A STUDY ON FNAC AND BIOPSY CORRELATION OF THYROID LESIONS - IMMUNOHISTOCHEMISTRY OF THYROID MALIGNANCY

A dissertation submitted
in partial fulfilment of the requirements
for the award of degree of

DOCTOR OF MEDICINE IN PATHOLOGY
M.D DEGREE
(BRANCH - III)

THE TAMIL NADU
DR.M.G.R.MEDICAL UNIVERSITY
CHENNAI - 600 032.

APRIL 2015

CERTIFICATE

This is to certify that this dissertation titled **"A STUDY ON FNAC AND BIOPSY CORRELATION OF THYROID LESIONS – IMMUNOHISTROCHEMISTRY OF THYROID MALIGNANCY"** is the original and bonafide work done by **Dr.REVATHY.M,** under my guidance and supervision, at the Govt. Kilpauk Medical College and Hospital, Chennai – 600 010, during the tenure of her course in M.D. (Branch-III) PATHOLOGY from May 2012 to April 2015 held under the regulations of The Tamil Nadu Dr. M.G.R. Medical University, Guindy, Chennai - 600 032.

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DECLARATION

I hereby declare that this dissertation entitled **"A STUDY ON FNAC AND BIOPSY CORRELATION OF THYROID LESIONS-IMMUNOHISTOCHEMISTRY OF THYROID MALIGNANCY"** has been prepared by me during the period of study as a postgraduate of Pathology from May 2012 to April 2015 at the Govt. Kilpauk Medical College, Chennai – 600 010, under the guidance and supervision of **DR. J.BHARATHI VIDHYA JAYANTHI., M.D,** Professor and HOD, Department of Pathology, Govt. Kilpauk Medical College, Chennai – 600 010 in partial fulfillment of regulation for the award of M.D Pathology degree examination to be held in April 2015 by the Tamilnadu Dr. M.G.R Medical University, Guindy, Chennai – 600 032.

I also declare that this topic has not been submitted for the award of a Master or Diploma degree by any other medical university in India in the recent past.

Place: Chennai.
Date: **Dr. Revathy .M**

ACKNOWLEDGEMENT

I express my profound gratitude to **Prof.Dr.N.Gunasekaran,M.D**. **DTCD**, Dean, Kilpauk medical College-10 for permitting me to use all the needed resources for this dissertation work.

I would like to express my gratitude and reverence to the Head of the Department of Pathology and my guide**, Prof.Dr.J.Bharathi Vidhya Jayanthi,M.D.,** Kilpauk Medical College, Chennai, whose guidance and help has elevated me to this level, to conduct the study successfully. I sincerely thank her expert guidance and constant encouragement to conduct this study.

I take immense pleasure in thanking **Prof.Dr.M. Saraswathi,M.D**, who have offered many valuable suggestions and encouragement during this period, whose help has been invaluable to me.

I thank **Prof.Dr.Pushpa,DGO,M.D., Prof.Dr.Andal,M.D, Prof.Dr.Venu Anand,M.D, Prof.Dr.Sahayaraj, M.D**., Department of pathology, Kilpauk Medical College and Hospital, Chennai-10 for their constant encouragement.

I also thank all my Assistant Professors, **Dr. Teleflo, M.D, Dr.Jaganathan, M.D, Dr.Premalatha, M.D, Dr.Chitrakala Sugumar, DGO, M.D, Dr.Geethalakshmi, M.D, Dr.Balaji, M.D, Dr.Surekha,**

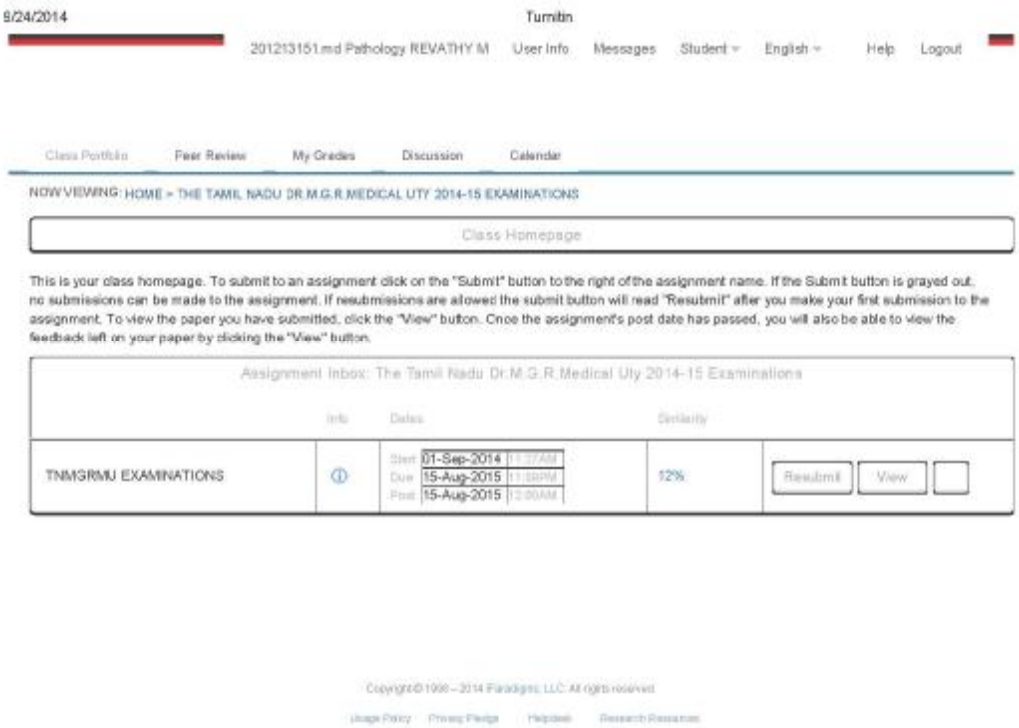
M.D, Dr.Gayathri, M.D., Dr. Martina, M.D, Dr.Vijayanandhi, DCP., Dr. Susruthan, M.D,. for their valuable advice and guidance.

