A DISSERTATION ON

# "EVALUATION OF A SCORING SYSTEM FOR PREDICTING THE RISK OF MALIGNANCY IN THYROID NODULES USING CLINICAL, LABORATORY AND SONOLOGICAL DATA"

Dissertation submitted to

**THE TAMIL NADU Dr.M.G.R.MEDICAL UNIVERISTY**

**CHENNAI**

with partial fulfilment of the regulations

for the Award of the degree

**M.S. (General Surgery)**

Branch –I


**INSTITUTE OF GENERAL SURGERY**,

**MADRAS MEDICAL COLLEGE ,**

**CHENNAI.**

**APRIL-2017**

# CERTIFICATE

This is to certify that the dissertation entitled "**EVALUATION OF A SCORING SYSTEM FOR PREDICTING THE RISK OF MALIGNANCY IN THYROID NODULES USING CLINICAL, LABORATORY AND SONOLOGICAL DATA**" is a bonafide original work of **Dr. S.SADHANA**, in partial fulfilment of the requirements for M.S.Branch–I (General Surgery) Examination of the Tamil Nadu Dr. M.G.R.Medical University to be held in APRIL 2017 under my guidance and supervision in 2015-16.

**Prof.Dr.R.A.PANDYARAJ M.S, FRCS**
Professor of General Surgery,
Guide and supervisor
Institute of General Surgery,
Madras Medical College,
Rajiv Gandhi Government
General Hospital
Chennai –600003.

**Prof.Dr.P.RAGUMANI M.S**
Director and Professor
Institute of General Surgery
Madras Medical College,
Rajiv Gandhi Government
General Hospital
Chennai - 600003

**Prof. Dr. M.K.MURALITHARAN M.S, M.Ch,**
Dean
Madras Medical College &
Rajiv Gandhi Government General Hospital,
Chennai-600003.

# DECLARATION

I hereby solemnly declare that the dissertation titled "**EVALUATION OF A SCORING SYSTEM FOR PREDICTING THE RISK OF MALIGNANCY IN THYROID NODULES USING CLINICAL, LABORATORY AND SONOLOGICAL DATA**" is done by me at Madras Medical College & Rajiv Gandhi Govt. General Hospital, Chennai during 2015-16 under the guidance and supervision of **Prof.Dr.R.A.PANDYARAJ, M.S. FRCS.** The dissertation is submitted to The Tamilnadu Dr.M.G.R. Medical University, Chennai towards the partial fulfillment of requirements for the award of M.S. Degree (Branch-I) in General Surgery.

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**Dr.S.SADHANA,**
Post Graduate student ,
M.S. General Surgery
Institute of General Surgery,
Madras Medical College,
Chennai-3.

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To
Dr.S.Sadhana
Post Graduate in MS(General Surgery)
Madras Medical College
Chennai 600 003

Dear Dr.S.Sadhana,

The Institutional Ethics Committee has considered your request and approved your study titled **"EVALUATION OF A SCORING SYSTEM FOR PREDICTING THE RISK OF MALIGNANCY IN THYROID NODULES USING CLINICAL, LABORATORY AND SONOLOGICAL DATA" - NO.10022016.**

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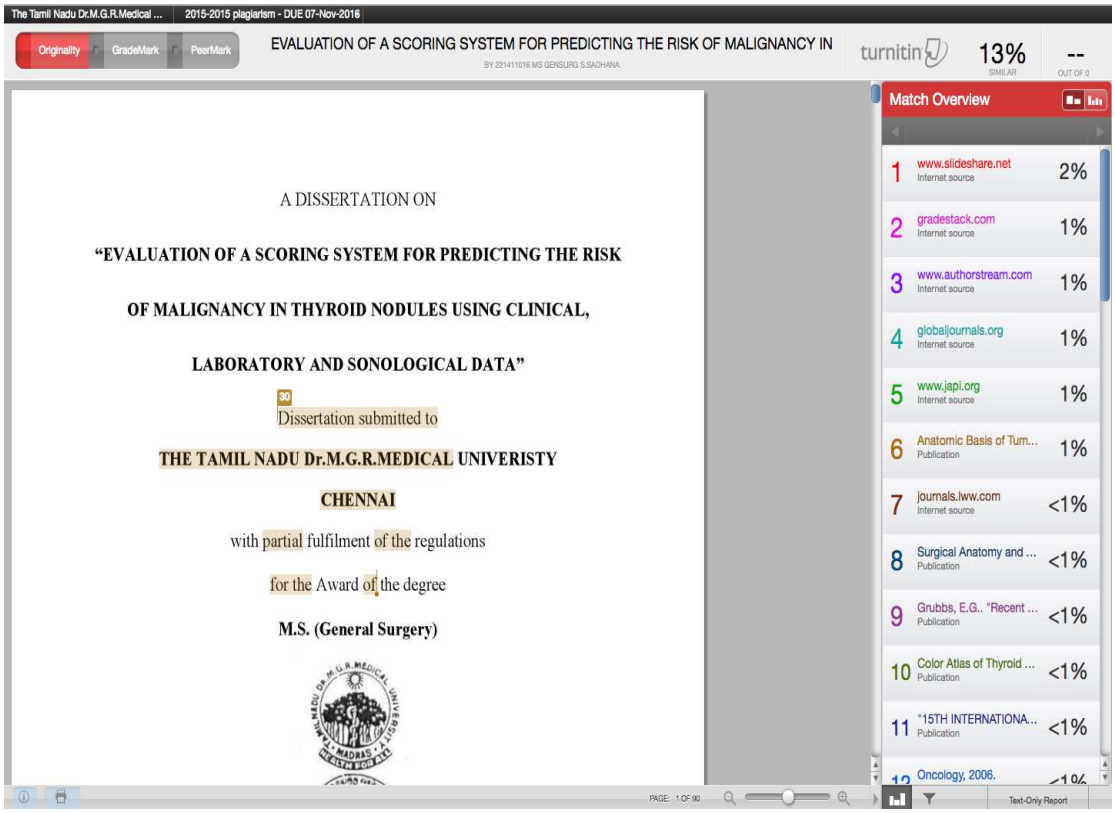
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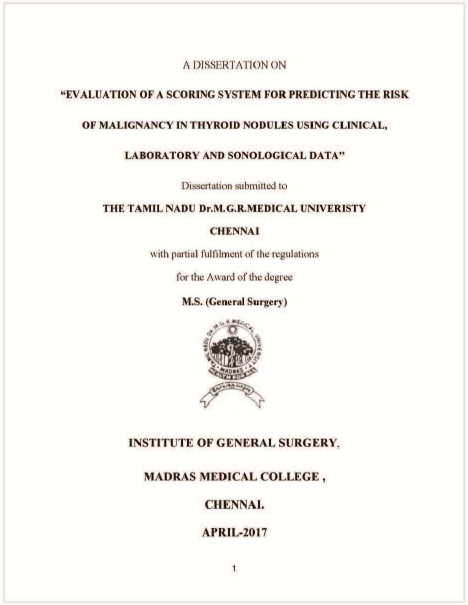

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## ACKNOWLEDGEMENT

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I am very grateful to **Prof.Dr.R.A.PANDYARAJ M.S, FRCS** Professor of Surgery, Institute of General Surgery, and my Assistant Professors **Dr.R.MANIVANNAN, Dr.J.SELVARAJ, Dr.D.MANIVANNAN, DR.D.VINODH** and **DR.G.VIMALA,** Madras Medical College & Rajiv Gandhi Government General Hospital who guided and trimmed my work throughout the period of my study.

I would like to express my deep sense of gratitude to **Prof. Zahir Hussain M.S, M.Ch,** Associate Professor, Department of Surgical Endocrinology, MMC for guiding me throughout the study.

I am extremely thankful to all the Members of the INSTITUTIONAL ETHICAL COMMITTEE for giving approval for my study. I also thank all the patients who were part of the study and my Professional colleagues for their support and criticisms.

With deep reverence, I salute my parents **Mr. V.U. Shankar** and **Mrs. K. Jayanthi**. I thank the almighty for blessing me with a wonderful family, to whom I dedicate this thesis and leave unsaid what they mean to me.

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# ABBREVIATIONS

| | | |
|---|---|---|
| ATC | : | Anaplastic Thyroid Carcinoma |
| CEA | : | Carcino Embryonic Antigen |
| EBRT | : | External Beam Radiotherapy |
| ELN | : | External Laryngeal Nerve |
| FNAC | : | Fine Needle Aspiration Cytology |
| FN | : | Follicular Neoplasm |
| MIT | : | Mono Iodo Tyrosine |
| MNG | : | Multi Nodular Goitre |
| MTC | : | Medullary Carcinoma Thyroid |
| RAI | : | Radio Active Iodine |
| RIA | : | Radio Iodine Ablation |
| RLN | : | Recurrent Laryngeal Nerve |
| T3 | : | Triiodothyronine |
| T4 | : | Tetraiodothyronine / Thyroxine |
| Tg | : | Thyroglobulin |
| TPO | : | Thyroid Peroxidase |
| TRH | : | Thyroid Releasing Hormone |
| TSH | : | Thyroid Stimulating Hormone |
| WDC | : | Well Differentiated Carcinoma |

# ABSTRACT

## INTRODUCTION

Many patients present to the surgical department with a thyroid nodule. However not all require surgery and only 5-6% of these are malignant. There are many methods to diagnose and predict malignancy in thyroid nodules. This study throws light on the usefulness of combining clinical, radiological and laboratory investigations into a single scoring system which is used to predict the risk of malignancy in thyroid nodules thereby helping the surgeon to make appropriate decisions regarding the operative management and follow up of the patient.

## AIMS AND OBJECTIVES

To evaluate a scoring system using clinical, laboratory and sonological data for predicting the risk of malignancy in patients with thyroid nodules, in a tertiary care centre in South India, which caters mostly for an economically underprivileged population.

## MATERIALS AND METHODS

This prospective observational study involved 50 patients admitted in MMC, Chennai with thyroid nodules. Analysis of a scoring system was done which combined clinical findings, radiological features and laboratory findings such as TSH level and FNAC report. The final scores

were compared with the post-operative histopathology of the patient and the risk of malignancy was predicted.

## OBSERVATION AND RESULTS

The scoring system had a maximum score of 26. The observed score ranged from 3 to 19. The mean score was 11. All the malignant cases observed in our study had a score greater than 11. The incidence of thyroid carcinoma for scores of 1 to 11 was 0%, 12 to 13 was 20%, 14 to 18 was 75% and ≥19 was 100%. The average risk of malignancy for a score ≤11 was 0% and for a score >11 was 54.166%.The sensitivity and specificity of the scoring system was 70.2% and 100% respectively.The positive and negative predictive value for the scoring system was 100% and 43.83% respectively.The greater risk of malignancy demonstrated for patients above a score of 11 was statistically significant ($p<0.0001$, $\chi^2 = 14.965$, df = 1). The risk of malignancy increased with increasing scores and was found to be 100% for a score ≥16.

## CONCLUSION

This scoring system has proved to be accurate in predicting the risk of malignancy in patients with thyroid nodules by combining various parameters derived from the patient's history, clinical examination and simple, cost-effective investigations like thyroid function test, ultrasonogram and FNAC. Each of these factors has variable reliability,

but their combination has proven to be a better predictor of malignancy. It can be routinely introduced in every hospital for pre-operative assessment of patients presenting with thyroid nodules, thus helping the surgeon to make rational and individualized decision while treating such patients.

# CHAPTER – 1

# INTRODUCTION

# INTRODUCTION

## 1. BACKGROUND

The incidence of thyroid nodules is on the rise and so is the incidence of thyroid malignancy. One of the greatest challenges for a clinician is the evaluation and follow-up of patients presenting with thyroid nodules. It is essential to identify the patients harboring a malignant disease and those having a benign lesion.

Several clinical characteristics, laboratory investigations and imaging modalities have been associated with the risk of malignancy in thyroid nodules[1]. These data have been integrated into various scoring systems. An ideal scoring system would reduce the need for costly imaging and unwanted exposure and at the same time increase the precision of decision making.

In our study we have put together a scoring system using clinical, laboratory and radiological data for evaluating the risk of malignancy in thyroid nodules. These risk factors have been analyzed in various other studies and found to have specific predictive value for malignancy[2]. The aim of our study is to evaluate this scoring system for predicting the risk of malignancy.

## 2. OBJECTIVES

1. To evaluate a scoring system for predicting the risk of malignancy in thyroid nodules using clinical, laboratory and sonological data.
2. To study the risk factors having high predictive value.

# CHAPTER - 2

# REVIEW OF LITERATURE

## 2.1 HISTORY[3,4,5]

The history of thyroid diseases can be traced back to ancient times. **Celsus and Galen** described goiters ( Latin: *guttur* = throat ) in 1st century A.D.

**Thomas Wharton** (1656) coined the term thyroid gland (Greek :*thyreoeides* = shield ) because of its appearance like a shield protecting the trachea.

**Andrea Vesalius** (1514 – 1564) coined the term "*glandulaelaryngis* " in his book De HumaniCorporisFabrica.

**Lorenz Heister** of Germany first described the surgery for removal of a thyroid.

**AnitonWolfler**was the first surgeon to describe the recurrent laryngeal nerve during thyroidectomy.

**Theodor Billroth** (1892 – 1894) and **Theodor Kocher** (1849 – 1917) were eminent surgeons who performed thyroid surgeries in the 19th century. Kocher became a Nobel laureate in 1909, being recognized for his work.

**IvarSandstrom** (1887) of Sweden discovered parathyroids and described their anatomy and blood supply.

**C. H.Mayo** of USA had tremendous experience in thyroid surgery. Reports from the Mayo clinic had been an important factor in

disseminating anunderstanding of the surgical technique and operative difficulties, which, in turn, greatly improved thyroid surgery.

**William Halstead** (1852 – 1922) of USA stressed the importance of preservation of parathyroids during thyroid surgery.

**Martin and Ellis** (1930) first described FNAC of thyroid.

**Duffy et al** (1950) studied relationship of papillary carcinoma of thyroid and neck irradiation in childhood.

**Hazard et al**, in 1950, discovered medullary carcinoma of thyroid.

**Sipple**(1960) observed that medullary carcinoma of thyroid was associated with pheochromocytoma.

Development in molecular medicine in the 1980s has provided major insight into the impact of genetic mutations leading eventually to thyroid carcinomas. This lead to the introduction of different surgical strategies.

## 2.2 ANATOMY OF THYROID GLAND[6]

The thyroid gland is butterfly shaped wit two lateral lobes, an isthmus, and occasionally a pyramidal lobe. it is brownish in color. On palpation, it is firm in consistency. It is located posterior to the strap muscles of the neck.10 percent of population may not have the isthumusand the pyramidal lobe is present only in 50 percent. The thyroid gland normally extends from C5 to T1 vertebra.

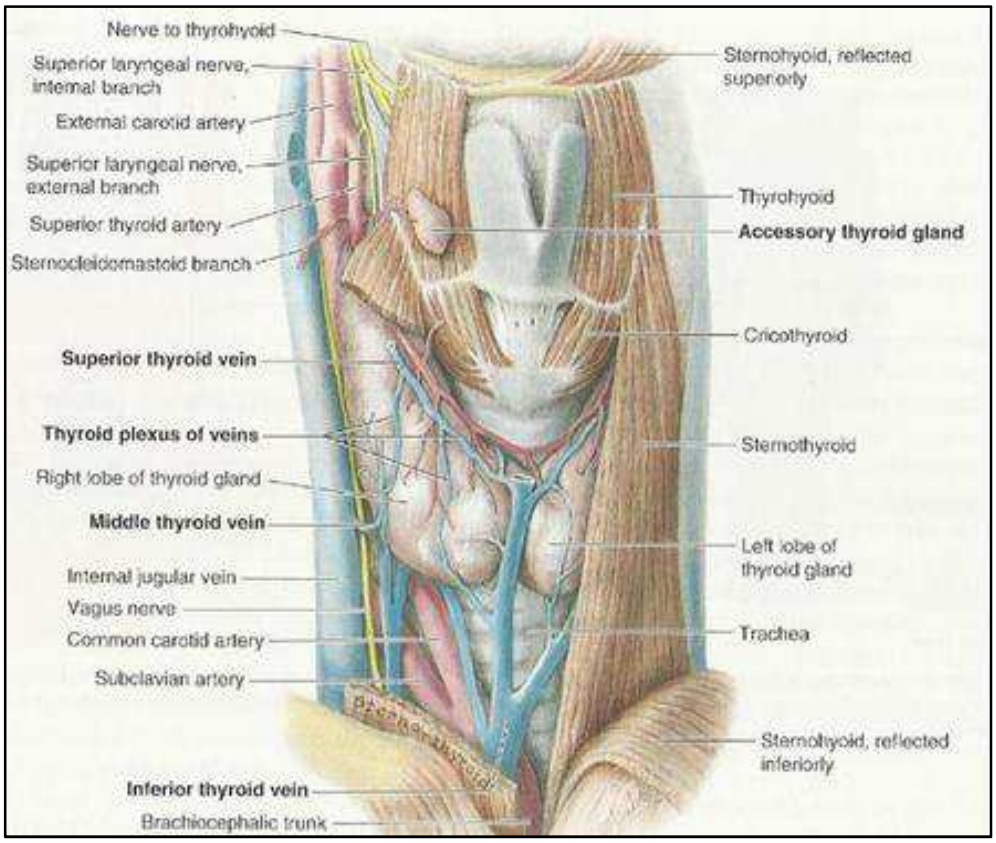



***Fig 1: Anatomy of thyroid gland***

The normal thyroid gland weighs about 30 g in the adult. The dimension of each lobe is about 5x3x2 cm. The isthmus connecting the

two lobes is about 1.3 cm in breadth. The lobes have a broad lower portion and a relatively conical apex.

## CAPSULE OF THE THYROID GLAND

The **true capsule** of the thyroid, continues with the septa, and makes up the stroma of the gland.

The **false capsule** lies outside the true capsule and is a derivative of the pre-tracheal layer of deep cervical fascia. It is thick anteriorly and laterally; posteriorly it becomes thinned out, allowing the gland to expand posteriorly. The false capsule is retained with the gland during thyroidectomy. The **ligaments of Berry** are thickened portions of the pre-tracheal fascia, which attach the gland to the cricoid cartilage.

## PARATHYROID GLANDS

Normal parathyroid glands weigh 30 to 50 mg and are approximately the size of a grain of rice (3 to 5 mm). The color, texture, and appearance of parathyroid glands vary considerably, ranging from golden to reddish brown and becoming a more pale yellow as the fat content increases.

The superior parathyroid glands are normally situated on the postero-medial surface of middle to superior thyroid lobe, near the trachea-esophageal groove. They reside under the superficial fascia of the

thyroid, posterior to the recurrent laryngeal nerve (RLN). When a tubercle of Zuckerkandl of the thyroid lobe is present, these glands are often found posteromedial to the tubercle. They are found between the two capsules.

Inferior parathyroid glands usually lie just under the lower part ofthyroid lobe and anterior to RLN. They may be between the two capsules or within thesubstance of the gland or on the surface of the false capsule.

## VASCULAR SUPPLY

The thyroid gland is supplied by the external carotid system via the superior thyroid artery and the subclavian system via the inferior thyroid artery. Sometimes there may be an additional artery, the thyroid ima artery arising from the brachiocephalic artery.

## SUPERIOR THYROID ARTERY

The superior thyroid artery is a branch of the external carotid artery. It reaches the superior pole of the gland by passing downwards and laterally. The artery runs close to the external laryngeal nerve in a part of its course. At the superior pole of the gland, it divides into an anterior and a posterior branch. The superior parathyroid gland is supplied by the posterior branch.

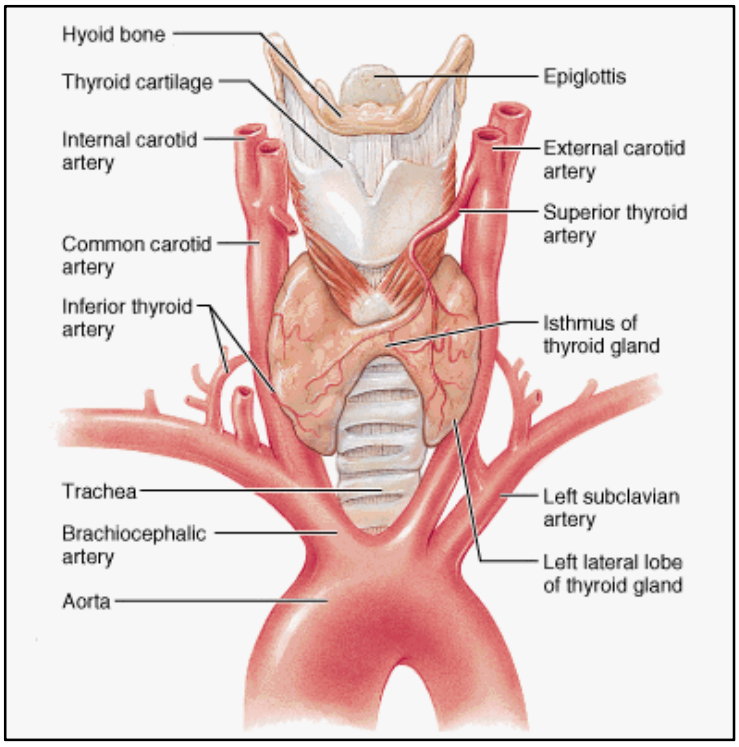



***Fig 2: Blood supply of thyroid gland***

## INFERIOR THYROID ARTERY

It originates from thyro-cervical trunk. In about 15% of cases, it arises directly from the sub-clavian artery. It pierces the pre-vertebral fascia and splits into 2 or more branches as it crosses the RLN. The recurrent laryngeal nerve has variable relations to the branches of the artery. One of the lower branches of the artery supplies the inferior parathyroid. The posterior part of the gland is supplied by the upper branch which ends by joining the descending branch of superior thyroid artery.

