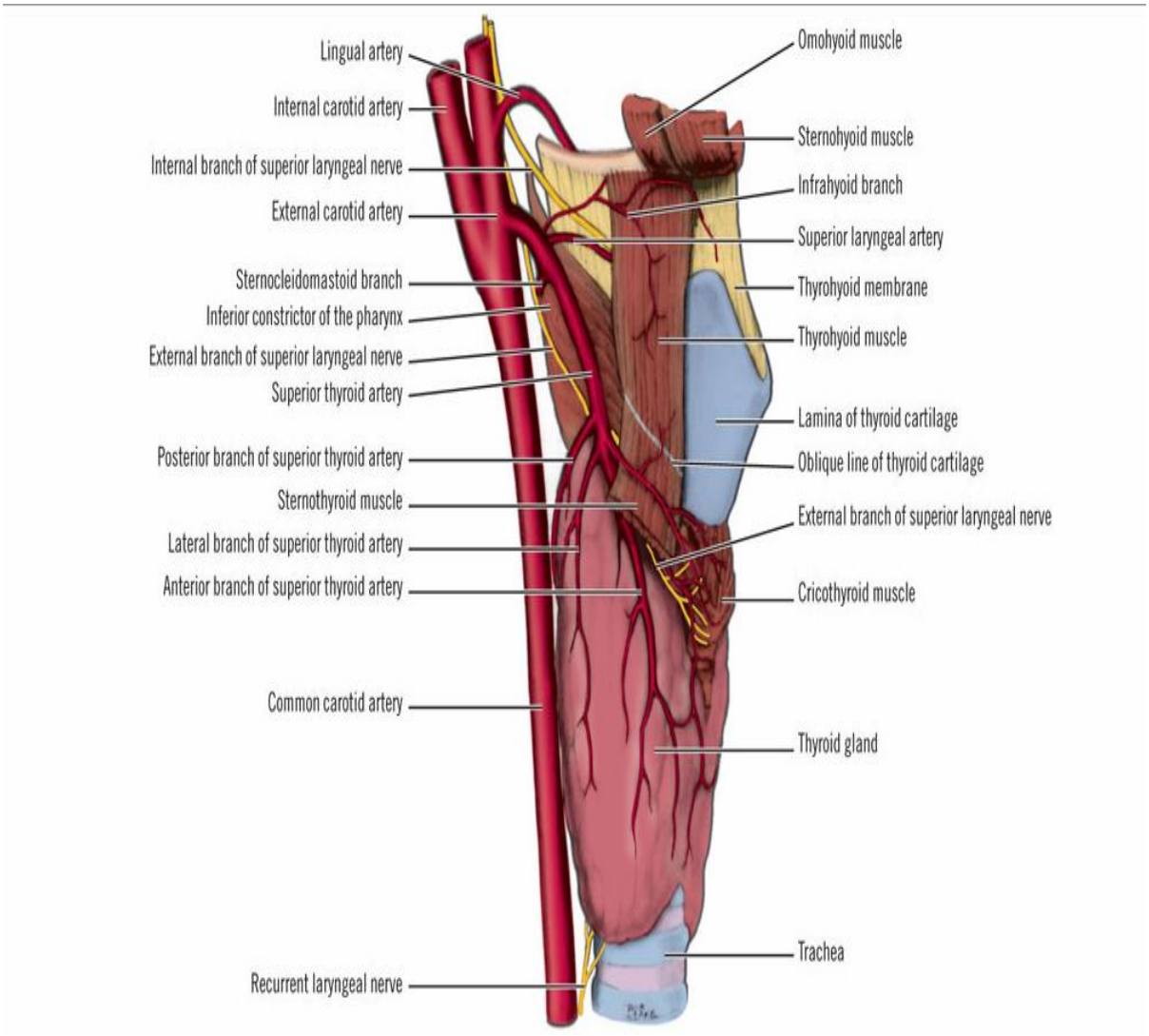

Fig 2:Thyroid Gland -Lateral view

Blood supply of the thyroid gland

It is supplied by two arteries which carry sympathetic fibres with them and is drained by three veins.

Arterial Supply

The thyroid gland is supplied by superior thyroid, inferior thyroid and sometimes by arteria thyroidea ima.

The superior thyroid artery, first branch of external carotid artery descends downwards and forwards in intimate relation with external laryngeal nerve. It enters the gland superficially. After piercing the pretracheal fascia, it divides into anterior and posterior branches. The anterior branch runs along the upper border of isthmus to anastomose with the fellow of the opposite side. The posterior branch descends along the posterior border to anastomose with ascending branch of inferior thyroid artery. The superior thyroid supplies upper 1/3 rd of lobe and upper ½ of isthmus.

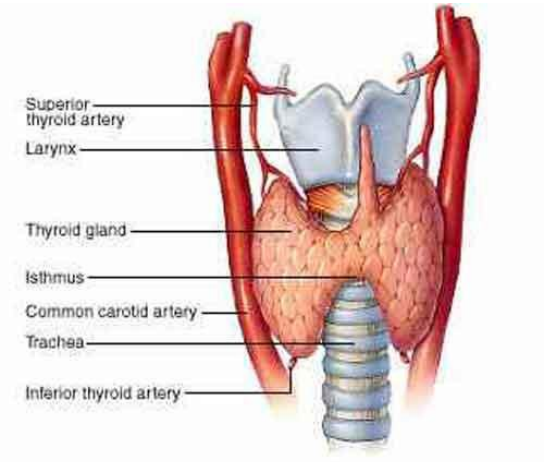

Fig 3: Arterial supply of thyroid gland

The inferior thyroid artery is a branch of thyrocervical trunk, which in turn is a branch of subclavian artery. It is related to the posterior surface of gland. During the course it passes behind the carotid sheath and middle cervical ganglion but in front of the vertebral vessels. Its terminal part is intimately related to recurrent laryngeal nerve. It divides into 4 to 5 branches and one ascending branch anastomoses with posterior descending branch of superior thyroid artery. The inferior thyroid artery supplies the lower 2/3rd of the lobe and lower ½ of isthmus with parathyroid glands. This makes a major share in thyroid blood supply.

The thyroidea ima artery enters the lower part of the isthmus and arises from the arch of aorta, or brachiocephalic trunk, or right common carotid artery and supplies the isthmus.

Venous drainage:

From a venous plexus on the surface of the gland the superior thyroid vein follow superior thyroid artery and runs along the outer border of omohyoid to terminate in internal jugular vein. The middle thyroid vein is a short channel, which leaves the gland at its middle, crosses the common carotid artery to enter into internal jugular vein. It bleeds torrentially if torn during surgery due to its shortness.

The inferior thyroid vein leaves the isthmus at its lower border, runs down in front of trachea to end in the innominate vein of same side. Sometimes both inferior thyroid veins may join the left innominate vein.

Lymphatic drainage:

Thyroid is richly drained by lymphatics. It has extensive intraglandular and intralobar lymphatics that encircle the thyroid follicle. The capsular lymphatics may cross –communicate with isthmus and that of the opposite lobe. The gland is drained by two sets of medial and lateral channels. The medial ascending channels leave the upper border of isthmus and drain to the gland on the cricothyroid membrane that is, the prelaryngeal lymph nodes. The ascending lateral vessels leave the upper pole of the gland and run with superior thyroid artery to the deep cervical nodes. Descending lateral vessels pass from deep surface of the gland to small nodes placed on recurrent laryngeal nerve, called nodes of recurrent chain.

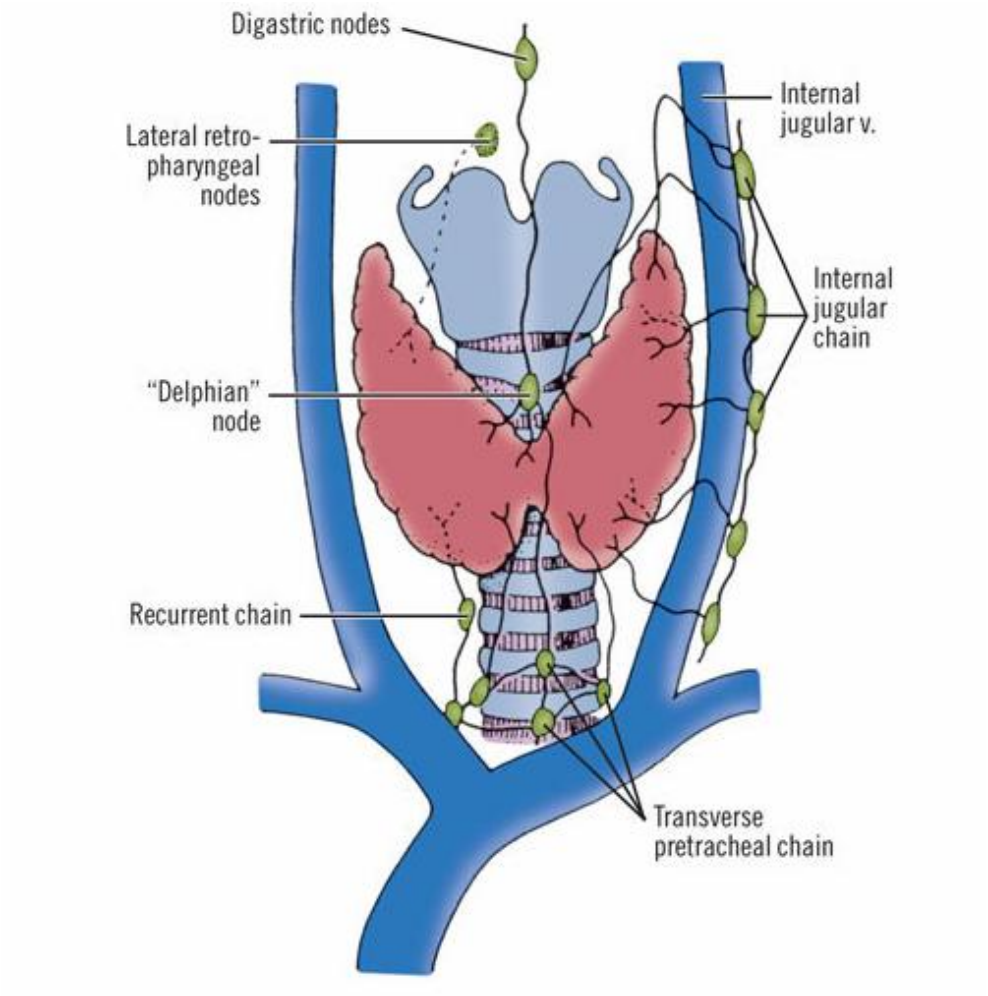

Fig 4: Lymphatic supply of thyroid gland

Nerve supply:

Sympathetic nerves are mainly derived from middle cervical ganglion and partly from superior and inferior cervical ganglion which accompany the thyroid arteries.

Microscopic anatomy:

The thyroid consist essentially a mass of more or less rounded follicles containing varying amounts of colloid. These follicles are lined by a single layer of cuboidal epithelium, which form the walls of the follicles. These follicles are arranged in subunits of 20-40 lobules each being supplied by an individual arteriole. These cells secrete Thyroxine **(**T4**)** and tri-iodothyronine (T3). The parafollicular or 'C' cells lie in between the follicles, which secrete calcitonin, which in turn promotes deposition of calcium salts in the skeleton.

NERVES RELATED TO THYROID

Two nerves, the external branch of superior laryngeal nerve and recurrent laryngeal nerve are in intimate relation with thyroid gland. So protection of these nerves is very important in thyroid surgery.

The external laryngeal nerve, which supplies inferior constrictor and cricothyroid muscle, is in real danger while ligating the superior thyroid artery. The nerve descends just deep to the artery. The best way to avoid injury to the nerve is to ligate the upper pole of the gland with the vessel as close to the gland as possible.

The recurrent laryngeal nerve is related to the posterior surface of the gland and in intimate relation with inferior thyroid arteries. The nerve can be identified in a triangle formed by common carotid artery laterally, trachea medially, and thyroid lobe superiorly, which lies in between trachea and larynx.

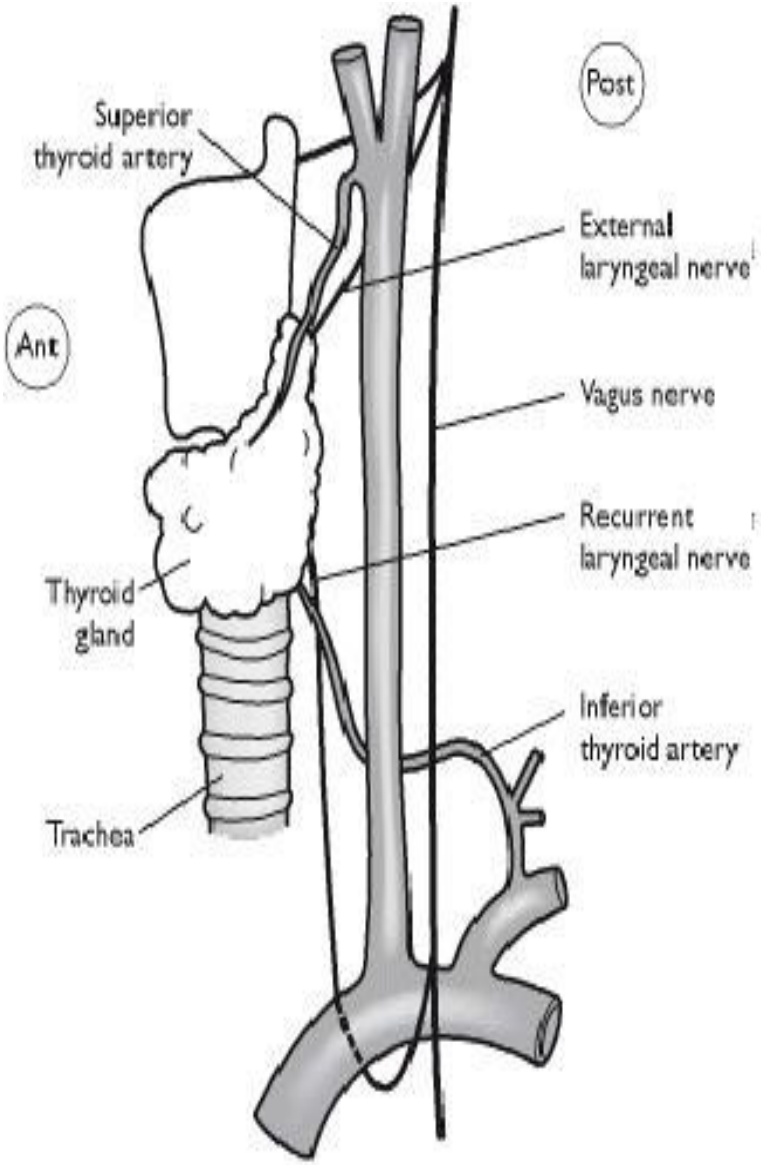

Fig 5: nerves related to thyroid gland

Variations in position of recurrent laryngeal nerve are

1. The nerve penetrates and traverses through the gland which is a dangerous position.
2. The nerve courses through the area of greatest adherence of the gland to larynx i.e ligament of Berry – not in the gland but very near to it.
3. The nerve passes posterior to the joint between inferior cornu of thyroid cartilage and the cricoid cartilage.
4. Right nerve may not be recurrent in some cases, arising directly from vagus above the level of cricoid cartilage. These are associated with anomalous origin of right subclavian artery.

