A STUDY ON SOLITARY NODULE OF THYROID

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CERTIFICATE

Certified that this is the Bonafide dissertation done by **Dr. N.V. Sathish** and submitted in partial fulfillment of requirement for degree of **MASTER OF SURGERY** Branch 1 of **General Surgery of the Tamilnadu Dr.M.G.R. Medical University, Chennai.**

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DECLARATION

I solemnly declare that the dissertation titled **"A STUDY OF SOLITARY NODULE OF THYROID"** was done by me at Coimbatore Medical College and Hospital, Coimbatore during the period of September 2003 to September 2005 under the guidance and supervision of **Prof.Dr. A.RAMAMOORTHY M.S.**

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A STUDY ON SOLITARY THYROID NODULE

INTRODUCTION

Solitary thyroid nodule can be defined as a goitre which on clinical examination appears to be a single nodule in an otherwise normal thyroid gland[1]. Solitary thyroid nodule remains a common clinical problem.

Virtually any disease of the thyroid can present as a solitary nodule. A solitary nodule has a high risk of being malignant (10-20%) than the multiple palpable nodules of a multinodular goitre (5%).

A solitary nodule may become cosmetically distressing to a patient and occasionally causes pressure symptoms. Less frequently, an autonomously hyperfunctioning single nodule may cause hyperthyroidism. However, in the greater proportion of patients the major concern relates to the potential of malignancy with in such a nodule.

Until recently, many clinicians have advised and practiced the routine surgical resection of all solitary thyroid nodules for definitive histological assessment. Thyroid surgery, even in experienced hands is associated with definite morbidity and should not be undertaken lightly. It is logical to propose a more selective surgical policy for a patient with a solitary thyroid nodule, advising operation only for those individuals in whom cancer has been diagnosed or suspected or who are otherwise at risk of their goitre.

The incidence of thyroid cancer in patients with solitary thyroid nodule ranges from 11 to 20% (Kendall & Condon, 1969) [20].

The vast majority of thyroid nodules are benign and do not require removal. The physician or surgeon should be able to perform an accurate clinical assessment of any thyroid nodule, appreciate the risk factors for thyroid cancer, and be able to evaluate which patient would benefit from surgery.

Conservative management is appropriate when malignancy can be reasonably excluded.

AIM OF STUDY

1. To review the data regarding the prevalence of solitary thyroid nodule and analyse its distribution with respect to age, sex, etc.

2. Discussion of the clinical presentation and the significance of solitary thyroid nodule.

3. To evaluate the risk factors associated with occurrence of malignancy in a solitary nodule of thyroid.

4. To find out the percentage of malignancy in solitary nodule.

5. To study the clinicopatholgical correlation of solitary thyroid nodules

6. To study the correlation of FNAC and biopsy. To study the sensitivity and specificity of FNAC.

7. To provide a clinically applicable and cost-effective approach to the evaluation and management of solitary thyroid nodule.

MATERIALS AND METHODS

This is a prospective study of randomly selected patients with clinically palpable, solitary thyroid nodule diagnosed and treated at Coimbatore Medical College Hospital. Total duration of study was two years, from 2003 September to 2005 September.

Each patients Symptoms and signs were entered in a proforma (given at the end of this dissertation) with detailed clinical examination in relation to the thyroid swelling and lymph

node involvement and a routine systemic and general examination was done.

All patients were subjected to basic investigations like complete hemogram, Blood sugar, Blood urea, serum cholesterol, urine analysis, chest radiogram and radiogram of neck. Tissue diagnosis was obtained by fine needle aspiration cytology in all the patients.

Thyroid profile was done in selected patients with features of hyper or hypofunctioning of the gland. Radio isotope scan was not done since the facility was not available at our hospital. Ultrasound of neck and Computed Tomogram scan of skull and chest were done in selected cases. All operated specimens were subjected to Histopathological examination.

Preoperative and postoperative complications were analysed. Most cases were regularly followed up throughout the study period. All the observations were analysed and compared with other studies.

SURGICAL ANATOMY

The thyroid gland occupies an important position in the centre of the visceral compartment of the neck, lying astride the trachea, just above the thoracic inlet. It normally weighs about 25 g.

The gland consists of two symmetrical lobes, united in front of the second, third and fourth tracheal rings by an isthmus of gland tissue. The extent of the gland is from the thyroid cartilage to the 5th or 6th tracheal ring or from C_3 to T_1[2].

Each lobe is pear shaped, consisting of a narrow upper pole and a broader lower pole.

The right lobe is often larger than the left. The Thyroid gland is covered by fascia and the strap muscles, and more laterally, it is tucked under the diverging anterior borders of the sternomastoid muscles and adjacent to the lobes on the medial side, is the carotid sheath.

Because of its fascial attachments, the gland moves upwards with swallowing. The normal gland is impalpable - though can be felt in thin necks. It is soft and supple and the tracheal rings can be palpated through it.

THE MUSCULO FASCIAL COVERINGS

The strap muscles are ensheathed by the general investing layer of cervical fascia, and this unites them in the midline.

These muscles are applied to the anterior surface of the gland, but separated from it, by a loose condensation of fascia derived from the pretracheal fascia. This false capsule covers the gland which is enclosed by its diaphonous true capsule with its very rich blood supply, clearly visible just beneath its surface. The pretracheal fascia is attached above to the thyroid cartilage and cricoid cartilage and this suspension of the gland from the larynx is responsible for its movement with deglutition.

In the surgical approach to the thyroid gland, the musculo fascial envelope is incised down the midline, which is relatively avascular, and the space between the two capsules of the gland is entered. This loose plane is easily developed and the gland exposed by retracting the strap muscles.

The nerve supply of these muscles, the sternohyoid and sternothyroid, comes from Cervical roots 1, 2 and 3 via branches from the ansa cervicalis. This branches enter the muscle at its lateral border and on the deep surface and the muscles may be divided transversely to facilitate access to the gland, provided they are resutured, there does not appear to be any impairment of function.

The other important implication of the musculofascial covering of the gland is that at the end of thyroid operations, the divided fascial envelope is resutured in the midline and this again closes the visceral space. If there is post operative haemorrhage into this closed space, respiratory embarrassment from tracheal compression results and requires release of sutures to restore the airway.

BLOOD SUPPLY

Superior thyroid artery is the first branch from the anterior aspect of the external carotid artery, after giving off its sternomastoid and superior laryngeal branches, pierces the pretracheal fascia as a single vessel to reach the summit of the upper pole. It divides on the gland into an anterior branch that runs down to the isthmus and a posterior branch that runs down the back of the lobe and anastomoses with an ascending branch of the inferior thyroid artery from the lower pole.

The inferior thyroid artery, arises from the thyrocervical trunk, and passes behind the carotid sheath, and then runs transversely across the space between this and the Thyroid gland to enter the deep surface of the gland as several separate branches close to the tracheothyroid groove.

The recurrent laryngeal nerve lies normally behind this branches or may be related anteriorly or posteriorily to the branches.

The Thyroideima artery enters the lower part of the isthmus in 3 percent of individuals. It springs from the branchiocephalic trunk (or) direct from the arch of aorta.

The venous return from the upper pole follows superior thyroid artery. This superior thyroid vein, enters either internal jugular vein (or) common facial vein.

The middle thyroid vein, short and wide, passes from the middle of the lobe, directly into the internal jugular vein.

From the isthmus and lower poles the inferior thyroid veins form a plexus that lies in the pretracheal fascia, in front of the cervical part of the trachea and drain into the

brachiocephalic veins.

LYMPHATIC DRAINAGE

The lymphatics follow the arteries. From the upper pole, they enter the antero superior group of deep cervical lymph nodes. From the lower pole, they pass with the inferior thyroid artery back to its point of origin from the subclavian behind the carotid sheath, into the posteroinferior group. A few pass downwards into pretracheal nodes, following the course of thyroidea ima artery.