## THYROID-IMA ARTERY

The thyroid-ima artery originates from the brachiocephalic artery or directly the aortic arch. It occurs in about 10 percent of individuals, according to Montgomery.

## VENOUS DRAINAGE

Three pairs of veins - the superior, middle and inferior thyroid veins, drain the thyroid gland.

## SUPERIOR THYROID VEIN

It emerges from the upper pole of the thyroid, passes across the common carotid artery and omo-hyoid muscle and enters the internal jugular vein.

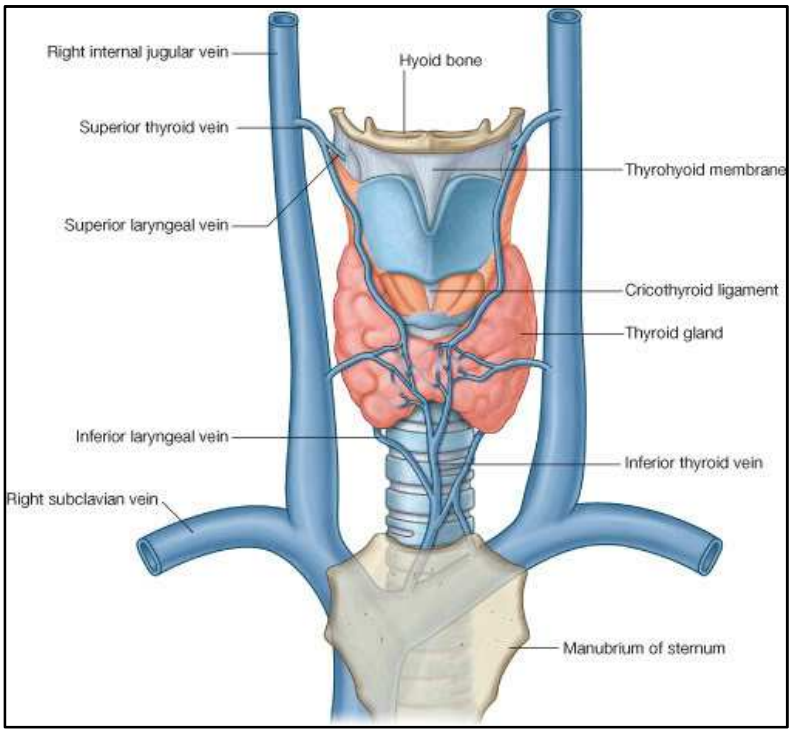



***Fig 3: Venous drainage of thyroid gland***

## MIDDLE THYROID VEIN

The middle thyroid vein arises on the lateral surface of the gland. It does not have an accompanying artery. It travels across the common carotid artery and opens into the internal jugular vein.

## INFERIOR THYROID VEIN

It is the largest vein arising from the thyroid.It drains into the brachiocephalic vein. The thyroid-ima vein is a common trunk formed occasionally by the union of right and left veins.

## FOURTH THYROID VEIN OF KOCHER

It may emerge between the middle and the inferior thyroid veins and drains into the internal jugular vein.

## LYMPHATIC DRAINAGE

The thyroid gland has an extensive supply of lymphatics. The lymphatic drainage can be divided into four zones (Hollinshead).

## 1. MEDIASTINAL SUPERIOR DRAINAGE

From the upper part of the isthumus and the inner margins of the lobes. Drains primarily into the digastric lymph nodes and into the pre-laryngeal (Delphian) nodes just above the isthumus. Secondarily it may drain into the upper jugular nodes or into pre-tracheal.

## 2. MEDIAN INFERIOR DRAINAGE

Lymphatics draining the inferior part of the isthumus and the infero-medial portions of the lobes. They drain into the pre-tracheal and brachiocephalic nodes.

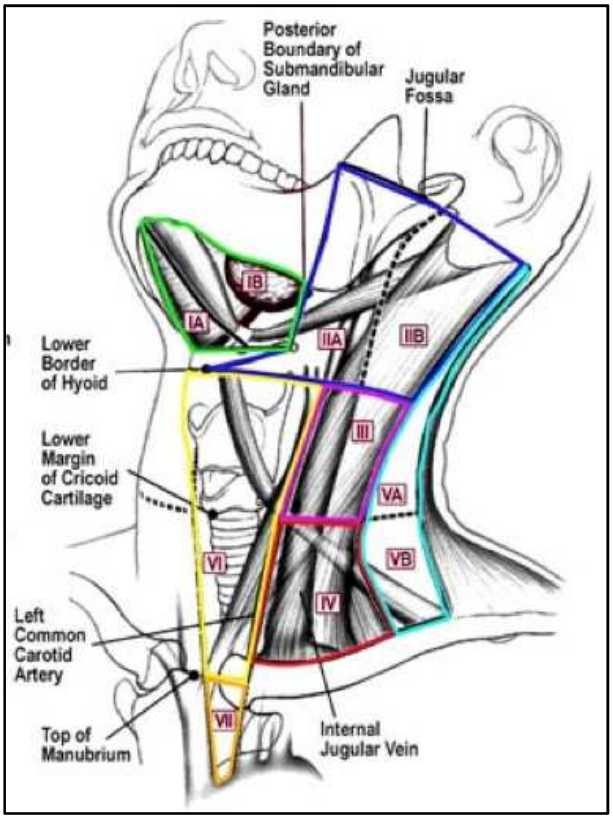



***Fig 4: Lymph node levels in the neck***

## 3. RIGHT AND LEFT LATERAL DRAINAGE

Superiorly follow superior thyroid artery and vein. Inferiorly they follow the inferior thyroid artery.

## 4. POSTERIOR DRAINAGE

Drains into the retropharyngeal nodes.

The thyroid lymphatics drain first into the level-VI nodes (central

compartment) containing the pre-tracheal and para-tracheal nodes and subsequently into the level II-IV nodes (lateral jugular).

## NERVE SUPPLY

The thyroid gland is supplied by the sympathetic system from the cervical chain. But in thyroid surgery the recurrent and superior laryngeal nerves of the parasympathetic (vagus) system are of utmost importance.

## EXTERNAL LARYNGEAL NERVE

It is a branch of the Superior Laryngeal Nerve of Vagus. It passes deep to the sternothyroid, posterior and medial to the superior thyroid vessels. The nerve innervates the cricothyroid muscle. Cernea et al. stated that injury to this nerve would most likely cause a permanent voice change for professional vocalists. Fatigue, also, is common after injury

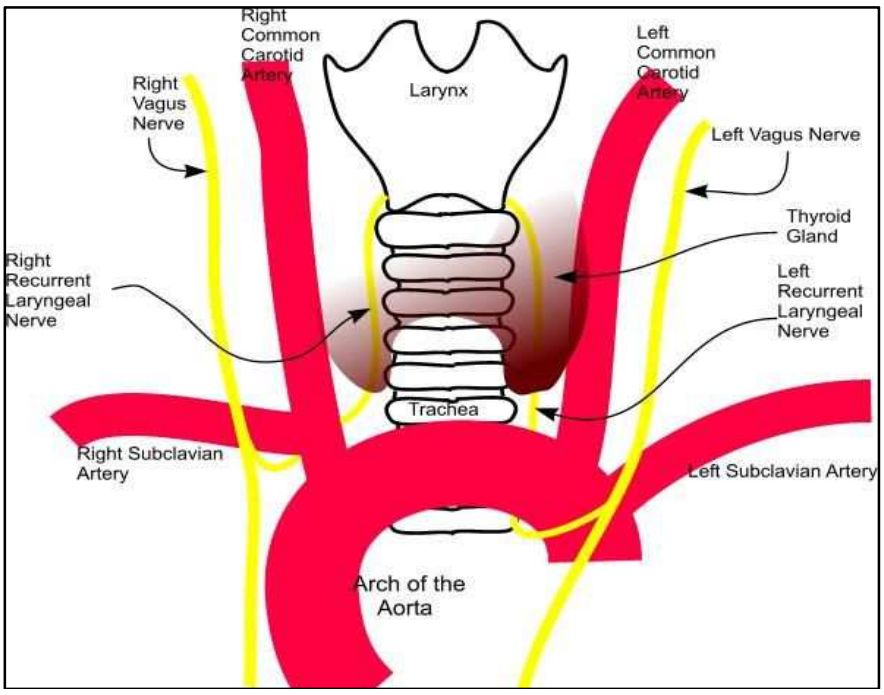



***Fig 5: Nerve supply of thyroid gland***

## RECURRENT LARYNGEAL NERVE

It is intimately related to the thyroid gland. They innervate all the intrinsic laryngeal muscles except cricothyroid. On the right side, it arises from the vagus as it crosses the right sub-clavian arteryand hooks around the subclavian artery and ascends in the trachea-esophageal groove. It courses behind the right lobe and enters the larynx behind the cricothyroid articulation.

The left recurrent nerve arises where the vagus nerve crosses the aortic arch. It winds around the ligamentum-arteriosum and aorta, and ascends similar to the right nerve. It is related to the inferior thyroid artery near the middle-third of the gland.

Exposing the nerve during surgery is a goodpractice. The nerve can be recognized where it enters the larynx just behind the inferior-cornu of the thyroid cartilage. If not found, a non-recurrent nerve ought to be looked for, particularly on the right. Pelizzo et al. advised that the best way to locate the recurrent laryngeal nerve during thyroidectomy is the ***Zuckerkandl'stuberculum***, which is located on the lateral portion of each of the thyroid lobes. It is the posterior-most portion of the lateral lobes at the level of the Berry’s ligament.

## EMBRYOLOGY[7]

An epithelial proliferation arises in the floor of the tongue at the foramen caecum which gives rise to the thyroid gland.Subsequently it descends as a bilobed diverticulum in front of the pharynx. The attachment to the tongue forms the thyroglossal duct. This duct usually vanishes by the 6$^{th}$ week. The gland descends in front of the hyoid bone, and reaches its final stationby the 7$^{th}$ week. The gland develops two lateral lobes connected by the isthmus.It starts functioning by the 3$^{rd}$ month. The cells of the ultimo-branchial body becomethe C (calcitonin) cells among the thyroid follicles.

## HISTOLOGY[6,7]

The thyroid capsule is a slender layer of connective tissue. From the capsule, several septa extend within the thyroid parenchyma, which is subdivided into several lobules. Epithelial cells (cuboidal or squamous) form the thyroid follicles; they are separated by thin connective stroma, which is rich in both lymphatic and blood vessels. There is a colloidal gelatinous collection in the center of the follicle. Each follicle has two types of cells: follicular and parafollicular cells, or C cells.

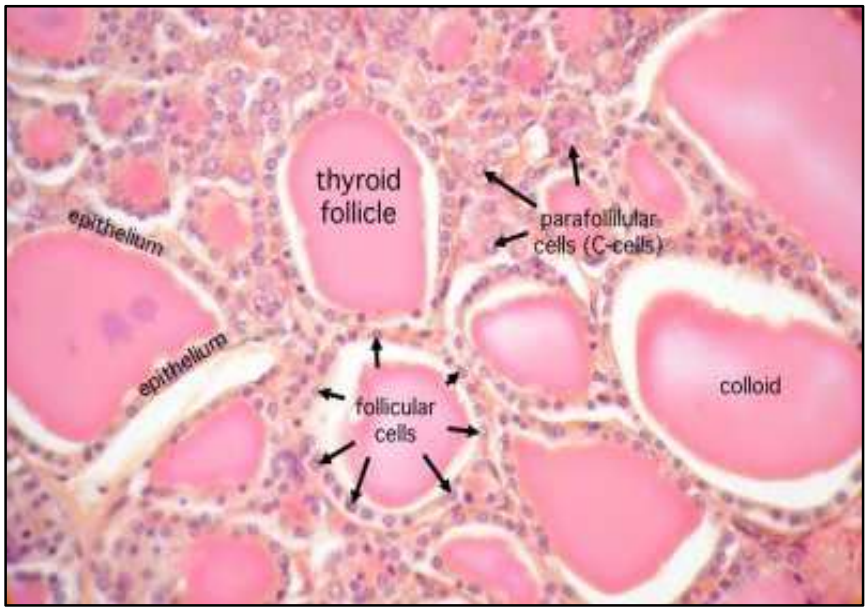



***Fig 6: Histology of thyroid follicle***

The follicular cells are responsible for the following actions: synthesis of thyroglobulin, iodination, storage of thyroglobulin, resorption of thyroglobulin, hydrolysis of thyroglobulin, and release of thyroid hormone into the blood and lymphatics. The parafollicular, or C cells, can be found in the connective stroma between the follicles or in the follicular epithelium. Characteristically, they contain several secretory granules.

## 2.3 PHYSIOLOGY OF THYROID GLAND[8,9]

The normal thyroid gland secretes three hormones – triiodothyronine (T3) and tetraiodothyronine (T4) from the follicular cells to normalize growth and development, body temperature and energy levels. Calcitonin the third hormone is produced by parafollicular cells and regulates calcium metabolism.

### THYROID HORMONE SYNTHESIS

Iodine in diet is converted to iodides which are utilized by the thyroid gland to synthesize thyroid hormones. Thyroglobulin (Tg) is a glycoprotein manufactured in the thyroid cells. By exocytosis, it is secreted into the colloid.

### STEPS

### 1. IODIDE TRAPPING

Iodide is actively transported across the basement membrane of the thyrocyte in an ATP dependent manner.

### 2. OXIDATION

Iodide is oxidizedinto iodine. The tyrosine residues on thyroglobulin become iodinated to form monoiodotyrosines (MIT) and diiodotyrosines (DIT). This step is catalyzed by thyroid peroxidase (TPO).

**3. COUPLING**

2 DIT molecules combine to form tetra-iodothyronine or thyroxine (T4). A DIT molecule joins with an MIT molecule to form 3,5,3'-triiodo-thyronine (T3) or 3,3',5'- triiodo-thyronine reverse (rT3).

**4.HYDROLYSIS**

Thyroglobulin undergoes hydrolytic breakdownto release free T3, T4,mono and di iodotyrosines.

**THYROID HORMONE RELEASE AND TRANSPORT**

In the euthyroid state, the thyroid gland produces most of T4 but only 20% of the total T3. Most of the T3 is produced by peripheral deiodination of T4 by 5'-mono-deiodinase. Some amount of T4 undergoes deiodination of inner ring to form rT3.

The hormones are carried in serum bound with proteins like T4-binding globulin, T4-binding pre-albumin and albumin.Only 0.02% is unbound and is the physiologically active form. T3 is more potent of the two thyroid hormones, although its circulating plasma level is much lower than that of T4. T3 is less tightly bound to plasma proteins than T4 so it enters tissues easily. It is three to four times more active than T4 per unit weight, with a half-life of one day compared to approximately seven days for T4.

## REGULATION OF THYROID HORMONES

The hypothalamic – pituitary-thyroid axis controls the secretion of hormones. The hypothalamus produces the thyrotropin-releasing-hormone(TRH). This in turnexcites the pituitary to discharge TSH or thyrotropin. TRH is transported to the pituitary by the porto-venous circulation.

## THYROID STIMULATING HORMONE (TSH)

It is a glycoprotein containing 211 aminoacids. It is secreted in a pulsatile manner from the anterior-pituitary gland. There are two subunits: the α-subunit is similarto the rest of the anterior-pituitary hormones; the β-subunit is exceptional to TSH. Once TSH binds to the receptor (TSH-R) on thyroid cells, it interacts with a 'G-protein', which in turn stimulates the synthesis of cyclic-adenosine-monophosphate (cAMP). This is thekeyhormone synthesizing pathway. The biological half-life of human TSH is about 60 minutes. It is degraded mostly in the kidneys and to a certain extent in the liver. The normal secretion rate is about 110 microgram/day. The average plasma level is 2 microgram/mL.

TSH secretion is regulated by a negative feedback loop. Its secretion is augmented by TRH and repressed by circulating fT4 and fT3 by a negative-feedback mechanism. Stress also inhibits TSH secretion. In experimental animals, it is decreased by warmth and increased by cold.

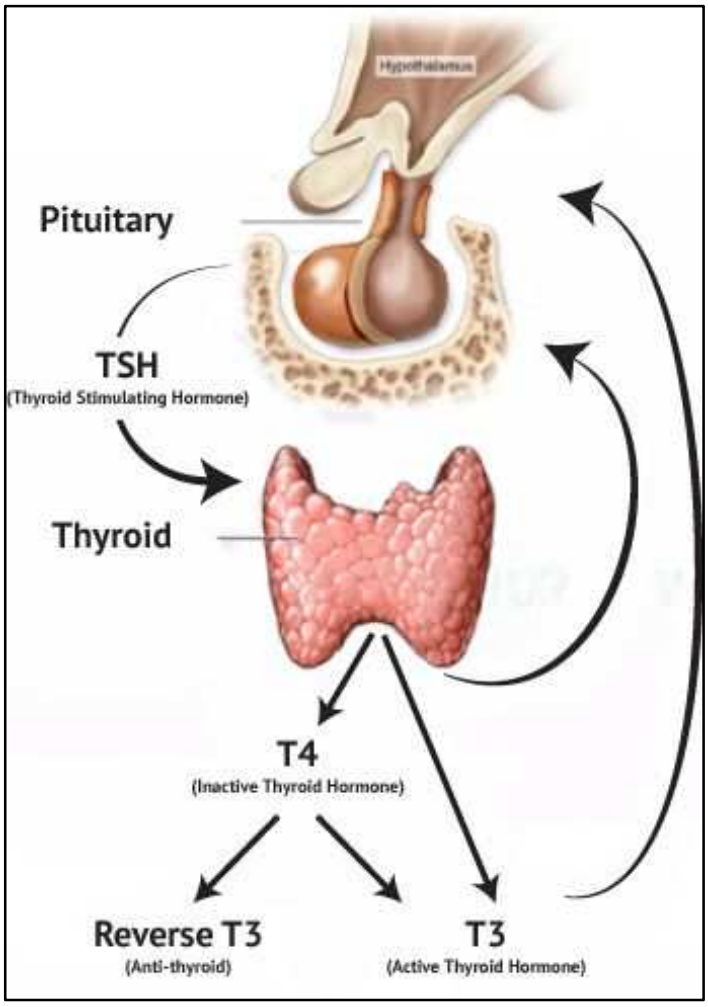



***Fig 7: Regulation of thyroid hormones***

Excessively large doses of iodide cause increased organification and termination of production. This is known as ***Wolf–Chaikoff effect.***

## 2.4 THYROID MALIGNANCIES[6,10,11]

Among the endocrine malignancies, thyroid malignancies are the commonest. They account for 94.5% of total new cases and 66% of all endocrine carcinoma related deaths. Majority of thyroid cancers present as nodules. The risk of development of malignancy in each thyroid nodule is 5-10% in the total population. The risk is higher for males and in the extremes of age. There is a 33-37% chance of malignancy in patients with history of childhood neck irradiation. A solitary-nodule has greater risk of malignancy (15-25%) than a multinodular goiter (1-6%). A history of rapid increase in size, breathlessness, difficulty in swallowing, hoarseness of voice is highly suspicious of malignancy.

**CLASSIFICATION OF THYROID MALIGNANCIES**

**PRIMARY**

1. Arising from the follicular epithelium
    a. Well differentiated (90%) – Papillary, Follicular
    b. Undifferentiated (1-2%) – Anaplastic
2. Arising from parafollicular cells (5-9%) – Medullary
3. Arising from lymphoid cells (1-3%) – Lymphoma
4. Arising from stromal cells (1%) – sarcomas

**SECONDARY**

Metastatic

## ETIOLOGY OF THYROID MALIGNANCY

### RADIATION EXPOSURE

Exposure to radiation is asignificant risk factor for development of well-differentiated thyroid tumors. The younger the age at exposure, the greater is the risk. The risk is proportional to the exposure dose (minimum dose of 10cGy). Latent period after childhood exposure is 3-5 years. Majority of cases develop between the second and third decade.

### SEX

Well-differentiated carcinomas are around two and a half times more common in women. The median age at which it is diagnosedis also earlier in females than in males.

### FAMILY HISTORY

There is a four to ten fold amplified risk of differentiated tumors in 1st degree relations.

### DIET

Iodine deficient diets lead to elevated TSH and may begoitrogenic. Excessive iodine consumption in seafood is associated with a higher incidence of papillary carcinoma.