SYNTHESIS OF THYROID HORMONES

The primary function of thyroid gland is the production of sufficient thyroid hormones for proper regulation of cellular metabolism throughout the body.

Iodine metabolism

Iodine is taken in the form of Iodides sea fish; egg and milk are good dietary source of iodide. Dietary iodide is absorbed from upper gastrointestinal tract and carried as inorganic iodide in plasma. Normally thyroid, salivary glands and kidney compete for iodide but thyroid and kidney are the principal organs that compete for iodide.

The adult man requires 0.14 mg of iodide per day and an adult female requires 0.10 mg. Growing children, pregnant and lactating women require more. The daily requirement is met by balanced diet and drinking water, exception being hilly areas where food and water may be deficient in iodine.

The synthesis of thyroid hormones is divided into four steps:

a) Iodine trapping

The thyroid traps the plasma iodine in the inorganic form. It is essentially an active process and stimulated by TSH. It is competitively inhibited by Thiocynates and perchlorates.

b) Iodine binding

The inorganic iodide is oxidized to inorganic iodine at the thyroid follicular cells with the help of an enzyme peroxidase. Iodine combines with amino acid tyrosine in the globulin molecule within the follicular cells to form monoiodotyrosine and diiodotyrosine (MIT and DIT). This process is inhibited by Thiouracil group of antithyroid drugs and by PAS and chloroquine.

c) Coupling

Thyroxine (T4) is formed by coupling of two molecules of DIT and Tri-iodothyronine (T3) by coupling of one molecule of each MIT and DIT. The coupling reaction occurs at the Thyroglobulin molecule. They are oxidative reactions and need peroxidase enzyme.

d) Hormonal release

Thyroglobulin is first taken up by thyroid follicular cells. Under the influence of TSH a protease acts on thyroglobulin to release T4, T3, MIT and DIT. MIT and DIT are deiodinated within the cell and iodine is reutilized for iodinating globulin. From the follicular cells T4 and T3 directly enters the circulation.

On entering the circulation the thyroid hormones are largely bound to specific protein called thyroxine-binding globulin (TBG), thyroxine binding albumin (TBA) and thyroxine binding prealbumin (TBPA).

This protein has got more affinity to Thyroxine than to the tri-iodothyronine. The protein bound iodine (PBI), which is about 4-8 μg per 100 ml mainly, reflects plasma T4 level.A small amount of hormone remains free in the serum in equilibrium with the protein bound hormone and is biologically active. The free hormone is physiologically active and protein bound fraction acts as a reserve. Thyroid hormones are disposed by de-iodination 80% and 20% excreted in the stools. About 40% of circulating T4 is converted to T3 peripherally called “Reverse T3”. This is inhibited by propranolol and glucocorticoids.

Differences between T3 and T4

T3 has quicker onset of action and is effective in very small doses. The onset of action of T3 is within 6-8 hours and that of T4 is 4-14 days. After cessation of therapy the hormonal effect lasts for several days with T4 but vanishes quickly with T3. T3 is the more important physiological hormone and is also produced in the periphery by conversion from T4. Reverse T3 is an inactive form of T3.

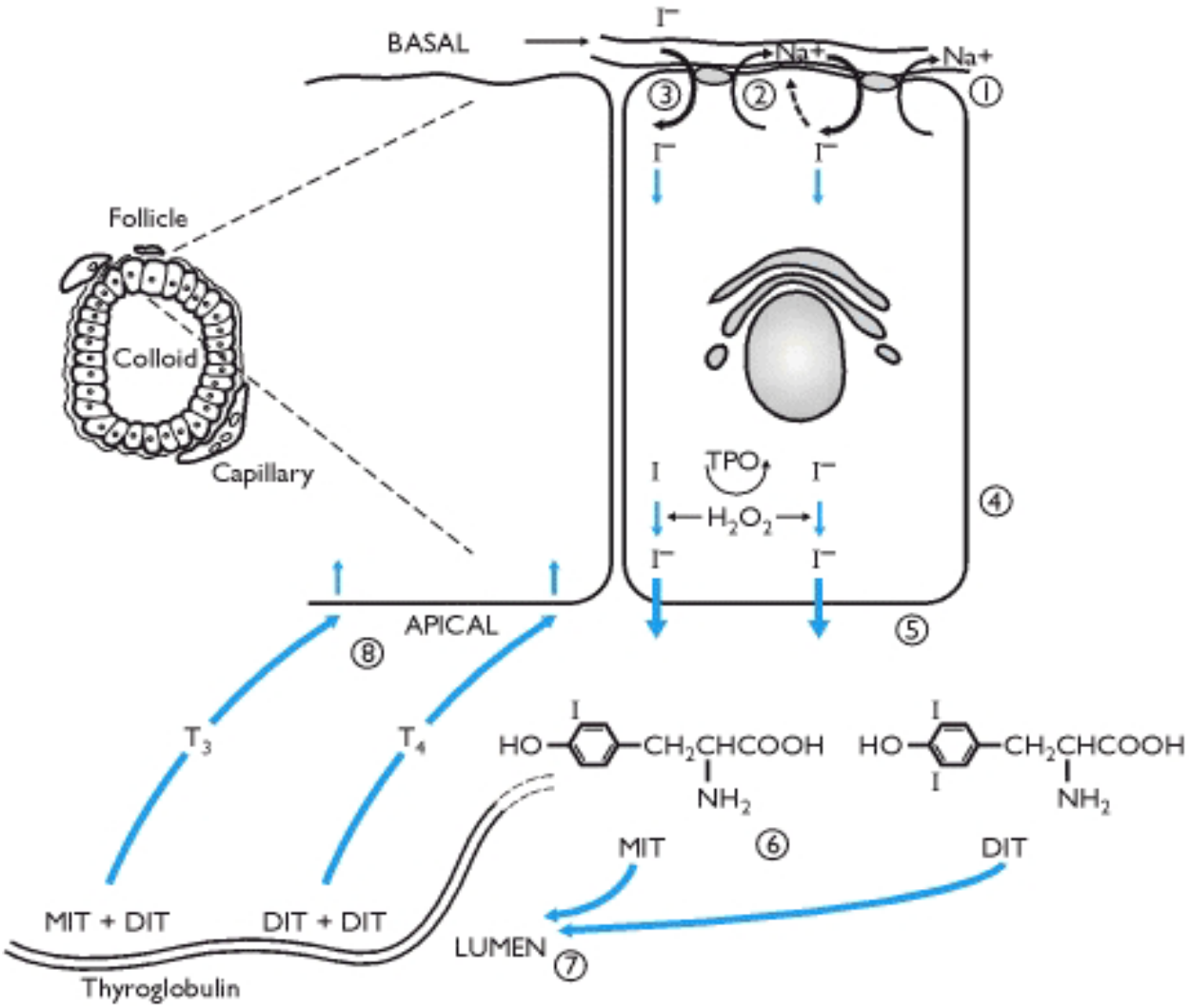

Fig 6: Steps in synthesis of thyroid hormones

Mechanism of action of thyroid hormones

In normal levels, the thyroid hormones act at chromatin of molecules and stimulate synthesis of mRNA molecules. These later synthesize protein molecules including enzymes at cytoplasm, which has anabolic, growth promoting, and calorigenic actions. But in unphysiological higher concentrations they act at mitochondria and uncouple oxidative phosphorylation. Thus oxygen consumption and heat production is increased.

Theories concerning the mechanism of action of thyroid hormones

- Uncoupling of oxidative phosphorylation at mitochondria.
- Increased activity of Na+, K+ dependent ATPase.
- Increased synthesis of specific enzymes.
- Stimulation of adenyl cyclase at plasma membrane.

Regulation of thyroid function

Thyroid function is regulated by two mechanisms, namely suprathyroid and intrathyroid. The suprathyroid regulation is by thyroid stimulating hormone (TSH) released from basophilic cells of the anterior pituitary. TSH stimulates thyroid hypertrophy and hyperplasia. All steps in the synthesis and secretion of thyroid hormones are enhanced and the synthesis of thyroglobulin is increased. These actions of TSH are due to binding of hormone to receptors on thyroid follicular cell membrane. Regulation of TSH secretion is by two opposing mechanisms.

The thyrotrophic-releasing hormone (TRH)/ (TSHRH) of hypothalamic origin stimulates synthesis and secretion of TSH and thyroid hormones. TRH is synthesized in the hypothalamus, reaches anterior pituitary by portal blood system and binds to receptor on thyrotrophic cells. This is called pituitary – thyroid axis.

The intrathyroidal regulation is also called auto-regulatory mechanism, but this is not to mean that thyroid controls hormone production in the absence of TSH stimulation. The gland reduces the iodine trapping mechanism whenever there is sudden increase in the supply of iodide and this occurs without the negative feedback mechanism.

Thyroid stimulating antibodies

A family of IgG immunoglobulins binds with TSH receptor sites (TRAbs) and activates TSH receptors on the follicular cell membrane. They have a more protracted action than TSH (16-24 hours versus 1.5-3 hours) and are responsible for virtually all cases of thyrotoxicosis not due to autonomous toxic nodules. Serum concentrations are very low and not routinely measured. Measurement of antithyroglobulin and thyroid antimicrosomal antibodies is helpful in autoimmune thyroiditis.

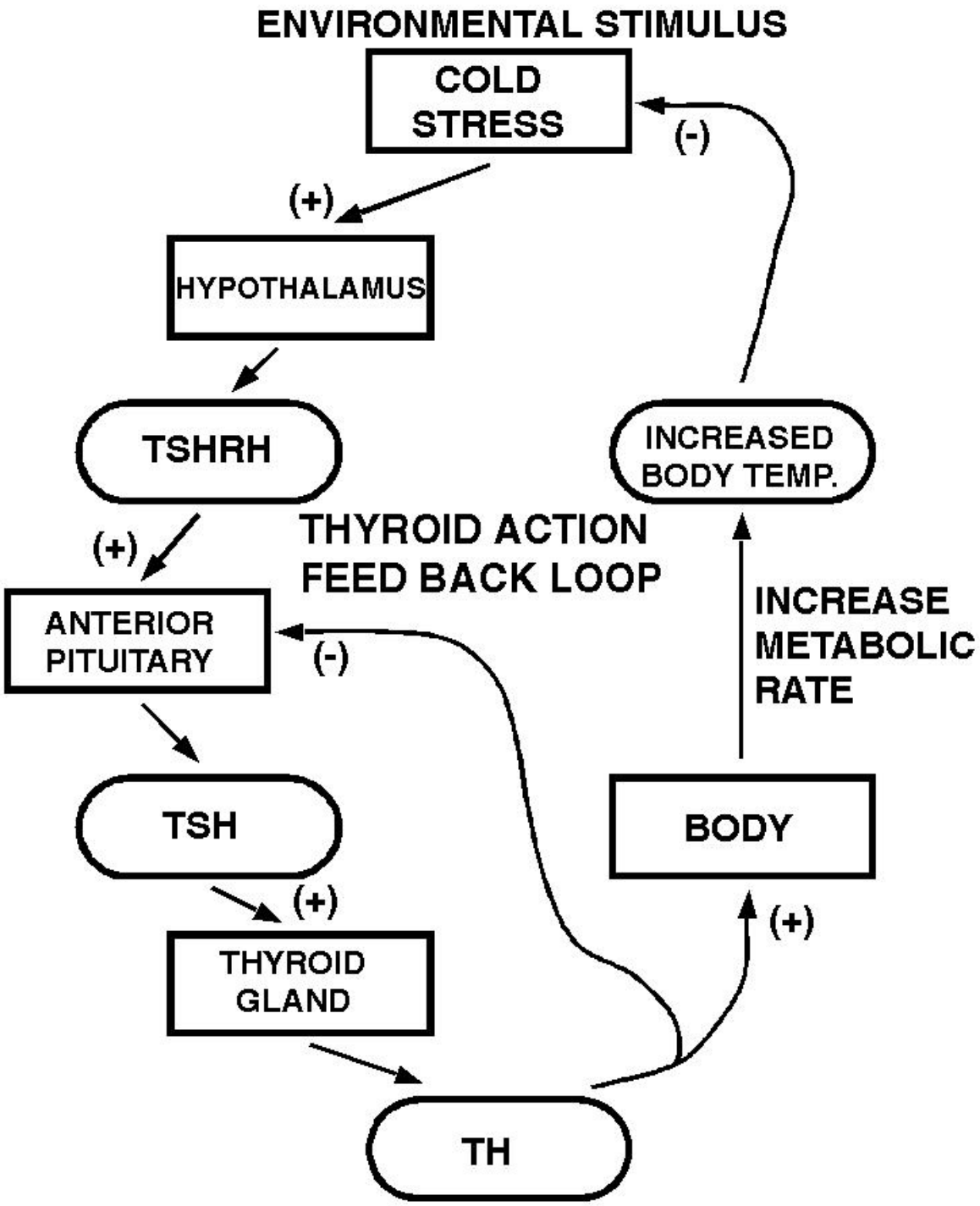

Fig 7: Regulation of thyroid hormone secretion

CAUSES OF SOLITARY THYROID NODULES

Solitary nodule of thyroid can occur from diverse diseases. They are

1. Cyst (pure and complex)
2. Adenomatous nodule (colloid nodule)
3. Thyroid neoplasms
    a. **Benign**- Follicular adenoma, Hurthle cell adenoma
    b. **Malignant-**
        i. Primary-
            Papillary carcinoma
            Follicular carcinoma
            Medullary carcinoma
            Anaplastic carcinoma
            Lymphoma
        ii. Metastatic-
            Renal cell carcinoma
            Breast carcinoma
            Lung carcinoma
            Melanoma
            Colonic carcinoma
            Pancreatic carcinoma

4. Thyroiditis-

Acute thyroiditis

Subacute thyroiditis

Hashimoto’s thyroiditis

Riedel’s thyroiditis

5. Infections-

Abscess

Tuberculosis

6. Infilterative diseases-

Sarcoidosis

Amyloidosis

PATHOLOGY

1. Adenomatous Nodule

Nodule ranges from half a centimetre to several centimetres in diameter.