NERVE SUPPLY

The gland receives its innervation from the sympathetic and parasympathetic divisions of the autonomic nervous system. The sympathetic fibres arise from the cervical ganglion and enter with blood vessels and are vasomotor in action. While the parasympathetic fibres are derived from the vagus and reach the gland via branches of the vagus and reach the gland via branches of the laryngeal nerves[26].

The Thyroid gland's relation to the recurrent laryngeal Nerve and to the external branch of superior laryngeal nerve is of major surgical significance.

Hunt reported the anatomy of recurrent laryngeal nerve in 100 cases. The right recurrent laryngeal nerve resided in the tracheoesophageal groove in 64% of cases, whereas the left nerve was similarly located in the left side in 77% of cases.

The nerve was lateral to the trachea in 33% of cases on the right side and 22% on the left side. On one occasion on the right side, a direct recurrent laryngeal nerve was given off in the neck without looping around the subclavian artery. Sometimes the nerves can run anterolateral to trachea (Tr. 8%, Lt 6%), with a maximum risk of injury during surgery.

The inferior thyroid artery is often used as a landmark for demonstration of recurrent laryngeal nerve. In most of the cases, the recurrent laryngeal nerve passes posterior to the inferior thyroid artery or its branches. (60% of cases), in about 30% of cases, the nerves pass anterior to the artery and the rest, between the branches of the artery.

In 50% of cases, the nerve is embedded in the ligament of Beny, which is of importance, because traction on the gland will put the nerve on stretch and make it subject to section. Damage to the recurrent laryngeal nerve results in paresis or paralysis of the intrinsic musculature of the larynx on that side which results in vocal cord paralysis.

The non recurrent laryngeal nerves occurs in 1% of cases and almost invariably on the right side; the nerve from the vagus, runs directly to the gland along the superior thyroid pedicle, and may be at a risk, when this is transected.

The superior laryngeal nerves arises from the vagus, near the base of the skull, runs medial to carotid sheath, divides at the level of hyoid bone into external (muscular) and internal (sensory) branches.

External branch of superior laryngeal nerve innervates the cricothyroid muscle which is a tensor of the vocal cord. In most cases the superior laryngeal nerve lies adjacent to the vascular pedicles of the superior poles of the Thyroid gland, requiring that the vessels to be ligated with care to avoid injury, which are individually ligated and divided low on the gland, dissected laterally to the cricothyroid muscle.

HISTOLOGY OF THYROID GLAND

The thyroid gland is enclosed by a dense connective tissue capsule. The lobes are divided into multiple lobules formed of follicles variable in size and shape. There is an average of about 3 x 106 follicles in each gland, each measuring 30 micro m. Within the follicles is the clear viscid colloid. The follicles are lined by flattened cuboidal or columnar epithelium depending on glandular activity. Sparsely intermingled between the follicular cells and also within the interfollicular spaces are the parafollicular cells (the calcitonin secreting C cells). They are slightly larger than the follicular cells and have large nuclei and cytoplasmic granules. They are located in the upper poles of the thyroid lobes, reflecting their origin as neuroectodermal cells derived from the ultimobranchial bodies and part of the APUD series. The follicles are supported by a heavily vascularised connective tissue frame work.

EMBRYOLOGY

The Thyroid develops as an endodermal tubular structure from the posterior aspect of the fetal tongue, and grows downwards in front of the developing hyoid and larynx, bifurcating and fusing with growth elements from the 4th branchial pouch. The stem of the down growth forms the thyroglossal duct whose upper end remains as the foramen caecum of the tongue; the lower end forms the pyramidal lobe of the thyroid. Thyroglossal duct usually atrophies but may remain in whole or in part and produce

abnormalities in later life. The transient ultimobranchial pouches (part of 4th) contribute to the development of thyroid, an element which becomes parafollicular (Calcitonin Secreting) cells. It is a matter of surgical importance that the 4th branchial pouches also produce the superior parathyroids which maintain close relationship to the superormedial aspect of thyroid lobes. The inferior parathyroids develop from 3rd branchial pouches and their relationship is more to thymus than thyroid. They normally come to lie between the apex of the thymus and the lower pole of the thyroid or along the fibrous band, the thyrothymic ligament which unites them.

PHYSIOLOGY

Iodine Metabolism

The average daily requirement of Iodine is 0.1 mg. Iodine is converted to iodide in the stomach and duodenum and after absorption, distributed uniformly, actively transported into the thyroid, by an ATP - dependent process. The normal serum - thyroid 12 - ratio is about 1:5. But can be as high as 1:500.

Thyroid hormones T_3 and T_4 are bound to thyroglobulin within the colloid. Synthesis within the thyroglobulin complex is controlled by several enzymes in distinct steps.

(i) Trapping of inorganic iodide

ii) Oxidation of iodide to iodine

iii) Binding of iodine with tyrosine to form iodotyronine

iv) Coupling of monoiodtyronines and diodotyronines to form T_3 and T_4, rT_3.

All the steps are accelerated by TSH acting through a specific membrane receptor, via the cAMP second messenger system. The coupling and oxidation of iodide are catalysed by a peroxidase enzyme, in the presence of H_2O_2.

When hormones are required the complex is reabsorbed in to the cell by endocytosis and thyroglobulin broken down by lysosomal action. This results in formation of T_3, T_4, rT_3, MIT & DIT; the MIT & DIT are deiodinated and 12 reused T_3 & T_4 enter the circulation and are transported bound to thyroxine binding globulin (TBG), thyroxine binding pre-albumin (TBPA) and albumin. About 99.98% of hormones are protein bound.

The circulating plasma levels of T_3-T_4 are in a ratio of 1:20, but T_3 is less protein - bound, So is the more potent hormone, with a half life of 1 day compared to about 7 days for T_4. T_3 is the more important physiological harmone. Approximately 85% of T_3 is produced by mono-deiodination of T_4 in other tissues such as liver, muscle and Kidney.

Pituarty Thyroid Axis

Synthesis and liberation of thyroid hormones is controlled by TSH from anterior pituitary. Secretion of TSH depends on the level of circulating thyroid hormones and is modified in a classical negative feed back manner. Regulation of TSH secretion also results from the action of thyrotropin releasing hormone (TRH) produced in the hypothalamus.

Action of Thyroid Hormones

Thyroid hormones influence and speed up many metabolic processes in the body.

They are essential for normal growth, mental development and sexual maturation.

They also increase the sensitivity of the cardiovascular and central nervous systems to catecholamines and so influence cardiac output and heart rate. many of these actions are mediated by T_3 which by binding to specific receptors in cell nuclei alters the expression of some genes.

The thyroid hormones are deiodinated and the rest are excreted as glucoronide conjugates.

Thyroid Function Tests

There are variety of tests available to assess the function of thyroid. No single test is diagnostic and therefore a combination of tests are indicated.

1. Measurement of Thyroid hormones in the serum

Total T_4 and T_3 represents total protein bound T_4 an T_3 and are not measurements of free active thyroid hormones. Total T_4 and T_3 are influenced by the thyroxine binding proteins in the serum. False high levels are seen in pregnancy and those who are taking oral contraceptive pills. False low values are seen in hypoproteinaemic states such as nephrotic syndrome. Drugs such as salicylates, penicillin compete with T_3 and T_4 for protein binding. So measurements of free T_3 and T_4 by Radioimmunoassay is specific.

FT_4 measurement helps in detecting early toxicity, when TT_4 levels are normal. In patients with end-organ resistance to T_4 (Refetoffs sndrome). T4 levels are raised, but TSH levels are usually normal. T_3 levels may be low in patients with reduced peripheral conversion of T_4 to T_3 due to starvation (low T_3 syndrome) or due to drugs (eg. Propranolol). T_3 thyrotoxicosis is a rare condition, in which levels of TT_4 in the hyperthyroid patient are normal and RATU is normal, but TT_3 levels are raised. It is seen in patients with endemic goitres and small solitary thyroid nodules.