I wish to express my thanks to my collegues **Dr. Jeyasambavi, Dr.Rajeshwari, Dr. Subhitha and Dr. Lokesh kumar** and technical staff members **Mrs. Komala, Mrs. Lalitha, Mrs. Jayanthi, Mrs.Gnanamani, Mrs. Suganthi** and the attender **Mrs. Jeyalakshmi.**

No words are enough to express my pride and deep sense of reverence I have for my parents **Mr.Mahendran & Mrs.Vijayalakshmi**, my brothers **Dr.Manoj and Dr.Naveen**, My Parents in law **Mr.Mohanraj & Mrs.Shanthi**, who have not only showered their love on me, but made me what I am, instilling in me the courage to believe in my convictions.

Words can hardly express my thanks to my husband **Mr.Vimal Raj** who always supported me as a friend in times of joy and distress to keep my confidence afloat, whose advice and encouragement have were probably the most valuable.

Above all, I remember the master of ceremonies, the powerful **God, The Almighty** who gave me courage, enthusiasm and vigour to accomplish this work.



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File size:	1.09M
Page count:	111
Word count:	10,553
Character count:	57,582
Submission date:	24-Sep-2014 01:44PM
Submission ID:	453963198

INTRODUCTION

ABBREVIATIONS

FNA	–	Fine needle aspiration
FNAC	–	fine needle aspiration cytology
H & E	–	hematoxylin and eosin
IHC	–	Immunohistochemistry
HPF	–	high power field
TRIS	–	tris (hydroxymethyl)amino methane
WHO	-	world health organisation
TG	-	thyroglobulin
T3	–	triiodothyronine
T4	-	thyroxine
TSH	-	thyroid stimulating hormone
TRH	-	thyrotropin releasing hormone
DPX	-	distrene pthalide in xylene
SV 40	-	simian virus 40
MW	-	molecular weight
KDa	-	kiloDalton

Wt p53	-	wild type p53
HPE	–	histopathology
PTC	–	papillary carcinoma thyroid
HTA	-	hyalinising trabecular adenoma
Min	–	minutes
LI	–	labelling index
M	-	Male
F	-	Female

TABLES OF CONTENTS

INTRODUCTION

The thyroid gland (Greek, Thyreos – Shield + eidos - Form)[24] is a butterfly shaped organ situated in anterioinferior region of neck. It is composed of two lobes joined together by isthmus. As it is superficially located, any pathological changes resulting in enlargement of the gland create masses that can be palpable or easily visible. The functional effects of hormonal changes also create different clinical manifestations that prompt investigation[20].

The Incidence of thyroid nodules constitute about 4-7% of adult population. Only 5% of these nodules are malignant and remaining are either nonneoplastic or benign[21]. Thyroid malignancies constitute about 1.5%[70] of all cancers and are more common among Females.

Fine Needle Aspiration (FNA) is a cost effective and more reliable test for diagnosing thyroid Nodules[22]. Inorder to avoid unneccessary surgery[38], preoperative distinction between non neoplastic, benign and malignant lesions are of utmost importance[23]. FNA is a serves as a useful tool to categorise non neoplastic and neoplastic lesions and thereby guide in therapy. It is also helpful in diagnosing and monitoring clinically equivocal cases and cases where biochemical and immunological parameters are normal or marginally abnormal.

Most of the thyroid tumors are readily diagnosed by using definitive histological criteria, but there are certain conditions like variants of carcinomas derived from follicular epithelial cells where this distinction becomes subtle. For this reason ancillary technique like immunohistochemistry is used.

In this study first we analyse cytological and histopathological correlation in thyroid lesions. Furthermore the study also evaluates the role of immunohistochemical analysis for differentiating benign and malignant tumours by using immunological markers.

AIMS AND OBJECTIVES

- To study the incidence of thyroid lesions.
- To study the age, sex and clinical presentations of thyroid lesions.
- To assess the cytological and histological correlation of thyroid lesion.
- To estimate the incidence of p53 positivity and Ki-67 index in Thyroid malignancies

REVIEW OF LITERATURE

The thyroid gland is a butterfly shaped endocrine gland situated in the anterior aspect of the root of the neck. Disorders of thyroid comprise a group of commonly encountered endocrinologic disease.

STUDIES DONE EARLIER:

History of FNAC:

The importance of scientific contribution in medicine requires both synthesis of a number of observations and the elixir of time. The ultimate acceptance of medical facts and development of medical procedures are influenced by social and economic factors. The history of fine needle aspiration biopsy was also influenced by such factors. The roots of FNAC can be traced back to Scandinavian countries.

The British Medical Journal "Lancet" in 1833 first reported the use of aspiration by aspirating large liver mass at St. Bartholomeus Hospital in London by Edward Stanley. The mass was found to be a hydatid cyst and not a tumour [1].

In 1847 & 1851 Kun and Lebert described the use of a cannula to extract cell samples from palpable tumours and they also explained microscope can be used to identify cell morphology[5].

In 1853 James Paget in his lectures advocated aspiration forms a basic means of diagnosing the lesions.

In 1863, Pritchard used grooved needle for aspiration in breast lesion. He also gave an excellent description for cytology of fat necrosis[7]

Dungeon and Patrick, in 1927, emphasied scrape or touch preparation as cytological method to tissue biopsy, which is essentially a duplicate of the typical method used in fine needle aspiration. They reported 200 cases with accuracy of 98.6%3.

The major impact in the development of aspiration biopsy was given by two physicians in Sweden and Newyork . Their diagnostic methods combined both cytologic and histologic features from cell block preparation.

In 1926 Martin & Ellis introduced the method of aspiration in diagnosis of tumours at memorial Hospital, New York [2]. In 1933 Steward by studying 45 cases, he felt that the procedure was useful in diagnosing anaplastic carcinoma but ambiguous for the

differentiating papillary and follicular carcinoma from colloid nodules [3].

Stewert analysed 2500 tumours in Memorial hospital by aspiration method and emphasied certain points to be considered for optimal results. They are:

- Technique of aspiration and preparation of the sample.
- Aspirated material should be interpretated along with clinical information.
- Compare the picture of the smear with conventional histology.
- Pattern of the smear should be taken into consideration along with detailed individual cytological features for correct interpretation.
- Limitations of aspiration biosy is also taken into consideration along with usefulness of this method.