Macroscopically, nodule shows cystic changes, focal haemorrhages, fibrosis and calcification.

Microscopically, nodules appear as clusters of small active looking follicles within lobules. Small follicles become colloid cyst due to loss of their walls. Focal areas of necrosis with collection of red cells and macrophages laden with hemosiderin are also seen.

2. Follicular adenoma

Almost all thyroid adenomas show follicle formation to a varying degree. Follicular adenomas are usually cellular but may contain variable amount of colloid. The most important clinically relevant fact about follicular adenoma is that it cannot be distinguished from follicular carcinoma by FNAC as vascular or capsular invasion cannot be made out from FNAC. It is only by histopathological examination that these adenomas can be differentiated from carcinoma. About 5% of adenomas are prone to be follicular carcinoma. It is also difficult to differentiate between an adenoma and nodule of adenomatous goitre. If the gland appears otherwise normal and there is a well-demarcated capsule, it goes in favour of an adenoma.

Microscopically, follicular adenomas show a consistent pattern of follicles. Tumour is surrounded by fibrous capsule that often contains wide vascular spaces. The tumour cells form large and small follicles, which confine to the inner margin of the capsule.

According to the size of follicles and to the degree of follicle formation, follicular adenomas are further classified as:

a. Embryonal adenoma

b. Micro-follicular adenoma

c. Normo-follicular adenoma

d. Macro-follicular adenoma

Variants of follicular adenoma are Hurthle cell adenoma, adenolipoma and atypical follicular adenoma.

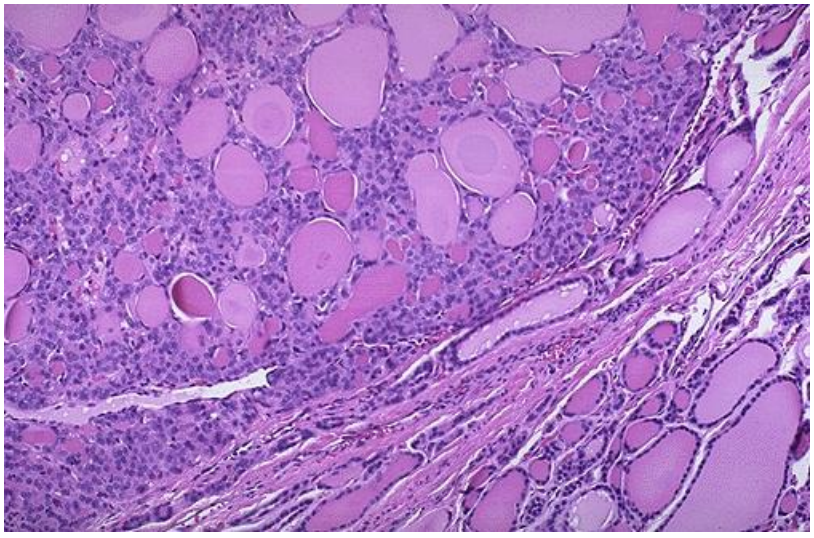

Fig 8: FOLLICULAR ADENOMA

Hurthle cell adenoma

It is an uncommon variant composed of solid trabecula of large cells with abundant granular oxyphilic cytoplasm and vesicular nuclei. The tumor cells do not form follicles and contain little stroma.

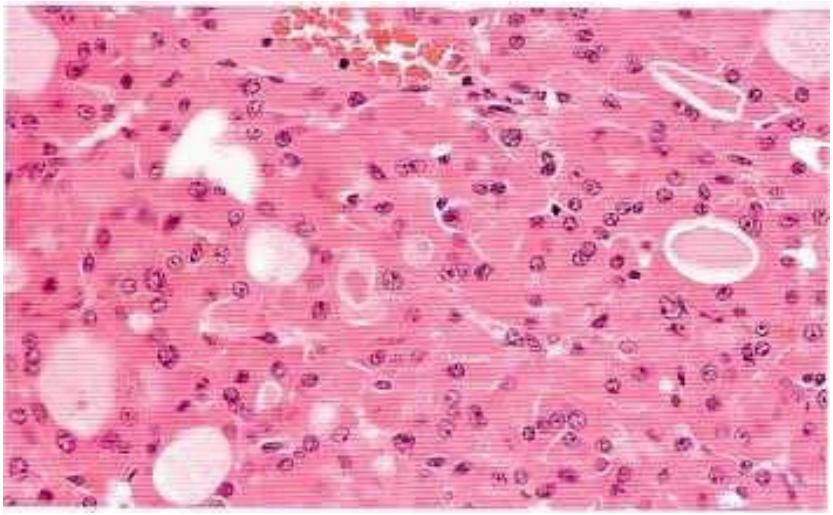

Fig 9: HURTHLE CELL ADENOMA

3. Papillary carcinoma

It is typically a slow growing malignant tumor. Most often it presents as an asymptomatic solitary nodule. Predominant spread is by lymphatics. Involvement of regional lymph nodes is common but distant metastasis is rare.

Microscopically, the carcinoma is composed of columnar thyroid cells arranged in papillary projections with connective tissue vascular stalks. Distinctive nuclear features include large size, pale staining, ground glass appearance. These optically clear nuclei termed' Orphan Annie eyed' nuclei are usually not perceived in frozen section but are well seen in fixed tissue. Another

characteristic feature is presence of deep nuclear groove that are seen in more than 80% of patients.

Psammoma bodies are calcified degenerative changes in the papilla that appear laminated basophilic stromal structures that are present in 40-50% of papillary carcinoma.

Multicentricity of the primary tumor is one of the important features of this carcinoma. Multicentricity has often been incriminated due to lymphatic spread. Tumor cells invade the capsule but vascular invasion is quite rare.

Papillary carcinoma is divided into 3 sub groups (Woolner classification) namely occult, intra-thyroidal and extra-thyroidal.

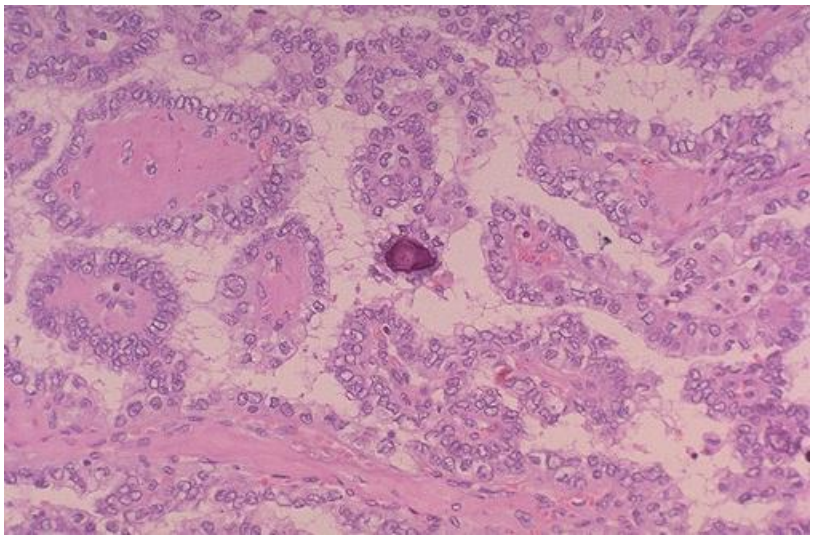

Fig 10: PAPILLARY CARCINOMA

4. Follicular carcinoma

It can present as either solitary nodule or as an irregular firm thyroid enlargement. It is a slow growing tumour. Regional metastasis to lymph nodes is rare, but distant metastasis is common especially to lungs and bones.

Macroscopically, follicular carcinoma presents as solitary, well demarcated, red to brown tissue mass, often surrounded by thick capsule with areas of haemorrhage, necrosis and cyst formation.

Microscopically, follicular carcinoma is composed of follicles of various sizes and show trabecular or solid pattern with existence of lumen in the lining acini which may or may not contain colloid. The tumour cells contain hyperchromatic nuclei and cytoplasm resembling that of normal follicular cells.

Vascular invasion and direct extension to involve the adjacent structures are significant features of follicular carcinoma. This carcinoma usually does not metastasize to regional or distant lymph nodes. Multicentricity is also much rare in this carcinoma.

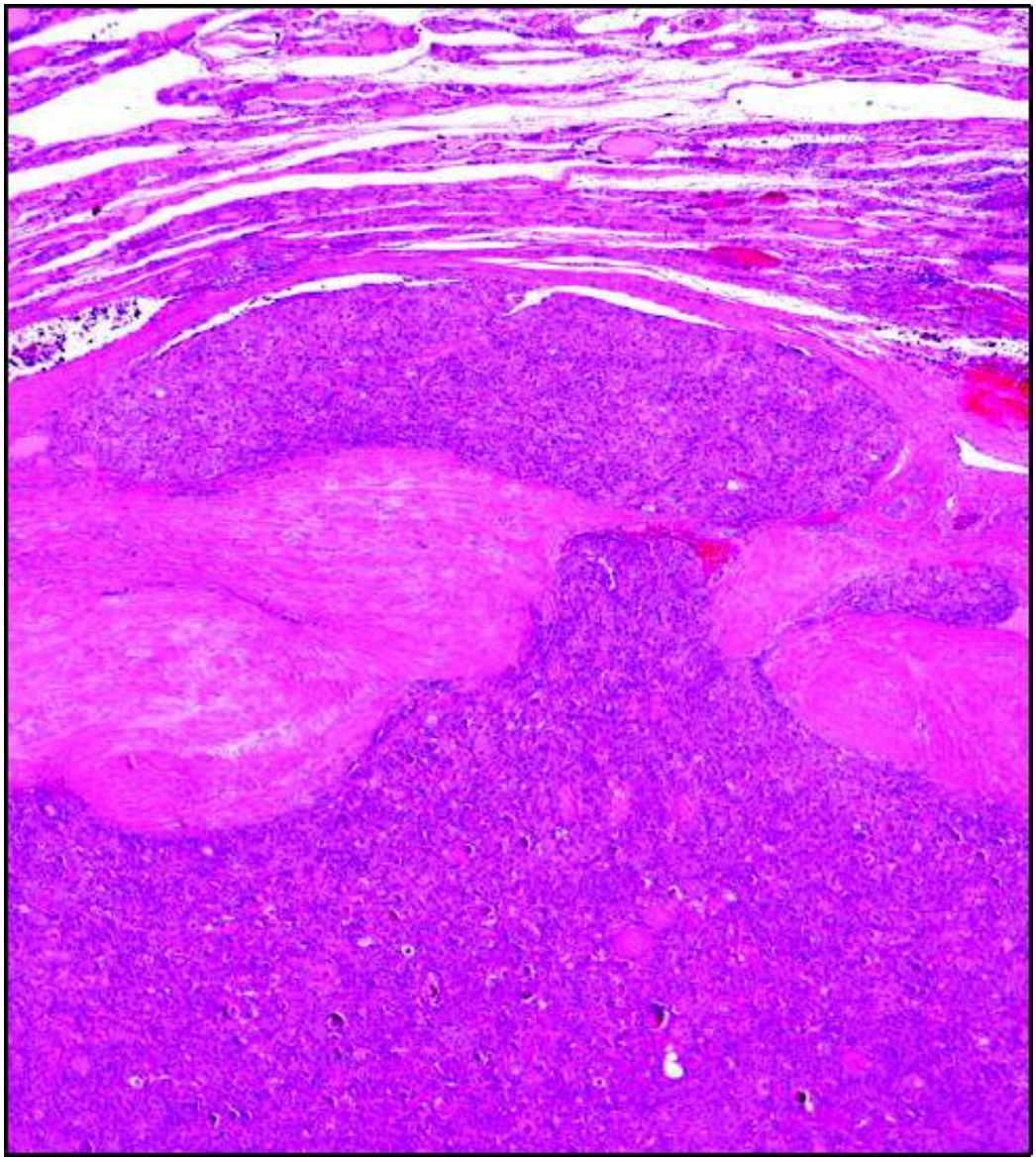

Fig 11: FOLLICULAR CARCINOMA

5. Anaplastic carcinoma

It is one of the most aggressive and difficult to treat human malignancies and subsequently one of the most lethal malignancies. It is rare for an anaplastic carcinoma to present as solitary thyroid nodule.

It usually occurs in 7th-8th decade of life. It extensively invades the adjacent structures. It metastasis both to regional lymph nodes as well as to distant organs such as lungs and brain.

Macroscopically, the tumour is white and firm with areas of necrosis and haemorrhages.

The tumour is poorly differentiated, shows either papillary or follicular carcinoma in better differentiated areas.

Microscopically, the tumour is composed of 3 types of cells namely small cells, spindle cells, and giant cells.

Small cell carcinoma consists of closely packed small cells having hyperchromatic nuclei and numerous mitotic figures.

Spindle cell carcinoma consists of spindle resembling sarcoma.

Giant cell carcinoma is composed of highly anaplastic giant cells showing numerous atypical mitosis, bizarre and bi-lobed nuclei.

6. Medullary carcinoma

It comprises 5% of all thyroid carcinoma. It has 3 distinct features. They are its genetic association, secretion of calcitonin and amyloid stroma. It has an association with multiple endocrine neoplasia. Sporadic or non-familial cases accounts for 60-70% of cases.

Medullary carcinoma is found in equal number in males and females.