2. Serum Protein Bound Iodine (PBI)

Normal range 3-5.8 mg/ 100 ml. It lacks specificity in that it measures non hormonal forms of iodine in the blood. False positive results are seen in

pregnancy, persons taking iodides, expectorants containing potassium iodide and in those taking oral contraceptive pills.

T_3 Resin uptake:

Patients serum is incubated with radioactive T_3 so that the latter becomes fixed to unoccupied sites of Thyroid binding globulin. Naturally in hypethyrodism the unoccupied sites are low and in hypothyroidism the unoccupied sites are high. Then a secondary binder, a resin is added to the system, Resin uptake of T_3 is more in thyrotoxicosis and low in hypothyroidism. The test serves as indirect measurements of unbound T_4. From this free Thyroxin index can be calculated.

Free Thyroxine Index = Serum T_4 x T_3 uptake %[26].

Measurement of Serum TSII:

Normal range is upto 0.15-4.2 micro u/mi. Levels over 40 micro u/mi are present in gross thyroid deficiency. The test is invaluable in the early detection of mild degrees of hypothyroidism seen after surgery for thyrotoxicosis or after radioiodine. Old RIA methods have been replaced with more sophisticated immunometric assays using monoclonal antibodies that target two separate sites on TSH molecule allowing reading with an accuracy down to 0.005 micro u/mi. Estimation of these low concentrations aids the distinction of hyperthryoidism from euthyroidism.

TRH Test

When thyroid hormones are high as in hyperthyroidism, TSH is suppressed and I.V. Injection of TRH does not result in rise of TSH. When thyroid hormones are normal or low, TRH injection increases TSH level. Serum TSH is estimated at the beginning of the test and again 20 minutes and 60 minutes after injection of 200 micro gram of TRR. In euthyroid TSH level increases just above the basal level. In hypothyroidism there is an exaggerated response. This test is infrequently used but it is useful if thyroid hormones and TSH levels are discrepant, in Grave' diseases, hypothyroidism due to pituitary or hypothalamic disease.

Radioactive Iodine Uptake Test (RAIU)

RAIU indicate rate of thyroid hormone synthesis and release. 5-25 mci of radioiodine 1231 is given orally. Then after 24 hours thyroid content of 1231 is measured by a counter. It is measured after 24 hrs because it is convenient to the patient and also the value at 24 hrs is usually near its plateau. But in very severe hyperthyroidism measurement is taken earlier since the uptake and release is rapid.

Increased RAIU

Inference is increased hormone synthesis, causes

i) Hyperthyroidism (except T_3 toxicosis and increased body iodide)

ii) Ablation in hormones synthesis e.g. ineffectively or inefficiently used iodine.

iii) Acute or chronic iodine deficiency.

iv) Withdrawal of factors that lead to thyroid hormone depletion e.g. withdrawal of antithyroid drugs, recovery from subacute thyroiditis, withdrawal of exogenous hormones.

v) Compensatory increase in hormone synthesis after hormone loss e.g. Nephrosis, chronic diarrhoea, soya bean ingestion.

Decreased RAIU:

i) Hypothyroidism

ii) Antithyroid agents

iii) Primary biosynthetic defects of hormone

v) Hashimoto's disease

v) Subacute thyroiditis

vi) Increased availability of iodine

vi) Very severe hyperthyroidism due to increased release.

PATHOLOGY

A single palpable nodule in otherwise impalpable thyroid gland is called solitary nodule of thyroid. A single discrete nodule in a palpable thyroid gland is called dominant nodule[1].

The problem of solitary nodule of thyroid is that about 10-20 % of solitary nodule of thyroid is malignant and the physical signs of malignancy may not be evident in thyroid as noticed elsewhere.

Formation of nodules

A loss of co-ordination between iodine metabolism,. epithelial multiplication, thyroglobulin synthesis and coiloid endocytosis are important in the genesis of nodule.

Iodine deficiency and ingestion of goitrogens are the commonest cause of goitre formation. Iodine deficiency or goitrogens or hereditary factors lead to decrease in serum thyroid hormones with followed by increase in TSH which will produce diffuse hyperplastic goitre. The patient will become euthyroid because of normal thyroid hormone level, TSH level drops down and goitre disappears. If it persists after that it is a colloid goitre with inactive follicles. Because of fluctuation in TSH level, and varied response of cells to TSH, mixed active and inactive follicles are formed. In active follicles, because of high vascularity haemorrhage occurs with central necrosis. Growth stimulating antibodies are also responsible for multinodular goitre. Patient is usually euthyroid. Firm painless nodules are palpable; hardness may be due to calcification. Pain and sudden increase in size may be due to

haemorrhage and simulate malignancy. Many thyroid disorders, both benign and malignant may manifest as solitary nodule[31].

CAUSES OF SOLITARY NODULE

A. CYST

Simple

Mixed - Cystic and Solid or Complex

B. PALPABLE NODULE OF TRUE MULTINODULAR GOITRE
C. THYROIDITIS .

Hashimoto's

Sub acute

D. Th4FECTION

Granulomatous disease

Abscess

E. ADENOMA - 30%

F. TOXIC ADENOMA

G. MALIGNANCY

Carcinoma - Primary * Differentiated

- Papillary
- Follicular
- Medullary thyroid carcinoma

* Undifferentiated

- Anaplastic
- Metastatic

Lymphoma

Clinically palpable nodule of a multinodular goitre is the most common cause of solitary nodule thyroid.

ADENOMA

Virtually all adenomas of thyroid present as a small discrete solitary nodule.

They occur most commonly in young and middle aged women. They rarely exceed 3 cm. Almost all adenomas are of follicular variety. Rare types are papillary cystadenoma and Hurthle cell adenoma.

The Differentiation of a nodule within a multinodular goitre from an adenoma is difficult not only clinically but also anatomically.

The morphologic criteria used to identify adenoma are.

1. Complete fibrous encapsulation.
2. A clear distinction between the architecture inside and outside the capsule.
3. Compression of the thyroid parenchyma around the adenoma.
4. Lack of multinodularity in the remaining gland.

Histological classification of Adenoma

Type-I

A. Embiyonal Adenoma

The follicles are premature, very cellular and arranged in the form of cords.

B. Fetal Adenoma

Small follicles are arranged closely packed with a abundant connective tissue stroma.

C. SIMPLE ADENOMA

Composed of closely packed follicles of normal size.

D. Colloid Adenoma

Contains dilated follicles filled with colloid.

E. Hurthle Cell Adenoma

Composed of large granular cells identical to those encountered in various non - neoplastic thyroid lesions usually arranged in trabecular pattern.

Type II

A. Microfollicular
B. Macrofollicular
C. Atypical adenoma

Exhibits nuclear atypia, variability in cell morphology, including the presence of spindle shaped cells.

Follicular adenoma are differentiated from follicular carcinoma by the absence of capsular or vascular invasion. Thus careful sampling of capsule is required to exclude carcinoma.

Adenomas attain certain size and remain in that because the expansile pressure restricts blood supply. It may suddenly enlarge and may be painful because of haemorrhage within the nodule. Adenomas occasionally have some dependence on TSH, so it regresses after

administration of thyroid hormones.

Adenomatous goitre

Adenomatous goitre is usually multinodular but a few may present as solitary nodule. Most patients are euthyroid. Whether single or numerous, adenomatous nodules have similar appearances.

Typical features include

1. Nodularity created by islands of colloid filled or hyperplastic follicles.
2. Random irregular scarring.
3. Focal haemorrhages and haemosiderin deposition.
4. Focal calcification in areas of scarring
5. Microcyst formation.