Lipton and Abel in 1947, measured aspirated cells to evaluate hyperthyroidism. Tempka and his associates studied aspirates from colloid goiter in 1948.

Soderstom (1952); Eihorn & Franzen (1962) & Cohen & Choi (1988) evaluated importance of FNAC in selecting the patients for surgical or medical management [3].

Mazzaferri EL stated that FNAC is an important diagnostic tool for evaluation of a palpable thyroid mass [4].

The first international course in aspiration cytology was held in the year 1970 in Stockholm by Karolinska cytologists.

Frable WJ (1989) used small needles (25G or higher gauge) for aspiration of thyroid nodules and he also preferred plain slides instead of frosted slides for smear making. He used papanicolaou, May Grunwald Giemsa (MGG), Metachrome B and hematoxylin Eosin stains[5].

In 1988, Non-aspiration fine needle cytology, a new technique was pioneered in France to study the nodular thyroid disease. This technique employs insertion of the syringe and eliminates active aspiration which is replaced by the principle of capillary suction of fluid or semisolid material into the hub of the needle[92].

Harach HR in 1989 studied 142 cases of nodular goiters and he classified follicular lesions into type I (benign) type II (atypical benign) and typeIII(suspicious for malignancy)[7]. These observations

along with increase of surgically resected specimens indicated FNAC as accurate diagnostic modality.

Shah A studied 262 thyroid lesions and found overall diagnostic accuracy for FNAC to be 84.66%, 97.13% for nonneoplastic and 80.45% for neoplastic lesions. He concluded that FNA is a useful tool in diagnosing thyroid lesions and to differentiate between nonneoplastic and neoplastic lesions [25].

Carpi et al advocated the use of scintiscanning and ultrasonography to be used along with Fine Needle Aspiration (FNA) [8].

Yang et al used of ultrafast papanicolaou stain in identifying nuclear abnormalities in papillary carcinomas of thyroid[9].

In 1989, Sharo Mair et al, performed both aspirational and non-aspirational technique in 100 consecutive superficial mass in various body sites and concluded that non-aspirational technique produced superior quality material while aspirational technique produced adequate material.

Shukla PK(1993) used simple reusuable device from the barrel of 10ml disposable plastic syringe to hold a piston of 20ml disposable syringe so as to produce continuous negative pressure. He found this method to be satisfactory and inexpensive.

EMBRYOLOGY

Thyroid is the first endocrine gland to appear in the embryo as early as 24 days of gestation. Thyroid gland developes as median endodermal down growth from the primitive pharynx in between first and second pharyngeal pouch. This median anlage form a hallow diverticulium that descends into the anterior neck which maintains its connection with the tongue by a narrow tube, the thyroglossal duct.

The tip of the tubular duct bifurcates and divides the whole mass into a series of double cellular plates from where isthmus and lateral lobes of thyroid develops, which reaches the final position anterior to trachea at about seven weeks of gestation. The thyroglossal duct usually disappears at this stage, but the remnants of the duct may persist at any level during the course and later may develop as ectopic thyroid tissue and a median cyst.

The foramen caecum of the tongue represents the vestigial opening of the thyroglossal duct. The ultimobrachial body is derived from fourth and fifth pharyngeal pouch which fuses with the median thyroid anlage and becomes part of the lateral lobe of thyroid. The progenitors of “C” cells which are derived from the neural crest migrate to the ultimobrachial body before their incorporation into the developing thyroid gland. During fourteenth week the gland consists of well formed follicles lined by follicular epithelial cells and contains thyroglobulin positive colloid in the lumen.

ANATOMY:

The normal adult thyroid gland weighs about 16-25gm. It is composed of right and left lobe connected by thin isthmus in midline. Each lobe has pointed superior pole and a blunt inferior pole26. There is a thin remnant of tract of decent at superior end of isthmus called as pyramidal lobe.

Isthmus lies close to the ventral aspect of trachea covering 2nd, 3rd and 4th tracheal rings. Each lobe is 5cm length and extends from the oblique line of the thyroid cartilage to 6th tracheal ring. It is covered by pretracheal fascia which is firmly attached posteriorly to 2nd, 3rd and 4th tracheal rings[30,31,53].

Arterial Supply : Thyroid gland is supplied by superior and inferior thyroid arteries which are the branches of external carotid arteries and thyrocervical trunk respectively[31].

Venous Drainage : Thyroid is drained by the superior, middle and inferior thyroid veins. Superior and middle thyroid veins drains into external jugular vein, while inferior thyroid vein drains into brachiocephalic vein[31].

Nerve Supply : Nerves to thyroid are mainly derived from cervical sympathetic ganglions. These are vasoconstrictor.

Lymphatic Drainage : Thyroid is drained by upper and lower deep cervical nodes.

Upper part of the gland drains into upper deep cervical nodes either directly or through prelaryngeal nodes. Lower part of the gland drains into lower deep cervical nodes either directly or via pretracheal or paratracheal nodes[31,53].

The parafollicular cells are usually seen at the junction of upper 1/3rd and lower 2/3rd of lateral lobes. They are the neural crest derivative and reaches thyroid via ultimobranchial body.

HISTOLOGY:

The thyroid gland is enclosed by tense connective tissue capsule which extends into substance of the gland dividing into multiple lobules. Each lobule is made up of 20-40 follicules supplied by an end artery.

The functional and morphological unit of thyroid gland is follicles lined by single layer of follicular epithelial cells filled with colloid. The follicules vary in size with average diameter of 200microns. The follicules are surrounded by rich network of capillaries, veins and lymphatics.

According to the functional activity of the gland, the size and lining of the follicule, staining intensity of the colloid varies. In inactive gland, follicules are lined by flattened epithelial cells whereas in functional gland follicules are lined by tall cylindrical follicular epithelial cells.In hyperfunctioning gland colloid will be scant whereas it is dense, homogenous and intensly eosinophilic in hypoactive gland.

The second minor component of the thyroid gland are represented by parafollicular “C” cells. With the standard technique the parafollicular cells are difficult or impossible to distinguish from

follicular epithelial cells without using special staining procedure. They are large polygonal or spindle shaped cells than follicleswith lightly granular nucleus and small indistinct nucleolus [30,31].