Macroscopically, it may be circumscribed or infiltrative, yellow in colour, hard in consistency.

Microscopically, it has a well defined organoid pattern, forming nests of tumour cells separated by fibrovascular septa and amyloid containing stroma. The tumour cells may be arranged in sheets, pseudo-papilla or small follicles.

The nuclei of medullary thyroid carcinoma resemble those of neuroendocrine tumors in other areas of the body. They are usually round and have a stippled **"pepper and salt"** chromatin.

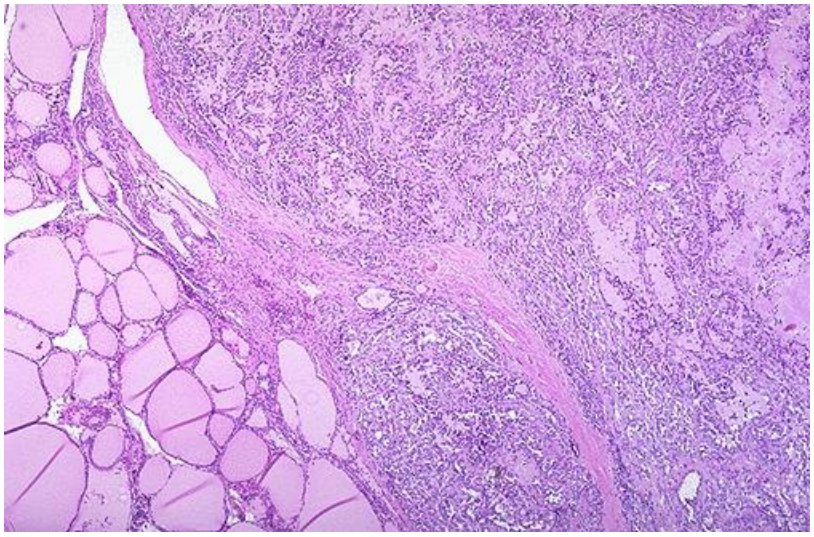

Fig 12: MEDULLARY CARCINOMA

Medullary thyroid cancer is rare in children and most often occurs with multiple endocrine neoplasia (MEN). Although medullary thyroid cancer usually affects the entire thyroid gland, it uncommonly may present as a solitary thyroid nodule, especially in adolescents with sporadic incidents of medullary cancer. This tumor involves the parafollicular C cells and is a calcitonin secretor. However, the tumor may also secrete adrenocorticotropic hormone (ACTH), melanocyte-stimulating hormone (MSH), histaminase, serotonin, prostaglandins, somatostatins, or beta-endorphin. It is an aggressive tumor treated by total thyroidectomy, but surgical cure is possible if spread is limited to the central compartment of the neck.

MEN is a hereditary syndrome of endocrine tumors. Medullary thyroid carcinoma occurs in MEN 2A and MEN 2B. MEN 2A consists of medullary thyroid cancer, adrenal pheochromocytoma, and hyperparathyroidism. MEN 2A is characterized by autosomal dominant inheritance and usually becomes clinically evident when the individual is aged 12-30 years. The associated thyroid malignancy is more aggressive in younger patients and metastasizes early to perithyroid lymph nodes, liver, lung, and bone.

MEN 2B causes mucosal neuromas, typical facies, marfanoid body habitus, and medullary thyroid carcinoma. The associated thyroid cancer is especially aggressive and often appears when the individual is aged almost 5 years. In both syndromes, because of disease aggression, early genetic identification is recommended with prophylactic thyroidectomy.

Medullary thyroid cancer and anaplastic or undifferentiated carcinomas are much more rare. Thyroid cancer is more common and aggressive in children than in adults, often with cervical lymph node metastases at the time of initial evaluation. Thyroid malignancy also metastasizes to the lungs in 10% of individuals. These metastases sometimes occur without lymph node spread, especially in individuals with follicular carcinoma. Cancer is also found in the contralateral lobe in as many as 66% of individuals with thyroid malignancy. Other sites of spread include the spinal cord, base of the tongue, and bone, especially the skull, tibia, and costochondral junction. Even metastatic thyroid cancer responds to treatment.

The prognosis of a solitary thyroid nodule is generally quite good, even with diagnosed malignancy. Despite early metastasis and the relative aggressiveness of disease in the pediatric population, the 10-year and 20-year mortality rates are almost zero. Because of this, survival rates are often based on the progression-free survival rate.

In a study of 329 pediatric patients with thyroid cancer, Newman et al found that the progression-free survival rate was 67% at 10 years and 60% at 20 years. [8] They reported only 2 disease-related deaths. Factors contributing to less favorable prognosis vary among studies; however, patients younger than 10 years are generally considered to have an increased risk for poor outcomes. Other risk factors for poor prognosis are residual cervical disease after thyroidectomy, extensive pulmonary metastases, and tracheal and laryngeal invasion. Unfortunately, younger patients with thyroid cancer are likely to have more extensive disease on diagnosis than older patients, confusing the independence of these risk factors. Genetic markers indicating poor prognosis include nondiploid DNA, overexpression of p21 ras, and mutations of the n-ras gene.

7. Lymphoma

It is a rare disease accounting for less than 1% of all lymphomas and accounting for 2% of extra nodal non-Hodgkin's lymphoma. Almost all thyroid lymphomas are non- Hodgkin's type, with most being intermediate grade and the remainder higher grade. Median age for diagnosis is in 7th decade of life.

Macroscopically, lymphomas of thyroid appear as fleshy tan to gray masses often extending outside the thyroid capsule.

Microscopically, the thyroid lymphoma resembles that of lymphomas occurring at other sites. The most common histologic type is large cell diffuse malignant lymphoma. Some tumors demonstrate a plasmacytoid appearance; others show features of immunoblastic sarcoma.

8. Hashimoto's thyroiditis

It is an autoimmune disease where in the thyroid gland appears to be sensitive to its own thyroglobulin and cell constituents.

In 80% of cases, there is diffuse involvement of the thyroid gland. In the remaining the enlargement may be asymmetric with nodularity and firmness. Lymphoadenoid tissue predominates. There is disruption and fragmentation of the follicular basement membrane. The remaining epithelial cells are larger and demonstrate oxyphilic changes known as Askanazy cells. The lymphocytic infiltration may be focal or diffuse.

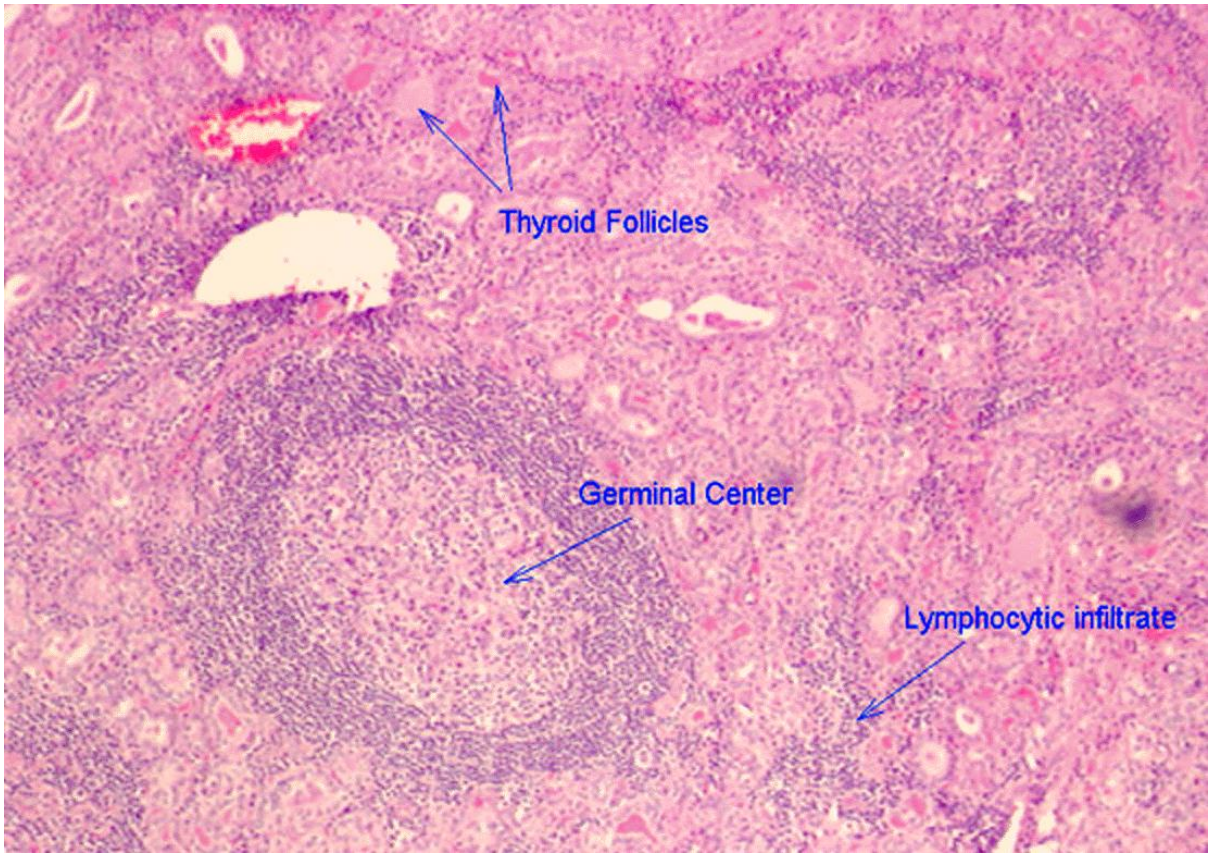

Fig 13: HASHIMOTO'S THYROIDITIS

9. Sub-acute thyroiditis

It is also called as **De Quervain's** thyroiditis in which there is rapid and painful enlargement of the thyroid gland. It appears to be caused by viruses. It is common in females and in forties.

Microscopically, the architecture of the gland is totally disrupted. There is marked destruction on follicles and follicular cells which are desquamated. Giant cells and granulomas are characteristic and their presence has been attributed to a reaction to the exposed colloid. Thus, the acute phase is followed by sub-acute phase and finally the recovery phase.

10. Riedel's thyroiditis

It is a very rare disease, affecting mainly middle aged females. There is chronic inflammatory process that extends beyond the limit of thyroid gland to surrounding fascia, muscles, nerves, trachea and esophagus.

Microscopically, the thyroid follicles become small and few in number which are replaced by dense fibrous tissue.

APPROACH TO SOLITARY THYROID NODULE

The thyroid nodule may be palpable or hidden and symptomatic or asymptomatic. The thyroid nodules of less than 1-2 cms are not palpable. The gland may be normal or abnormal in structure and function.

Case history

The symptoms are important evidence to know whether hyper or hypothyroidism is associated with goitre. The patient and family members may have noticed alteration in mental activity irritability or excitability.

The patient may give history regarding alteration in temperature tolerance, perspiration and change in weight, bowel habits and appetite or eye changes or palpitation. Pressure symptoms like dysphagia, hoarseness of voice, or dyspnoea may occur with goiter.

A history regarding diet, ingestion of goitrogenic foods like cabbage, soya beans and drugs should be elicited. History of having stayed in endemic area and family history of similar swelling should be recorded.

General physical examination

Here the signs of hyper or hypothyroidism are to be recorded. Tachycardia during sleep and loss of weight in hyperthyroidism, whereas bradycardia and weight gain are seen in hypothyroidism.

The extremities will be hot and moist in hyperthyroidism and cold and dry in hypothyroidism. Tremors of hand and tongue are seen in hyperthyroidism.

Eye signs are characteristic of primary thyrotoxicosis and these include Stellwag's sign, Von Graffe's sign, Joffroy's sign and Moebius sign.

In secondary thyrotoxicosis the eye signs are not the characteristic feature, instead they present with palpitations, ectopic heart beat, paroxysmal supra-ventricular tachycardia etc.

Local examination

Inspection

Patient in sitting position with neck slightly extended

Swelling:

Site:

Size:

Shape:

Surface:

Margins :

Skin over the swelling:

Extent of the swelling:

Moves with deglutition:

Movement with protrusion of tongue:

Plane of the swelling:

Lower border of the swelling:

Position of trachea:

Visible pulsations:

Dilated veins:

Cervical lymph nodes:

Palpation

Patient in sitting position with neck slightly flexed

Warmth

Tenderness

Swelling:

Site:

Size:

Shape:

Surface:

Consistensy:

Margins :

Mobility:

Skin over the swelling:

Extent of the swelling:

Lower border of the swelling:

Kocher’s test:

Trachea position:

Carotid pulsation:

Examination of cervical lymph nodes:

Percussion:

Direct percussion over manubrium sterni-to look for retrosternal extension

Auscultation:

To look for bruit.