Microscopically adenomatous nodules are composed of follicles of vaiying size. Some follicles are distended with colloid and lined by flattened epithelium, where as others are small and are more active appearing.

CARCINOMA

Papillary Carcinoma: (70%)

Common in adults and children. Responsible for 30% of the thyroid carcinoma occurring below 40 yrs. More common in women. It grows slowly. Metastasis to cervical lymphnodes are common. About 10-20% may present as only cervical lymphnode metastates.

The primary is occult (lateral abelTant thyroid). All the lesions below 1.0 cm are called as occult or micro carcinoma. Blood spread is unusual. Prognosis is good. 10 year survival rate is about 70-80%.

Histology

Complicated branching tree like pattern of cells outlined by papilliferous axial fibrovascular stroma. Pale, empty nuclei (Orphan Annie eyed nuclei) and Psammoma bodies are present. Papillary carcinoma is subjected to the influence of pituitary T.S.H.

Follicular carcinoma (25%)

It is a well differentiated carcinoma of the thyroid but more aggressive than papillary carcinoma. More common in women. Peak incidence occurs in 5th and 6th decade.

Two types:

i) Encapsulated - less common

ii) Invasive mass

Haemorrhages, cystic degeneration and necrosis are common. Microscopically picture is that of adeno carcinoma with considerable range in size and differentiation of glands. Blood spread occurs in 70% cases. Commonest sites are lungs, bones, brain etc. Regional lymphnodes are involved in only 5% of cases.

Medullary carcinoma

Derived from parafollicular cells (C cells). It is an APUDOMA. 80% occur sporadically usually in adults. 10-20% occur in children and teenagers with associated syndromes.

MEN Ila : MTC, Phaechromocytomas, parathyroid tumours

MEN lIb: MTC, Phaechromocytomas + Mucosal neuroma, Marfanoid features, ganglioneuromatosis.

90% of the patients secrete calcitonin. Less frequently histamine, prostaglandins, ACTH and serotonin are secreted. It may present as a single nodule
or multiple nodules. Sporadic forms occur in 5th - 6th decades. Often present in advanced forms. Familial type presents in second decade. Associated endocrine abnormalities bring the patient early. Diarrhoea is present in upto 30% of patients. Metastasis is usually to regional nodes (50%), lung, liver and bone. Medullaiy carcinoma is not TSH dependent. It does not take up radio iodine. Diagnosis of medullary carcinoma can be made by stimulating calcitonin secretion by Pentagastrin and calcium infusions.

Anaplastic carcinoma

Usually occurs in 7th and 8th decades of life, it is a rapidly growing, locally infiltrative tumour with very poor prognosis.

It spreads by lymphatics and by blood stream. Two histological types are small cell carcinoma and giant cell carcinoma. 1 year survival is about 20%.

Other tumours like lymphoma, sarcoma and secondaries also occur in thyroid. Secondary tumours usually arise from kidney, breast, colon, melanomas.

Thyroiditis

(i) Hashimoto's Thyroditis

It is a an autoimmune thyroiditis. It is the commonest cause for goitrous hypothyroidism in places where iodine intake is adequate. It is a major cause for nonendemic goitre in children. The goitre is due to thyroid growth immunglobulins like auto antibodies to thyrotrophin receptors, follicular microsomes, thyroglobulin. Thyroid parenchyma is replaced by fibrous tissue because of the infiltration by lymphoid cells. So eventually hypothyroidism develops. Sometimes in the midcourse patient may develop thyrotoxicosis called 'Hasitoxicosis'. More common in women at menopausal age. Usually both the lobes are involved. Nevertheless one lobe is larger than the other. It is lobulate and rubbery in consistency. It may be associated with pernicious anaemia, vitiligo, Rheumatoid arthritis etc.

Histology

Excessive replacement of parenchyma by lymphocytes, plasma cells, macrophages, lymphoid germinal centers. Follicular cells are transformed into eosinophilic granular cystoplasmic cells called Hurthle cells (or oncocytes or Askanazy cells). Diagnosis rests on measurement of serum auto antibodies by Radio Immuno Assay. It is positive in over 85% of cases. Lymphoma may develop in Hashimoto's thyroiditis.

(ii) Subacute Thyroiditis (De Quervain's Thyroiditis)

Causative agent is a virus, probably mumps virus. Patient has flu like illness followed by pain and rapid onset of swelling of thyroid. Swelling may be diffuse or asymimetrical, and tender on palpation. During active phase patient may develop hyperthyroidism, then due to extensive destruction hypothyroidism develops[30].

Histology:

Aggregation of macrophages admixed with multi nucleated giant cells; It is a self limiting condition.

Acute bacterial thyroiditis is rare. Commonest organisms are staphylococcus.

(iii) Riedel's Thyroiditis (Lignious Thyroiditis).

Aetiology is unknown. There is extensive fibrosing reaction that destroys more or less all the thyroid gland. The fibrous tissue may extend beyond the capsule and involve other structures in the neck. More common in females.

It is characterised by painless enlargement of thyroid, woody hard in consistency, asymmetrical, pressure symptoms may be present especially tracheal compression. It may be associated with retropentoneal fibrosis. Occasionally it may be associated with sclerosing cholangitis. About 25-50% of the patients are hypothyroid.

Toxic Adenoma:

This type produces hormones in sufficient quantity to give rise to hyperthyroidism. Thyroxine output is not controlled by TSH or LATS. It is an autonomous tumour. Patient has increased metabolic rate, loss of weight, intolerance to heat, tremors, fibrillations. Usually there is no exophthalmos. Radioiodine scan shows it to be a hot nodule.

Thyroid Cyst:

30% of Clinically palpable swellings are cystic.

Causes:

i) Colloid degeneration (50%)

ii) Degeneration of follicular adenoma

iii) 10-15% are malignant.

CLINICAL PRESENTATION

Patients with solitary nodule in thyroid may present for:

- Toxic symptoms (autonomous, hyper functioning nodule).
- Pressure symptoms - dyspnoea, dysphagia, hoarseness of voice and rarely superior venacaval obstruction.
- Metastatic disease in the neck lymph nodes
- Distant metastasis.
- Cosmetic reasons.

CLINICAL RISK FACTORS

Age

The risk of cancer in a solitary thyroid nodule is more than 10% in adults. This risk is more in teenagers and after 60 years of age (30% .40%).

Sex

Nodules in men are more likely to harbour malignancy than in women.

Growth patterns

A nodule that has appeared recently or one that has undergone progressive enlargement over months is suspicious of malignancy. However sudden painful enlargement of a nodule is usually due to haemorrhage with in the nodule.

IRRADIATION

The finding of solitary thyroid nodule in an individual with a history of external irradiation[31] therapy over face, neck and chest should be regarded with a high degree of suspicion for the presence of malignancy.

FAMILY HISTORY

The presence of a solitory nodule in a patient with a family history of thyroid malignancy increases the risk for malignancy in the nodule.

PHYSICAL CHARACTERISTICS OF THYROID NODULE

1. Single Versus multiple:

Malignancy occurs in 10-20% of single thyroid nodules but in only *3-5%* multi nodular goitre.

2. Consistency and fixation:

Hard consistency and the clinical impression of fixation implying invasion of adjacent structures also suggest malignancy. Indeed the majority of cancers occurring in single nodules are mobile and indistinguisable from benign lesions.

3. Recurrent nerve paralysis.

In the absence of previous neck surgery, it is virtually pathognomonic of malignancy.

4. Obstructive signs:

Clinical evidence of obstruction of the airway or of the great veins of neck and mediastinum by a solitary thyroid nodule is rare, but when present, should raise the suspicion of malignancy.

5. Lymphnodes

Associated palpable cervical lymph adenopathy points strongly to cancer 6. Distant metastasis.