## THYROID ONCOGENESIS[11]

Numerous tumor suppressor genes and oncogenes are implicated in thyroid oncogenesis. One of them is the RET proto-oncogene (chromosome 10) which codes a receptor - tyrosinekinase that binds several growthfactors. Germ-line mutations in the RET protooncogene predisposes to MEN2A, MEN2B and familial medullary thyroid cancers. The tyrosinekinase of RET fuses with other genes by re-arrangement. These products function as oncogenes and have been incriminated in the genesis of papillary cancer. BRAF mutations have been identified in40% papillary carcinomas. Mutated *RAS* oncogenes have been recognized in upto 40% of follicular adenomas/carcinomas, papillary and anaplastic cancers. Mutation of p53 tumor suppressor gene is common in undifferentiated thyroid carcinomas and carcinoma cell lines. The oncogene resulting from the union of the DNA-binding domain of transcription factor PAX8 gene with the PeroxisomeProliferator-Activated Receptor Gamma 1 (PPAR-y1) is known to play avital role in the oncogenesis of follicular cancer.

## PAPILLARY CARCINOMA

This carcinoma accounts for eighty to eighty-five percent of malignant thyroid carcinomas. It can present as

1. solitary painless nodule thyroid
2. solitary nodule with lymph node metastasis
3. lymph node metastasis with occult primary – Lateral aberrant thyroid

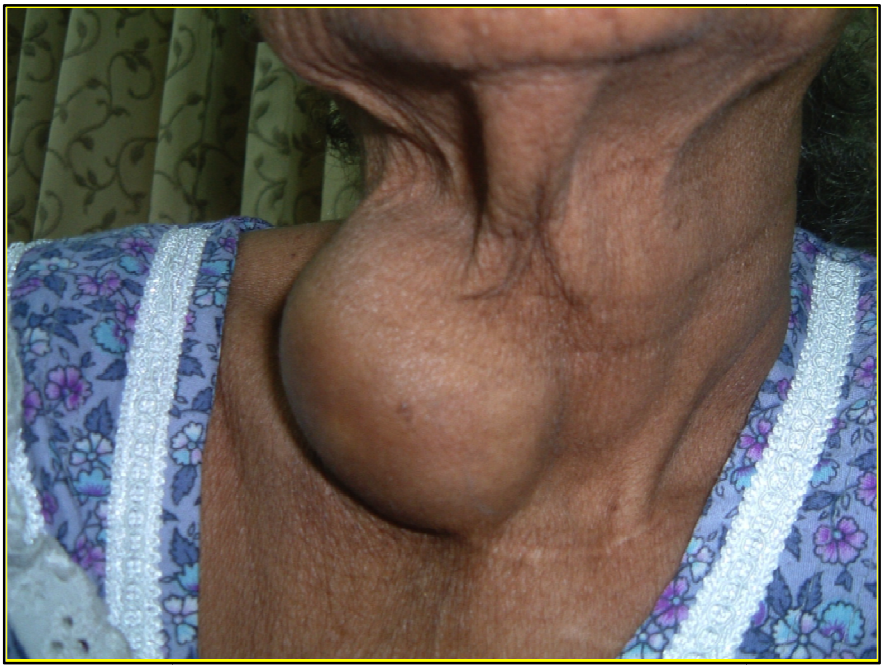


***Fig 8: patient presenting with thyroid nodule***

## PATHOLOGY

It is the commonest thyroid tumor in children as well as those exposed to ionizing radiation. There is a 2:1 female to male ratio.The patients usually present at thirty to forty years of age. A slowlygrowing painless mass in the neck is the most common presentation. Metastasis to

lymphnodes is very usual (80%) and may be one of the initial presenting features.

On gross examination, it is hard and appears whitish on cut-section. Histologically, they reveal papillary structures, mixed papillary with follicular pattern, or a purely follicular pattern (Follicular Variant). They contain cuboidal cells with abundant pale cytoplasm andclosely packed nuclei demonstrating “grooving”. There are intra-nuclear cytoplasmic inclusions called***Orphan Annie***nuclei which is characteristic. ***Psammoma bodies***, which are clumps of calcified sloughedcells are also present. Multifocality is common in papillary carcinoma.

Minimal/occult or microcarcinoma are tumor ≤1 cm in dimension, without localinvasion or lymphatic metastases.

## FOLLICULAR CARCINOMA

They comprise ten percent of thyroid carcinomas. They occurfrequently in iodine-insufficient regions. It can present as

1. solitary nodule
2. MNG
3. Distant metastasis

The female to male ratio is 3:1. They usually present at 50 years of age.Unlike papillary carcinomas, lymphnode metastasis occurs in 5% cases, whereas blood-borne metastasis occurs in 90% of cases. FNAC cannot distinguish benign follicular lesions from follicular carcinomas.

## PATHOLOGY

Follicular carcinomas are capsulated. Microscopically, it contains follicles,but the lumen may not contain colloid. Malignancy can be identified by the occurrence of capsular or vascular invasion. Minimally invasive carcinomas are encapsulated but have microscopic penetration into the capsule without invasion in to parenchyma. Tumors that are widely invasive, show penetration of large vessels or tumor capsule. In contrast to papillary carcinoma, follicular carcinoma is unifocal in origin.

## HURTLE CELL CARCINOMA

They account for 3% of all thyroid malignancies. Theyare considered a variation of follicular carcinoma. FNAC cannot be used for diagnosing Hurthle cell carcinoma as they are characterized by capsular and vascular invasion. They contain areas of eosinophilic cells which are laden with mitochondria derived from oxyphilic cells. They are more often multifocal.30% of tumors are bilateral. They usually do not take up RAI. Twenty-five percentage of them metastasize to local nodes. They have a higher mortalityrate of about twenty percent at ten years. Treatment includes a total thyroidectomy with neck dissection. It is radio resistant.

## MEDULLARY CARCINOMA

Parafollicular“C-cells” are the cells of origin. It has an incidence of 3-12% of thyroid cancers. There are two types of MTC namely sporadic form (60-70%) and familial form (30%). There are three distinct syndromes associated with familial MTC – MEN 2A, MEN 2B and Familial non-MEN MTC. These syndromes occur due to germ-line mutations in RET proto-oncogene.

## PATHOLOGY

Sporadic disease is usually associated with unilateral presentation. Multicentricity is found in familial disease. Ninety percent of familial patients have a bilateral presentation. Familial disease is also linked with “***C-cell hyperplasia***”, a pre-malignant lesion.

Histologically, the presence of ***amyloid*** is a diagnostic feature, but immunohistochemical staining for calcitonin isuniversally considered a diagnostic tumormarker.

The age of presentation is usually fifty to sixty years. Familial cases present at anearlier age.The usual presentation is a thyroid mass associated with palpable cervical lymph nodes (15-20%). Pain is more common in this tumor and local invasion may produce symptoms of compression of adjacent structures. Distant blood-borne metastasis to the

liver, bone and lung occurs later. Patients with extensive metastatic disease often develop paraneoplastic symptoms like diarrhea and about 2-4% of patients develop Cushing's syndrome due to ectopic production of ACTH.

**TREATMENT**

If it is associated with pheochromocytoma, this has to be operated first. The surgery of choice for patients with MTC is total thyroidectomy. A prophylactic bilateral level-V nodal dissection must be routinely done as the central group of nodes are involved early in the disease. If the central or lateral group of nodes are palpable, then a Modified Radical Neck Dissection is done. Patients havingunresectable residual tumor or recurrent tumor can be treated with externalbeam radiotherapy. Chemotherapy is not very effective.

## ANAPLASTIC CARCINOMA

It is a lethal malignancy with the worst prognosis of all thyroid malignancies. The patients usually survive only for four to five months after diagnosis. The mean age of diagnosis is the sixth and seventh decade with male to female ratio of 1:1.5. It usually develops due to de-differentiation of prior well differentiated carcinoma. Other organs of metastasis include bone and liver.

Microscopy shows cells with striking cytological atypia. The mitotic activity of the cells is high. Necrosis of tumor and vascular invasion isusual. 33% of cases show coexisting areas of well-differentiated cancer.

**CLINICAL FEATURES**

A rapidly growing neck mass is the usual presentation. Infiltration into the adjacent vital structuresis often present at diagnosis. Death occurs mainly due to loco-regional invasion leading to airway compromise.

**TREATMENT**

Survival after diagnosis is very poor. Radiotherapy has limited success. It is used to treat locally recurrent tumor. The most effective chemotherapeutic agent is doxorubicin.Doxorubicin with platinum is more efficient than monotherapy with doxorubicin alone.

## THYROID LYMPHOMA

Thyroid lymphoma is rare constituting <1% of all lymphomas. Majority are non-Hodgkin’s lymphoma of intermediate grade. Many are thought to be Mucosa Associated Lymphoid Tissue-omas (maltomas) showingplasmacytic differentiation. Most of the cases have cervical or mediastinal lymph nodes at presentation. Thyroid lymphomas have a

strong preponderance for females with a female to male ratio of 8:1. They present between the $6^{th}$ and $7^{th}$ decade of life. Symptoms include hoarseness, breathlessness with stridor or difficulty in swallowing. Patients may be hypothyroid with Hashimoto's thyroiditis. Treatment includes combination of surgery, EBRT and chemotherapy according to the histo-pathological type.

## METASTATIC CARCINOMA TO THYROID[12,13]

Comprises <1% of thyroid malignancies. Renal cell carcinoma is the most common primary responsible for twenty three percent cases. The other common primary sites are breast (16percent), lung (15percent), melanoma (5percent), colon (4.5percent) and larynx (4.5percent). Diagnosis is by FNAC. Treatment is mainly palliative. Surgery may be indicated in case of obstructive symptoms.

## 2.5 DIAGNOSTIC STUDIES

### LABORATORY INVESTIGATION[14]

### THYROID STIMULATING HORMONE (TSH)

Thyroid function tests can be used to diagnose asymptomatic thyroid dysfunction. TSH is routinely done if the thyroid nodule is more than one centimeter. A radio-isotope scan is indicated when the TSH is less than normal and this isassociated with a low risk of cancer. Thyroid cancers are infrequentlyassociated with thyrotoxicosis.Elevated TSH suggests hypothyroidism and isassociated with a greater risk of malignancy.

### THYROGLOBULIN (Tg)[8]

Serum thyroglobulin (Tg) is a highly specific marker in the follow-up of patients after initial treatment of thyroid cancer.Tg levels must be less than 2ng/mL while the patient is taking T4. If the patient is hypothyroid, it must be less than 5ng/mL. Thyroglobulin level >2ng/mL isindicative of residual thyroid tissue or metastatic deposits. Tg and antiTg anti-body levels are followed up at six month intervals in the beginning and then yearly until the patient is disease free. Rising titres of thyroglobulin or anti-Tg antibodies is highly suspicious of recurrence of the disease.

## CALCITONIN

The serum calcitonin level should be measured whenever there is a suspicion of medullary carcinoma. Patients with sporadic medullary carcinoma have a high baseline calcitonin level, but it is normal in thirty percent of patients with familial medullary carcinoma or multiple endocrine neoplasia (MEN) type 2. After curative surgery for MTC, serum calcitonin levels fall to undetectable levels over several weeks. If they remain elevated postoperatively, this is usually an indicator of residual cancer, either from local lymph node spread or from distant metastases. If previously undetectable or very low postoperative serum calcitonin levels are found to have increased, disease recurrence or spread is highly likely and further diagnostic evaluation is warranted.

## RADIOLOGICAL IMAGING[15]

## ULTRASOUND

Ultrasound imaging is central to the investigation of most thyroid nodules Ultrasound is commonly used to assist in FNAC. It can be used for monitoring patients who are managed conservatively. Ultrasound featuresthat are suggestive of malignancy are the presence of micro-calcifications, increased vascularity, irregular borders, hypoechogenicity and having a shape with height more than width on transverse view.

Patterns of sonographic features may be used to classify a given thyroid nodule as having high, intermediate, low, or very low suspicion for malignancy. When combined with the size of the nodule, these characteristics can be used to guide decisions to proceed with FNA biopsy. When a thyroid nodule is detected, it also is appropriate to assess the neck sonographically for pathologic adenopathy. If pathologic nodes are detected, biopsy may be targeted to the pathologic node. If metastatic thyroid cancer is found in a node, surgical planning may proceed from there.

| **USG FEATURE** | **SENSITIVITY (%)** | **SPECIFICITY (%)** |
|---|---|---|
| Microcalcification | 26 – 59 | 86 - 95 |
| Hypoechogenicity | 27 - 87 | 43 - 95 |
| Irregular margins | 17 - 78 | 39 - 85 |
| Increased vascularity | 54 - 74 | 79 - 81 |
| Taller than wider shape | 33 | 93 |

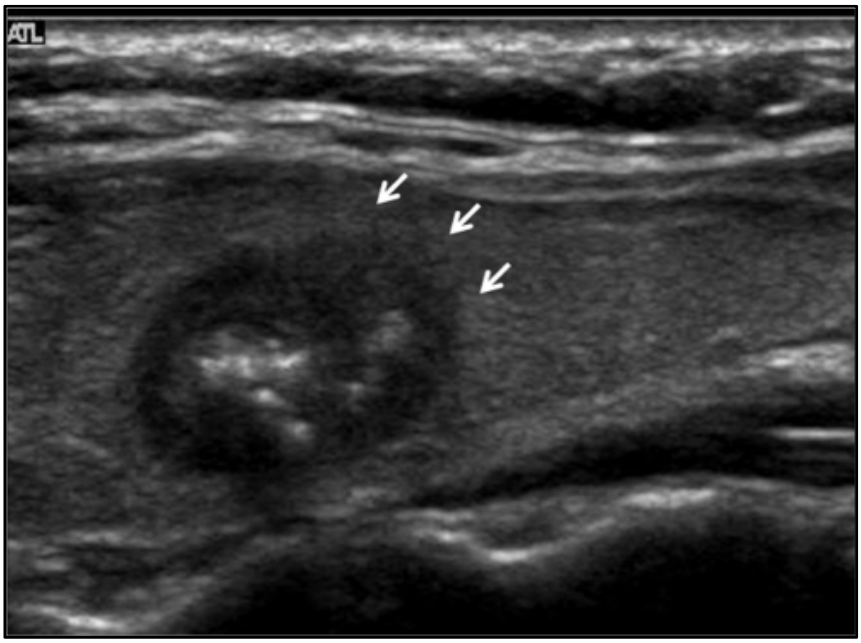



***Fig 9: USG feature of malignant thyroid nodule (hypoechogenicity, irregular margins and calcification)***

**COMPUTED TOMOGRAPHY AND MAGNETIC RESONANCE IMAGING**

Theyare useful in evaluating local extension in cases of thyroid tumors. It is particularly suitable for a suspicious nodule with bulky cervical lymphadenopathy. It is also useful for post-operative monitoring. CT is also helpful in preoperative evaluation of larger thyroid masses that are believed to have a sub-sternal component based on physical examination, ultrasound or chest radiograph.

## RADIOISOTOPE SCANNING

RAI is indicated for thyroid nodules more than one centimeter in size that are associated with a decreased serum TSH level. Technetium-99m pertechnetate (99mTc) is absorbed quicklyby follicular cells. However it does not undergoorganification. 99mTc has a brief halflife and smallradiationdose. Its rate of uptake shows whether the nodules are hyperfunctioning (“hot”) or hypofunctioning (“cold”). 99mTc is also taken up by uptake salivary glands and major vascular structures, hence the results are carefully interpreted.

Iodine scintigraphy with $I^{123}$ and $I^{131}$ is used to estimate the functional status of the gland. $I^{123}$ and $I^{131}$ are taken up by follicular cells and organified.$I^{123}$ produces small dosage of radiation (30 mrad) with a brief half-life of twelve to thirteen hours.

$I^{131}$ has a lengthier half-life of eight days and releasesgreaterintensities of beta radiation. It is ideal for imaging thyroid cancer. It is the ‘screening modality of choice’ for the assessment of metastases. Malignancy is present in 15% to 20% of cold nodules and in less than 5% of hot nodules.

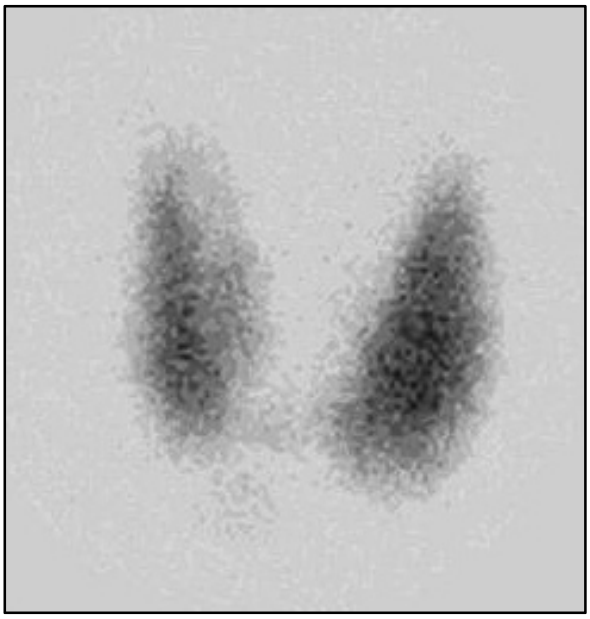


***Fig 10: Radioiodine scan showing normal thyroid uptake***

## FINE NEEDLE ASPIRATION CYTOLOGY (FNAC)[15]

FNAC is a key investigativeprocedure in theassessment of thyroid nodules. Patients with nodules having high-risk or intermediate-risk sonographic features should undergo FNAC if the nodules are 1 cm or larger in size, patients with nodules with low-risk sonographic features should undergo FNAC if the nodules are 1.5 cm or larger, and patients with nodules with very low suspicion sonographic features should undergo FNA biopsy if the nodules are 2 cm or larger.

FNAC is performed using a twenty-three to twenty-seven gauge needle and may be performed with capillary or suction technique. It is associated with a low frequency of complications, while maintaining diagnostic accuracy. USGguided FNAC can be donefor

palpableheterogenous nodules, and for non-palpable swellings.Results of FNAC should be reported using the Bethesda System for Reporting Thyroid Cytology.

| BETHESDA SCORE | CATEGORY | RISK OF MALIGNANCY (%) |
|---|---|---|
| 1 | Not satisfactory | 1% - 4% |
| 2 | benign | 0% - 3% |
| 3 | Atypia or follicular lesion of unknown significance | 5% - 15% |
| 4 | Follicular neoplasm / suspicious for follicular neoplasm | 15% - 30% |
| 5 | Suspicious for malignancy | 60% - 75% |
| 6 | malignant | 97 %- 99% |

Papillary carcinoma has discrete cellular cytologic characteristics that make FNAC extremely accurate in securing this particular diagnosis. In contrast, the diagnosis of FTC is not made based on cellular features but instead on demonstration of capsular or vascular invasion by follicular cells. This architectural finding cannot be determined by

FNAC. Although FTCs do not have the same cytologic appearance as benign thyroid tissue, they often are categorized as suspicious for follicular neoplasm, and the diagnosis not made until final pathology is available.

Another issue that must be understood is sampling error. A fine needle by definition is sampling only a small portion of a lesion. The false-negative rate of FNAC is 1% to 6%.

## 2.6 MANAGEMENT OF WELL-DIFFERENTIATED THYROID CARCINOMA

The mainstay of management of well-differentiated carcinoma (WDC) is surgery.

### SURGERIES FOR WELL-DIFFERENTIATED CARCINOMA

1. Total thyroidectomy – removal of entire gland with capsule.
2. Near-total thyroidectomy – entire gland is removed preserving a small portion near the posterior capsule of the gland.
3. Hemi-thyroidectomy – removal of ipsilateral lobe containing the lesion along with the isthumus.

Total thyroidectomy removes all malignant tissue, but there is no normal thyroid tissue. So the patient requires life-long thyroid hormone supplementation. Also there is thehazard of bilateral injury to nearby important structures. Alternatively, conservative procedures may leave residual cancer.

The current recommendation for near-total or total thyroidectomy are[16]:

1) Prinary tumor greater than 1.5 cm.
2) Nodules on the opposite lobe.

3) Metastasis.
4) History of radiotherapy to the head and neck.
5) History of differentiated thyroid carcinoma in a first-degree relative.
6) Age above forty-five years.
7) Tumors (4cm) with marked atypia.
8) Unfavourable histology – tall cell variant, diffuse sclerosing variant, poorly differentiated, Hurthle cell carcinoma and follicular cancer (except microinvasive).