Other system examination

Cardiovascular system:

S1S2 heard

Murmur:

Respiratory system:

Breath sounds:

Added sounds:

Abdomen:

Tenderness :

Organomegaly :

Central Nervous System:

Neurological defect:

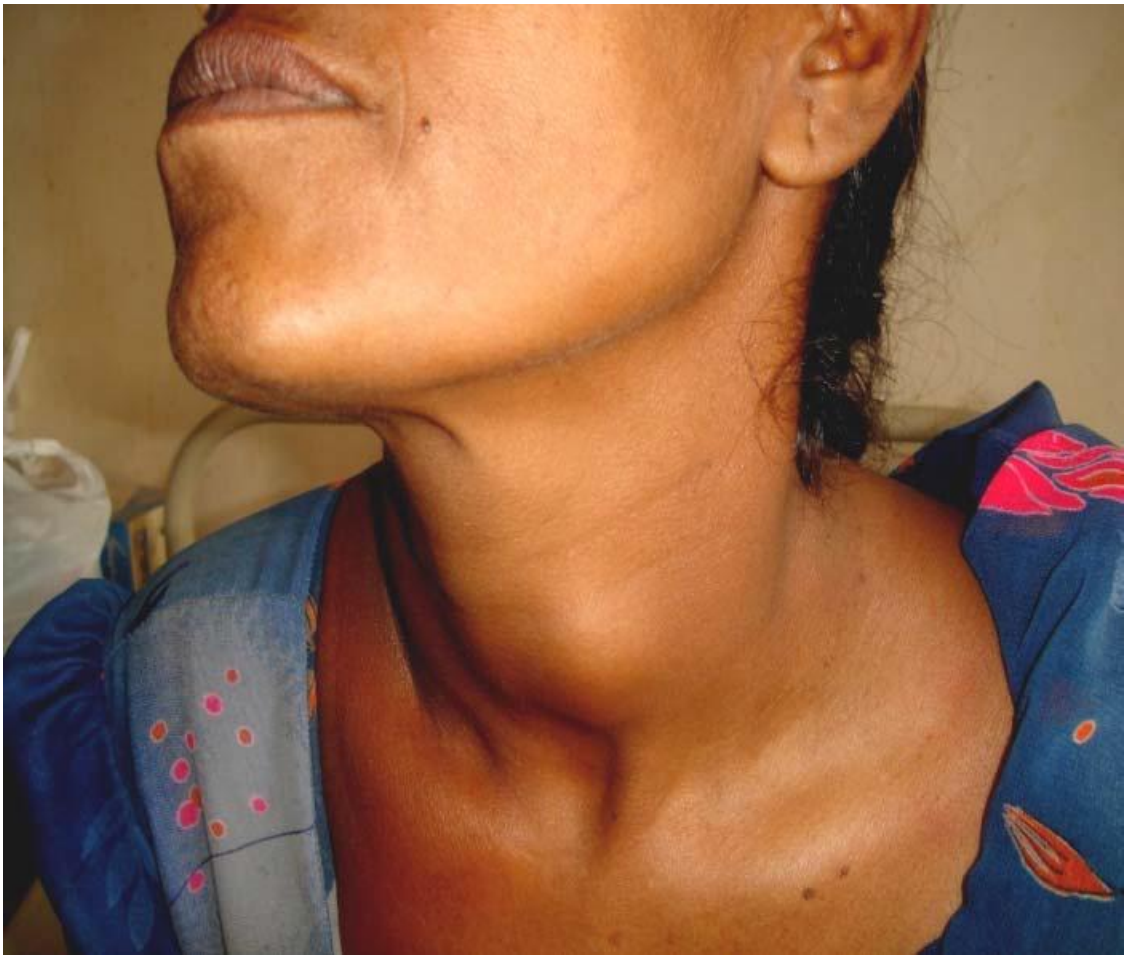

Fig 14: Solitary nodule Thyroid- clinical photograph

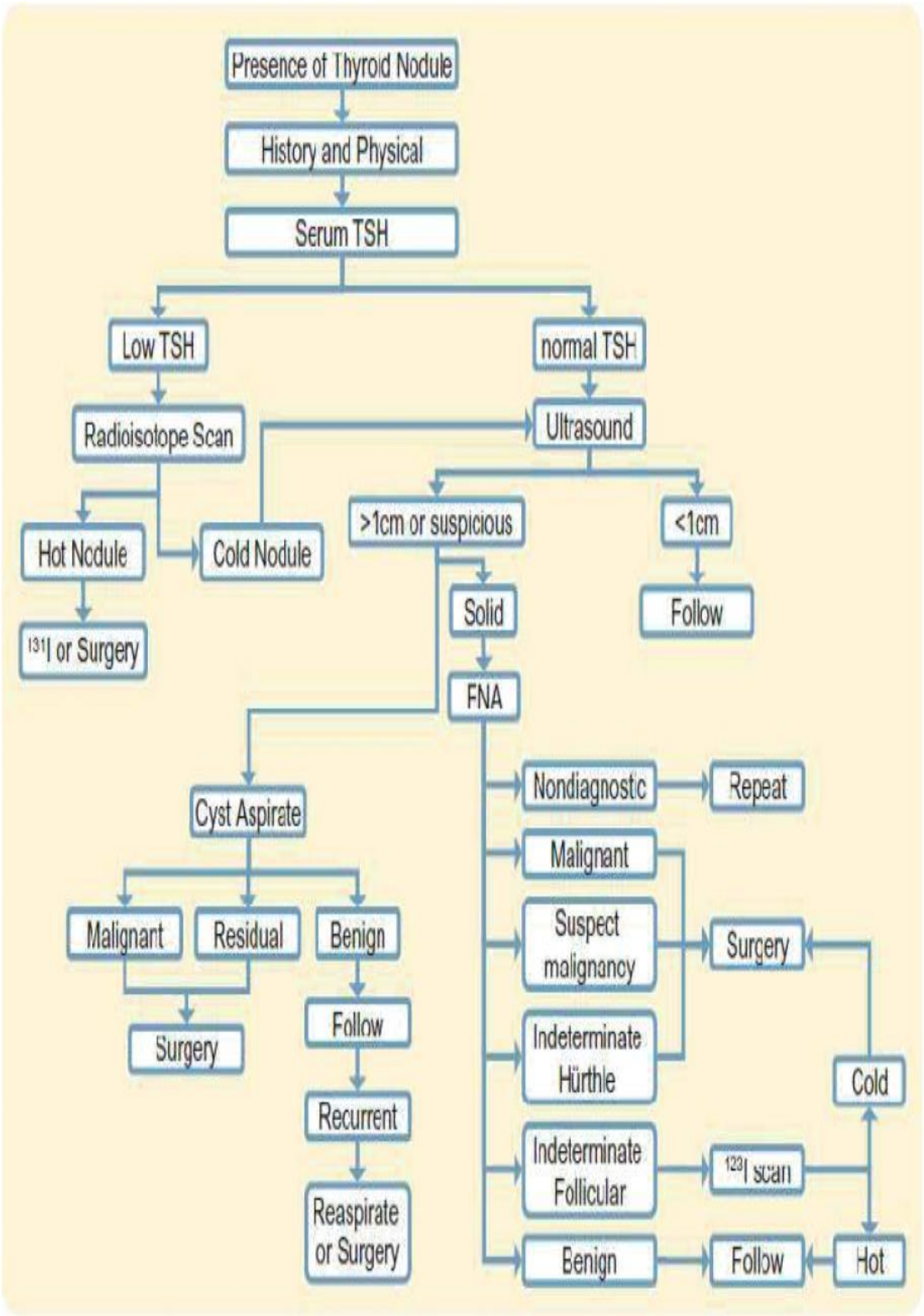

Fig 15:Evalutaion of Solitary Thyroid Nodule

INVESTIGATIONS

1. Thyroid function test
2. FNAC
3. Imaging techniques

    a.Ultrasound neck

    b. X-ray neck AP view and Lateral view

    c.CT neck

    d.Radionucleotide imaging

4. Indirect Laryngoscopy

1. **Thyroid function tests**

Most of the patients with solitary thyroid nodule will be euthyroid.

Serum TSH:

The tests for serum TSH (normal 0.5 to 5 μU/mL) are based on the principle that monoclonal TSH antibodies are bound to a solid matrix and bind serum TSH. The amount of serum TSH is proportional to the amount of bound secondary antibody (immunometric assay). Older radioimmunoassays for TSH were able to detect elevated TSH levels in hypothyroidism, but were not sensitive enough to detect suppressed levels of TSH characteristic of hyperthyroidism. Newer, second-generation, "sensitive" TSH assays can measure levels less than 0.1 μU/mL and third generation or "supersensitive or ultrasensitive" assays can detect TSH levels as low as 0.01 μU/mL. Serum TSH levels reflect the ability of the anterior pituitary to detect free T4 levels. There is an inverse relationship between the free T4 level and the logarithm of the TSH concentration—small changes in free T4 lead to a large shift in TSH levels. Thus, the ultrasensitive TSH assay has become the most sensitive and specific test for the diagnosis of hyper- and hypothyroidism and for optimizing T4 replacement and suppressive therapy.

Total T4 and Total T3 :

Total T4 (reference range: 55 to 150 nmol/L)

Total T3 (reference range: 1.5 to 3.5 nmol/L)

It is measured by radioimmunoassay and measure both the free and bound components of the hormones. Total T4 levels reflect the output from the thyroid gland, whereas T3 levels in the non-stimulated thyroid gland are more indicative of peripheral thyroid hormone metabolism and are, therefore, not generally suitable as a general screening test. Total T4 levels are increased not only in hyperthyroid patients, but also in those patients with elevated thyroglobulin levels secondary to pregnancy, estrogen/progesterone use, or congenital diseases. Similarly, total T4 levels decrease in hypothyroidism and in patients with decreased thyroglobulin levels caused by anabolic steroid use and by protein-losing disorders such as nephrotic syndrome. Individuals with these latter disorders may be euthyroid if their free T4 levels are normal. Measurement of total T3 levels is important in clinically hyperthyroid patients with normal T4 levels, who may have T3 thyrotoxicosis. As discussed previously, total T3 levels are often increased in early hypothyroidism.

Free T4 and Free T3:

These radioimmunoassay-based tests are a sensitive and accurate measurement of biologically active thyroid hormone. Free T4 (reference range: 12 to 28 pmol/L) estimates are not performed as a routine screening tool in thyroid disease. Use of this test is confined to cases of early hyperthyroidism in which total T4 levels may be normal but free T4 levels are raised. In patients with end-organ resistance to T4 (Refetoff syndrome), T4 levels are increased, but TSH levels usually are normal. Free

T3 (reference range: 3 to 9 pmol/L) is most useful in confirming the diagnosis of early hyperthyroidism, in which levels of free T4 and free T3 rise before total T4 and T3. Free T4 levels may also be measured indirectly using the T3 resin-uptake test. If free T4 levels are increased, fewer hormone-binding sites are available for binding radiolabeled T3 that has been added to the patient's serum. Therefore, more T3 binds with an ionexchange resin and the T3 resin uptake is increased.

2. **FNAC**

FNAC is one of the commonest investigations done today for solitary thyroid nodule since last 2-3 decades. It was popularized by Dr. Torsten Lowhagen from Sweden.

Fine needle aspiration biopsy cytology is the most important investigation in the initial evaluation. It is safe, inexpensive and an out- patient procedure. If done properly and with appropriate patient selection, the false negative rate is less than 5% and false positive rate of 1-5%. It has a sensitivity of 83% and specificity of 92%.

The Bethesda System for Reporting Thyroid Cytopathology: Recommended Diagnostic Categories

I. Nondiagnostic or Unsatisfactory

Cyst fluid only

Virtually acellular specimen

Other (obscuring blood, clotting artifact, etc)

II. Benign

Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc)

Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context

Consistent with granulomatous (subacute) thyroiditis

Other

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

IV. Follicular Neoplasm or Suspicious for a Follicular Neoplasm

Specify if Hürthle cell (oncocytic) type

V. Suspicious for Malignancy

Suspicious for papillary carcinoma

Suspicious for medullary carcinoma

Suspicious for metastatic carcinoma

Suspicious for lymphoma

Other

VI. Malignant

Papillary thyroid carcinoma

Poorly differentiated carcinoma

Medullary thyroid carcinoma

Undifferentiated (anaplastic) carcinoma

Squamous cell carcinoma

Carcinoma with mixed features (specify)

Metastatic carcinoma

Non-Hodgkin lymphoma

Other

The Bethesda System for Reporting Thyroid Cytopathology: Implied Risk of Malignancy and Recommended Clinical Management

Diagnostic Category	**Risk of malignancy**	**Treatment**
Nondiagnostic or Unsatisfactory	1-4%	Repeat FNA with ultrasound guidance
Benign	0-3%	Clinical follow-up
Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance	5-15%	Repeat FNAC
Follicular Neoplasm or Suspicious for a Follicular Neoplasm	15-30%	Surgical lobectomy
Suspicious of malignancy	60-75%	Near total thyroidectomy or lobectomy
Malignant	97-99%	Total thyroidectomy

- Accuracy of FNAC depends upon experience of the cytologist.

- Analysis of the data suggests a false negative rate of 1-11%; a false positive rate of 1-8%; a sensitivity of 68-98% and a specificity of 72-100%.

- Ultrasound guided aspiration is useful if the solitary nodule is < 1cm, when it is difficult to place the needle.

- Follicular carcinoma cannot be differentiated from follicular adenoma by FNAC.

- The routine use of FNAC for patient with thyroid nodules reduces the incidence of unnecessary surgery. FNAC is alone sufficient to identify most patients at risk and is therefore cost effective.

- Dorairajan N and Jayashree N in their study consisting of 100 cases of solitary thyroid nodule found the usefulness of Fine Needle Aspiration Cytology in the diagnosis. They suggested that pre operative fine needle aspiration cytology is a must for the diagnosis and deciding the line of treatment.

3. **Imaging procedures**

A) Ultrasound Neck

Ultrasound examination of thyroid accurately measures the size of the gland, the number of nodules within and dimensions of the nodule. Most of the solitary nodule on clinical examination turns out to be multinodular goiter on ultrasound.

Conventional B-mode or gray scale ultrasound can classify nodules as solid, cystic or mixed and cystic lesions with accuracy of more than 90%. A cystic lesion is usually characterized by sonoluscent pattern with well defined walls. Solid nodules have characteristic ultrasonic echo. Cystic lesions can again be classified as purely cystic which are rarely malignant and complex cyst where there is solid component within the cyst. Presence of echogenic component in nodules increases chances of malignancy. Ultrasound also aids in FNAC of complex cystic lesion. High resolution ultrasonography with real time capability visualizes nodules as small as 5mm. Purely cystic lesions greater than 4cm can be managed by aspiration.

Ultrasonographic feature of thyroid malignancy are

- Microcalcification
- Hypoechogenicity
- Irregular margins
- Absence of halo
- Intra nodular vascularity
- Solid
- Taller than width

High suspicious nodules:

A solid hypoechoic nodule or cystic nodule with solid component that is hypoechoic and has at least one of the above mentioned malignant features are considered high risk nodules. This group has been found to carry risk of malignancy of 70-90%

Intermediate suspicious nodules:

Hypoechoic solid nodules with smooth margins and lacking microcalcifications,extrathyroidal or taller than wide shape are of intermediate suspicion. This pattern has highest sensitivity for identification of PTC but lacks specificity. These nodules are considered for FNAC at 1cm threshold.

Low suspicious nodules:

Hypoechoic or isoechoic solid nodules or partially cystic nodules with an eccentric solid component have lower risk of malignancy. The threshold for FNAC for these nodules is 1.5cm

Very low suspicious nodules:

Nodules that are partially cystic without above mentioned features have very low risk of malignancy. Such nodules are observed and considered for FNAC if larger than 2 cm.