CLINICO PATHOLOGICAL STAGING OF THYROID CARCINOMA; (DEGROOT) [13]

I A Unilateral confined to thyroid

B. Bilateral or multifocal

II. A**.** Unilateral Significant cervical nodes

B. Bilateral cervical or mediastinal lymphnodes

III. Local invasion with or without positive nodes

IV. Distant metastasis

TNM classification is separate for each type of thyroid carcinoma.

Definitions of• low risk and high risk for differentiated carcinoma as per lahey clinic.

- AGES scale : Age, Grade of Tumour, Extent of disease, Size of fumor
- MACIS Scale: Metastases : Age, extent of Clearance, Invasion, Size of tumour
- AMES scale : Age, Metastases, Extent of invasion, Size of tumour.

Low risk group

- Men of 40 years and younger, women of 50 years and younger without distant metastases.
- All older patients with intra thyroid papillary carcinoma or follicular carcinoma with minor capsular involvement, in association with tumors less than *5* cm in diameter and no distant metastases.

High risk group

- All patients with distant metastases
- All older patients with extra thyroid papillary carcinoma or follicular carcinoma with major capsular involvement and tumors *5* cm in diameter or larger regardless of extent of disease.

INVESTIGATION

Following investigation are required for evaluating a case of solitary thyroid nodule.

I. BIOCHEMICAL ASSESSMENT

Serum T_3 T_4 and TSH

In a hyper functioning nodule T_3 and T_4 will be high where as TSH will be low; but most patients with thyroid nodules are euthyroid. Risk of malignancy in a toxic nodule is negligible. Post - opTSH after thyroxine treatment should be about 0.1 micro u/ml in low risk group and < 0.1 micro u/ml in high risk group.

Plasma Calcitonin

A raised level of plasma calcitonin strongly suggests medullary carcinoma. Serum Calcitonin can be measured after a challenge with calcium or pentagastrin; can also be used for post-operative follow-up in MTC.

Thyrologlobulin assay.

Mainly useful after total thyroidectomy for malignancy. A raised level is a marker of early recurrence. After total thyroidectomy, the levels should be <2 ng/ml when patient is on thyroxine and when not, it should be <3 ng/ml.

Serum levels of CEA, histaminase, CGRP and serotonin are elevated in cases of MTC. CEA can also be used for post op follow up. Serum calcium levels should be observed to rule out, co-existent parathyroid disorders.

24-h urinary values of VMA (Vanillyl mandelic acid), catecholamine and metanephrine should be done to rule out co-existent phaeochromocytoma.

These biochemical investigations were done only for few cases in this series.

II. STANDARD RADIOGRAPH

Routine chest radiogram was done for all patients planned for surgery to assess the respiratory system. Radiogram of neck also was taken, they showed the position of trachea, any compression over it and rarely calcification in the nodule

III. ISOTOPE SCANNING

With appropriate apparatus, isotopically labelled materials that are differentially accumulated by thyroid tissue can be detected and quantified. Radio Isotopes used are ^{99m}Tc Pertechnetate, ^{131}I, ^{125}I and ^{123}I

^{99M}TC PERTECHNETATE[4]

Actively concentrated by the thyroid but unlike iodide undergoes negligible organic binding. Half life is six hours, so requires only single patient visit. Also it delivers very low irradiation to the thyroid tissue so it provides information about iodide-transport function of thyroid and not about organic binding and retention. The stay in the thyroid gland is brief and hence imaging done early. It is inappropriate for metastasis and substernal goitre.

Route - Single IV bolus and imaging performed 4-6 hour later. Apparatus used is scintillation camera.

^{125}lodine:

Half life 60 days. Its low energy emission precludes scanning from deep sources such as

sternal goitre or distant metastasis.

^{123}Iodine:

Half life 13 hours. Radiation to the thyroid tissue is about 1% of that is delivered by ^{131}I since there is absence of beta radiation. So it is the ideal isotope.

^{131} Iodine:

Half life 8 days. Useful to find out functioning metastatic lesions of thyroid carcinoma.

Tc-Pentavalent - dimercaptosuccinate Scanning (DMSA)

DMSA Scintigraphy scanning has been shown to be more accurate in localising medullary carcinoma than the more standard techniques such as USG, CT and MRI scanning. Tc-Pentavalent DMSA shows high concentration in lesions in about 80% of patients with medullary carcinoma thyroid.

Tc99m - Sestamibi Scan, MIBG (Meta- Iodo Benzyl - Guanidine) Scan and PET scan can also be used in cases of recurrent / metastatic MTC. Tc99m sestamibi scan also be used for recurrent Hurthle cell cancer.

USE OF THYROID SCAN

To define areas of increased or decreased function from the reminder of the gland provided these areas are 1 cm or more in diameter. Better visualisation of small nodules can be achieved by oblique or lateral view along with antero -posterior view.

About *85%* of nodules are “cold” of which 10-25% are malignant. About *5%* of nodules are hot, of which < 1% are malignant.

Though majority of cold nodules are not malignant, lack of function increases the chance of developing malignancy particularly if only one nodule is present. Conversely hot nodules are unlikely to be malignant.

Scans performed after exogenous thyroid hormone administration (suppression scans) can reveal autonomous nodules.

Thyroid scans are also useful in detecting retrosternal goitres and ectopic thyroid tissue in the neck or ovary.

The most important use is to trace metastasis from thyroid carcinoma. (differentiated type), which can be detected and treated by radioactive iodine in *75%* of cases. Screening can be facilitated by removal of all thyroid tissue which is the most compelling of all arguments in favour of total thyroidectomy in differentiated thyroid malignancies, except Hurthle cell carcinomas. Scanning is more sensitive to detect pulmonary micro metastases than chest x-ray or CT scan.

Histologically radioisotope imaging has played a major role in the work up of thyroid nodules, however with the advent of fine needle aspiration cytology, this role has become less clear. Because thyroid scans add little in determining which nodules require surgical excision, they should no longer be a routine part of the evaluation of a solitary thyroid nodule.

IV. Ultrasonogram of thyroid

It is useful to know whether a nodule is cystic or solid and will often detect other impalpable nodules ; can be utilised for guided aspiration of cysts. USG can be used for follow-up of nodules after thyroxine suppression.

V. CT scan

Useful in assessing the extent of primary tumor and neck node metastases.. Also useful to detect pulmonary or brains metastasis. MRI can be used to differentiate suspicious recurrent tumours from scar tissue.

VI. Tissue Diagnosis

- Fine needle aspiration cytology
- Core needle biposy

a. Fine Needle Aspiration Cytology (FNA C) [18]

FNAC is the gold standard investigation for evaluation of solitary nodule and should be done for all cases. Its use in the recent years has resulted in a significant decrease in the number of thyroid surgeries being performed, while increasing the yield of malignant lesions of patients who have undergone operation.

ADVANTAGES

1. Most valuable in diagnosis
2. Safe, doesn't require experience, and can be repeated several times.
3. Has given better selection of patients for surgical removal of nodules
4. Diagnostic accuracy - 96%.
5. No complications.
6. Is therapeutic in cases of simple thyroid cysts.

MATERIALS

1. Disposable hypodermic needle 2 1-23 size and length of 1-1.5 inches.
2. Disposable 20 cc syringe, pistol syringe holder (cameco) preferred
3. Swabs and spirit to clean.
4. 76 x 26 mm microscopic slides which are suitably numbered and labelled.

5. Koplin jar for keeping smeared slides in the fixative i.e., isopropyl alcohol.
6. Transport box
7. Laboratory requisition form with full clinical details.
8. Stain - Haematoxylin & Eosin stain or May - Grounwald Giemsa stain.