Solid cell rests[29] are remnants of ultimobrachial bodies which are usually found along central axis of the middle and upper third of the lateral lobes. They mainly composed of polygonal or oval cells admixed with occasional clear cells.

Other structures that are found in the thyroid are parathyroid glands, normal thymus, salivary gland remnants, and occasional teratomatous elements like cartilage[28].

PHYSIOLOGY:

Thyroid secretes two hormones thyroxine(T3) and triiodothyronine(T4) which is controlled by thyroid stimulating factor(TSH) secreted by anterior pituitary gland, which in turn controlled by thyroid hormone releasing hormone(TRH) secreted by hypothalamus by classical negative feedback loop . It also secretes another hormone calcitonin which plays a major role in calcium metabolism[30].

The steps involved in thyroid hormone synthesis are as follows:

1. Iodide trapping – sodium iodide symporter transports iodide from blood to thyroid follicules
2. Oxidation of iodidie ion – by the enzyme peroxidase
3. Organification of thyroglobulin(TG) – Binding of iodine with tyrosine portion of TG
4. Iodination of tyrosine and formation of thyroid hormones by coupling reaction.

The iodotyrosine residues are condensed to form the biologically active thyroid hormones, T3,T4 which are stores as thyroglobulin in colloid. When the gland is stimulated, there will be

endocytosis of colloid and proteolysis of thyroglobulin by lysosomal enzymes and release of T3&T4 into the circulation.

After the hormones are secreted they are released into circulation, peripheral conversion of T4 to T3 occurs by deiodination. Triiodothyronine(T3) has high affinity and greater activity when compared to T4[27,30].

Calcitonin, 32 aminoacid peptide secreted by parathyroid gland,mainly controls calcium metabolism in the body.

Common clinical manifestations:

Diseases of thyroid gland are grouped into three categories

- Hyperthyroidism - excessive release of thyroid hormones.
- Hypothyroidism – deficiency of thyroid hormones.
- Mass lesions of thyroid[32]

HYPERTHYROIDISM:

The common symptoms of increased secretions of thyroid hormone are

- Weight loss.
- Excessive appetite.
- Heat intolerance.
- Sweating.
- Palpitations.
- Tremors.
- Emotional liability.
- Tiredness.
- Diarrhea.

The signs of hyperthyroidism are

- Tachycardia.
- Hot moist palms.
- Exophthalmos.
- Eyelid retraction / lid lag.
- Agitation.
- Goiter.

HYPOTHYROIDISM:

The common symptoms of decreased secretions of thyroid hormones are

- Weight gain.
- Constipation.
- Cold intolerance.
- Menstrual disturbances.
- Lethargy.
- Tiredness/weakness.
- Hoarseness of voice.

The signs of hypothyroidism are

- Bradycardia.
- Cold extremeties.
- Dry skin and hair.
- Periorbital puffines.
- Hoarseness of voice.
- Bradykinesis.
- Delayed relaxation of ankle jerk.
- Carpeltunnel syndrome[24,31]

CYTOLOGY:

The interpretation of cytological features depends on evaluation of cellularity, architectural pattern of tissue fragments in low power, cytological features in high power and background characteristics[33].

A cytological sample is considered satisfactory when four to six clusters of follicular epithelial cells are seen in atleast two slides prepared from two needle passes[10]

The cytology of normal thyroid gland includes

- Follicular epithelial cells.
- Colloid.
- Skeletal muscle.
- Cartilage.
- Tracheal epithelium.

Follicular epithelial cells:

Follicular epithelial cells are dispersed or in small clusters. Some of the follicules are fragile, loses their cytoplasm and appear as bare nuclei similar to normal small lymphocyte. These follicules

are cuboidal cells with regularly spaced nuclei, pale cytoplasm arranged around lumen with or without colloid[34,35].

Colloid:

Colloid has different staining character with different stains and fixation procedures. It stains pink with alcholol fixed H&E stain. They stain pale green to orange pink with cracking artefact and clumping in PAP stain. Colloid stain deep magenta in air dried Romanowsky stain[36,35,22,34]. Sometimes colloid may be washed away during processing, but parched earth or crazy pavement like artefact may be seen indicating the presence of colloid.

The cytological features[19,22] of individual thyroid lesions are described below:

Thyroid cyst:

The fluid aspirated from a thyroid cyst usually contains numerous foamy macrophages, sometimes haemosiderin laden (siderophages), altered blood, colloid and small clusters of benign thyroid epithelial cells. Papillary carcinoma thyroid also present as cystic lesion and the presence of psammoma bodies in the aspirated fluid should cause concern while reporting.

Thyroiditis:

Thyroiditis includes lymphocytic thyroiditis, Hashimoto thyroiditis, De Quervain's thyroiditis and Riedel's thyroidits. Large number of lymphocytes and plasma cells are present in both lymphocytic and Hashimoto thyroiditis but presence of Hurthle cells, multinucleated giant cells and epitheloid histiocytes differentiates hashimoto thyroiditis from lymphocytic thyroiditis. Cytology of De Quervain's thyroiditis shows large multinucleated giant histiocytes, nuclear debris, inflammatory cells including neutrophils, lymphocytes and presence of abundant colloid. Usually there will be history of viral illness followed by thyroid enlargement in de quervain's thyroiditis.

Simple colloid goiter:

Smears usually show normal cytological appearance of follicular epithelial cells along with presence of abundant very thick colloid.

Nodular goiter:

Smears in nodular goiter usually shows

- Abundant thick and thin colloid
- Follicular epithelial cells in monolayered sheets, poorly cohesive groups

- Globular colloid masses superimposed with follicular epithelial cells
- Plenty of bare nuclei
- Large hyperplastic follicular epithelial cells with abundant vacuolated cytoplasm and fire flares
- Hurthle cells, pigment laden histiocytes and cell debris

Follicular neoplasm:

Follicular adenoma and follicular carcinoma are distinguished only in histology with presence of capsular and vascular invasion. These two groups along with follicular variant of papillary carcinoma of thyroid comes under follicular neoplasm.