Benign nodules:

Simple cyst are very unlikely to be malignant and donot require FNAC for diagnostic purpose.FNAC is required for relief of compressive symptoms with drainage of cystic contents. In such cases a small amount of aspirate is also sent for cytological examination.

Lymph node evaluation:

Because of high frequency of nodal metastasis in thyroid cancer and the impact that sonographically suspicious nodes have on prognosis and management it is important to examine all patients with a nodule for the presence of suspicious lymph nodes in the anterior neck. The sensitivity and specificity of ultrasound for detecting nodal metastasis is variable depending on the experience of the sonographer.

Benign lymph node sonographic appearance:

The classical appearance of benign node is fusiform shaped hypoechoic structure with hyperechoic stripe in the center. The hilar stripe represents the entry of vasculature and lymphatic outflow from the node.

Malignant lymph node sonographic appearance:

Neoplastic infiltration typically begins at the outer cortex of the node. Disappearance of the hilum may be the earliest indication of malignant transformation. A more suspicious finding may be seen as the node converts from oval to rounded appearance with progression of peripheral infiltration. A malignant node may be hyperechoic or isoechoic. Cystic degeneration within a lymph node is a common finding with metastatic thyroid cancer. Calcification within a lymph node are also highly specific for malignancy.

B) X-Ray

The X-ray neck AP and lateral view is indicated to look for retrosternal extension of thyroid enlargement and tracheal compression.

C) CT Scan :

These are sometimes indicated in evaluation of thyroid nodules. The anatomic structure of the neck and mediastinum that may be involved in thyroid carcinoma is best evaluated by contrast enhanced C.T

C.T. scan detect airway invasion and demonstration of cartilage destruction coupled with iodinated contrast material, also C.T. can be used to detect regional node metastases.

M.R.I. provides better contrast between muscle, tumor and lymph nodes than C.T. vascular imaging is superior in MRI. It can also provide both coronal and sagittal sections.

Indications for CT:

a. To determine the exact location and degree of invasiveness of large tumour.

b. To evaluate substernal or retrosternal extension.

c. Regional node metastases.

d. To detect local recurrence.

D) Radionucleide imaging

Based on the distribution of radioactive substance, the nodule can be classified as cold (non-functioning), warm (normally functioning) and hot (hyper functioning).

Cancer of the thyroid is characterised by lack of affinity for radioactive drugs and therefore appear as cold.

Nodules must be greater than one cm in diameter and have 20% less uptake than the surrounding parenchyma to show up as cold nodule.

In Aschraff and Van Herle's review, 84% of nodules were cold, 10.5% were warm and 5.5% were hot. Malignant disease was found in 16% of the cold nodules, 9% of warm nodules and less than 4% of hot nodules.

A normal thyroid gland traps 10-35% of ingested radioiodine through sodium iodide symporter (NIS). NIS is also present in salivary gland and breast but only thyroid NIS is stimulated by TSH. Thyroid NIS cannot differentiate between radioactive and non radioactive iodine. More than 20 radionuclide of iodine are recognised but only I-123 and I-131 are commonly used for clinical purposes.

I-123 is used for diagnostic testing as it has short half life and emits only gamma rays. I-131 has a half life of 8 days and emits both beta as well as gamma rays. This makes it useful for diagnostic and therapeutic purpose.

Technetium 99m pertechnetate (Tc-99m) is now more widely used than I-123 because of its easy availability and low cost. Unlike I-123 which is both concentrated and organified within the thyroid Technetium 99m pertechnetate (Tc-99m) is only concentrated in the thyroid. Disadvantage of Technetium 99m pertechnetate (Tc-99m) it also gets concentrated in salivary gland.

111 In-pentreotide is a somatostatin analogue used in imaging medullary thyroid cancer.

Other radionuclide used are thallium-201 ,99mTc methoxyisobutylisonitrile, 99mTc tetrafosamin

Indications:

- Evaluation of solitary thyroid nodule
- Thyroid remnant survey after surgery
- Detection of functioning thyroid cancer metastases
- Evaluation of focal functional thyroid abnormalities

Contraindications:

- Hypersensitivity reaction to iodine
- Pregnancy
- Breastfeeding
- Severe Grave ophthalmopathy

4. **Indirect Laryngoscopy**:

Routine laryngoscopic examination should be done before thyroidectomy. Pre-operative vocal cord examination is done for medicolegal purposes. 3-5% of patients have asymptomatic paresis or paralysis of one vocal cord probably due to exanthema during childhood. It is also helpful in diagnosing involvement of recurrent laryngeal nerve by the tumor.

Other relevant investigations

Tumor markers

Thyroid cells are the only source of thyroid in the human body and hence circulating thyroglobulin levels serve as biomarker of persistent or recurrent disease in differentiated thyroid carcinoma follow up. It has a half life of 65hrs and the levels typically nadir 6-8 weeks post total thyroidectomy.

Thyroglobulin levels should be measured initially at 6 month intervals. In low risk patients, who have low suppressed Thyroglobulin levels in the first year, serum Thyroglobulin should be measured after T4 withdrawal or recombinant TSH stimulation approximately 12 months after ablation. Patients with undetectable stimulated Thyroglobulin levels can be followed annually with clinical exam and Thyroglobulin levels on T4 replacement.

A single rTSH-stimulated Thyroglobulin level of <0.5 ng/mL (with absent antibodies) has a 98% to 99.5% probability of identifying patients completely free of disease on follow-up. A Thyroglobulin level of >2 ng/mL following rTSH stimulation is highly sensitive in identifying patients with recurrent tumor.

Calcitonin: It is a useful tumor marker in detection and follow up of medullary carcinoma.

Anti-thyroid antibodies: Antithyroglobulin (TGHA) and microsomal antibodies (MCHA) may help to determine the pathologic state of the involved gland. High antibody titres are found in Hashimoto's thyroiditis or Graves disease.

Molecular markers of thyroid malignancy:

Galectin 3 immunodetection is one of the most widely studied markers of malignancy in follicular lesion with indeterminate cytology. Bartolazzi et al examined Gal 3 expression in 1009 thyroid lesion samples and 226 FNAC cytological results which showed 98% sensitivity and 99% specificity to differentiate benign from malignant lesion. Pennelli et al corroborated these results by observing 80% sensitivity and 86% specificity in group of one hundred indeterminate cytological nodules.

The BRAF mutation which is characteristic of PTC has provided greater diagnostic accuracy for nodules with indeterminate cytology and nodules suspicious of malignancy. While researching the BRAF (V600E) mutation, Kim et al. studied 1074 patients with thyroid nodules and observed an increase in the FNAB sensitivity from 67.5 to 89.6% and an increase in the accuracy from 90.9 to 96.6%. In another analysis, Nikiforov et al. reviewed 470 cytology specimens from 328 patients for BRAF mutations, RAS mutations, RET/PTC markers, and PAX8/PPAR gamma mutations. BRAF mutations were the most

common finding, and the presence of three mutations was predictive of a malignancy diagnosis in 97% of the confirmed cases.

Cerruti et al. analyzed four protein markers from cytology material (FNAB) to evaluate thyroid nodules with suspected malignancy. Greater diagnostic accuracy was observed when both proteins derived from chromosome 1 (chromosome 1 open reading frame 24, C1orf24) and membrane protein 1 (integral membrane protein 1, ITM1) were present. Additionally, the BRAF mutation (V600E) was verified in 48% of the 120 papillary carcinoma cases evaluated and occured more frequently in the classic PTC cases (66%) than in the follicular PTC variant (21%). Furthermore, there was a strong association between the BRAF (V600E) mutation and extra-thyroid invasion, lymph node metastasis, and recurrence risk, indicating that the mutation is an important prognostic marker for classic PTC.

According to Fadda et al. , it is possible to identify two risk categories (high and low) in nodules with indeterminate cytology (follicular neoplasms) based on HBME-1 and Gal-3 expression. Indeterminate cytology was present in 50 of 120 surgically treated cases. In these 50 indeterminate tumors, a positive immunohistochemical panel was observed in 76.9% of the cases with malignant nodules in the final histology, and a negative panel (no positive markers) was observed in almost all (96.8%) of the benign cases. These data were corroborated by Kang et al. (88) in an analysis of the BRAFV600E mutation in (preoperative) FNAB samples from 200 surgically treated thyroid nodules. The

mutation was present in 63.3% of the malignant cases with initially indeterminate cytology. Therefore, for nodules with indeterminate cytology (Bethesda categories III and IV), negative tumor markers (HBME-1 and Gal-3) in the FNAB sample suggests conservative management, and a positive immunohistochemical panel suggests surgical treatment.

TREATMENT

The optimal management of solitary thyroid nodule continues to be a source of controversy and operative intervention is recommended by most surgeons is not always divine by some physicians who advocate either observation or suppressive therapy.

Though majority are benign, significant proportion (10-25%) are malignant. In light of our present knowledge, the only curative therapy for thyroid malignancy is complete surgical removal.

After FNAC, surgery is advised in following circumstances:

- All proven malignancies.
- All cytologically diagnosed follicular adenoma.
- Cystic nodules, which recur even after 3 aspirations.

Surgery should also be considered in following circumstances:

- Presence of hard, irregular, fixed nodule.
- Recurrent laryngeal nerve paralysis.
- Thyroid nodule with history of prior irradiation to head and neck.
- Patients under 20 and over 70 years of age.

Treatment options are:

For papillary carcinoma of thyroid, there are two schools of thoughts.

One advocates Total thyroidectomy in all cases, second advocates hemithyroidectomy.

Most surgeons prefer total thyroidectomy because:

a. Intra-glandular tumor of opposite lobe occurs in 30-87.5% patients.
b. Recurrent thyroid carcinoma occurs in the opposite lobe in about 7% of patients.
c. About 50% of patients, who die of thyroid cancer, die of "Central Neck recurrence".
d. Radioiodine can be used to detect recurrent or residual thyroid carcinoma and to ablate residual tumours once the entire gland is removed.
e. The 1% chance of well differentiated carcinoma turning into anaplastic carcinoma is decreased.

If frozen section is not available, one has to wait for histopathological report. If report is positive for malignancy and is obtained within 7 days, total thyroidectomy is performed as oedematous and fibroblastic reaction in the operated field doesn't hinder dissection or identification of vital structures.

If the report is delayed for more than 7 days, it's better to wait for 2-3months to allow the reaction to settle completely. After 2-3months, total thyroidectomy is

performed. In patients with apparent lymph node metastasis, modified radical neck dissection is performed.

In anaplastic carcinoma, the median survival in most series is less than 5months from the time of diagnosis. It is one of the most rapidly lethal tumors known in surgical oncology.

Early diagnosis with aggressive surgical therapy supplemented by external beam radiation and doxorubicin based chemotherapy is the most appropriate treatment for patients with anaplastic carcinoma of thyroid.

The optimal treatment for thyroid lymphoma has evolved with success of combination of chemotherapy used in treatment of Non-Hodgkin's Lymphoma. Role of surgery in this disease is simply to obtain adequate tissue for diagnosis. If diagnosis has to be confirmed by surgery, a near total thyroidectomy is done. After histopathological diagnosis, the first course of MOPP (nitrogen mustard, oncovin, procarbazine, and prednisolone) therapy is given, followed by external beam radiation (total dose 40-60 cGy) and then remaining five courses of chemotherapy.

MATERIALS AND METHODS

The case material for the present study was taken from Tirunelveli Medical College Hospital,Tirunelveli. This study of solitary thyroid nodule is based on 52 cases admitted in Surgery Department between July 2017 to June 2019.The patients were studied and examined in detail clinically and recorded in a performa, Routine investigations and specific investigations including FNAC of the nodule, Thyroid profile, IDL, Plain X-ray neck, USG neck were done in all cases. Frozen section were done for all cases which were reported as Follicular Neoplasm in FNAC.

Inclusion Criteria:

All patients with solitary nodule were included in the study.

Exclusion Criteria:

Patients diagnosed as multinodular Goitre clinically or sonographically were excluded from the study.

RESULTS

TABLE 1: AGE DISTRIBUTION

AGE DISTRIBUTION		
GROUP	**NUMBER**	**PERCENTAGE**
20-29	**3**	**5.8**
30-39	**19**	**36.6**
40-49	**15**	**28.8**
50-59	**9**	**17.3**
60 AND ABOVE	**6**	**11.5**

TABLE 2: SITE OF INVOLVEMENT

LOCATION	NUMBER	PERCENTAGE
RIGHT	**29**	**55.8**
LEFT	**23**	**44.2**

TABLE 3:FNAC REPORT

FNAC	NUMBER	PERCENTAGE
NODULAR GOITRE	31	59.6
FOLLICULAR NEOPLASM	18	34.64
PAPILLARY CARCINOMA	3	5.76

TABLE 4:TYPE OF SURGERY

PROCEDURE	NUMBER	PERCENTAGE
HEMITHYROIDECTOMY	43	82.7
TOTAL THYROIDECTOMY	9	17.3

TABLE 5:HISTOPATHOLOGICAL REPORT

HPE	NUMBER	PERCENTAGE
NODULAR GOITRE	14	26.9
COLLOID GOITRE	15	28.8
FOLLICULAR ADENOMA	15	28.8
FOLLICULAR CARCINOMA	2	3.9
PAPILLARY CARCINOMA	6	11.6