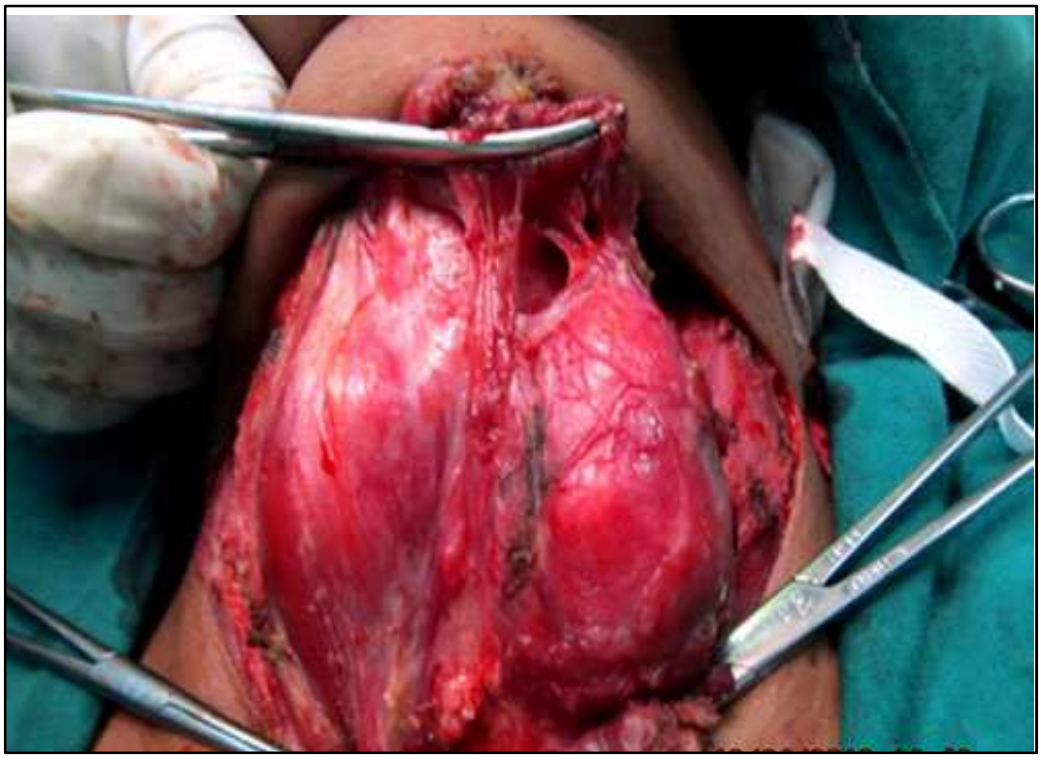


***Fig 11: Intra-operative picture of MNG***

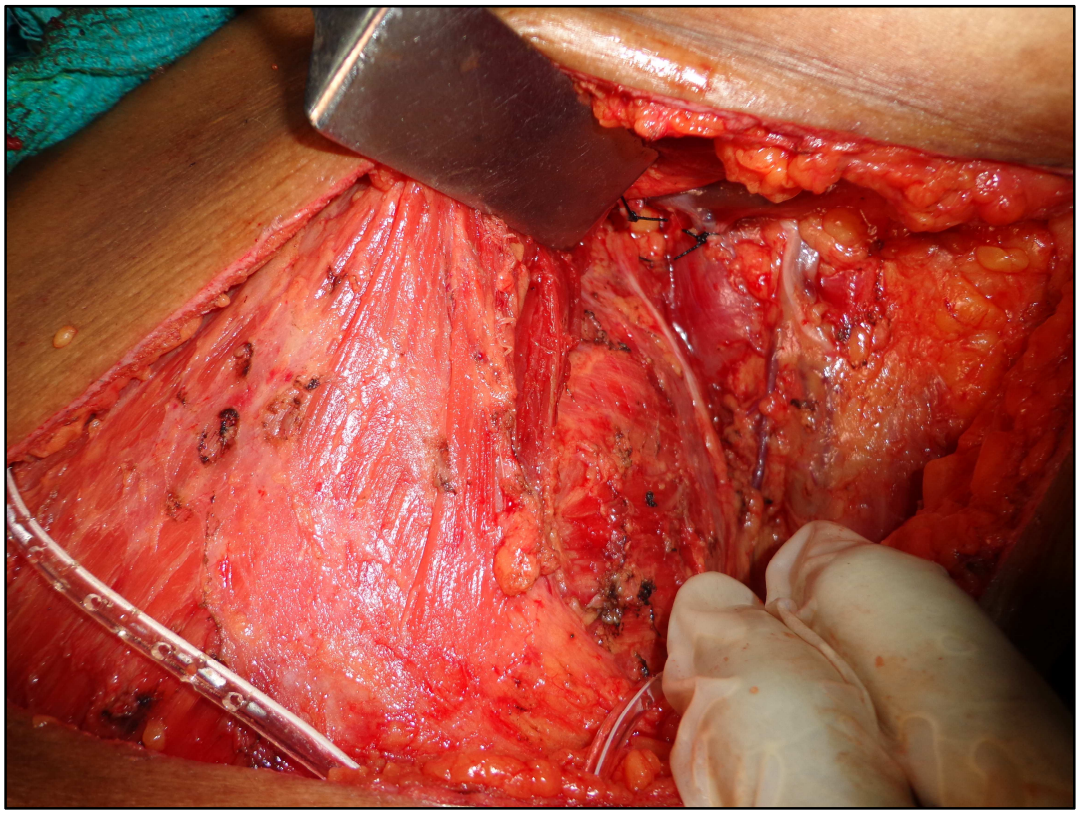


***Fig 12: Recurrent laryngeal nerve***

**Advantages of total thyroidectomy in well-differentiated carcinomas are:**

1) Better survival rate even for lesions >1.5cm.
2) Low recurrence rate and prevention of recurrence in contralateral lobe.
3) Decreased incidence of pulmonary metastasis.
4) Mortality and morbidity is similar to lobectomy.
5) Enhanced sensitivity of Tgas anindicator for persistent/recurrent disease.
6) Radioactive iodine can be used to treat persistent / recurrent disease.

Hemithyroidectomy is done in differentiated cancers <1.5 cm in size without extrathyroidal extension and no distant metastasis.

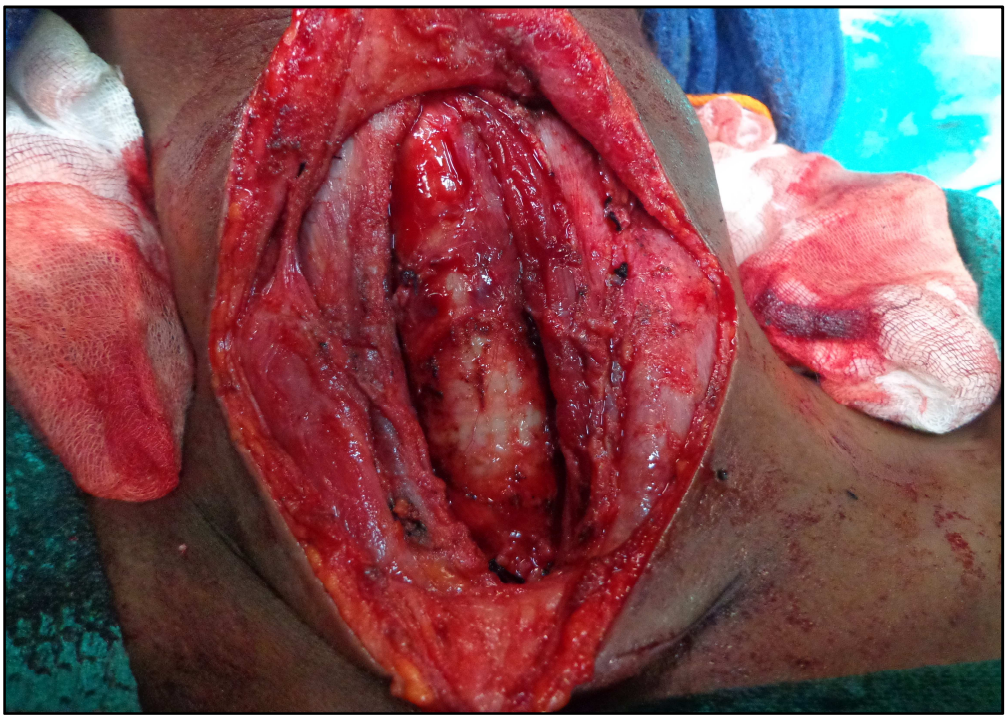


***Fig 13: Thyroid bed following total thyroidectomy***

**ARGUMENTS FAVOURING HEMITHYROIDECTOMY**

1) Differentiated thyroid cancer is an indolent disease and in a majority of patients has a very low recurrence and mortality rate.
2) Hypoparathyroidism and damage to recurrent laryngeal nerve are potential problems of total thyroidectomy.

## LYMPH NODE DISSECTION

Approximately eighty percent of papillary thyroid carcinoma patients have microscopic regional lymph nodal metastasis. Adjuvant radioactive iodine ablation of occult micro-metastasis can be done.Palpable enlargement of nodes is seen in twenty to thirty percent of adults and is arationalization for lymph node dissection[17]. As the central group or level VI lymph nodes are mainly involved in thyroid malignancy, it is recommended that dissection of these groups of nodes be done in all cases of WDC. Studies have demonstrated an improved survival rate and reduced recurrence rate after prophylactic central compartment dissection[17,18,19]. The current American Thyroid Association Guidelines recommends a staging or prophylactic level VI dissection for all cases undergoing thyroidectomy for well-differentiated thyroid cancer.

## LATERAL NECK NODE DISSECTION

Dissection of lateral jugular nodes (levels II-V) is vitalfor nodes involved by disease. Level based resection of lateral neck nodes is preferred over “berry picking”. Studies show that there is no improvement in survival rate following prophylactic lateral neck node dissection. However, followup of patients by detailed examination and USG, can recognize patients with lateral neck nodal disease that can then be properly treated by therapeutic compartmental node dissection.

# POST OPERATIVE MANAGEMENT OF DIFFERENTIATED THYROID CANCER AND FOLLOW UP

## Thyroid Hormone / TSH suppression

Thyroxine (T4) replacement therapy for patients who underwent total or near-total thyroidectomy suppresses TSH thereby eliminating the stimulus for any residual tumor cells. TSH suppression reduces tumor recurrence rates, particularly in young patients with papillary and follicular thyroid cancer. The goal of therapy should be to keep TSH level at around 0.1mU/L in low risk patients, or <0.1mU/L in high risk patients.

## Thyroglobulin (Tg) measurement

Thyroglobulin is a highly specific marker for follow up. Tg levels should be below 2ng/mL ifthe patient is on T4 and <5ng/mL if the patient is hypothyroid. Thyroglobulin >2ng/mL is indicative of residual normal thyroid tissue or metastatic deposits. Tg and antiTg anti-body levels are estimated bi-annually in the beginning and then yearly. Rising titres is highly suspicious of recurrence of disease.

**Imaging modalities**

A USG of the neck and CT or MRIscanof the neck and mediastinum is done in high risk patients for promptdiscovery of any recurrent or persistent disease.

**Radioactive iodine scan**

Post surgery screening and radioactive iodine $I^{131}$ is more sensitive for detecting metastasis. T4 therapy is discontinuedfor four to six weeks before scanning with $I^{131}$. During that period, patients are put on T3 to reduce the incidence of hypothyroidism. T3, having ashorter half-life than T4, iswithdrawn for two weeks to permit TSH levels to increase prior to treatment. Hypo-iodide diet is advised throughout thisphase. The standardpractice involves administering a screening dose of about 2mCi of $I^{131}$ and quantifying uptake twenty-four hours later. The uptake is less than 1 percent after total thyroidectomy. A “hotspot” in the neck after primary screeningdenotes residual normal tissue. If a significant uptake is shown, a therapeutic radio-ablative dose of $I^{131}$must be given to patient.

## RADIOACTIVE IODINE ABLATION (RIA)

Radio-iodine therapy given as $I^{131}$ is a veryefficient nonsurgical treatment for well-differentiated thyroid cancer. $I^{131}$ emits beta radiationwhich destroys cancer cells. $I^{131}$ uptake is reliant onsufficient

stimulation by TSH.Radio-iodine ablation is used increasingly post-operatively in treatment of welldifferentiated thyroid carcinoma. The goal is to prevent loco-regional recurrence and destroy residual tissue. Studies[16] show anadvantage with $I^{131}$ ablation in cases with a) tumors >1.5cm, b) multifocal tumors, c) residual disease and d) nodal metastases.

**AMERICAN THYROID ASSOCIATION GUIDELINES FOR RIA**

1) Stage III or IV disease.
2) Stage II disease, younger than 45 years.
3) Most of the patients older than 45 years.
4) Selected patients with stage I disease – tumors >1.5 cm, multifocal, residual disease, nodal metastasis, vascular invasion and intermediately differentiated histology.

Post-operative ablation is done 6 weeks after surgery.

DOSE: Residual / recurrent thyroid bed disease – 150mCi

Diffuse lung metastasis <150mCi.

Some patients may need another $I^{131}$ treatment after 6-12 months until 1 or 2 negative scans are obtained.

**Side effects of radio-iodine**

Short term complications include radiation thyroiditis, painless neck edema, sialoadenitis, nausea, tumor hemorrhage, temporary bone marrow depression and amenorrhea / oligomenorrhea. Late complications include secondary malignancies in bone, soft tissue, colo-rectal, salivary glands and leukemia.

## ROLE OF RADIOTHERAPY AND CHEMOTHERAPY FOR WDC

Radiotherapy is sometimesnecessary to control unresectable, locally invasive or recurrent tumor and to treat skeletal metastasis. Single and multi-drug chemotherapeutic agents have been used with limited success in disseminated thyroid carcinoma. The frequently used drugs are Adriamycin and taxol.

## MANAGEMENT OF PATIENTS WITH METASTATIC DISEASE

The preferred treatment for metastatic disease includes the following:

1) Surgical excision of loco-regional disease -with sparing of vital structures.
2) External beam radiation.
3) Surveillance of patients with stable asymptomatic disease.

4) Tentative chemotherapeutic trials.
5) A small portion of patients may benefit from radio frequency ablation; ethanol ablation or chemo-embolization.

## TREATMENT OF PULMONARY METASTASIS

The management of patients with pulmonary metastasis depends uponmetastatic lesion size, avidity of radioiodine uptake and response to prior therapy. Pulmonary micro-metastases are treated with radioiodine therapy, given every six to twelve months as long as disease continues to respond. Radioiodine is also used to treat larger pulmonary metastases if they are iodine avid. Non radioiodine avid pulmonary disease requires chemotherapy withcisplatin and doxorubicin.

## MANAGEMENT OF PATIENT WITH BONE METASTASIS

The management of patients with bone metastasis depends onseveral factors. Studies show abetter survival rate associated with complete surgical resection of isolated bone metastasis, particularly in patients younger than 45 years of age. Radioiodine therapy can also be used for iodine-avid bone metastasis and is associated with better survival. External beam radiation can be given when skeletal metastatic lesions produce severe pain, fracture or neurologic complications. Un-resectable painful lesions are treated by a combination of options or

individual treatment like radioiodine, external beam radiotherapy, intra-arterial embolization, radio-frequency ablation, periodic zoledronate or pamidronate infusions or bone seeking radio-pharmaceuticals such as strontium-8 or samarium-153.

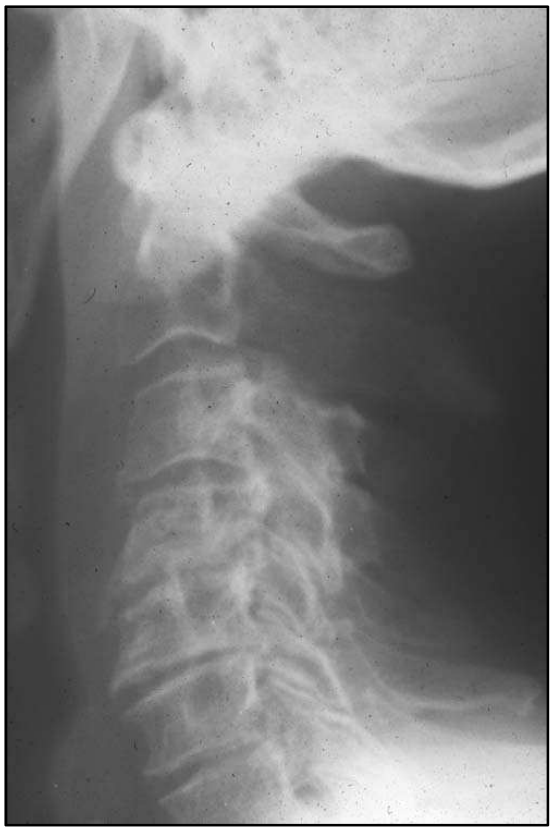


***Fig 14: Cervical vertebral metastasis***

**TREATMENT OF BRAIN METASTASIS**

Brain metastasis carries a poor prognosis. Surgical excision and radiotherapy is the mainstay of treatment. Targeted therapy (like radio-surgery) is employed to limit the radiation exposure of the surrounding brain tissue. Radioiodine can be used for CNS metastasis that take up radio-iodine.

## AJCC CLASSIFICATION OF THYROID CANCER[20]

### PRIMARY TUMOR (T)

TX: Primary tumor cannot be assessed

T0: No evidence of primary tumor

T1: Tumor ≤2cm in diameter, limited to thyroid

T2: Tumor >2cm but <4cm in diameter, limited to thyroid

T3: Tumor >4cm in diameter limited to thyroid, or any tumor with minimalextra-thyroidal invasion.

T4a: Any size tumor extending beyond capsule to invade subcutaneous soft tissue, larynx, trachea, esophagus, or recurrent laryngeal nerve, or intra-thyroidal anaplastic cancer

T4b: Tumor invading prevertebral fascia, or encasing carotid artery or mediastinal vessels; or extra-thyroidal anaplastic carcinoma

### REGIONAL LYMPH NODES (N)

NX: Regional lymph nodes cannot be assessed

N0: No regional lymph node metastasis

N1: Regional lymph node metastasis

N1a: Metastases to level VI nodes

N1b: Metastases to unilateral, bilateral, or contralateral cervical or superior mediastinal lymph nodes

**DISTANT METASTASIS (M)**

MX: Distant metastases cannot be assessed

M0: No distant metastasis

M1: Distant metastasis

**STAGE GROUPINGS**

**PAPILLARY AND FOLLICULAR CARCINOMA**

| STAGE | TNM |
|---|---|
| **<45 y** | |
| I | Any T, any N, M0 |
| II | Any T, any N, M1 |
| **≥45 y** | |
| I | T1, N0, M0 |
| II | T2, N0, M0 |
| III | T3, N0, M0; T1–3, N1a, M0 |
| IVA | T4a, N0–1a, M0; T1–4a, N1b, M0 |
| IVB | T4b, any N, M0 |
| IVC | Any T, any N, M1 |

**MEDULLARY CARCINOMA**

| STAGE | TNM |
|---|---|
| I | T1, N0, M0 |
| II | T2–3, N0, M0 |
| III | T1–3, N1a, M0 |
| IVA | T4a, N0–1a, M0; T1–4a, N1b, M0 |
| IVB | T4b, any N, M0 |
| IVC | Any T, any N, M1 |

**ANAPLASTIC CARCINOMA**

| STAGE | TNM |
|---|---|
| IVA | T4a, Any N, M0 |
| IVB | T4b, Any N, M0 |
| IVC | Any T, Any M, M1 |

## PROGNOSIS OF WELL-DIFFERENTIATED CARCINOMA

Papillary carcinomais associated with 90%-95% long-term disease-free survival; follicular carcinoma with70%-80% long-term disease-free survival. 20% of patients having follicular cancer develop local recurrence and a small proportion develop distant metastasis.

## PROGNOSTIC FACTORS

**AMES criteria (Lahey Clinic):** based on age, metastatic disease, extra-thyroidal extension and size.

| | **Low mortality risk** | **High mortality risk** |
|---|---|---|
| A: age | Men less than 41 years<br>Women <51 years | Men greater than 41 years<br>Women >51 years |
| M: metastasis | Absent | Present |
| E: extent of primary tumor | Intrathyroidal papillary cancer; Follicular cancer with minor capsular involvement | Extrathyroidal papillary cancer; Follicular cancer with major capsular involvement |
| S: size of primary tumor | <5 cm | ≥ 5 cm (regardless of extent) |

**AGES criteria (Mayo Clinic):** based on age, grade of tumor, extent and size.

Score = (0.05 x Age [if age >40] + 1 [if grade 2] + 3 [if grade 3 or 4] + 1 [if extra-thyroidal] + 3 [if distant metastasis] ) + (0.2 x tumor size [maximum diameter in cm])

**20 year survival score**

<3.99 = 99%

4-4.99 = 80%

5 - 5.99 = 67%

>6 = 13%

The **MACIS** scale is a more sophisticated post-operative scale.It includes distant metastasis, age at presentation, completeness of original surgical resection, extra-thyroidal invasion and size of original lesion (in cm).

**OTHER PROGNOSTIC SCORING SYSTEMS**

- **Ohio state:** size, cervical metastasis, multiplicity, invasion, distant metastasis
- **Sloan–Kettering:** age, histology, size, extension, metastasis
- **NTCTS:** size, multifocality, invasion, differentiation, cervical metastasis, extra-cervical metastasis

## METASTASIS

Approximately 33%-61% of patients with PTC have cervical lymph node involvement at the time of diagnosis, whereas in follicular cancers, it is between 5%-20%. Only a tiny proportion of patients have metastatic disease during initial presentation, which is a strong predictor of very poor outcome.

# CHAPTER - 3

# MATERIALS AND METHODS

# 3. MATERIALS AND METHODS

**3.1 Type of study** : Prospective and Observational Study

**3.2Study approval** : Prior to commencement of this study – Thesis & Ethical Committee of Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai has approved the thesis protocol.

**3.3 Place of study** : Rajiv Gandhi Government General Hospital, Chennai.

**3.4 Period of study** : Duration starting from 01 August 2015 to 31 July 2016

**3.5 Sample size** : 50 cases

**3.6 Selection of patients:**

a) **Inclusion criteria-** Patients havingclinically palpable thyroid nodule at initial presentation.

b) **Exclusion criteria –**1.Patients having non-palpable thyroid nodules.2.Patientswhose FNAC samplesturned out to beunsatis factory.