In FNAC, the follicular neoplasm includes

- Repetitive microfollicular pattern
- Rosettes, syncytial groups and equal sized follicular epithelial cell clusters
- Bloody and colloid free background

Papillary carcinoma thyroid (PTC):

Smears are usually cellular with numerous papillary fragments and three dimensional clusters of follicular epithelial cells. Sometimes

papillae are removed intact but appear as flat sheets with distinct anatomical borders. PTC has distinct nuclear features which are well visualized in cytology. They are

- Nuclear crowding
- Nuclear overlapping
- Nuclear grooving
- Intranuclear inclusions
- Ovoid pale nuclei with fine granular powdery chromatin

Scanty viscous chewing gum colloid is one of the striking feature in papillary carcinoma. The background shows macrophages, debris, multinucleated giant cells, lymphocytes and cystic degeneration.

Medullary carcinoma:

Smears are usually cellular with round, polygonal and spindle cells some are plasmacytoid cells with eccentric nucleus and moderate amount of cytoplasm and well defined cell margins. The nucleus show anisocytosis and fine stippled or coarsely granular cytoplasm. Sometimes amyloid may also be detected in the smear.

Anaplastic carcinoma:

These are the most aggressive tumours of thyroid. Smears contains three major patterns or in combination of either giant cells, spindle cells and squamoid cells along with necrotic background with dissociated pleomorphic malignant cells and abnormal mitosis

Lymphomas can also occur in thyroid either as primary tumour or as part of systemic tumours. Presence of monotonous population of atypical malignant lymphocytes as on Non-Hodgkin's lymphoma or Reed steinberg cells as in Hodgkin's lymphoma favours diagnosis

Metastatis to thyroid are usually rare. Breast, kidney, lung , gastrointestinal malignancies metastatis to thyroid. Smears are similar as their histology.

Sometimes extraneous cells like muscle can be seen when needle is passed through muscle.

There are no absolute contraindication for Fine needle aspiration in thyroid lesions if patient is cooperative [36,22].

COMPLICATIONS:

There are certain rare complications that can occur during needle aspiration in thyroid. They are

- Local hemorrhage due to needling and occasionally hematoma in anterior neck[11,12]
- Airway compression.
- Carotid hematoma[13.]
- Transient vocal cord paralysis.
- Acute transient goiter[14]
- Acute suppurative thyroiditis[15]
- Chemical neuritis[16]
- Puncturing of trachea causes coughing.
- Occasionally hemorrhage, necrosis or infarction obscure histological pattern of thyroid neoplasms.

TERMINOLOGY & REPORTING:

There has been variety of terminology used for reporting thyroid FNA. They are

1. The Papanicolaou Society task force[17] on standards of practice in 1996 produced the following reporting scheme:

- Inadequate.
- Benign Nonneoplastic.
  - Colloid nodule.
  - Nodular goiter.
  - Cystic goiter.
  - Thyroiditis.
- Cellular follicular lesion.
  - Favour hyperplastic (adenomatous) nodule.
  - Follicular neoplasm.
- Hurthle cell neoplasm.
- Malignant.

2. The most recent terminology has been given by National cancer Institute – sponsored Thyroid Fine Needle Aspiration State of the Science conference[18] and the guidelines are:

- Nondiagnostic(unsatisfactory).
- Benign.
  - Colloid nodule.
  - Nodular goiter.
  - Hyperplastic (adenomatoid) nodule.
  - Chronic lymphocytic thyroiditis.
- Follicular lesion(atypia) of undetermined significance.
- Neoplasm.
  - Follicular neoplasm.
  - Hurthle cell neoplasm.
- Suspicious for malignancy.
- Malignant.

3. The Bethesda system of reporting[19] includes 6 categories.

- Nondiagnostic.
- Benign.
- Atypia of undetermined origin.
- FN/ Suspicious of FN.
- Suspicious of malignancy.
- Malignant.

Principle lesions in thyroid aspiration cytology are (Koss GL)[37]

- Cysts.
- Colloid goiter(adenomatous, nodular, diffuse).
- Thyroiditis (acute, subacute, lymphocytic/ autoimmune).
- Adenoma.
- Carcinoma.
  - Papillary carcinoma and its variant.
  - Follicular neoplasms.
  - Medullary carcinoma.
  - Anaplastic carcinoma.
    - Large cell.
    - Small cell.
- Malignant lymphoma.
- Metastatic tumours.

WHO Classification of thyroid tumours:

a) Tumours of thyroid follicular or metaplastic epithelium

1. Follicular adenoma (including Hurthle cell adenoma)

i. Follicular carcinoma (including Hurthle cell carcinoma)

   a. Minimally invasive.

   b. Widely invasive.

ii. Papillary carcinoma.

iii. Poorly differentiated thyroid carcinoma, including insular carcinoma.

iv. Anaplastic (undifferentiated) and squamous cell carcinoma, including so-called carcinosarcoma.

v. Columnar cell carcinoma.

vi. Mucoepidermoid carcinoma.

vii. Sclerosing mucoepidermoid carcinoma with eosinophilia.

viii. Mucinous carcinoma.

b) Tumours showing C-cell differentiation :

Medullary carcinoma.

c) Tumours showing both follicular and C-Cell differentiation:

i) Collision tumor: Follicular/papillary and medullary carcinoma.

ii) Mixed follicular: Parafollicular carcinoma (differentiated thyroid carcinoma, intermediate type)

d) Tumours showing thymus or related branchial pouch differentiation:

i) Ectopic thymoma.

ii) Spindle Epithelial tumour with thymus like element (SETTLE).

iii) Carcinoma showing thymus like element (CASTLE) or intrathyroid thymic carcinoma.

e) Tumours of lymphoid cells :

i) Malignant lymphoma

ii) Plasmacytoma

f) Intrathyroid parathyroid tumour :

i) Parathyroid adenoma.

ii) Parathyroid carcinoma.

g) Mesenchymal and other tumours :

i) Benign and malignant mesenchymal tumours, such as solitary fibrous tumours, smooth muscle tumour, peripheral nerve sheath tumour, angiosarcoma.

ii) Paraganglioma.

iii) Teratoma.