TECHNIQUE

The lesion should be fixed between two fingers and needle placed in the centre of nodule for small lesions (1-2 cms) and at periphery for larger lesions (2-4 cms). With suction maintained several passes (usually 4-6) of the needle are made through the tissue preferably with a slight change of angle during each pass.

The plunger is released to equalise the pressure, the needle is withdrawn and the contents is expelled on a series of glass slides, smeared, air dried and stained.

DISADVANTAGES

1. More likelihood of insufficient material.
2. To differentiate follicular adenoma from follicular carcinoma.

b. Core Needle Biopsy:

It produces a small cylinder of tissue which is submitted to histopathological examination. Also useful in diagnosing follicular carcinoma, lymphoma and anaplastic carcinoma. This procedure has a high risk of haemorrhage and injury to adjacent structures, hence not routinely done.

VII. Indirect laryngyoscopy

To find out functional status of vocal cords. This was done in all patients submitted for

surgery.

Selective venous Catheterisation

This is done for cases of suspicious recurrent / metastatic MTC. Hepatic and jugular veins are catheterised and a rise in calcitonin levels of sample, after pentagastrin stimulation is diagnostic.

GENETIC STUDIES

This is done in cases of MTC to look for RET protoncogene (Cur. 10) Point mutation and if positive family members

MANAGEMENT

Management opted for solitary thyroid nodule are

1. Surgical
2. Non-Surgical

SURGICAL

Advised after cytological impression

Indications:

1. All proven malignant nodules
2. All cytologically diagnosed follicular neoplasm
3. All lesions exhibiting an atypical pattern but non-diagnostic cellular pattern on cytology.
4. All papillary adenomas

5. Cystic lesion which recurred following aspiration; > 4 cm in size; complex in nature.
6. High suspicion of malignancy on clinical grounds even if cytology suggests benign disease and presence of high risk factors.

7. Hyperfunctioning nodule resulting in hyperthyroidism.
9. Obstructive symptoms, actual or potential
9. Patient anxiety
10. Cosmesis.

The standard surgical procedure in a benign single nodule should be Hemithyroidectomy. The line of resection should be extended to the junction of the isthmus & the contralateral lobe.

Patients with toxic nodule may be treated by surgery. Ideal procedure is Hemithyroidectomy. Prior to surgery patient should be brought to euthyroid state with propranolol and carbimazole. Surgical treatment is safe, certain and without morbidity. Patients with toxic nodule over the age of 45 years can be treated with radioiodine.

In patients with differentiated thyroid carcinoma, there are two schools of thought,

1. HEMI THYROIDECTOMY
2. TOTAL or NEAR TOTAL THYROIDECTOMY

The Treatment Objectives in differentiated thyroid cancer are

1. Eradicate primary disease
2. Reduce the incidence of local / distant recurrence
3. Facilitate the treatment of metastasis.
4. Cure the maximum number of patients
5. Achieve all of the above with minimal morbidity

In case of minimal papillary carinoma, and minimally invasive follicular carcinoma and the rare encapsulated papillary carcinoma, hemi thyroidectomy is the treatment. In all other cases of differentiated thyroid cancers total thyroidectomy is the procedure of choice.

There are several arguments for treatment of differentiated thyroid cancer by total / near total thyroidectomy.

i) Multifocal disease

ii) decreased incidence of local recurrence

iii) reduced risk of anaplasia in any residual tissue.

iv) facilitation of diagnosing unsuspected metastatic disease by radioactive iodine scanning or treatment with I^{131}.

V) Greater sensitivity of blood thyroglobulin levels to predict persistent / recurrent disease.

If total thyroidectomy is contemplated, it is not better than near total thyroidectomy in which 1 - 2 gms of normal thyroid tissue is preserved on the contralateral side to protect blood supply to one or more parathyroid glands.

If conservative surgery has been done TSH is suppressed by levothyroixine 0.2- 0.3 mg/ day. But TSH suppression is of doubtful value in Low risk patients.

In preparing patients for isotope scanning, T_4 is stopped 8 weeks before and T_3 is used for the first 6 weeks and stopped only 2 weeks before so that the patient will not develop thyroid insufficiency. A low iodine diet is also recommended during those 2 weeks.

If lymphnodes are affected by secondary deposits in cases of papillary carcinoma or MTC and if a nodule of MTC is > 2 cm in size, modified neck dissection is performed on the ipsilateral side. Routine central neck node dissection is done for Hurthle cell carcinoma and MTC and in cases of involved central nodes bilateral neck dissection should be done.

If distant metastasis are found, they are treated with large doses of '~'I. The alternative

is TSH suppression with T_3.

In patients with medullary carcinoma the treatment of choice is total thyroidectomy with central neck node dissection and T_3 replacement therapy. Close relatives are screened by estimating serum calcitonin in both basal and after pentagastrmn or calcium. If rise in serum calcitonin is observed, prophylactic thyroidectomy is done. Phaeochromocytoma should be excluded before surgeiy, Screening of family members with RET protooncogene point mutation has replaced the provocation tests.

In case of anaplastic carcinoma, total thyroidectomy with modified neck dissection is treatment of choice but in almost all patients it is not resectable. Isthmusectomy is done to decompress trachea and to obtain tissue for histology. External irradiation should be given in all cases for palliation of pain and dyspnea. Chemotherapy with adriamycin or adriamycin, chlorambucil and vincristine combination are advised.

In case of lymphoma, radical surgery is unnecessary. Once the diagnosis is established by biopsy, isthmusectomy is done for tracheal decompression. Lymphoma responds well to radio therapy.

THYROIDECTOMY PROCEDURE[29]

For Hemi thyroidectomy

1. Patient in supine position, neck extended with the help of a sandbag placed between the shoulders and rotation of the head is avoided by keeping the head on a ring.
2. A transverse collar incision is made about two finger breadth above the clavicle.

3. Elevation of upper & lower flaps in the plane between platsyma and deep cervical fascia.
4. Vertically incise the deep cervical fascia in the midline.
5. Vertically split infrahyoid muscles.
6. Ligate and divide middle thyroid vein.
7. Ligate and divide superior thyroid pedicle
8. Inferior thyroid artery to be ligated incontinuity away from the gland.
9. The thyroid isthmus is clamped at the junction with contralateral lobe and divided.

For total tyroidectomy:

The same technique to be followed on contralateral side also. The parathyroids are carefully separated and left insitu.

NON SURGICAL MANAGEMENT

Thyroid surgery, even in experienced hands, is associated with definite morbidity and should not be undertaken lightly.

When the question of malignancy within a solitary thyroid nodule has been eliminated by FNAC and in the absence of obstructive symptom, it is reasonable to offer the patient a conservative line of management.

Review the patient after 6 months, carry out a full cervical examination and repeat the FNAC. Provided there is no clinical suspicion of cancer and the cytology again is unequivocally benign, the individual is seen on an annual basis for re examination and further

FNAC.

Suppressive dose of exogenous T_4 to inhibit further growth of solitary thyroid nodule is a controversial question.

ASTWOOD[6] et al, Celani et al 1990, reported successful reduction in size of nodules but other workers, in equally well documented reports, draw the contrary conclusion (Reverter et al 1992)

OBSERVATION

PREVALENCE OF SOLITARY THYROID. NODULE

TABLE :1

No. of Thyroid Cases Admitted	Solitary Thyroid Nodules	Percentage
390	75	19.2

Solitary thyroid nodule represents thyroid pathology in about 19.2% of case.

Out of 75 patients, 65 were females and 10 were males. This gives a Male:Female ratio = 1:5. Solitary thyroid nodule is *5* times more common in women. In C.F.Nagori[22] **22** series the male female ratio was 1:3.5

TABLE 2

SEX DISTRIBUTION

Sex	No. of Patients	percentage
Female	65	86.7%
Male	10	13.3%

This distribution is in accordance with most of the reported series in our country and else where.