**3.7 Study procedure:**

All the necessary information regarding the study was explained to the patients or their valid guardian. Informed written consent was taken

from the patientsready to participate in the study. Detailed history was taken from the study group to establish proper diagnosis as per the proforma (Annexure 1). Thorough physical examination was done in each case.FNAC, USG neck and Thyroid function test was done for all the patients. Data collection sheets were filled in by the investigator. All of the preoperative factors related to the patient were noted down in the data sheet.Patients were then explained about their disease process and the possible line of management. After proper evaluation and preparation, patients who required surgical management were taken up for surgery. Strict aseptic precautions were followed during the operation. Meticulous techniques were practiced as far as possible. The operation procedure and related peroperative factors were observed directly and recorded in the data collection sheet instantly. The post operative HPE report was collected. After completing the collection of data it was compiled in a systematic way.

### 3.8 Ethical consideration

All the patients/ legal guardians were given an explanation of the study and about the investigative and operative procedures with their merits and demerits, expected results, and possible complications. If he/she agreed then the case had been selected for this study. The study did not involve any additional investigation or any significant risk. It did

not cause economic burden to the patients. The study was approved by the institutional ethical committee prior to commencement of data collection. Informed consent was taken from each patient/guardian. Data were collected by approved data collection form.

### 3.9 Data collection

Data were collected by pre-tested structured questionnaire. Data were collected from all the respondents by direct interview after getting informed written consent from them or from their legal guardian.

### 3.10 Data analysis

Data analysis was done both manually and by using computer. Calculated data was arranged in systemic manner and presented in various table and figures. Statistical analysis wasdone. Results on continuous measurements are presented as Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Chi-square test has been used to find the significance of study parameters on categorical scale between two or more groups.

**SIGNIFICANT FIGURES:**

+ Suggestive significance (P value: $0.05<P<0.10$)

* Moderately significant (P value: $0.01<P<0.05$)

** Strongly significant (P value: $P\leq0.01$)

**STATISTICAL SOFTWARE**

The statistical software namely SAS 9.2, SPSS 15.0, Stats 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of data and Microsoft Word and Microsoft Excel have been used to generate graphs, tables, etc.

# CHAPTER – 4

# OBSERVATION AND RESULTS

# OBSERVATION AND RESULTS

This was a prospective study done in the Institute of General Surgery at Madras Medical College, Chennai. The study period was August 2015 to July 2016.

Total number of cases = 50

Total number of cases confirmed with malignancy = 13

## STUDY DESIGN

A prospective study with a sample size of 50 patients was conducted at the Institute of General Surgery, Madras Medical College, Chennai. Patients with palpable thyroid nodules were included. The preoperative clinical, radiological and TSH levels were analyzed and a cancer risk score was assigned to each patient as per the scoring system designed. This score was compared with the post-operative HPE report to predict the risk of malignancy. The observed results were subjected to statistical analysis. The following observations were made. The risk factors used in the scoring system were assigned scores based on the existing McGill Thyroid Nodule Scoring System. The parameters were assigned scores based on the previously demonstrated sensitivity and specificity of each parameter for carcinoma. A maximum cancer risk score of 26 is attainable with this scoring system.

# THE SCORING SYSTEM

**1. CLINICAL DATA:**

| FACTOR: | ASSIGNED SCORE: | PATIENT'S SCORE: |
|---|---|---|
| AGE (>45 YEARS) | **1** | |
| GENDER (MALE) | **1** | |
| EXPOSURE TO IONIZING RADIATION (+) | **3** | |
| FAMILY HISTORY OF THYROID MALIGNANCY (+) | **3** | |
| CONSISTENCY OF GLAND (HARD) | **2** | |
| TSH LEVEL (>1.4mIU/L) | **1** | |

**2. ULTRASONOGRAM OF NECK:**

| FACTOR: | ASSIGNED SCORE: | | PATIENT'S SCORE: |
|---|---|---|---|
| SHAPE (TALLER THAN WIDE) | **1** | | |
| SIZE | 2-2.9CM | **2** | |
| | 3-3.9CM | **3** | |
| | 4CM AND ABOVE | **4** | |
| NODULARITY | MULTIPLE | **1** | |
| | SOLITARY | **2** | |
| ECHOGENICITY (HYPOECHOIC) | **1** | | |
| CALCIFICATION (+) | **1** | | |
| CERVICAL LYMPH NODES (+) | **2** | | |
| VASCULARITY INCREASED | **1** | | |

**3. FNAC:**

| FEATURE: | ASSIGNED SCORE: | PATIENT'S SCORE: |
|---|---|---|
| BENIGN | **1** | |
| SUSPICIOUS OF MALIGNANCY | **2** | |
| MALIGNANT | **3** | |

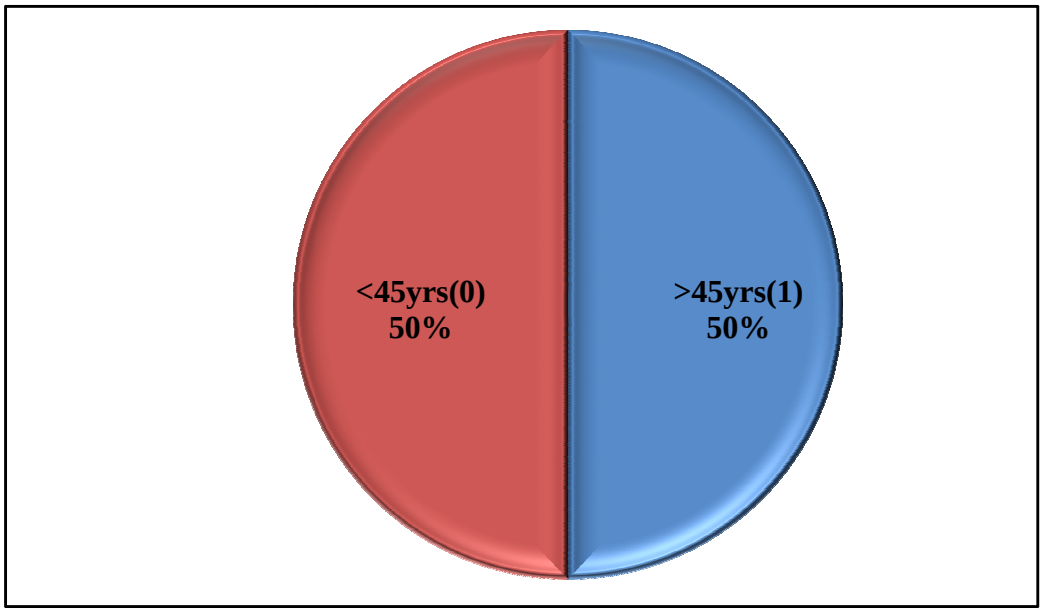
**TOTAL SCORE:**

# RESULTS

## AGE DISTRIBUTION

### Table 1: Age distribution of patients

| AGE IN YEARS | BENIGN | MALIGNANT | TOTAL |
|---|---|---|---|
| <45 (0) | 18 | 7 | 25 |
| >45 (1) | 19 | 6 | 25 |

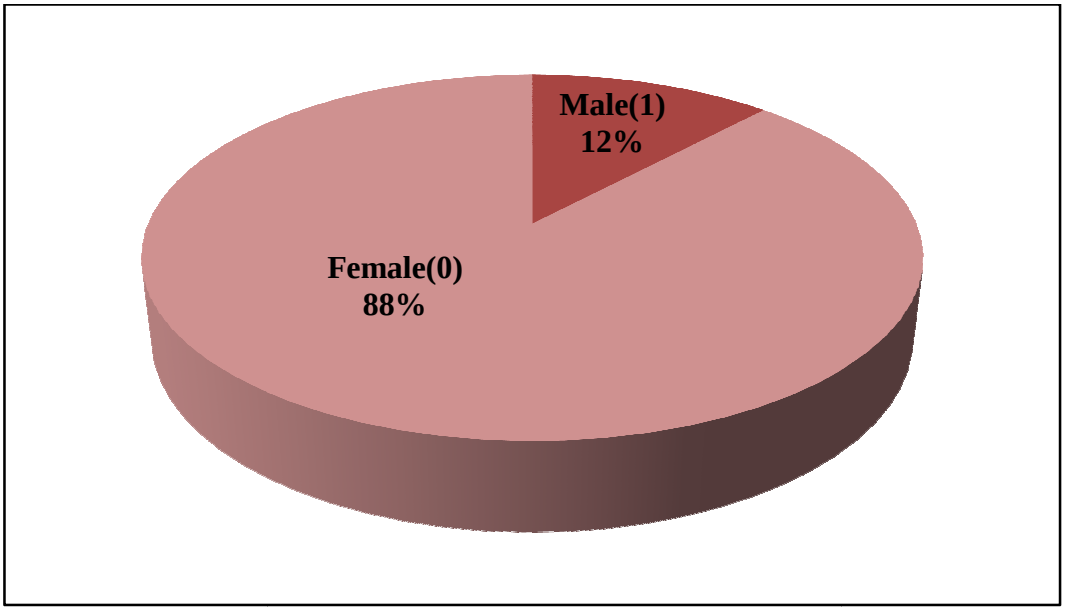



In our study 50 patients were included out of which 25 patients were aged more than 45 years and 25 patients were aged less than 45 years. Among the patients proven to have malignancy, 6 were aged over 45 years. Patients over 45 years of age were given a score of 1.

## GENDER DISTRIBUTION

### Table 2: Gender distribution of patients

| GENDER | BENIGN | MALIGNANT | TOTAL |
|---|---|---|---|
| FEMALE (0) | 34 | 10 | 44 |
| MALE (1) | 3 | 3 | 6 |

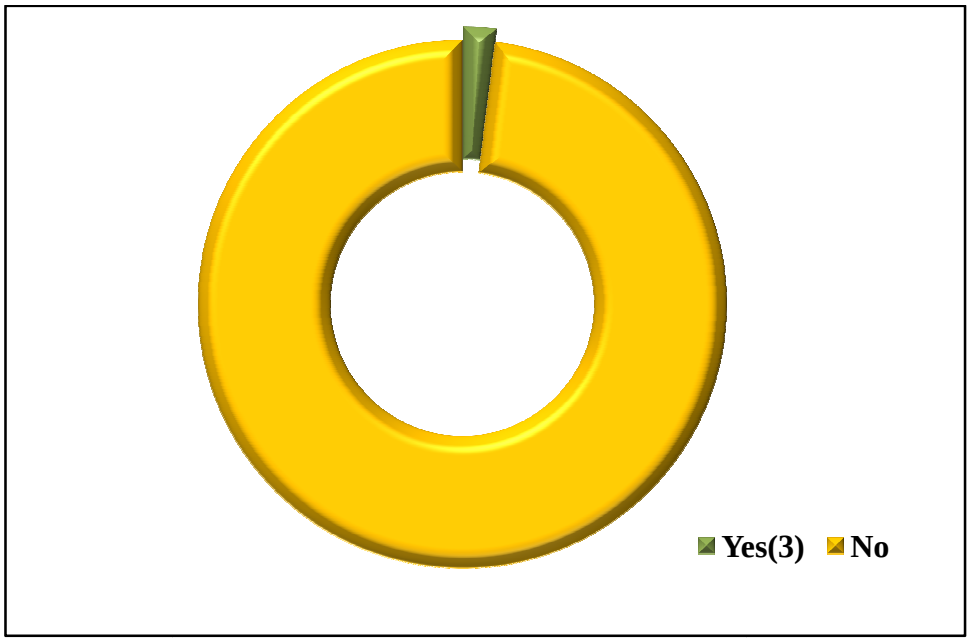



Among the 50 patients 44 were female and 6 were male. Among the cases proved to be malignant, 3 were male. Male gender was given a score of 1.

## FAMILY HISTORY OF MALIGNANCY

**Table 3: Distribution according to family history of malignancy**

| FAMILY HISTORY OF MALIGNANCY | BENIGN | MALIGNANT | TOTAL |
|---|---|---|---|
| PRESENT (3) | 0 | 1 | 1 |
| ABSENT (0) | 37 | 12 | 49 |




Among the 50 patients, only 1 patient had a family history of thyroid malignancy and this patient was also diagnosed with malignancy post operatively.

## EXPOSURE TO IONIZING RADIATION

### Table 4: Distribution according to history of exposure to ionizing radiation

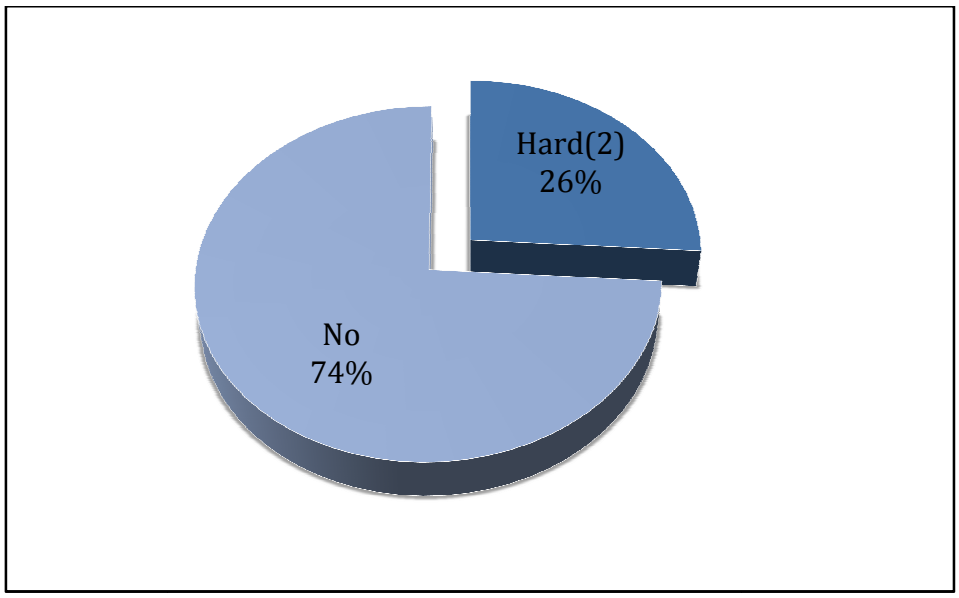
| EXPOSURE TO IONIZING RADIATION | BENIGN | MALIGNANT | TOTAL |
|---|---|---|---|
| PRESENT (3) | 0 | 0 | 0 |
| ABSENT (0) | 37 | 13 | 50 |

Among the patients studied, none had history of exposure to ionizing radiation. The presence of this history was given a score of 3.

## CONSISTENCY OF GLAND

**Table 5: Distribution of patients with hard consistency of gland**

| HARD CONSISTENCY | BENIGN | MALIGNANT | TOTAL |
|---|---|---|---|
| PRESENT (2) | 1 | 12 | 13 |
| ABSENT (0) | 36 | 1 | 37 |

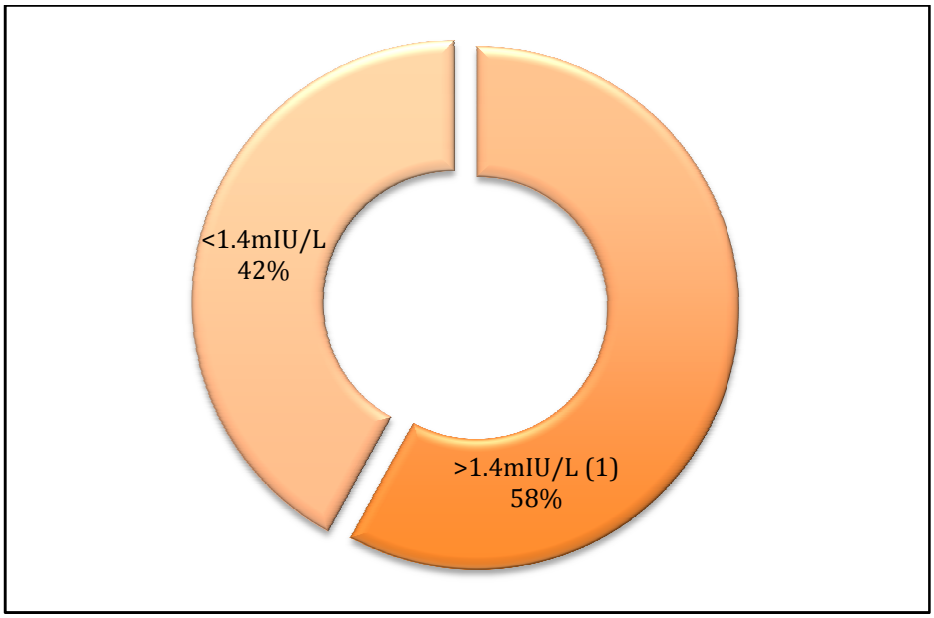



Among the 50 patients studied, 13 patients on clinical examination had hard consistency of the thyroid gland. Among those diagnosed with malignancy, 12 had hard consistency of gland. The presence of hard consistency was given a score of 2.

## TSH LEVEL

**Table 6: Distribution of patients depending upon TSH level**

| TSH LEVEL | BENIGN | MALIGNANT | TOTAL |
|---|---|---|---|
| > 1.4 mIU/L (1) | 17 | 12 | 29 |
| < 1.4 mIU/L (0) | 20 | 1 | 21 |

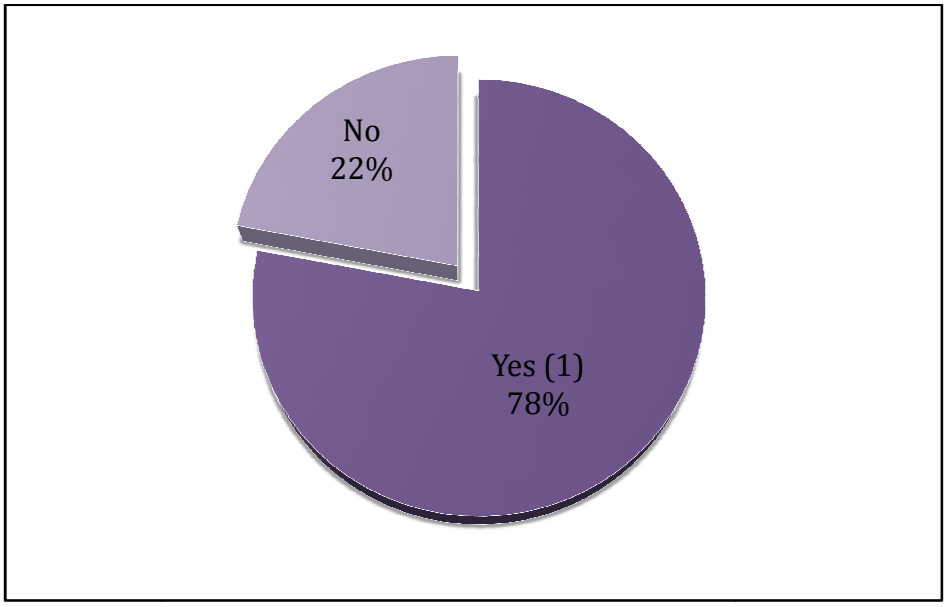



Among the 50 patients studied, 29 had serum TSH level >1.4mIU/L and 21 had TSH level <1.4mIU/L. Among those diagnosed to have malignancy, 12 had TSH level >1.4IU/L. A serum TSH level >1.4IU/L was given a score of 1 in our study.

## SHAPE OF THE GLAND

**Table 7: Distribution of patients with USG feature of taller than wider shape**

| TALLER THAN WIDER SHAPE | BENIGN | MALIGNANT | TOTAL |
|---|---|---|---|
| PRESENT (1) | 29 | 10 | 39 |
| ABSENT (0) | 8 | 3 | 11 |

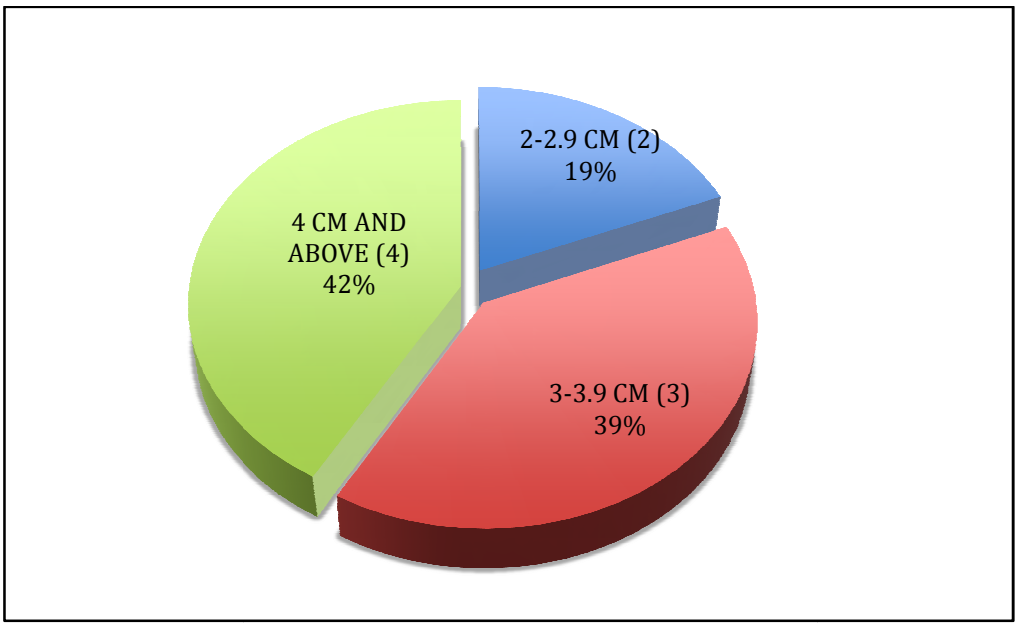



39 patients had USG feature of taller than wider shape of their thyroid. Among these patients 10 patients were diagnosed with malignancy post operatively.This feature was given a score of 1 in our scoring system.