IMMUNOHISTOCHEMISTRY IN THYROID:

Immunohistochemical analysis has been widely used in diagnosing many unequivocal thyroid tumours. Thyroid lesions with nodular architecture and follicular growth pattern often pose diagnostic difficulty during the assessment of cytologic and histologic specimens. The diagnosis of follicular neoplasm on cytology or follicular tumor of uncertain malignant potential on histology is likely to cause confusion and delay effective management of these lesions. Occasionally, thyroid tumors represent unusual or metastatic lesions and their accurate diagnosis required for proper management.

Most thyroid tumors can be readily diagnosed using histopathologic criteria, thereby allowing the pathologist to differentiate between benign and malignant lesions and to make an accurate classification for the majority of the variants of carcinomas derived from follicular epithelial cells. However, in most cases, this distinction becomes subtle. The decision favouring one or another has its clinical consequences and implies different modalities of treatment. At first, there should be a need to avoid excessive treatment and psychological discomfort to the patient. Secondly, patients with aggressive disease course need to have effective management at the initial stages when it is still curable.

For this reason, the approach to these challenging tumors should include ancillary techniques, like immunohistochemistry and molecular profiling, which can improve the standard morphologic assessment both in cytological samples and surgical specimens[28].

Several immunohistochemical markers using different antibodies, either alone or combined in panels, have been postulated to improve the diagnostic accuracy of thyroid lesions.

So, in this study we are using the two immunohistochemical markers namely

- p53
- Ki-67

p53 gene

p53 (Tp53) protein was first identified in the year 1979 as a transformation- related protein[39] and a cellular protein. These protein accumulates in the nuclei of cancer cells and binds tightly to the simian virus 40 (SV40) large T antigen[40,41].

p53 is a nuclear phosphoprotein of MW 53 kDa, and encoded by a 20-Kb gene containing 11 exons and 10 introns[41], which is located on the short arm of chromosome 17[42]. There are two other members in this family of genes, p63 and p73.

Structure of p53:

Wild-type p53 protein contains 393 amino acids and is composed of several structural and functional domains. It has an N-terminus containing an amino-terminal domain and a proline-rich region, a central core domain and a C terminal region containing an oligomerization, a strongly basic carboxylterminal regulatory domain, a nuclear localization signal sequence and 3 nuclear export signal sequence[42].

The amino-terminal domain is required for transactivation activity and interacts with various transcription factors like acetyltransferases and MDM2 (murine double minute 2). The proline-rich region plays a vital

role in stability of p53 regulated by MDM2, where it becomes more susceptible to degradation by MDM2 if this region is deleted.

The central core of this protein is made up of DNA-binding domain required for sequence-specific DNA binding. The basic C-terminus of p53 also functions as a negative regulatory domain and has a role in induction of cell death. C terminal tail of p53 regulates core DNA binding domain. If this interaction is disrupted by posttranslational modification, the DNA binding domain will become more active, thus inducing an enhanced transcriptional activity[43,44].

Most of the p53 mutations found in human cancers are missense mutation in central DNA binding domain. In p53 family of proteins both p63 and p73 show considerable homology with p53 but at the same time have structural and functional differences.

Physiology of p53:

p53 is an important tumor suppressor gene, as it integrates with multiple stress signals and regulates cell response to DNA damage by the induction of series of target genes, which regulate cell cycle arrest. This allows DNA damage repair or apoptosis of severely damaged cells. These biological effects are elicited by p53 binding to responsive promoters which, in turn, activate the transcription of several genes like

p21 (G1 cell growth arrest), Bax, and PUMA. Another major target gene of p53 is Mdm2, an ubiquitin ligase that binds to the N-terminus of the p53 protein and causes p53 inactivation, nuclear export and degradation. Mdm2 along with p53 acts as amajor negative feedback loop aimed at reducing

p53 proapoptotic function and thus allowing cell repair. p53 is also a major regulator for cell senescence. Telomere shortening caused by cell replications triggers p53 activation, thereby blocking cell cycle and favours the cell entry into the stage of senescence.

As a consequence, p53 inactivation or mutation may contribute to the increased number of cell replications and accumulation of genetic abnormalities in human cancers[42,43,44,49] .

Mutation of p53:

The p53 gene is often found to be genetically altered in most of the tumors, and is one of the frequently inactivated genes in the human cancers. Aberrant stimulation of cell proliferation leads to DNA replication stress, DNA double standard breaks, genomic instability, activation of the DNA damage checkpoint, and ultimately leads to p53-dependent apoptosis. p53 mutation is frequently seen in 70% of lung

cancer, 60% in colon, head and neck, ovary, and bladder and 45% in stomach cancer[43,44,49].

Because of the short half life of wild type p53, they remain undetectable when analysed by IHC, whereas mutated p53 can be readily detected by IHC in various malignancies because of its long half- life[69].

There are two forms of p53, wild (normal) type and mutated type. Wild type (wt) p53 are mainly responsible for series of biological consequences like cell cycle regulation, induction of apoptosis, development, differentiation, gene amplification and cellular senescence[44]. Hence p53 gene was known as “Guardian of genome”[43].

Because of the short half life of wild type p53, they remain undetectable when analysed by IHC, whereas mutated p53 can be readily detected by IHC in various malignancies because of its long half- life[69].

p53 gene in thyroid:

Mutated p53 is seen in most of the human cancers[45] accounting for 50% of cases[48], but they are expressed as late genetic event in thyroid neoplasms accounting for 10% of cases[49,51,52]. p53 is expressed mainly in anaplastic and poorly differentiated thyroid carcinomas[50] and rarely in well differentiated tumours like papillary and follicular carcinoma as well as in medullary carcinoma thyroid.

These observations suggests that p53 plays minor role in thyroid cancers where its mutation indicates tumour progression to aggressiveness or invasive subtypes.

Positive p53 immunoreactivity in thyroid neoplasms acts as an independent prognostic factor for the survival of patients with thyroid cancer[46,47].

Ki-67 gene

Ki-67 gene was first described in the year 1983 by Gerdes et al91 after immunising mice with Hodgkin's lymphoma cell line L428. The antibody was named after its production in the city of Kiel (Hence Ki), Germany. 67 referes to the clone number on 96 well plates from which it was found. The Ki-67 gene was located on the long arm of chromosome 10(10q25) with half life of 60-90mins.