Considering the total number of admission of any thyroid swelling the female incidence is more partly because of increased prevalence and partly because of increased cosmetic awareness among young females.

TABLE 3

AGE DISTRIBUTION

Age In years	No. of Patients	Percentage
Upto2O	8	11
21-30	27	36
31-40	22	29
41-50	14	18
51-60	2	3
6landAbove	1	1

In this study the youngest patient was 14 years old and the oldest was 65 years old. 80% of solitary nodules occurred during the age between 2 1-50 years. The highest incidence of 36% was recorded during the third decade of life.

TABLE 4

SYMPTOMS AND SIGNS

Symptoms & Signs	No. of Patients	Percentage
Swelling Thyroid region	75	100
Pain	6	8
Toxic Symptoms	2	2.6
Dyspnoea	3	4
Dysphagia	14	18.6
Sudden Increase in size	7	9.3
Regional Palpable Lymphnode	2	3
Hoarseness of voice	1	1.3
Hard consistency	4	5.3

All the patients had only single palpable nodule. Toxic symptoms were present in 2 patients. Clinical evidence of obstruction to airway or of the great veins of neck by a solitary thyroid nodule is rare. The presence of stridor, respiratory wheeze; engorgement of neck veins should be interpreted with caution and the possible existence of a second pathology with in the mediastinum or lungs should be considered.

Seven patients complained of a sudden increase in size; while hoarseness of voice was present, only in one patient. On examination the only finding was hard consistency in 4 cases.

In this study, 2 patients had regional lymphs node enlargement; which on FNAC proved to be secondary deposits from papillary carcinoma. 14 patients had difficulty in swallowing and 6 patients, pain over the swelling. 3 patients had difficulty in breathing, which was mostly uncharacteristic, neither exertional nor positional.

TABLE 5

HORMONAL STATUS (CLINICAL)

Hormonal Status	Total No. of Patients	percentage
Euthyroid	73	97
Hypothyroid	2	3
Hyperthyroid	-	-

Most of our patients were clinically in Euthyroid status. Only 2 patients came with toxic symptoms.

DIAGNOSTIC WORK UP

In this study the following investigations were done in included Urine analysis,. Blood urea, Blood sugar, serum radiograph of Neck, IDL scopy chest radiogram and fine needle aspiration cytology.

Ultrasound and CT Scan were done in few cases. Serum T_3, T_4 and TSH estimation were done in two patients admitted with toxic symptoms and confirmed toxicity. USG was done in a few patients suspected to have thyroid cysts, while CT scan, was done in a patient with extensive neck secondaries.

Radio nucleotide scanning was not done for any of the patients due to the non-availability of the facility in our hospital.

Fine Needle Aspiration Cytology represents a reliable method of providing a tissue diagnosis and is the investigation of choice for solitary thyroid nodule.

In this study FNAC was a very dependable and an easy investigation without complications.

TABLE 6

FNAC REPORT

S.No	FNAC Report	No. of Patients
1	Follicular Neoplasm	34
2	Nodular Goitre	30
3	Papillary Carcinoma	4
4	Hashimoto's Thyroidits	1
5	Thyroid cyst	1
6	No Report Possible	*5*

Amongst the FNAC reports, follicular neoplasm was the commonest to be reported with the inability to identify vascular/capsular invasion. Adenomatous goitre, presenting as a solitary nodule was next commonest eventuality. 4 cases were reported as papillary carcinoma with two of them showing deposits in the neck nodes. No cases of MTC / Hurthel cell carcinoma were reported in our series. No report was possible in *5* cases.

TABLE *7*

MANAGEMENT GIVEN

S.No.	Management Given	No. of Patients
1	Hemithyroidectomy	62
2	Subtotal Thyroidectomy	4
3	Near Total Thyroidectomy	1
4	Total Thyroidectomy with block dissection	2
5	Total Thyroidectomy without block dissection	1
6	Conservative & follow up	3
7	Not willing for Surgery	2
Total		75

Out of 75 patients, 70 were submitted for surgery with below mentioned indications. 2 patients were given conservative line of management because of Ischaemic heart disease. One another patient with Hashimoto's thyroditis also was put on conservative treatment. 2 patients were not willing for surgery. These patients were advised regular follow up, on a half yearly basis for re-examinations and repeat FNAC. Repeat FNAC was done in 2 of these patients and were reported as benign.

Provided there is no clinical suspicion of cancer and the cytology is again unequivocally benign, the individual is seen on an annual basis for re-examination and further FNAC (RUSSEL).

TABLE 8

INDICATIONS FOR SURGERY

S.No	Indications for Surgery	No. of Patients
1	Cytology proven Malignancy	4
2	Cytology diagnosis as Follicular neoplasm	34
3	Clinical Suspicion of Malignancy with Benign cytology	1
4	Thyroid Cyst	1
5	Patient anxiety & cosmesis	30
	Total	70

This study includes two cases of solitary thyroid module with hyperthyroidism with benign cytology report. For these patients hemithyroidectomy was done after preparation with antithyroid drugs, on the assumption that the solitary nodule is the overactive tissue, since Radioisotope scan was not available to study the functional status of the nodule and these patients had no recurrence of thyrotoxicosis.

Total thyroidectomy was done for three patients of papillary carcinoma with neck node dissection (FND) in two patients, whereas neck node dissection was not done in 1 case.

Near total thyroidectomy was done for a patient with papillary carcinoma leaving behind a strip of tissue on the side other than the nodule.

Sub-total thyroidectomy was done for 4 patients who had nodules on contralateral lobe preoperatively.

Hemi-thyroidectomy, the standard surgical procedure for solitary thyroid nodule was done in 62 patients i.e., about 88% of patients who underwent surgery.

Surgery was done in a patient with an inconclusive FNAC report, based on clinical suspicion of malignancy. All resected specimens were submitted for histopathological examination.

TABLE 9

HISTOPATHOLOGICAL REPORT

HPE REPORT	No. of Patients	Percentage
CARCINOMA: Papillary Carcinoma and Follicular variant of papillary carcinoma Follicular carcinoma.	8 6 2	11.4
Follicular Adenoma	30	43
Nodular Goitre	28	40
Thyroiditis Hashimoto's	2	2.8
Thyroid Cyst	2	2.8
Total	70	

Histology proven malignancy in this series of study of solitary thyroid nodule is 11.4%., of which 75% (6 cases) were of papillary carcinoma and the rest 25% (2 cases) were of follicular carcinoma types. Of these, four cases were diagnosed preoperatively and were offered the confirmative treatment the rest four cases were diagnosed only on HPE reporting and then underwent completion total thyroidectomy without neck resection. All these patients are under regular follow-up with suppressive doses of thyroxine.

DISCUSSION

The Incidence of thyroid cancer in patients with a solitary thyroid nodule.

Study by Kendall & Condon l969[17]}

Pnarras et al 1972} 11-20%

Study by Cohn F J Russel at Royal Victoria}

Hospital, BELFAST., U.K.} 13%.

Study at Coimbatore Medical College Hospital

Coimbatore 2003-2005 11.4%

This compares well with the other international studies.

In our study 40% of solitary nodule in males proved to be malignant whereas in females only about 6% of the solitary nodules harboured malignancy.

TABLE 10.
AGE AND SEX DISTRIBUTION OF BENIGN AND MALIGNANT NODULE

Age in Years	Males			Females		
	Benign	Malignant	Total	Benign	Malignant	Total
Upto 20	1	1	2	10	2	12
21-30	1	0	1	22	0	22
3 1-40	1	0	1	15	1	16
41-50	2	2	4	6	0	6
51-60	1	1	2	2	0	2
61 and above	0	0	0	1	1	2
Total	6	4	10	*56*	4	60

According to Matheson 1986, the malignant potential of a nodule in a man is approximately three times that for a women of comparable age and in our study, the risk has been almost six times.