## SIZE OF THE GLAND

**Table 8: Distribution based on size of the gland determined by USG**

| SIZE | BENIGN | MALIGNANT | TOTAL |
|---|---|---|---|
| 2 – 2.9 CM (2) | 8 | 3 | 11 |
| 3 – 3.9 CM (3) | 15 | 4 | 19 |
| ≥ 4 CM (4) | 14 | 6 | 20 |

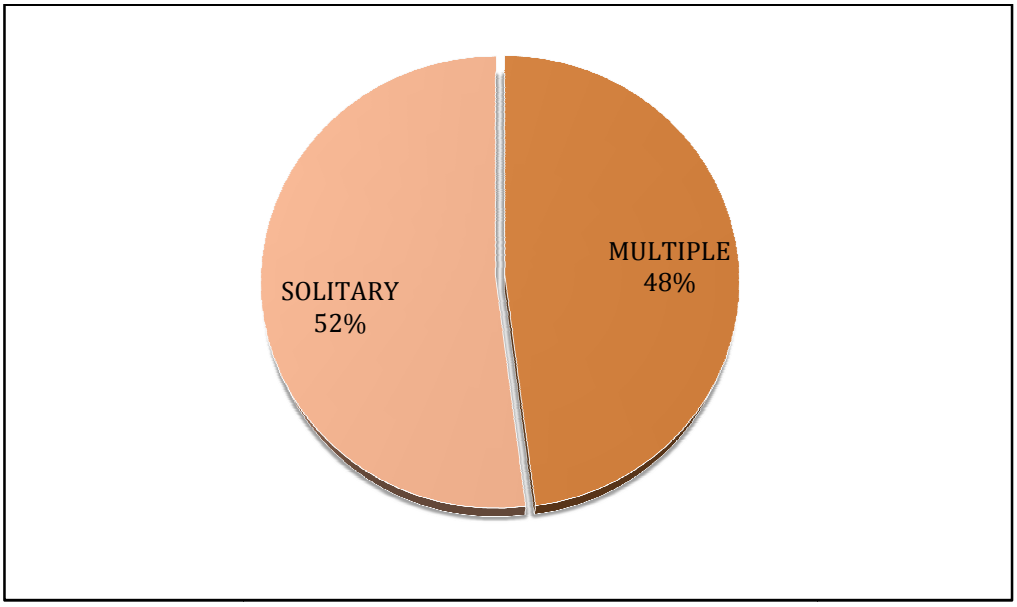



Among the patients diagnosed with malignancy, 3 patients had size of gland between 2–2.9 cm, 4 had size between 3-3.9 cm and 6 had size ≥4 cm. Each of these sizes were given a score of 2, 3 and 4 respectively.

## NODULARITY OF GLAND

### Table 9: Distribution based on nodularity

| NODULARITY | BENIGN | MALIGNANT | TOTAL |
|---|---|---|---|
| SOLITARY (2) | 19 | 7 | 26 |
| MULTIPLE (1) | 18 | 6 | 24 |

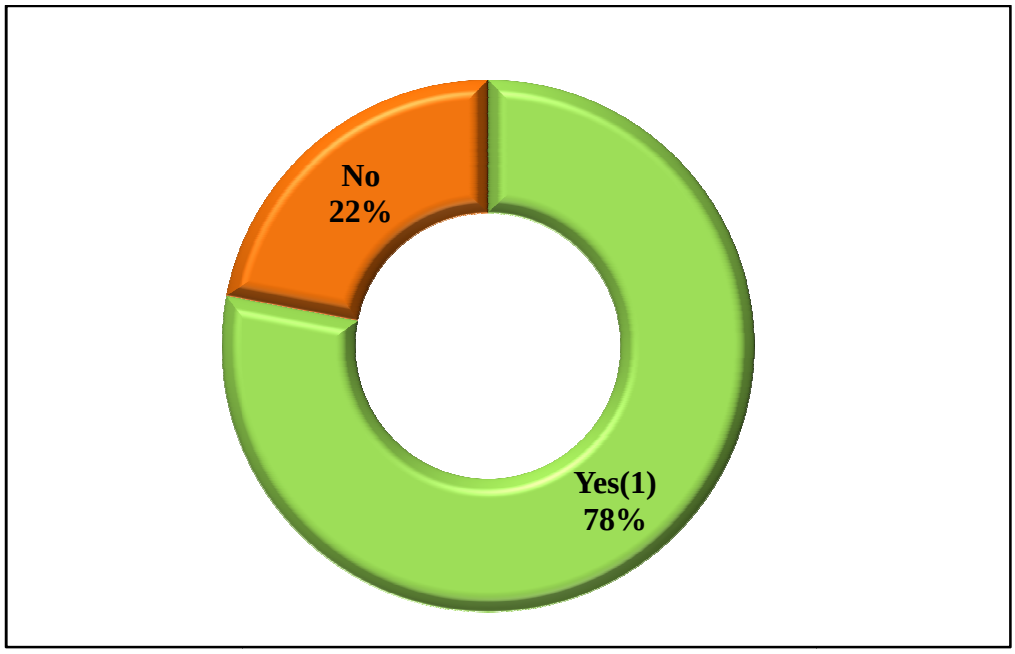



26 patients had solitary nodular goiter and 24 patients had multinodular goiter. 7 patients with malignancy had solitary nodule and 6 patients with malignancy had multinodular goiter. Solitary nodule was given a score of 2 and multinodularity was given a score of 1, both of which were determined by USG.

## ECHOGENICITY OF GLAND

**Table 10: Distribution based on USG determined echogenicity of gland**

| HYPOECHOGENICITY | BENIGN | MALIGNANT | TOTAL |
|---|---|---|---|
| PRESENT (1) | 26 | 13 | 39 |
| ABSENT (0) | 11 | 0 | 11 |

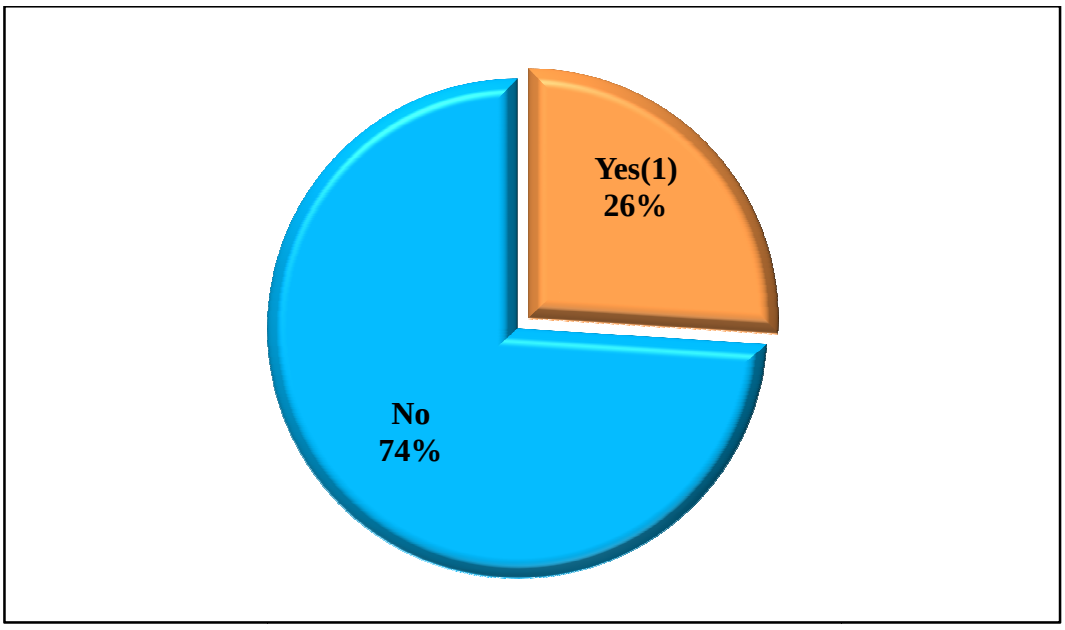



39 patients showed the presence of hypoechoic nodules on USG. All the patients diagnosed with malignancy had hypoechoic nodules on USG.

## CALCIFICATION OF GLAND

**Table 11: Distribution based on presence of calcification within the gland**

| CALCIFICATION | BENIGN | MALIGNANT | TOTAL |
|---|---|---|---|
| PRESENT (1) | 3 | 10 | 13 |
| ABSENT (0) | 34 | 3 | 37 |

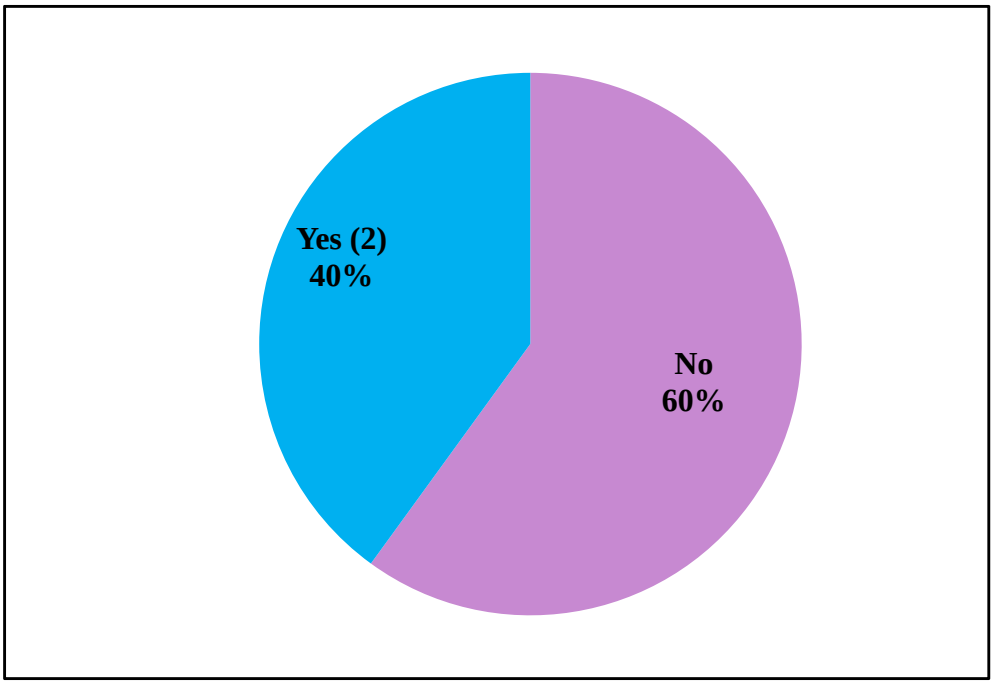



13 patients had intra-glandular calcification determined by USG. Among these patients 10 were confirmed to have malignancy post-operatively. The presence of calcification on USG was given a score of 1.

## CERVICAL LYMPH NODE INVOLVEMENT

**Table 12: Distribution based on cervical lymph node involvement**

| CERVICAL LYMPHADENOPATHY | BENIGN | MALIGNANT | TOTAL |
|---|---|---|---|
| PRESENT (2) | 9 | 11 | 20 |
| ABSENT | 28 | 2 | 30 |

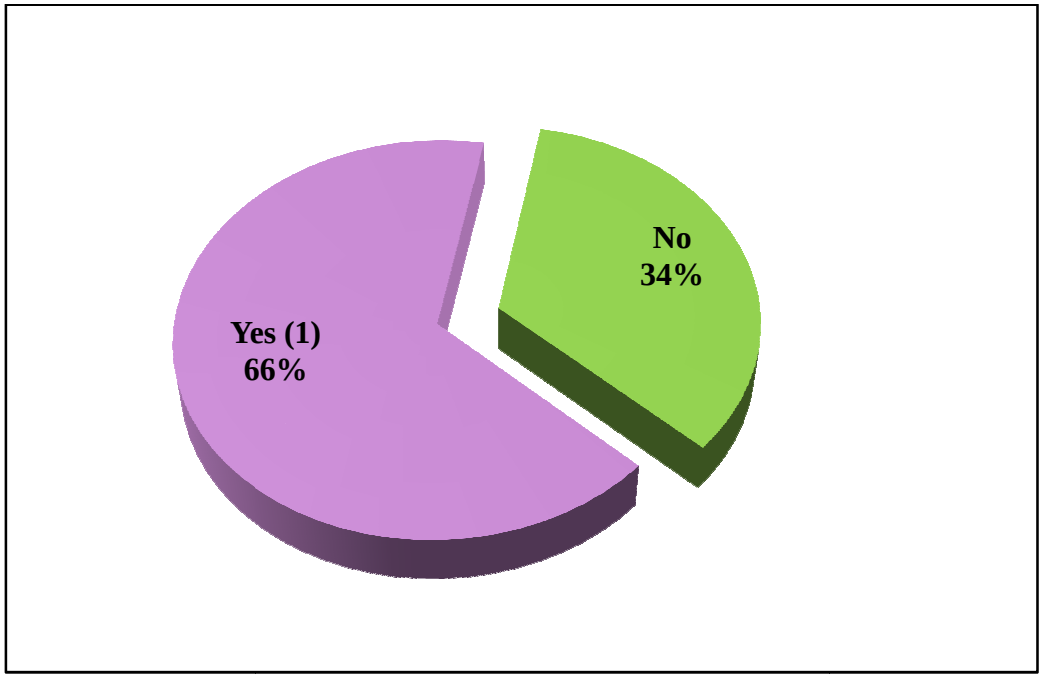



Of the 50 patients evaluated, 20 had cervical lymphadenopathy confirmed radiologically and 30 did not have lymphadenopathy. 11 patients with proven malignancy had lymphadenopathy. The presence of cervical lymphadenopathy was given a score of 2.

## VASCULARITY OF THE GLAND

**Table 13: Distribution based on vascularity of gland**

| VASCULARITY | BENIGN | MALIGNANT | TOTAL |
|---|---|---|---|
| INCREASED (1) | 20 | 13 | 33 |
| NORMAL (0) | 17 | 0 | 17 |

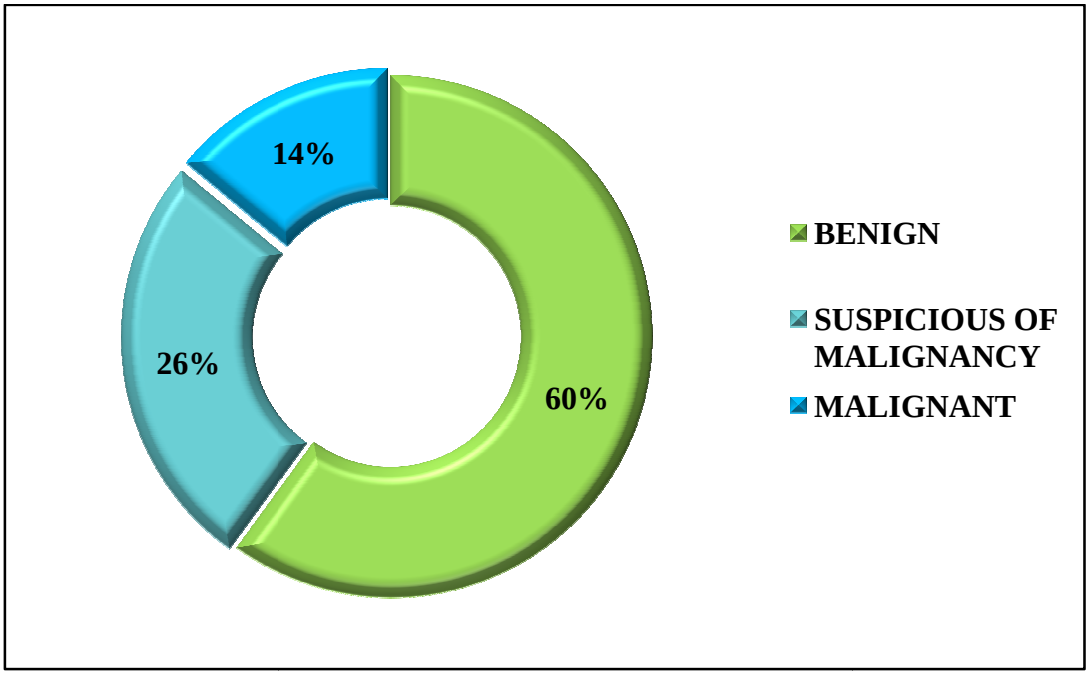



Among the patients studied, 33 patients showed increased vascularity of the gland on USG. All the 13 patients with malignancy had increased vascularity. The presence of increased vascularity was given a score of 1.

## FINE NEEDLE ASPIRATION CYTOLOGY

### Table 14: Distribution based on FNAC report

| FNAC REPORT | NUMBER OF CASES |
|---|---|
| BENIGN (1) | 30 |
| SUSPICIOUS OF MALIGNANCY (2) | 13 |
| MALIGNANT (3) | 7 |




The FNAC report of 30 patients under study was found to be benign, 13 patients had a lesion suspicious of malignancy and 7 patients had outright malignancy. Among the patients whose FNAC report was suspicious of malignancy, 6 out of 7 turned out to be malignant. Benign, suspicious of malignancy and malignant lesions were given a score of 1, 2 and 3 respectively.

**Table 15: Final pathology according to the scoring system**

| SCORE | BENIGN | MALIGNANT | PERCENTAGE OF MALIGNANCY (%) |
|---|---|---|---|
| **1** | 0 | 0 | 0 |
| **2** | 0 | 0 | 0 |
| **3** | 1 | 0 | 0 |
| **4** | 1 | 0 | 0 |
| **5** | 1 | 0 | 0 |
| **6** | 3 | 0 | 0 |
| **7** | 4 | 0 | 0 |
| **8** | 5 | 0 | 0 |
| **9** | 4 | 0 | 0 |
| **10** | 4 | 0 | 0 |
| **11** | 3 | 0 | 0 |
| **12** | 4 | 1 | 20 |
| **13** | 4 | 1 | 20 |
| **14** | 2 | 1 | 33.33 |
| **15** | 1 | 1 | 50 |
| **16** | 0 | 3 | 100 |
| **17** | 0 | 1 | 100 |
| **18** | 0 | 3 | 100 |
| **≥19** | 0 | 2 | 100 |

The scores ranged between 3 and 19, with a mean score of 11. The incidence of thyroid carcinoma for scores of 1 to 11 was 0% (0 out of 24 patients), 12 to 13 was 20% (2 out of 10 patients), 14 to 18 was 75% (9 out of 12 patients) and ≥19 was 100% (2 out of 2 patients). A score ≤11 correlated with a 0% risk of malignancy, whereas a score>11 implied a 54.166% risk of malignancy. This greater risk demonstrated for patients above a score of >11 is statistically significant ($p<0.0001$, $\chi^2 = 14.965$, df = 1).

**Table 16: Score versus HPE report**

| | | POST OP HPE: | | TOTAL |
|---|---|---|---|---|
| | | BENIGN | MALIGNANT | |
| SCORE | ≤11 | 26 | 0 | 26 |
| | >11 | 11 | 13 | 24 |
| TOTAL | | 37 | 13 | 50 |

**Table 17: Result of Chi Square Test**

| | Value | df | Asymp. Sig. (2-sided) |
|---|---|---|---|
| Yates Chi-Square | 16.32 | 1 | < 0.0001(S) |
| Pearson Chi-Square | 19.03 | 1 | < 0.0001 (S) |
| N no. of cases | 50 | | |

# CHAPTER – 5

# DISCUSSION

Thyroid nodules often present a considerable management dilemma for the thyroid surgeon, pathologist, endocrinologist, and patient alike owing to their diagnostic ambiguity. There is an imperative need for a reliable analytical test to help determine preoperatively the nature of a thyroid nodule, before committing patients to surgery. Ideally, such a test would yield a high PPV for carcinoma, affirming the need for surgical excision while representing a high degree of specificity, which would help limit the number of patients subjected to thyroid surgery and its potential morbidities for excision of benign nodules.

Numerous attempts have been made to define clinical, sonographic and cytologicparameters useful for identifying patients at higher risk of malignancy. None of these parameters, however, have proven to be adequate on their own to guide clinical decision-making.

The concept of a combined scoring system was previously proposed by ***Rago and colleagues***[21]**,** who calculated a risk score derived from both clinical and echographic parameters and applied it exclusively to indeterminate lesions to describe the individual possibility of malignancy.

The ***McGill Thyroid Nodule Scoring system (MTNS)***[22]was proposed which summated 22 parameters. A multidisciplinary team, using existing evidencebased risk factors for thyroid cancer, developed the MTNS. These risk factors were categorized into eight

clinical/laboratory parameters, eight imaging (sonography/ positron emission tomography [PET] scan) features and six histopathologic criteria.