CHART 1: SPECTRUM OF THYROID

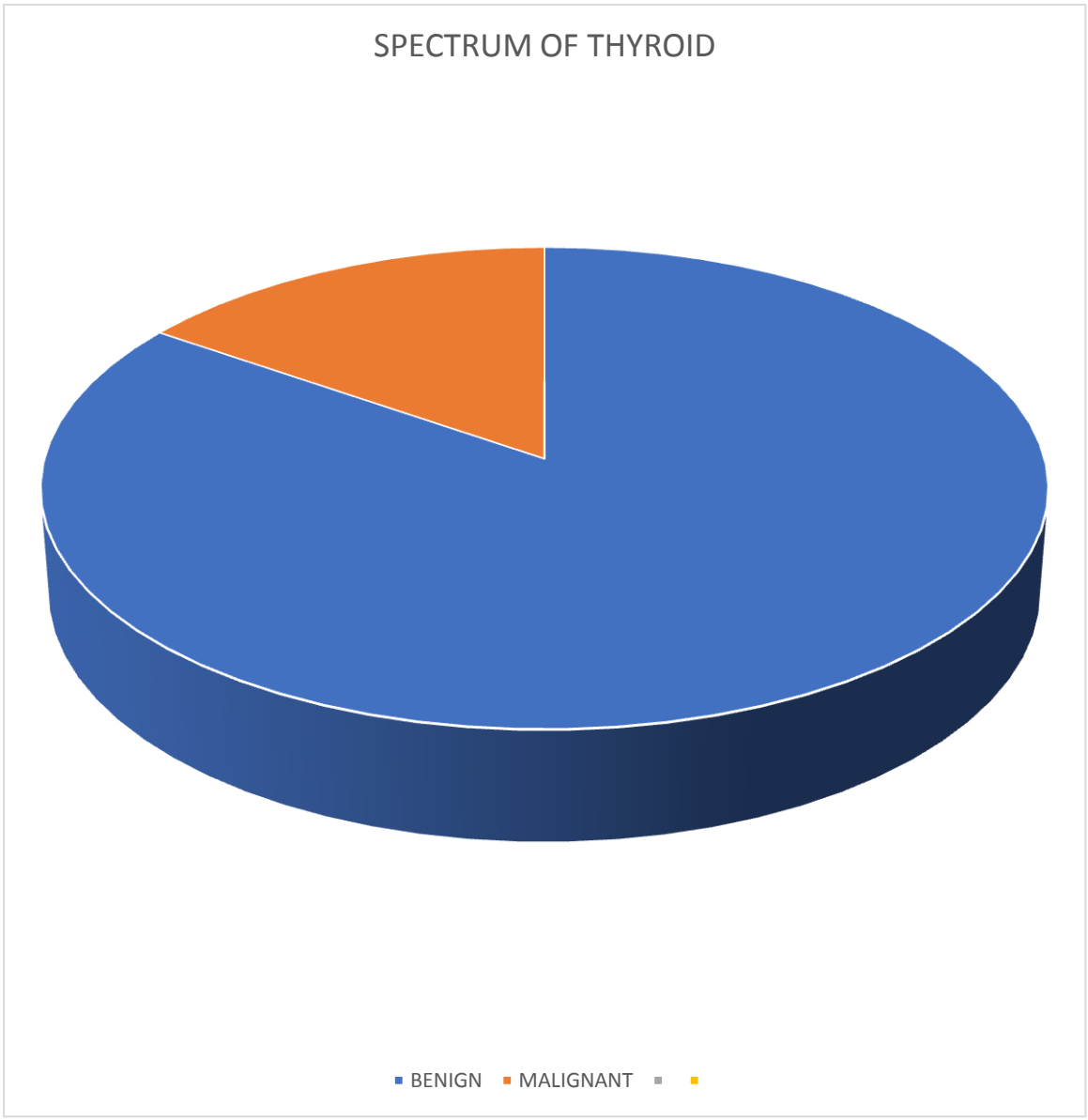

CHART 2: RATIO OF MALIGNANCY

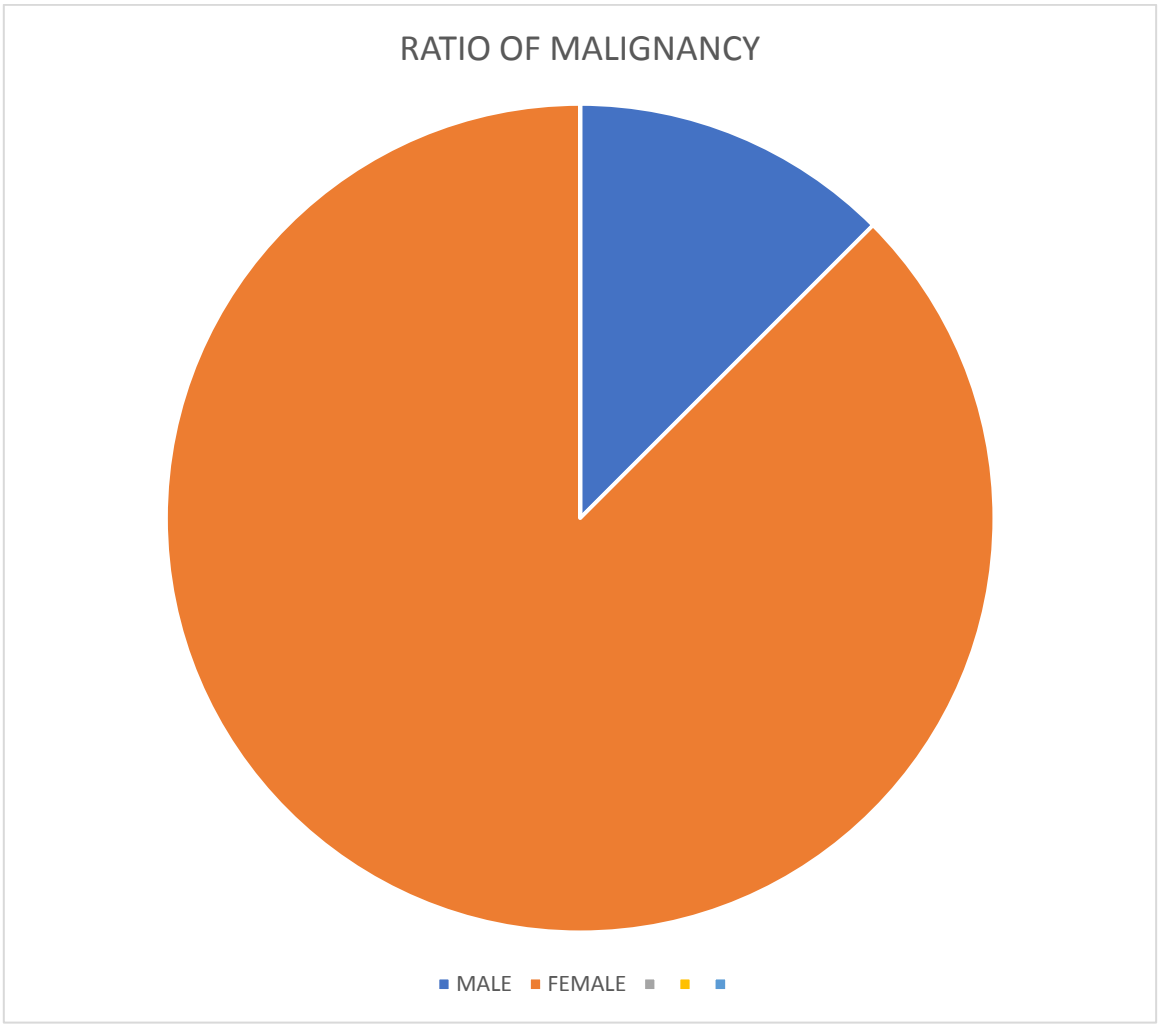

TABLE 6: CORRELATION OF FNAC WITH HPE

FNAC	FROZEN SECTION	TREATMENT	HPE
Follicular Neoplasm-18	Follicular adenoma-15	Hemithyroidectomy-15	Follicular adenoma - 15
	Papillary carcinoma-01	Total Thyroidectomy-01	Papillary carcinoma-01
	Follicular cacrcinoma-02	Total Thyroidectomy-02	Follicular Carcinoma –2
Nodular Goitre – 31		Hemithyroidectomy-14	Nodular Goitre – 14
		Hemithyroidectomy-12	Colloid Goitre-12
		Hemithyroidectomy Followed by completion thyroidectomy-02	Papillary Carcinoma – 2
		Total Thyroidectomy-03	Colloid Goitre -3
Papillary Carcinoma-3		Total Thyroidectomy-03	Papillary Carcinoma - 3

DISCUSSION

54 cases were taken up for our study out of which 2 where excluded as USG thyroid showed multinodular goitre.

In our present study age distribution of the patient ranges from 23-65 years with mean age of 43.14 years with male to female ratio of 1:16.3 which is comparable with Mitra et al study with age range was 16–70 and median age was 39.6 years. In Jose et al (2002) the age of patients ranged from 17-65 years with a median age 35.5 years. Kilopatricet al. study found female to male ratio of 14:1

Age distribution of the present study is also comparable with Taneri et al., where the mean age was 47 and the ranged being between 24 and 67 years and to a prospective study conducted by Sekhri et al (2001) where they found that thyroid swelling ranged between 9 years of age to 70 years with mean age of 33.9 years.

According to the study conducted by Prof .R.L. Gupta University College of medical science, Delhi right lobe involvement is more 51.4% compared to left lobe involvement of 38.8% which is comparable with our study with right lobe involving 55.8% and left lobe 44.2%.

The most common clinical presentation is swelling in the front of neck and majority of patients presented between 6months to 2 years.

Among FNAC report nodular goitre was most common cytological diagnosis followed by follicular adenoma.In our present study cytology showed benign lesion in 94.2% cases and malignant lesion in 5.8% cases which is comaparable with Gharibz and Goellnear study which showed benign lesion to be 96% and malignant lesion to be 4%.

Frozen section studies were done for all 18 cases of follicular neoplasm out of which 15 cases were diagnosed as follicular adenoma and hence proceeded with hemithyroidectomy. 2 patients were diagnosed to have follicular carcinoma and one patient had papillary carcinoma hence these 3 patients underwent total thyroidectomy.

In this study 43 patients underwent hemithyroidectomy based on preoperative and peroperative findings and 9 patients underwent total thyroidectomy.

Out of 9 patients who underwent hemithyroidectomy 6 patients were diagnosed pre and peroperatively to have malignant disease.

Remaining 3 patients underwent malignancy as USG thyroid showed suspicious of malignancy.

The incidence of malignancy in our series is 17.3% which is comparable with other studies as follows

s.no	Study	Year	Percentage
1.	C.Leigh	1969	20.9
2.	A K Sarda	1997	10.8
3.	Mazafferi	1998	12
4.	Aimal munir	2002-03	13.3
5.	Khairy	2004	13.9
6.	Talepoor	2005	15.8
7.	Catrheinelhre	2007	20.9
8.	Judy jin	2009	15
9.	Salim Ahmeed	2011	12.3
10	Abul Hossain	2014	28
11.	Majeedullah buzdar	2015	15.3
12.	Ramesh babu	2015	10.8
13.	Gopalakrishna	2016	18.35
14.	Hari Narayana	2017	22
15.	Our study	2019	17.3

The maximum incidence of malignancy (44.4%) was present during fourth decade of life.Histologically proven malignancy in this series is 8 cases of which 7 patients were female and 1 male patient.

Of these 8 cases six were papillary carcinoma and its variant and two cases were follicular adenoma. Of these six cases were diagnosed preoperatively and intra operatively and were offered definitive treatment, the rest two patients were diagnosed only by histopathological examination hence they underwent completion thyroidectomy.All the patients were under regular follow up with suppressive dose of thyroxine.

In our study 33% of solitary nodules in males proved to be malignant whereas in females only 16% of solitary nodules were malignant.

No medullary carcinoma,anaplastic carcinoma,lymphoma were reported in our study.

Completion thyroidectomy was done in two patients. Both were diagnosed as nodular goitre by cytology hence underwent hemithyroidectomy but histopathology was reported as papillary carcinoma and subsequently underwent completion thyroidectomy. The rate of completion thyroidectomy was 4.6% which is comparable with Naine et al study which shows completion rates to be 7.3%

Completion thyroidectomy rate of our study is also comparable with Giuseppe study which showed completion rates to be 6.5% and Bayaram Vyseller which shows completion rates to be 8.9%.

Out of two cases which underwent completion thyroidectomy one case showed papillary carcinoma in contralateral lobe. Barczynski study showed a rate of malignancy in the contralateral lobe to be upto 40% which is comparable with our study.

Out of 52 patients who were operated three patients developed transient hypocalcaemia in the post-operative period and were treated with intravenous calcium gluconate. There were no mortality during this study.

CONCLUSION:

FNAC is highly specific in diagnosing malignant lesion but lacks sensitivity. Frozen section studies had added additional value in differentiating follicular adenoma from follicular carcinoma which couldnot be done by FNAC. But definitive diagnosis is possible only with excision and postoperative histopathological examination of the nodule. Though FNAC is initial diagnostic modality of choice HPE remains final diagnostic proof. The incidence of malignancy is higher in case of Solitary Nodule Thyroid.

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PROFORMA OF QUESTIONAIRRE

Name :

I.P.No. :

Age :

Sex :

Address :

D.O.A :

DOS :

DOD :

II. CHIEF COMPLAINTS:

III HISTORY OF PRESENTING ILLNESS:

1. Swelling in the neck :
    Duration:
    Onset and Progression:
    Any sudden increase in size: yes/no
2. Pain in nodule: yes/no
3. Hoarseness of voice
4. Local pressure symptoms:
    Dysphagia:
    Dyspnoea:
    Change in voice:
5. Symptoms of hyperthyroidism in solitary thyroid nodule.
    a. Anxiety/Nervousness:
    b. Palpitation:
    c. Preference to cold/intolerance to heat:
    d. Weight loss:

6. Family history:

7. Clinical Examination:

A. General:

a. Nourishment: well/moderate/poor.

b. Build: moderate/thin/obese.

c. Anaemia:

d. Pedal edema:

e. Pulse: BP:

f. Tremors of extremities:

Of tongue:

g. Hands- normal/moist and warm/cold.

h. Skin condition:

i. Hair texture:

j. Any eye signs:

k. Thyroid status: euthyroid/hypothyroid/hyperthyroid.

B. LOCAL EXAMINATION:

1. Inspection:

a. Position of nodule: right lobe/left lobe/isthumus

b. Size and shape of nodule:

c. Extent:

d. Borders:

e. Skin over the swelling:

f. Any visible veins:

g. Any visible pulsation:

h. Movement with deglutition:

i. Position of trachea:

j. Plane of the swelling:

2. PALPATION:

a. Warmth:

b. Tenderness:

c. Size and shape:

d. Extent:

e. Border:

f. Consistency:

g. Mobility:

h. Lower limit of the swelling- can be reached/Cannot be reached

i. Carotid pulsations- position- normal/displaced

Volume- normal/weak

j. Position of trachea:

k. Plane of swelling:

3. PERCUSSION: Retrosternal extension

4. AUSCULTATION- Bruit.

C. REGIONAL LYMPH NODES:

a. Palpable/ not palpable:

b. Number:

c. Site:

d. Size:

e. Consistency:

f. Mobility:

D. SYSTEMIC EXAMINATION

a. CVS:

b. RS:

c. P/A:

d. CNS:

Any bony tenderness/swelling

8. CLINICAL DIAGNOSIS:

9. INVESTIGATIONS:

Routine Investigations:

Blood : Hb% TC DC

Urine: Alb B.T. C.T. E.S.R.