In males 75% of cancer occurred in more than 40 years age group.

Malignancy is more likely in a nodule in a child or a teenager or when a goitre develops in a patient aged 60 years or above (Hamming et al 1990, Caruso and Mazzaferri[9] 1991)

50% of thyroid cancers occurred in individuals under 40 years of age and of them 75% is papillary carcinoma. Fravenhofer[37] et al 1970 in his study of 125 cases of thyroid cancer found that 80% of thyroid cancers in individuals under 40 years of age was papillary carcinoma.

TABLE 11

HISTOLOGICALLY PROVEN MALIGNANCY

TYPE	No. OF PATIENTS	PERCENTAGE
PAPILLARY CARCINOMA	6	75
FOLLICULAR CARCINOMA	2	25
MEDULLARY CARCINOMA	0	0

No medullary carcinoma, anaplastic carcinoma and lymphoma was reported in our series.

The relative incidence of primary malignant tumours in our series is almost in accordance with most of the reported series (DUNHILL[36]).

In our study, 50% of the cases, all of them males, developed malignancy after 40 years, whereas in females, 75% of cases were younger than 40 years.

COMPARISON OF PRE OPERATIVE FNAC WITH POST OPERATIVE HISTOPATHOLOGICAL EXAMINATION:

Out of 70 cases operated 5 had different histopathology reports as compared to FNAC. If both FNAC & histopathology are benign or malignant they are considered true positive.

4 cytologicaly benign lesions were reported as malignant on histopathological examination. So FNAC was false negative in these cases.

TABLE 12

ACCURACY RATE OF FNAC

Result	True Positive case	False Negative	False Positive	Total
No. of Cases	66	4	0	70
Percentage	94	6	0	

In comparison on overall accuracy rate greater than 94% was achieved in the cytological diagnosis of a solitary nodule.

CANCER RISK IN FOLLICULAR NEOPLA'SM

The cytological appearances of follicular adenoma and follicular carcinoma are very similar. So a cytological diagnosis of follicular neoplasm is only possible, and confirmation of diagnosis of follicular carcinoma depends upon the visualisation of capillary & Vascular invasion in histopathological examination.

Although the Cancer risk is only 20%, CFJ RUSSEL, in common with others advises surgical resection of all solitary thyroid nodules reported as follicular neoplasm cytologically.

In this study, 34 cases were diagnosed as folhicular neoplasm cytologically and of these four were histologically malignant ..12% cancer risk.

SURGICAL PROCEDURES

CARCINOMA

We have done total thyroidectomy for three patients with or without neck node. dissection. All three were papillary carcinoma. Near total thyroidectomy was done for a case, also of papillary carcinoma.

Total Thyroidectomy is considered not only as a measure to reduce the recurrence rate of differentiated carcinoma but also as a means to prevent development of a highly malignant undifferentiated lesion. The percentage of radio iodine pick up can be increased several fold after total thyroidectomy and it also increases the sensitivity of thyroglobin as a post operative marker of residual / recurrent disease.

DISADVANTAGE

The risk of permanent hypoparathyroidsm or recurrent laryngeal nerve damage is high.

We have done near total thyroidectomy for one patient, a case of cytological proven papillary carcinoma, which was a small lesion (1.5 cm).

Near total thyroidectomy means leaving a fringe of thyroid tissue to preserve parathyroid.

Indications for near total thyroidectomy includes smaller lesions and better prognostic variants of papillary carcinoma thyroid.

Advantages of near total thyroidectomy are

1. Lesser incidence of permanent or transient hypo parathyroidism
2. Lesser incidence of recurrent laryngeal nerve palsy

Disadvantage of near total thyroidectomy are

1. Follow up is difficult
2. Remaining thyroid tissue has to ablated for control of metastasis.

Out of the four false negative patients (cytologically benign) all were treated with hemi-thyroidectomy. All these patients were taken up for completion thyroidectomy because they fell into the high risk group and they had an uneventful post operative period and follow up.

Ipsilateral lobectomy with isthmusectomy is what is required in all patients with differentiated carcinoma of favourable prognosis as given in AGES scoring system (HAY ID). The favourable prognostic factors are lesion less than 2 cm without cervical or distant

metastasis, age less than 40 years in males and less than 45 years in females.

So, the above patients were advised completion surgery with suppresive dose of thyroxine and regular follow-up.

The indications for isotope scanning after operation for differentiated cancer are.

1. Unresectable local recurrence
2. Metastatic disease
3. High risk patients and
4. Those with increase in serum Thyroglobulin level.

MALIGNANCY IN A TOXIC NODULE

Majority of cancers arise in hypo or cold thyroid nodules (ALDERSON et al 1976 COX et al 1991). The possibility of malignancy occurring with in a hot nodule is rare.

In our study, two patients with clinical toxicity were reported as follicular neoplasm cytologically and as folhicular adenoma histopathologically.

ADENOMA

Out of the 70 cases operated 30 cases were histolopathologically reported as adenoma. Most of them were macrofollicular adenoma. Hemithyroidectomy was done for all the patients.

Adenoma thyroid commonly occurred in the 3rd decade in this series of study.

NODULAR GOITRE

40% of operated cases were diagnosed as nodular goitre, hemithyroidectomy was done for most of them.

4 patients had nodules in the contra lateral lobe also, which were revealed peroperatively, hence sub-total thyroidectomy was done.

TABLE 13

ADENOMA AND NODULAR GOITRE HISTORICAL COMPARISON

Adenoma	Nodular Goitre
Usually single	Usually multiple nodules
Completely encapsulated	Partly encapsulated or unencapsulated
Compress the surrounding thyroid tissue	Doesn't compress surrounding thyroid tissue.
Compared of fairly uniform follicles smaller than rest of thyroid tissue	Heterogenous appearance often with larger follicles.
Degenerative changes uncommon	Hyperplastic follicles with focal haemorrhages, scarring, calcification and micro cyst formation.

OUT COME OF THERAPY

Complications

Out of the 70 patients operated, two developed features of hypocalcaemia in the immediate post operative period and were revived with intravenous, calcium gluconate and with no need for oral calcium supplementation.

Two patients had sluggish movement of left vocal cord after total thyroidectomy and improved later.

Seven patients had post operative wound infection. We had no mortality during this study.

Table 14

COMPARISION

Study by Cohn FJ Russel FRCS At Royal Victoria Hospital Belfast .U.K. 61 patients operated for solitary thyroid nodule			Study at Coimbatore Medical College Hospital Coimbatore 70 patients operated for solitary thyroid nodule	
FNAC Pathological Diagnosis	Number of Patients	Percentage	Number of Patients	Percentage
Nodular Goitre	30	49	28	40
Follicular Adenoma	19	31	30	43
Malignancy	8	13	8	11.4
Hashimotos	3	*5*	2	2.8
Dequervains	1	2	-	-
Simple cyst	-	-	2	2.8

CONCLUSIONS

1. FNAC is the gold standard for evaluation of Solitary Thyroid Nodule with an accuracy of 94% in our study.

2. 11.4 percentage of Solitary Thyroid Nodule were Malignant

3. Solitary Thyroid Nodule in males have more malignancy risk than female.

4. Suspect malignancy at extremes of age. Malignancy potential of Solitary Thyroid Nodule after 6th decade is 50%.

5. 50 percentage of thyroid cancer occurred in patients under 40 years of age, of them 75% were papillary carcinoma.

6. A selective surgical policy should be practised to resect Solitary Thyroid Nodule

7. Hemi thyroidectomy is the minimum, surgical procedure for single nodule.

8. Cancer risk in follicular neoplasm is 12%

9. Patient being submitted to Thyroidectomy should be counselled preoperatiely with regard to the risk of recurrent Laryngeal nerve paralysis.

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