Our scoring system also incorporates 14 parameters based on clinical, sonological and pathological data. Each of the 14 parameters was assigned a relative point score according to the current supporting evidence for that variable and the degree to which it was felt to impact the pretest probability for cancer.This observational study was conducted among 50 patients admitted in the Institute of General Surgery, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai.

## CLINICAL PARAMETERS AND LABORATORY TESTS

### AGE

Increasing age is long recognized as a well-established threat for thyroid malignancy. Age >45 years is incorporated into the American Joint Committee on Cancer (AJCC) staging[20]. A study of the Surveillance, Epidemiology, and End Results (SEER database) found, among 9904 patients with papillary thyroid cancer (PTC), that age >45 years was significantly associated with bad outcome on multivariate analysis[2]. Age >45 years was given a score of 1 in our study owing to limitations in specificity. 52% of malignant cases had age >45 years.

## GENDER

It is well known that thyroid malignancies are more common in females than males. But male gender, itself, is a solid risk factor for carcinoma and hence was given a score of 1. In our study 3 out of 13 patients diagnosed with malignancy were male (1:4.2) which is comparable to other studies.

## FAMILY HISTORY OF THYROID MALIGNANCY

A family history of thyroid cancer, or thyroid cancer in a first-degree relative, is also one of the few well-established risk considerations for carcinoma. Owing to the vast nature of support in the literature and the universally accepted nature of family history as a risk factor, it was also given 3 points within the scoring system[23]. In our study one patient had history of thyroid malignancy in mother, and this patient was also diagnosed with papillary cancer post operatively.

## EXPOSURE TO IONIZING RADIATION

Evidence of a linear dose–cancer association has been reported in studies of childhood survivors of the atomic bombings of Hiroshima and Nagasaki and in studies of children treated with either radiotherapy or iodine-131[24]. The Canadian National Dose Registry reported elevated standardized incidence ratios (SIRs) for thyroid cancer for both male (SIR 1.35; 90% CI 0.97–1.75) and female (SIR 1.42; 95% CI 1.19–1.69)

radiation workers[25]. As little doubt exists with respect to this association, a history of significant previous radiation exposure was given a score of 3 in the MTNS. None of the patients in our study had history of exposure to ionizing radiation.

**CONSISTENCY OF GLAND:**

A number of authors have agreed that nodules that are felt to be ‘‘stone’’ or ‘‘bone’’ hard on palpation indicate a higher likelihood of carcinoma. Raber[26] and colleagues demonstrated a predictive value of 57% and a relative risk of 2.6 for thyroid carcinoma in the presence of this feature (95% CI 1.2–5.6). Hence score of 2 was assigned. 12 out of 13 patients diagnosed with malignancy in our study had hard consistency of gland on clinical examination.

**TSH LEVEL**

Elevated serum thyroid-stimulating hormone level, even within the higher end of the range, is associated with augmented risk of malignancy. A well-designed study of over 800 patients conducted by Haymart et al[27]showed that the risk of carcinoma was significantly greater when TSH levels were between 1.40 and 4.99 mIU/L compared to lower levels (35% vs 25%, p = 0.002). Based on these findings, TSH serum levels >1.4 mIU/L was incorporated into the scoring system and given a risk score of 1. In our study 12 out of 13 patients diagnosed with malignancy

had a serum TSH level >1.4mIU/L which is comparable to the results of Haymart et al, Fiore et al and Jonklaas et al.

## ULTRASONOGRAPHY[28,29,30.31,32]

Ultrasonography attempts to distinguish malignant from benign nodules.Many recent studies have discussed the importance of distinctive sonographic features as predictors of malignant thyroid nodules.

### SHAPE OF THE GLAND

When imaging a nodule in the transverse direction, height greater than width, has been correlated with increased likelihood of malignancy (specificity range of 60– 93%)[32]. This is believed to represent aberrant, aggressive growth across the natural horizontal growth planes within the thyroid gland. It is also a reflection of tumor compressibility by an ultrasound probe. The sensitivity and specificity of this finding are variable, thus a score of only 1 was assigned. However in our study 92.30% of patients with malignancy demonstrated this feature on ultrasound.

### SIZE OF THE GLAND

Nodule size has been consistently associated with greater risk of malignancy. Tuttle and colleagues showed that nodules that were measured to be >4 cm to palpation had a 40% malignancy rate (vs 13%

for smaller lesions, p 5 .03). Raber and colleagues validated this correlation between size >4 cm and malignancy via sonography. Nodules measuring 3 cm or more on a sonogram conferred a 55% risk (vs 23% in smaller nodules, p , .0001) in another study. Yet smaller nodules(2 cm) have been demonstrated to represent a higher likelihood of cancer in other studies. To account for these discrepancies in the literature, we proposed that nodules of 2 to 2.9 cm be given a score of 2, nodulesof3to3.9cmascoreof3,and nodules >4cma score of 4 points. Our study too demonstrated a greater proportion of patients with malignancy (46%) having a size greater then 4 cm.

**NODULARITY OF THE GLAND**

Risk of malignancy in generalized swelling is about 3% and in solitary nodule of thyroid is about 15%. In a study conducted by Lema L.E.K, M.R.Aziz, N.A.Mbembati, H.A.Mwakyoma, malignancy was found in 10% of solitary nodule thyroid and 5% of multinodular goiter. In our study 53.8% of patients with malignancy had a solitary nodule and 46.2% demonstrated multinodular goiter.

**ECHOGENICITY, VASCULARITY AND CALCIFICATION OF GLAND**

Hypoechogenicity, increased Doppler flow and calcifications are the most widely recognized characteristics that increase the index of

suspicion for a malignant nodule. One study compounded the test characteristics for each feature of malignancy from seven additional studies and found hypoechogenicity to carry a 73% specificity, Doppler flow a 79% specificity andcalcifications a 91%specificity[28,29,31]. Because of high inter-observer variability and differing radiologic techniques, and because the various ultrasound findings are taken in constellation with one another, we assigned a score of 1 to each of these three features. In out study, 100 % of patients with malignancy demonstrated hypoechogenicity and increased vascularity of gland and 76.9% of patients with malignancy showed the presence of calcification within the gland.

**CERVICAL LYMPH NODE INVOLVEMENT**

Cervical lymphadenopathy is a common presentation in thyroid malignancy. The presence of cervical lymph nodes on ultrasound increased the predictive value of diagnosing thyroid cancer in suspicious nodules. Mazzaferri et al[30] demonstrated a 53–61% incidence of cervical lymphadenopathy in thyroid cancers. In our study, the incidence of cervical lymph node enlargement among malignant patients was 76.92% and was assigned a score of 2.

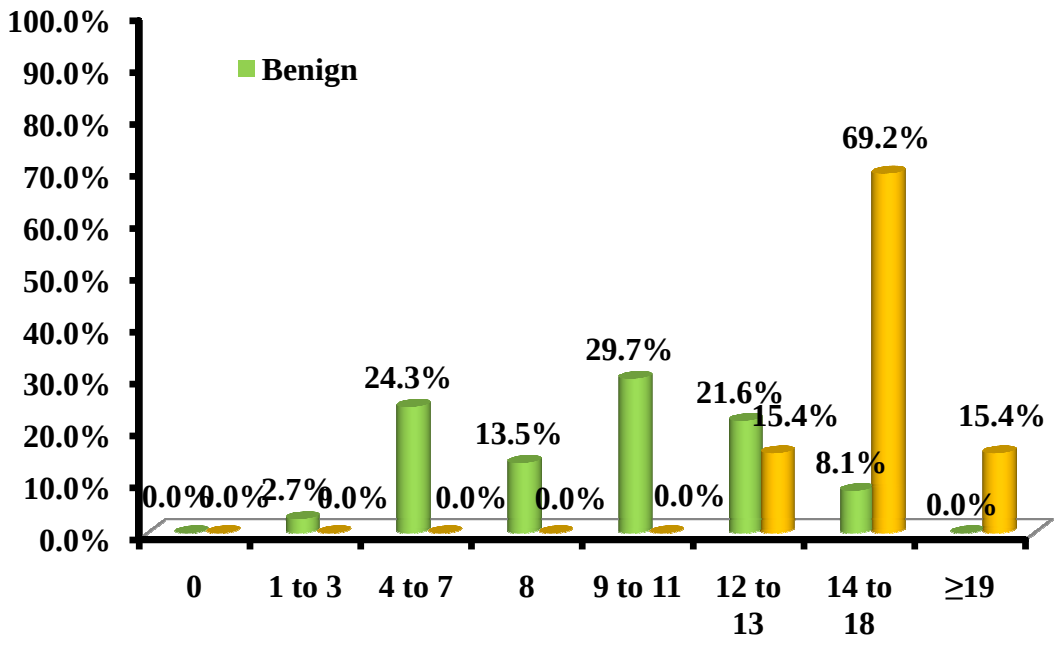
## FINE NEEDLE ASPIRATION CYTOLOGY

Cytologicatypia on FNAC has been shown to represent a higher likelihood of malignancy on a relatively consistent basis. In a study by Raparia et al, FNAC predicted malignancy with a sensitivity of 86.8%, a specificity of 67.0%, a negative predictive value of 87.5% and a positive predictive value of 65.5%[33,34,35]. Our study categorized FNAC report as benign, suspicious of malignancy and malignant and assigned a score of 1, 2 and 3 respectively. In our study, 53.8 % of patients with malignancy had a corelation between their FNAC and post operative HPE finding. The remaining 46.2 % of patients had an FNAC report which was suspicious for malignancy but their post operative HPE turned out to be malignant.

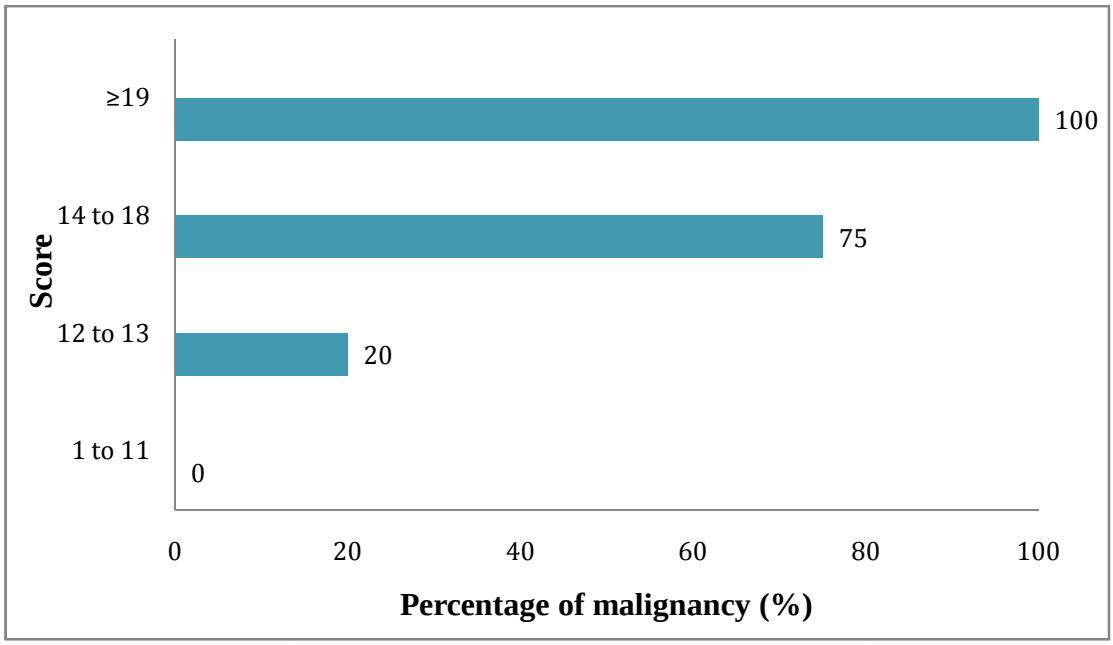
## THE SCORING SYSTEM

Our scoring system carried a maximum score of 26. The observed scores ranged between 3 to 19, with a mean score of 11.

## Score versus HPE status

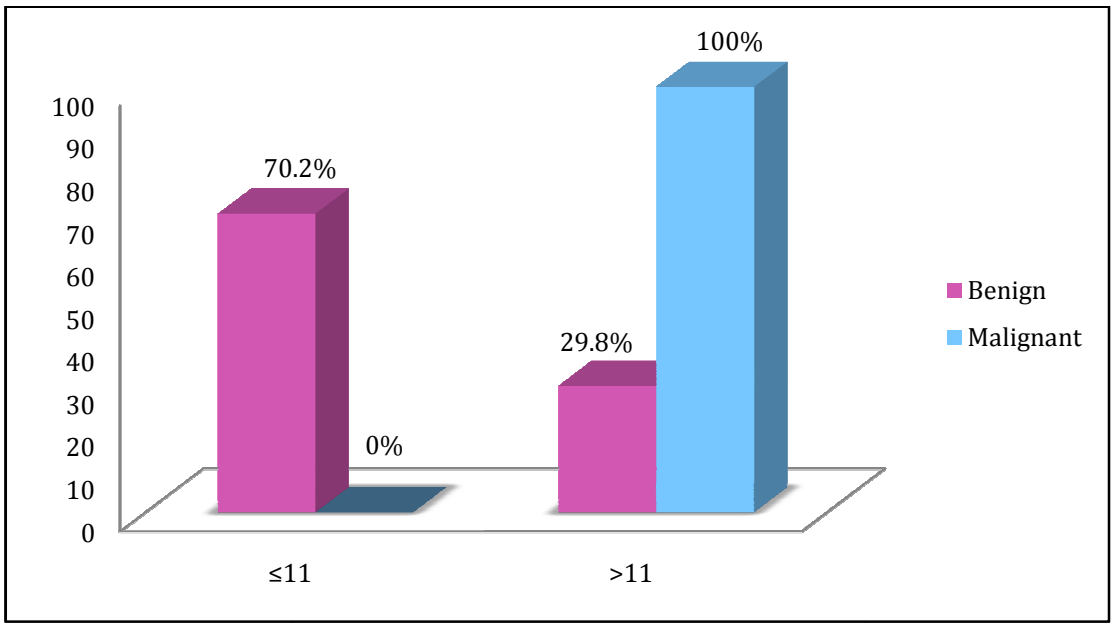



## Predictive value for malignancy

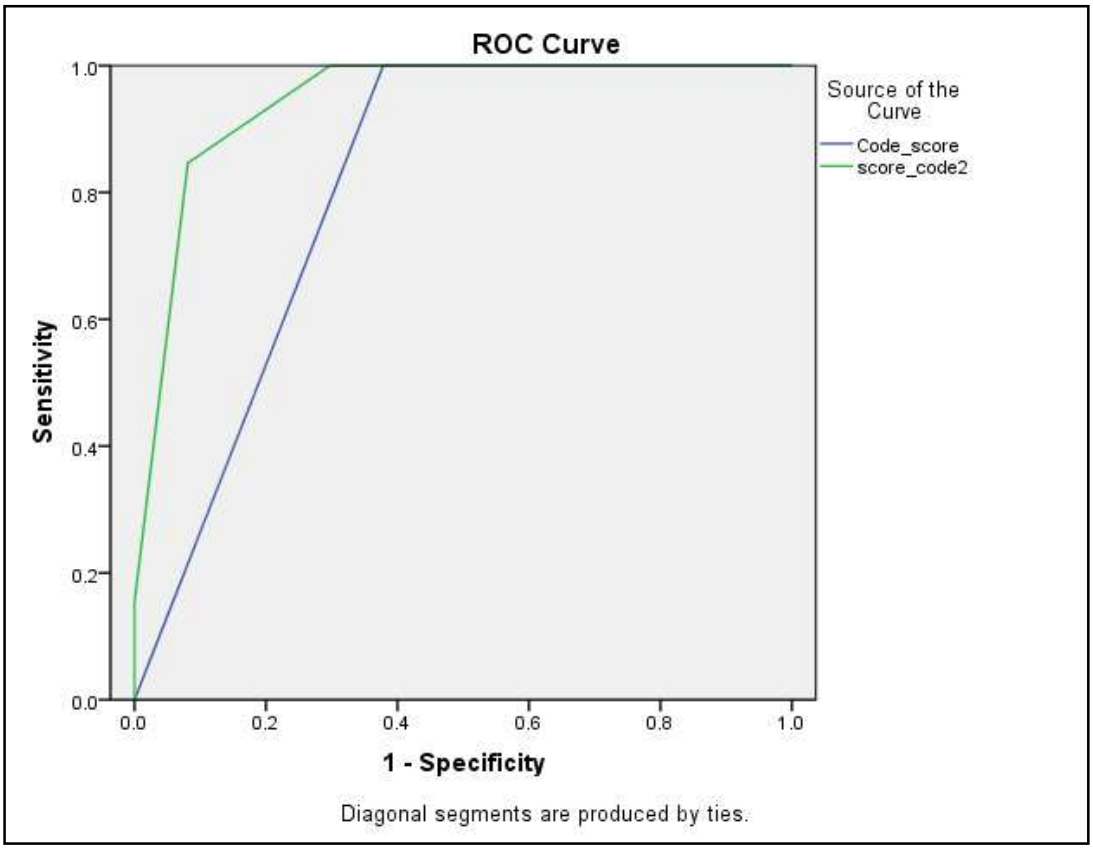


The incidence of thyroid carcinoma for scores of 1 to 11 was 0% (0 out of 24 patients), 12 to 13 was 20% (2 out of 10 patients), 14 to 18 was 75% (9 out of 12 patients) and ≥19 was 100% (2 out of 2 patients).

**Score versus cancer status**




In our study, all the malignant cases had a score >11. 70.2% of benign cases had a score ≤11 and 29.8% of benign cases had a score >11. The average risk of malignancy for patients with a score greater than the mean score of 11 was 54.166%. This greater risk demonstrated for patients above a score of 11 was also statistically significant ($p<0.0001$, $\chi^2 = 14.965$, df = 1).




The scoring system showed a favorable characteristic on the receiver operator curve (ROC). The area under the curve showed 81.1% sensitivity which is similar to that of the MTNS scoring system[22].

**Table 18: ROC curve analysis**

| Test Result Variable(s) | Area | Std. Error[a] | Asymptotic Sig.[b] | Asymptotic 95% Confidence Interval | |
|---|---|---|---|---|---|
| | | | | Lower Bound | Upper Bound |
| Mean score | .811 | .059 | .001 | .695 | .926 |
| MTNS score_ | .943 | .031 | .000 | .881 | 1.000 |

The sensitivity and specificity for carcinoma are 70.27% and 100% respectively. The positive and negative predictive values are 100% and 43.83% respectively. In our study, a score ≥16 was associated with 100% risk of malignancy.

In our study, 4 cases had pre-operative FNAC report as benign lesion. But all four patients had a score ≥15 according to our scoring system and their post operative HPE turned out to be malignant. Thus the scoring system helps to minimize the false-negative rates of FNAC. It can make pre-operative decision making much easier. Patients with a high score and thus a greater risk of malignancy can be carefully selected for surgery and a more vigilant post–operative follow up can be done.

## 5.2 LIMITATIONS OF THE STUDY

The study was carried out over a limited period of time with a restricted number of patients and there was lack of financial and infrastructural support, it could not have been large enough to be of reasonable precision. All the facts and figures mentioned here may considerably vary from those of large series covering wide range of time, but still then, as the cases of this study were collected from a tertiary level hospital in our country, this study has some credentials in applying a scoring system combining clinical, laboratory and sonological data, which are routinely documented pre-operatively, to predict the risk of malignancy in patients with thyroid nodules.

## 5.3 SUMMARY

Thyroid nodules are one of the frequently encountered diseases in the general surgery department. The incidence of malignancy in thyroid nodules is on the rise. Though there are many predictors of thyroid malignancy, none of them can conclusively predict the nature of a thyroid nodule. Our study aimed at evaluating a scoring system for predicting the risk of malignancy in thyroid nodules using clinical, laboratory and sonological data. The observations of this study can be summarized as follows:

- Our scoring system had a maximum score of 26. The observed scores ranged from 3 to 19.
- The incidence of thyroid carcinoma for scores of 1 to 11 was 0%, 12 to 13 was 20%, 14 to 18 was 75% and ≥19 was 100%.
- The mean score was found to be 11. The average risk of malignancy for a score ≤11 was 0% and for a score >11 was 54.166%.
- The sensitivity and specificity of the scoring system was 70.2% and 100% respectively.
- The positive and negative predictive value for the scoring system was 100% and 43.83% respectively.

- The greater risk of malignancy demonstrated for patients above a score of 11 was statistically significant ($p<0.0001$, $\chi^2 = 14.965$, df = 1).
- The risk of malignancy increased with increasing scores and was found to be 100% for a score ≥16.
- Among the risk factors studied, a family history of thyroid malignancy has a very high positive predictive value for development of thyroid carcinoma.
- Thyroid carcinomas are also frequently associated with increased TSH levels.
- Among the various USG features that predict malignancy, hypoechogenicity, calcification, increased vascularity and presence of cervical lymphadenopathy have a higher predictive value for malignancy.