FBS PPBS RBS

Blood Urea

Serum creatinine

ECG in all leads

X – Ray of the Chest

Specific:

a. Sleeping pulse rate:

b. Serum cholesterol:

c. Plain X-ray Neck: AP/Lateral

d. Indirect laryngocopy:

e. FNAC:

f. Thyroid profile:

g. Any other investigation:

10. TREATMENT:

a. Pre-operative:

b. Operative:

c. Post operative:

d. Pathological examination: gross/microscopy/final diagnosis

11. FOLLOW-UP:

ABBREVIATIONS

CG	-	Colloid Goitre
Comp	-	Complication
Consis	-	Consistensy
CT	-	Completion Thyroidectomy
F	-	Female
FA	-	Follicular Adenoma
FC	-	Follicuar Carcinoma
FN	-	follicular Neoplasm
FNAC	-	Fine Needle Aspiration Cytology
FV-PC	-	Follicular variant of Papillary Carcinoma
HPE	-	histopathological Examination
L	-	Left
LHT	-	Left Hemithyroidectomy
M	-	Male
MFA	-	Macrofollicular Adenoma
NG	-	Nodular Goitre
NG-CD	–	Nodular Goitre with Cystic Degeneration
PCT	-	Papillary Carcinoma Thyroid
R	-	Right
RHT	-	Right Hemithyroidectomy
Swe	-	Swelling
Tox	-	Toxicity
TP	-	Thyroid Profile
TT	-	Total Thyroidectomy
WD	-	Well Defined

நோயாளிகளுக்கு அறிவிப்பு மற்றும் ஒப்புதல் படிவம்
(மருத்துவ ஆய்வில் பங்கேற்பதற்கு)

ஆய்வு செய்யப்படும் தலைப்பு:
பங்கு பெறுவரின் பெயர்:
பங்கு பெறுவரின் வயது:

		பங்கு பெறுவர் இதனை ✓ குறிக்கவும்
1.	நான் மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்களை படித்து புரிந்து கொண்டேன். என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டுள்ளது என அறிந்து கொண்டேன்.	☐
2.	நான் இவ்வாய்வில் தன்னிச்சையாக தான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும், எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.	☐
3.	இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்காள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன்.	☐
4.	இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக் கொள்ள மறுக்க மாட்டேன்.	☐
5.	இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன் எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின் படி நடந்து கொள்வதுடன், ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ, அல்லது எதிர்பாராத, வழக்கத்திற்கு மாறான நோய்குறி தென்பட்டாலோ உடனே இதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்றேன்.	☐

பங்கேற்பவரின் கையொப்பம் / ..... இடம் .....
கட்டைவிரல் ரேகை
பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....
ஆய்வாளரின் கையொப்பம் /..... இடம் .....
ஆய்வாளரின் பெயர் .....
மையம் .....
கல்வியறிவு இல்லாதவற்கு (கைரேகை வைத்தவர்களுக்கு) இது அவசியம் தேவை
சாட்சியின் கையொப்பம் /..... இடம் .....
பெயர் மற்றும் விலாசம் ....

S.No	Name	Age	Sex	Ip	Clinical Prentation							Side	FNAC	USG			TP		Procedure	HPE	CT	HPE	Comp
					Swe	Pain	Tox	Pressure	Lymph	Voice	Consis				USG features	CT Neck		Frozen					
1	Arputhakani	29	F	47681	P	A	A	A	A	A	Firm	L	NG	SNG	well defined hyperechogenic	WD,HD,no calcification on left lobe	N	ND	LHT	CG	-	-	NO
2	Muthulakshmi	49	F	47641	P	A	A	A	A	A	Firm	L	NG	SNG	hyperechogenic,calcification	WD nodule in the left lobe	N	ND	LHT	NCG	-	-	NO
3	Essaki raja kumari	23	F	52317	P	A	A	A	A	A	Firm	R	FN	SNG	well defined solid lesion	ND	N	FA	RHT	MFA	-	-	NO
4	Manju	32	F	52106	P	A	A	A	A	A	Firm	R	FN	SNG	well defined hyperechogenic	ND	N	B	RHT	NCG	-	-	NO
5	Muthumari	40	F	65613	P	A	A	A	A	A	Firm	R	CG	SNG	soft,well defined lesion	WD,colloid nodule in right lobe	N	ND	RHT	CG	-	-	NO
6	Kamilabegam	47	F	70127	P	A	A	A	A	A	Firm	R	CG	SNG	well defined cystic lesion	WD with calcicifcation in right lobe	N	ND	RHT	NG-CD	-	-	NO
7	Lakshmi	65	F	71784	P	A	A	A	A	A	Firm	R	NG	SNG	hyperchogenic,cystic	WD nodule in right lobe	N	ND	RHT	CG	-	-	NO
8	DuraiRajammal	53	F	78107	P	A	A	A	A	A	Firm	L	NG	SNG	solid,hypoechoic lesion,microcalcification,irregular margin	WD nodule in the left lobe	N	ND	TT	CG	-	-	Transcient Hypocalcemia
9	Rajathi	48	F	78803	P	A	A	A	A	A	Firm	R	FN	SNG	solid,hypervascular lesion	ND	N	FA	RHT	FA	-	-	NO
10	Muthammal	40	F	79735	P	A	A	A	A	A	Firm	L	NG	SNG	welldefined,cystic,calcification	WD,Cystic nodule in left lobe	N	ND	LHT	NCG	-	-	NO
11	Radha	42	F	81236	P	A	A	A	A	A	Firm	R	CG	SNG	soft,well defined lesion	WD nodule in right lobe	N	ND	RHT	NG-CD	-	-	NO
12	Veyilmuthu	62	F	84072	P	A	A	A	A	A	Firm	R	NG	SNG	well defined,solid,calcifcation	ND	N	ND	RHT	FV-PC	Y	PCT	NO

13	Lakshmi	38	F	5957	P	A	A	A	A	A	Firm	L	FN	SNG	solid,hyperechogenic	ND	N	FA	LHT	FA	-	-	NO
14	Sumathi	36	F	8327	P	A	A	A	A	A	Firm	R	CG	SNG	soft,cystic lesion	WD cystic nodule in right lobe	N	ND	RHT	CC	-	-	NO
15	Guruthai	36	F	15041	P	A	A	A	A	A	Firm	R	NG	SNG	well defined,cystic lesion	WD,HD nodule in right lobe	N	ND	RHT	NCG	-	-	NO
16	Pandaram	44	M	15912	P	A	A	A	A	A	Firm	R	NCG	SNG	hyperechoic,well defined lesion	WD,HD nodule oi right lobe	N	ND	RHT	NCG	-	-	NO
17	Selvapakkiyam	63	F	18122	P	A	A	A	A	A	Hard	L	PCT	SNG	microcalcifications,hypoechoic nodule	ND	N	ND	TT	PCT	-	-	NO
18	Annathai	47	F	19104	P	P	A	A	A	A	Firm	R	CG	SNG	solid,hypoechogenic lesion,hypervascular	WD nodule in the right lobe	N	ND	TT	CG	-	-	NO
19	Kannammal	47	F	26300	P	A	A	A	A	A	Firm	L	FN	SNG	solid,hyperechogenic	WD,HD nodule pe light lobe	N	FC	TT	FC	-	-	NO
20	Mariammal	35	F	28300	P	A	A	A	A	A	Firm	R	FN	SNG	well defined,hyperechogenic	ND	N	FA	RHT	FA	-	-	NO
21	Kaliyammal	55	F	27145	P	A	A	A	A	A	Hard	R	FN	SNG	hypoechoic,irregular margin	WD.HD nodule with calcificaton	N	PC	TT	PC	-	-	NO
22	Usharani	32	F	28787	P	A	A	A	A	A	Firm	L	NG	SNG	cystic lesion	ND	N	ND	LHT	NCG	-	-	NO
23	Selvi	63	F	35126	P	P	A	A	A	A	hard	L	FN	SNG	well defined heterogenous lesion	ND	N	FA	TT	FA	-	-	wound haematoma
24	Muthulakshmi	33	F	35367	P	A	A	A	A	A	Firm	L	FN	SNG	well defined hyperechoic	ND	N	B	LHT	CG	-	-	NO
25	Chinnathambi	34	M	36821	P	A	A	A	A	A	Hard	L	FN	SNG	hypervascular, hpoechoic	ND	N	FC	TT	FC	-	-	NO
26	Latha	39	F	39786	P	A	A	A	A	A	Firm	L	CG	SNG	well defined lesion with calcification	WD,HD nodule in left lobe	N	ND	LHT	CG	-	-	NO
27	Sluchona	47	F	42465	P	A	A	A	A	A	Firm	R	NG	SNG	hypoechoic	ND	N	ND	RHT	NG-CD	-	-	NO

28	Esaiveni	34	F	42837	P	P	A	A	A	A	Firm	R	NG	SNG	well defined solid lesion,hypoechoic	WDnodule in right lobe	N	ND	TT	CG	-	-	NO
29	Indhumathi	34	F	48826	P	A	A	A	A	A	Firm	R	PC	SNG	microcalcifications,hypoechoic nodule	ND	N	ND	TT	PC-FV	-	-	NO
30	Raja	43	M	48991	P	A	A	A	A	A	Firm	L	CG	SNG	hyperchoic,cystic lesion	WD nodule filled withcolloid in left lobe	N	ND	LHT	NCG	-	-	NO
31	Meenatchi	60	F	49786	P	A	A	A	A	A	Firm	L	FN	SNG	well defined,solid	ND	N	FA	LHT	FA	-	-	NO
32	Subbulakshmi	39	F	50033	P	A	A	A	A	A	Firm	L	NCG	SNG	well defined hyperechoic	WD,HD,nodule calcification on left lobe	N	ND	LHT	PC	Y	no e/o malignnacy	NO
33	Subbulakshmi	35	F	53673	P	A	A	A	A	A	Firm	R	NG	SNG	soft, well defined hyperchogenic	Wdnodule noted in right lobe	N	ND	RHT	CG	-	-	NO
34	Usha	36	F	54582	P	A	A	A	A	A	Hard	R	PC	SNG	hypervascular, microcalcification	ND	N	ND	TT	PC	-	-	NO
35	Essakiammal	54	F	54860	P	A	A	A	A	A	Soft	R	NCYG	SNG	well defined cystic lesion	WD,HD nodule in right lobe	N	ND	RHT	NCYG	-	-	NO
36	Oorakali	60	F	5500	P	A	A	A	A	A	Firm	R	FN	SNG	well defined hypoechoic	WD,HD nodule in right lobe	N	FA	RHT	MFA	-	-	NO
37	Gandhi	33	F	60478	P	A	A	A	A	A	Firm	L	CG	SNG	soft cystic lesion	WD nodule in left lobe	N	ND	LHT	NCG	-	-	NO
38	Sudalai	33	F	69438	P	A	A	A	A	A	Firm	R	FN	SNG	well defined hypoechoic	ND	N	FA	RHT	FA	-	-	NO
39	Kanngi	56	F	78965	P	P	A	A	A	A	Frim	R	NCG	SNG	soft,cystic lesion	ND	N	ND	RHT	CG	-	-	NO
40	Sundari	31	F	82145	P	A	A	A	A	A	Firm	R	CG	SNG	well defined cystic lesion	WD cystic nodule in right lobe	N	ND	RHT	NCG	-	-	NO
41	Kumari	65	F	83125	P	A	A	A	A	A	Firm	L	FN	SNG	hypoechoic solid lesion with microcalcification	ND	N	FA	TT	FA	-	-	Transcient Hypocalcemia
42	Fathima	54	F	90154	P	P	A	A	A	A	Firm	R	NCG	SNG	soft,cystic lesion	ND	N	ND	RHT	CG	-	-	NO

43	Sumathi	55	F	91542	P	P	A	A	A	A	Firm	R	CG	SNG	soft,cystic lesion with calcifications	WD,HD nodule in right lobe	N	ND	RHT	CG	-	-	NO
44	Sudha	54	F	93754	P	A	A	A	A	A	Firm	L	FN	SNG	well defined hypoechoic	ND	N	FA	LHT	FA	-	-	NO
45	Thangam	45	F	93951	P	A	A	A	A	A	Firm	R	CG	SNG	cystic lesion with calcification	WD,HD,cystic nodule right lobe	N	ND	RHT	NG-CD	-	-	NO
46	Meenakshi	46	F	95214	P	A	A	A	A	A	Firm	L	NCG	SNG	well defined heterogenous lesion	WD nodule in left lobe	N	ND	LHT	CG	-	-	NO
47	Essakiammal	58	F	96523	P	A	A	A	A	A	Firm	R	FN	SNG	well defined hypoechoic	ND	N	FA	RHT	FA	-	-	NO
48	Vadivoo	65	F	97521	P	A	A	A	A	A	Firm	L	NCG	SNG	soft,cystic lesion	WD Colloid nule in left lobe	N	ND	LHT	CG	-	-	NO
49	Valli	54	F	98545	P	A	A	A	A	A	Firm	R	FN	SNG	solid,hypercoi c lesion	ND	N	FA	RHT	FA	-	-	NO
50	Deepika	36	F	99548	P	A	A	A	A	A	Hard	L	NG	SNG	microcalficati on with hypoechoic	ND	N	ND	LHT	CG	-	-	NO
51	Kamala	42	F	2548	P	P	A	A	A	A	Firm	L	NCG	SNG	soft,cystic lesion	WD,HD nodule in left lobe	N	ND	LHT	CG	-	-	NO
52	Devi	33	F	12567	P	A	A	A	A	A	Firm	R	FN	SNG	well defined hypoechoic	ND	N	FA	RHT	FA	-	-	NO