Ki-67 antigen represents nuclear nonhistone protein which is expressed by the cells in proliferative phase[53]. The Ki-67 protein is a large (395 kD) nuclear protein that is expressed during all active phases of the cell cycle except in G0 phase indicating there is correlation between Ki-67 immunoreaction and mitotic activity[55]. Since proliferation status is closely associated with tumor aggressiveness, the Ki-67 labeling index (LI) is considered as an established prognostic marker for various tumor types[54,56].

The Ki-67 is a protein phosphorylated via serine and threonine with a critical role in cell division and expressed in mitotically active cells.

The expression of the Ki-67 protein as an indicator of proliferation marker requires two criteria. frist the antigen should be continuously present during all phases of cell cycle and secondly,the antigen should rapidly disappear in non proliferative phase ie Go phase. Although it has been reported that Ki-67 antigen show staining faint or even undetectable at the onset of DNA synthesis it is generally accepted that the Ki-67 protein is expressed during all active phases of the cell cycle. Furthermore, all tissues tested showed positive Ki-67 staining in all proliferative phases of cell cycle[67,91].

Ki-67 expression correlates well with disease course and helps as a significant predictor for overall survival of the patients and presence of distant metastasis. The predictive value of Ki-67 labelling index has been studied in breast and prostate cancers. The prognostic value of the Ki-67 index is particularly important in those types of cancers in which the clinical course is difficult to predict based on histological criteria. Ki-67 labelling index is an independent and significant prognostic factor for disease-specific survival of the patient. Ki-67 labeling index also has a role in predicting how a tumor responds to a certain type of therapy[54,55].

Ki-67 in thyroid:

The Ki-67 labelling index will be lower in papillary carcinoma thyroid when compared to breast, colon or prostrate carcinoma. Ki-67 proliferation activity has limited role in diagnosing thyroid neoplasm whereas this marker is mainly used to differentiate benign and malignant thyroid lesions.

Follicular growth pattern pose a diagnostic difficulty wherein Ki-67 labelling index helps in differentiating follicular adenoma from follicular variant carcinoma. Ki-67 expression is maximum in medullary carcinoma thyroid but low in well differentiated tumours like papillary and follicular carcinoma[66,67,68].

IMMUNOHISTOCHEMISTRY

The two disciplines in immunohistochemistry are immunology and histology.

IHC is used to determine expression of antigen in tissues by using antibodies thereby aids in identifying lineage of cell population and define biologically distinct population of cells with same lineage.

Immunohistochemistry was first started by Coons and Jones[57] by using immunofluorescence technique in frozen sections. Later in 1966 Pierce modified this procedure and used in paraffin sections. In 1991 Shi and his associates introduced antigen retrivel technique. In this method paraffin processed sections are heated at high temperature before IHC staining. Depending on the sensitivity and specificity of antigen-antibody reaction antibodies are used in IHC which is provided by Hybridoma technique.

BLOCKING NON-SPECIFIC BACKGROUND STAINING:

Endogenous enzymes or non specific binding are responsible for background staining. Pre-incubating the sections with serum from same species minimizes nonspecific binding with primary antibody.

Peroxidise acts as endogenous enzymes which is seen both in normal and neoplastic tissues. These are abolished by peroxidise blocking or by using alternate systems such as immunogold technique.

Endogenous activity is overcomed by incubating the sections either in methanol containing 0.5% hydrogen peroxidise for about 10min at room temperature or by adding 0.1M concentration of levamisole to the enzyme substrate solution.

DETECTION SYSTEMS:

For visualisation of antigens antibodies are labelled or flagged with fluorescent substances, enzymes forming coloured reaction with suitable substrate or by using heavy metals. Enzymes are most commonly used in IHC. Incubation with a chromogen produces a stable end product suitable for light microscopy.

METHODS OF IHC

DIRECT LABELLING METHOD:

In this method antibody is attached with a label by chemical means and directly applied to tissue sections. The main advantage of this method is that it is rapid and easy procedure, but carries low sensitivity.

INDIRECT LABELLING METHOD:

In this method enzymes are labelled with secondary antibodies which are produced against primary antibody. This technique is more sensitive and easy to handle.

AVIDIN BIOTIN CONJUGATE METHOD:

In this method primary antibody is added followed by biotinylated secondary antibody and which in turn followed by preformed complexes of Avidin and Biotin horse radish peroxidise conjugate. This method is more specific but endogenous biotin produces background staining.

BIOTIN STREPTAVIDIN METHOD:

Instead of avidin, streptavidin is used in this method. Streptavin are more stable and also reduces background staining.

IMMUNOGOLD WITH SILVER ENHANCEMENT:

This technique represents the most sensitive and effective light microscopic immunohistochemical method currently available. In this method the gold particles are enhanced by the addition of several layers of metallic silver. Tih method is also used in ultrastructural immunolocalisation.

POLYMERIC METHOD:

In this method Dextran backbone are used for binding of large number of enzyme molecules to secondary antibody. This method increases sensitivity, minimizes non specific background staining and reduces total number of assay steps.

IMMUNOHISTOCHEMISTRY PROCESS:

In IHC the tissue has to undergo following steps like fixation, dehydration and paraffin embedding as in routine H&E sections.

FIXATION:

This is a critical step in interpretation of IHC as it preserves the tissue morphology. 10% buffered formalin is a ideal fixative for IHC. The main disadvantage of this fixation technique is that it masks the

antigens within the tissues which is overcome by antigen retrieval technique.

ANTIGEN RETRIEVAL:

This method involves unmasking of antigens. The following techniques can be used.

- Proteolytic enzyme digestion
- Microwave antigen retrieval
- Pressure cooker antigen retrieval
- Microwave and trypsin antigen retrieval

Pressure cooker antigen retrieval is most commonly used technique in IHC. Care should be taken to allow section to dry as this destroys antigenicity.

CONTROLS:

Control tissue is essential in IHC. Use of internal control protects against the effect of poor fixation.

MATERIALS AND METHODS

After obtaining ethical committee clearance in our college, Kilpauk Medical College, the study was conducted at the Department of Pathology.