## 5.4 CONCLUSION

This prospective observational type of study was conducted in Institute of General Surgery, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai, from 01 August 2015 to 31 July 2016. It can be concluded from the findings of the study that this combined scoring system can serve as an accurate predictor for thyroid malignancy. It will help physiciansto better assess the risk that a thyroid nodule is malignant, and therefore formulate clinical decisions accordingly, in conjunction with a more informed patient. This will also assist in the decision making with respect to the extent of surgery that will be performed: hemithyroidectomy or total thyroidectomy, with or without central compartment neck dissection. The scoring system brings high risk patients to the forefront and stands as an extremely powerful and valuable resource to surgeons to aid in their clinical decision making.

## 5.5 RECOMMENDATIONS

On the basis of the findings of the study, the following recommendations can be made:

- The scoring system can be introduced as a routine pre-operative assessment tool for patients presenting with thyroid nodules.
- Patients having a high score can be subjected to further evaluation before final decision making regarding the appropriate surgery.
- Further research is necessary in large scale for guidance regarding inclusion of additional risk factors to the scoring system thereby increasing its accuracy.

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# 8.ANNEXURES

## ANNEXURE – I: PROFORMA

## QUESTIONNAIRE:

Name: Age/Sex:
Address: Occupation:

**SYMPTOMS:**
Swelling in the neck- size, duration

**PAST HISTORY:**
Previous h/o surgery/ radiation/ chemotherapy

**FAMILY HISTORY:**
Thyroid malignancy+/-

**GENERAL EXAMINATION:**

**VITAL SIGNS:**

PR-
BP-
RR-

**LOCAL EXAMINATION:**
Examination of Thyroid gland-size, consistency, no. of nodules
Examination of cervical Lymph Nodes

**INVESTIGATIONS:**

FNAC

USG NECK

TSH LEVEL

**SURGERY DONE:**

**POST-OP HPE**

## ANNEXURE – II: INFORMATION SHEET AND CONSENT FORM

## INFORMATION SHEET

## TITLE: "EVALUATION OF A SCORING SYSTEM FOR PREDICTING THE RISK OF MALIGNANCY IN THYROID NODULES USING CLINICAL, LABORATORY AND SONOLOGICAL DATA

**Name of Investigator**: Dr.S.Sadhana. **Name of Participant:**

**Purpose of Research :**To evaluate the efficacy of a scoring system using clinical and laboratory data, ultrasound findings and fnac report for predicting the risk of malignancy in thyroid nodules.

S**tudy Design :**Prospective and Retrospective Observational Study

**Study Procedures :**Patient will be subjected to routine investigations, Thyroid function test, USG and FNAC.

**Possible Risks :**No risks to the patient

**Possible benefits:**

**To patient :**Patients treatment is tailored to their specific risk predictions.

**To doctor & to other people :**If this study gives positive results, it can help determine the treatment protocol for patients undergoing thyroid surgeries. This will help in providing better and complete treatment to other patients in future.

**Confidentiality of the information obtained from you :**The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared

**Can you decide to stop participating in the study :**Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time

**How will your decision to not participate in the study affect you :**Your decision will not result in any loss of benefits to which you are otherwise entitled.

Signature of Investigator Signature Of Participant

Date : Date:
Place : Place:

## ஆய்வில் பங்கேற்பவர்கானதகவல் அறிக்கை

**ஆய்வின் தலைப்பு:**மருத்துவவிவரங்கள்,நுண்ணதிர்வில் பரிசோதனைவிவரங்கள் மற்றும் ஆய்வகததகவல்களைபயன்படுத்திதைராய்டுகட்டியில்
ஏற்படக்கூடியபுற்றுநோய்க்கானவாய்பைகணிக்கஉதவும் ஒருமதிப்பீட்டுமுறையைபற்றியஆய்வு.

**ஆய்வாளரின் பெயர்** : மரு.ச.சாதனா (அறுவைசிகிச்சைஆய்வுபிரிவு)

**ஆய்வுமையம் :** ராஜீவ் காந்திஅரசுபொதுமருத்துவமனை,சென்னை.

இந்தஆய்வில் தங்களைபங்கேற்கஅழைக்கிறோம். இந்ததகவல் அறிக்கையில் கூறப்பட்டிருக்கும் தகவல்கள் தாங்கள் இந்தஆராய்ச்சியில் பங்கேற்கலாமாவேண்டாமாஎன்பதைமுடிவுசெய்யஉதவியாக இருக்கும். இந்தபடிவத்தில் உள்ளதகவல்கள் பற்றிஉள்ளசந்தேகங்களைநீங்கள் தயங்காமல் கேட்கலாம்.

**இந்தஆய்வின் நோக்கம் என்ன?**

தைராய்டுகட்டியில் புற்றுநோய் ஏற்படுவதற்கானவாய்பைமருத்துவவிவரங்கள்,ஆய்வுகூடசோதனைமற்றும் நுண்ணதிர்வில் பரிசோதனைதகவல்கள் மூலம் கண்டறியும் மதிப்பீடுஅமைப்புபற்றியஆய்வு. இதனால் சிகிச்சைமுறைமாறாது (அ) தாமதமாகாது.

**ஆய்வுமுறைகள்:**

விரிவானநோய்க் குறிப்புகளும்,மருத்துவபரிசோதனைகளும் முறையாகசெய்யப்படும். தைராய்டுகட்டிஉள்ளவர்களுக்குகட்டியின் தன்மை,தைராய்டு ஹார்மோன் அளவு,நுண்ணதர்வுபரிசோதனைவிவரம் மற்றும் கட்டியின் நுண்ணுசிதிரவப்படிவபரிசோதனையின் தகவல்கள் சேகரிக்கப்பட்டு இந்தமதிப்பீடுஅமைக்கப்படும். இந்தமதிப்பீட்டைஅவர்களுடையஅறுவைசிகிச்சைக்குபின் கிடைக்கும் பேத்தாலாஜி அறிக்கையுடன் ஒப்பிட்டுஅவர்களுக்குபுற்றுநோய் வருவதற்கானவாய்பைகண்டுஅறியப்படும்.

**ஆய்வினால் மக்களுக்குஏற்படும் நன்மைகள்:**

இந்தஆய்வின் முடிவில் கிடைக்கும் தகவல்கள் சமுதாயதிற்குபயனுள்ளதாகவும்,எதிர்காலத்தில் நோயாளிகளுக்குமருத்துவதீர்வாகவும் அமையும்.

**தங்களிடமிருந்துபெறப்படும் தகவல்களின் நம்பிக்கைத் தன்மை:**

தங்களிடமிருந்துபெறப்படும் தகவல்கள் பாதுகாக்கப்படுவதற்கான முழு உரிமையும் தங்களுக்குஉண்டு. இந்தபடிவத்தில் கையொப்பமிடுவதுடன் மூலம்,தாங்கள் தங்களைபற்றியவிவரங்களையும்,ஆய்வுவிவரங்களையும் ஆய்வாளர்,ஆய்வுநடத்தும் ஏனையோர் வரைமுறைஒழுங்குகுழுவினர் மற்றும் சட்டத்திற்குஉட்பட்டமருந்துகட்டுப்பாடு இயக்குநர் ஆகியோர் பார்வையிடஅனுமதிக்கிறேன். இந்தஆய்வில் காட்டப்படும் தகவல்கள் அறிவியல் நாளேடுகளிலோஅறிவியல் கூட்டங்களிலோசமர்ப்பிக்கப்படும் பட்சத்தில் தங்களதுஅடையாளம் வெளிப்படுத்தமாட்டாது.

**ஆய்வின் நடுவில் அதிலிருந்துவிலகிக்கொள்ளநினைத்தால்:**

இந்தஆய்வில் பங்கேற்பதுதங்களின் சொந்தவிருப்பமேமேலும் ஆய்வின் நடுவில் எந்தநேரத்திலும்,எக்காரணமும் கூறாமல் விலகிக்கொள்ளதங்களுக்கு முழு உரிமையும் உண்டு. இருப்பினும் விலகுவதற்குமுன் ஆய்வுகுழுவுடன் கலந்துஆலோசிப்பதுஉகந்ததுஎனபரிந்துரைக்கப்படுகின்றது.

ஆராய்ச்சியாளர் கையொப்பம் : பங்கேற்பவரின் கையொப்பம் :
தேதி : தேதி:

**PATIENT CONSENT FORM**

Study Detail : "EVALUATION OF A SCORING SYSTEM FOR PREDICTING THE RISK OF MALIGNANCY IN THYROID NODULES USING CLINICAL, LABORATORY AND SONOLOGICAL DATA"

Study Centre : Rajiv Gandhi Government General Hospital, Chennai.

Patient's Name :

Patient's Age :

Identification Number :

Patient may check (√) these boxes

a) I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ❑

b) I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ❑

c) I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ❑

d) I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms. ❑

e) I hereby consent to participate in this study. ❑

f) I hereby give permission to undergo detailed clinical examination and blood investigations as required.

Signature/thumb impressionSignature of Investigator

Patient's Name and Address: Study Investigator's Name:

## ஆய்வின் ஒப்புதல்

**ஆய்வின் தலைப்பு:**மருத்துவவிவரங்கள்,நுண்ணதிர்வில் பரிசோதனைவிவரங்கள் மற்றும் ஆய்வகதகவல்களைபயன்படுத்திதைராய்டுகட்டியில்
ஏற்படக்கூடியபுற்றுநோய்க்கானவாய்பைகணிக்கஉதவும்
ஒருமதிப்பீட்டுமுறையைபற்றியஆய்வு.

**ஆய்வாளரின் பெயர்** : மரு.ச.சாதனா (அறுவைசிகிச்சைஆய்வுபிரிவு)

**ஆய்வுமையம்** : ராஜீவ் காந்திஅரசுபொதுமருத்துவமனை,சென்னை.

_____ எனும் நான்,எனக்குகொடுத்துள்ளதகவல் தாளைபடித்துபுரிந்துகொண்டேன். நான் பதினெட்டுவயதைகடந்துள்ளதால்,என்னுடையசுயநினைவுடனும், முழு சுதந்திரதுடனும், இந்தஆராய்ச்சியில் என்னைசேர்த்துக் கொள்ளசம்மதிக்கிறேன்.

நான் எனக்குஅளிக்கப்பட்டஒப்புதல் படிவத்தையும்,தகவல்களையும் படித்துபுரிந்துகொண்டேன். ஒப்புதல் படிவத்தில் உள்ளதகவல்கள் எனக்குவிளக்கிக் கூறப்பட்டுள்ளன. ஆய்வின் தன்மைபற்றிஎனக்குவிளக்கப்பட்டுள்ளது. என்னுடையஉரிமைகளையும் பொறுப்புகளையும் ஆராய்ச்சியாளர் விளக்கிக் கூறினார். நான் இதுவரைஎடுத்துள்ளஅனைத்துவிதமானசிகிச்சைமுறைகளையும் ஆராய்ச்சியாளரிடம் கூறியுள்ளேன். இந்தஆராய்ச்சியினால் ஏற்படும் தீமைகள் பற்றிவிளக்கப்பட்டன.

நான் ஆராய்ச்சியாளருடன் ஒத்துழைப்பேன் என்றும்,எனக்குஏற்படக்கூடியஅசாதாரணமானநிகழ்வுகள் பற்றியும் உடனடியாகஆராய்ச்சியாளரிடம் தெரிவிப்பேன் என்றுஉறுதி கூறுகிறேன். இந்தஆய்விலிருந்துஎப்போதுவேண்டுமானாலும் எக்காரணமும் கூறாமல் என்னைவிடுவித்துக் கொள்ளலாம் என்பதைஅறிவேன்.

என்னிடம் இருந்துபெறப்படும் தகவல்களைஅரசு,வரைமுறைஅதிகாரிகள் ஆகியோர்களுடன் பகிர்ந்துகொள்ளஆராய்ச்சியாளர்களுக்குஅனுமதிஅளிக்கிறேன். என்னுடையசிகிச்சைக்கட்டுகளைபார்வையிடஉரிமைஉண்டு. என்னுடையதகவல்களின் அடையாளம் இரகசியமாகவைக்கப்படும் என்பதைஅறிவேன்.

இந்தஆராய்ச்சியில் பங்கேற்கதன்னிச்சையாகமுழுமனதுடன் சம்மதிக்கிறேன்.

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|---|---|
| பங்கேற்பவரின் கையொப்பம் / ரேகை : | ஆய்வாளரின் கையொப்பம் |
| பங்கேற்பவரின் பெயர் : | ஆய்வாளரின் பெயர் : ச.சாதனா |
| இடம் : | இடம் : |
| தேதி : | தேதி : |

| | | | | | MASTER CHART | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| SNO: | NAME: | AGE: | SEX: | IP NO: | CLINICAL DATA: | | | | | | ULTRASONOGRAM FINDINGS: | | | | | | | FNAC | TOTAL SCORE | POST OP HPE |
| | | | | | AGE >45 (1) | MALE SEX (1) | H/O EXPOSURE TO IONISING RADIATION (3) | FAMILY H/O THYROID MALIGNANCY (3) | HARD CONSISTENCY (2) | TSH >1.4mIU/L (1) | SHAPE TALLER THAN WIDE (1) | SIZE: 2-2.9=2 3-3.9=3 ≥4=4 | NODULARITY MULTIPLE (1) SOLITARY(2) | HYPOECHOIC (1) | CALCIFICATION + (1) | INCREASED VASCULARITY (1) | CERVICAL NODES + (2) | BENIGN (1) SUSPICIOUS(2) MALIGNANT(3) | | |
| 1 | Padma | 45 | F | 23116 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 3 | 1 | 1 | 0 | 0 | 0 | 1 | 8 | benign |
| 2 | Ellamal | 55 | F | 19136 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 4 | 2 | 1 | 0 | 1 | 0 | 1 | 12 | benign |
| 3 | Hajira | 22 | F | 20326 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 3 | benign |
| 4 | Amaravathy | 20 | F | 24758 | 0 | 0 | 0 | 0 | 2 | 1 | 1 | 3 | 1 | 1 | 1 | 1 | 0 | 3 | 14 | malignant |
| 5 | Jayachithra | 41 | F | 13872 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 4 | 2 | 1 | 1 | 1 | 2 | 1 | 14 | benign |
| 6 | Desammal | 30 | F | 23957 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 4 | 2 | 1 | 0 | 0 | 0 | 1 | 9 | benign |
| 7 | Mujbur Rahman | 54 | M | 44897 | 1 | 1 | 0 | 0 | 2 | 1 | 0 | 3 | 1 | 1 | 1 | 1 | 2 | 2 | 16 | malignant |
| 8 | Sumibaruda | 34 | F | 41561 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 3 | 2 | 1 | 0 | 1 | 0 | 2 | 11 | benign |
| 9 | Malathi | 38 | F | 23612 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 4 | 2 | 1 | 0 | 1 | 2 | 1 | 12 | benign |
| 10 | Kamalam | 70 | F | 13257 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 3 | 1 | 0 | 1 | 0 | 0 | 1 | 8 | benign |
| 11 | Malathy | 29 | F | 15640 | 0 | 0 | 0 | 0 | 2 | 1 | 1 | 2 | 2 | 1 | 0 | 1 | 0 | 2 | 12 | malignant |
| 12 | Jayalakshmi | 67 | F | 12836 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 2 | 1 | 0 | 0 | 0 | 1 | 9 | benign |
| 13 | Kodhai | 47 | F | 20626 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 2 | 1 | 0 | 0 | 0 | 1 | 8 | benign |
| 14 | Anandhi | 50 | F | 16454 | 1 | 0 | 0 | 0 | 2 | 1 | 1 | 4 | 2 | 1 | 0 | 1 | 2 | 3 | 18 | malignant |
| 15 | Jothi | 45 | F | 21471 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 3 | 2 | 1 | 0 | 0 | 0 | 1 | 9 | benign |
| 16 | Muthu | 34 | F | 36441 | 0 | 0 | 0 | 0 | 2 | 1 | 1 | 3 | 2 | 1 | 1 | 1 | 2 | 3 | 17 | malignant |
| 17 | Gangammal | 37 | F | 25016 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | 1 | 1 | 0 | 1 | 2 | 1 | 10 | benign |
| 18 | Sarala | 43 | F | 25295 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 3 | 2 | 1 | 1 | 1 | 0 | 2 | 11 | benign |
| 19 | Lalitha | 48 | F | 22941 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 1 | 6 | benign |
| 20 | Arul selvi | 16 | F | 46218 | 0 | 0 | 0 | 0 | 2 | 1 | 1 | 3 | 2 | 1 | 1 | 1 | 2 | 2 | 15 | malignant |
| 21 | Patchaiammal | 60 | F | 31276 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 3 | 2 | 0 | 0 | 0 | 0 | 1 | 9 | benign |
| 22 | Periyammal | 70 | F | 37311 | 1 | 0 | 0 | 0 | 2 | 1 | 1 | 4 | 1 | 1 | 1 | 1 | 2 | 3 | 18 | malignant |
| 23 | Ramaprabha | 40 | F | 24427 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | 0 | 0 | 1 | 5 | benign |
| 24 | Mariyammal | 35 | F | 21663 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 1 | 0 | 0 | 0 | 0 | 1 | 6 | benign |

| | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 25 | Gomathy | 30 | F | 22964 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 4 | 1 | 0 | 0 | 0 | 0 | 1 | 7 | benign |
| 26 | krishnaveni | 27 | F | 21731 | 0 | 0 | 0 | 0 | 2 | 1 | 1 | 2 | 2 | 1 | 1 | 1 | 2 | 2 | 15 | malignant |
| 27 | Kasthuri | 41 | F | 27119 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 2 | 0 | 0 | 0 | 0 | 1 | 4 | benign |
| 28 | Janani | 12 | F | 17818 | 0 | 0 | 0 | 3 | 2 | 1 | 0 | 2 | 1 | 1 | 1 | 1 | 2 | 2 | 16 | malignant |
| 29 | Kaliammal | 60 | F | 32312 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 3 | 1 | 0 | 0 | 0 | 0 | 1 | 7 | benign |
| 30 | Selvarasi | 40 | F | 28577 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 3 | 1 | 1 | 0 | 0 | 0 | 1 | 8 | benign |
| 31 | Arumugam | 54 | M | 21316 | 1 | 1 | 0 | 0 | 2 | 1 | 1 | 4 | 1 | 1 | 1 | 1 | 2 | 3 | 19 | malignant |
| 32 | Sasikala | 37 | F | 36958 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 4 | 2 | 1 | 0 | 1 | 0 | 1 | 11 | benign |
| 33 | radhika | 36 | F | 30532 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 3 | 1 | 0 | 0 | 1 | 0 | 1 | 7 | benign |
| 34 | Rani | 38 | F | 32764 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 3 | 2 | 1 | 0 | 1 | 0 | 1 | 10 | benign |
| 35 | Basilika Mary | 25 | F | 1E+05 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 4 | 1 | 1 | 0 | 1 | 2 | 2 | 13 | malignant |
| 36 | Rajendran | 50 | M | 32603 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 3 | 2 | 1 | 0 | 1 | 0 | 1 | 10 | benign |
| 37 | Sujatha | 42 | F | 21602 | 0 | 0 | 0 | 0 | 2 | 0 | 1 | 3 | 1 | 1 | 0 | 1 | 2 | 2 | 13 | benign |
| 38 | Mala | 32 | F | 33831 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 1 | 1 | 0 | 0 | 0 | 1 | 6 | benign |
| 39 | Shoba | 44 | F | 45412 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 4 | 2 | 1 | 0 | 0 | 0 | 1 | 10 | benign |
| 40 | minnala | 54 | F | 41961 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 4 | 2 | 1 | 0 | 1 | 2 | 2 | 15 | benign |
| 41 | Nobisha Beevi | 50 | F | 25837 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 3 | 1 | 1 | 0 | 1 | 2 | 2 | 13 | benign |
| 42 | Thillaiammal | 55 | F | 25982 | 1 | 0 | 0 | 0 | 2 | 1 | 0 | 4 | 2 | 1 | 1 | 1 | 2 | 3 | 18 | malignant |
| 43 | Subramaniam | 55 | M | 38292 | 1 | 1 | 0 | 0 | 2 | 0 | 1 | 4 | 2 | 1 | 1 | 1 | 2 | 3 | 19 | malignant |
| 44 | Arumugam | 70 | M | 40222 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 4 | 1 | 1 | 0 | 1 | 2 | 1 | 13 | benign |
| 45 | Vijaya | 45 | F | 39530 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 3 | 2 | 0 | 0 | 1 | 2 | 2 | 12 | benign |
| 46 | Navanetham | 64 | F | 48024 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 4 | 1 | 1 | 0 | 1 | 2 | 2 | 14 | benign |
| 47 | Gandhimathy | 45 | M | 12932 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 4 | 2 | 1 | 0 | 1 | 0 | 1 | 13 | benign |
| 48 | Noorinisha | 30 | F | 40316 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 4 | 2 | 1 | 0 | 1 | 0 | 1 | 12 | benign |
| 49 | Malliga | 50 | F | 26331 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 2 | 1 | 1 | 0 | 1 | 0 | 1 | 8 | benign |
| 50 | Noorinisha | 30 | F | 30237 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 1 | 1 | 0 | 1 | 0 | 1 | 7 | benign |