A total of 200 cases of thyroid lesons were included in study between the year June 2010 to June 2014 from three collaborative departments – Department of General surgery Kilpauk Medical College, Government Peripheral Hospital AnnaNagar and ESI Hospital Ayanavaram, Chennai.

Study designs were both prospective and retrospective. For retrospective study the case notes were retrieved from the records and information about age, sex, clinical presentation, biochemical results, cytological and histological diagnosis were reviewed. For prospective study all these findings were directly obtained from patients after getting consent and then cytological and histological diagnosis was done.

Immunohistochemical analysis was done in 50 cases using antibodies for Ki-67 and p53. In this study, various thyroid lesions like adenomatous goiter, toxic goiter, dominant nodule of nodular colloid goiter, hyperplastic nodule, colloid nodule/goiter are grouped under the spectrum of nodular goiter in cytology and histopathology.

CYTOLOGICAL STUDY:

After examining the patient, FNA was done by using 23-24 gauge needles with the patient in supine position and slight extension of neck to make the thyroid swelling more prominent. Without any negative pressure, aspiration was done by capillary suction, while instructing the patient to refrain from swallowing. Negative pressure was given in cases where colloid was aspirated. Aspirate was then expressed in a clean glass slide and smeared. At least three slides were made; all the slides were placed in 95% Isopropyl alcohol for 20mins for fixation and stained with Hematoxylin and Eosin stain.

Steps of staining procedure:

1. Harris hematoxylin – 5 mins.
2. Running tap water- 2 dips.
3. Decolourisation – 1% acid alcohol for 5-10 secs.
4. Blueing – running tapwater for 10-15 mins.
5. Counterstain – 1% aqueous eosin for 1-2 mins.
6. Wash in water.
7. Mounting with DPX.

Results:

Cytoplasm – Pink.

Nucleus – Blue.

Histopathological Study:

All thyroidectomy specimens were received in 10% Buffered formalin and left for overnight fixation. Grossing of the specimens was done and representative samples/bits were taken and sent for routine tissue processing.

Staining of Tissue Section:

Sections of about 4-5microns thick were cut from routinely processed paraffin embedded block and gently lowered on surface of water bath at 45 degree celsius to remove any folding.

Sections were then taken on alcohol cleaned glass slides smeared with thin film of egg albumin.

Slides were then warmed on a warmer at 58 degree Celsius for one hour, cooled and then stained.

Sections were then placed in two changes of Xylene for 2mins to remove the wax .

Sections were placed in 2 changes of Absolute alcohol for 2mins to remove Xylene.

Sections were treated with descending grades of alcohol with 90% alcohol for 1min and 80% and 70% alcohol for 1min.

Finally, sections were brought to De ionised water and then stained by routine Hematoxylin and Eosin stain.

Cytological diagnosis was correlated with histopathology and efficacy of FNAC was estimated by using the methodology of Galen and Gambino as follows:[58]

Sensitivity = TP/TP +FN x 100

Specificity = TN/TN+FP x 100

Efficacy = (TP+TN/TP+TN+FP+FN) x 100

TP = True Positive TN = True Negative

FP = False Positive FN = False Negative

These statistical values are interdependent statistical concepts showing accurate results.

Thyroid FNA is useful for

1. Detecting patients for thyroid malignancy (sensitivity).
2. Excludes patients without malignancy (Specificity).
3. Predicts the presence/absence of malignancy (positive & negative predictive value).
4. Classify patients who should have their nodules excised and who's excision is unnecessary (efficacy)

Immunohistochemistry

Immunohistochemistry was done in 50 cases. Paraffin blocks were chosen for IHC and stains used were p53 and Ki-67.

Sections were cut using the microtome with disposable blades. Slides are coated with chrom alum. Sections were subjected first to antigen retrieval using pressure cooker technique by citrate retrieval solution with pH 6. Then, sections are treated with Horse Radish Peroxidase (HRP) polymer technique for blocking endogenous antigens.

Immunohistochemical stains:

The following clones were used from Biogenex laboratories as immunohistochemical stains.

- Clone DO 7 for p53
- Clone v9 for Ki-67

Methodology:

1. Chrom alum coated slides were taken through following stages.
2. Treated with peroxidise block for inhibiting endogenous peroxidase in tissue for 5mins.
3. Washed two times in TRIS buffer for 5mins.
4. Application of power block for about 5mins for blocking non-specific antigen antibody reaction.
5. Washed two times in TRIS buffer for 5mins.
6. Primary antibody was added to the section for 60mins.
7. Wased two times in TRIS buffer for 5mins.
8. Secondary antibody tagged with Horse Radish Peroxidase enzymes were then added to the section for 30mins.
9. Washed two times in TRIS buffer for 5mins.
10. Super enhancer was applied to the section for 30mins mainly to enhance the final reaction product to increase the sensitivity of the antigen and antibody reaction.
11. Washed two times in TRIS buffer for 5mins.
12. DAB (Diamino benzidine) chromogen was then applied for 5mins.
13. Washed in distilled water for 5mins.
14. Counterstaining of the section was done by using hematoxylin.
15. Air dried and mounted with DPX.

Results:

Both p53 and Ki-67

Positive – nuclear stain – Brown

Methods of scoring for Ki-67

All slides were evaluated. Cells with brown granular nuclear staining were considered positive. An area with maximum proliferation was chosen to evaluate Ki-67 labelling index. A minimum of 1000 cells were counted in randomly selected areas. Labelling index was expressed as percentage of positively stained cells per 100 follicular epithelial cells.

Score was given according to the intensity of the nuclear stain.

0 – < 2% of nuclear staining.

1 – 2% to 5% of nuclear staining.

2 – 6% to 10% of nuclear staining.

3 – > 10% of nuclear staining.

Methods of scoring for p53

Cells with nuclear staining were considered as positive. Score was given according to the intensity of the nuclear stain.

0 – No staining

1 – Weak staining

2 – Moderate staining

3 – Strong staining

Percentage of positive cells[70]

0 – Negative staining

1 – The cells that is positive by less than 25%

2 - The cells that is positive by 26-50%

3 - The cells that are positive by >50%

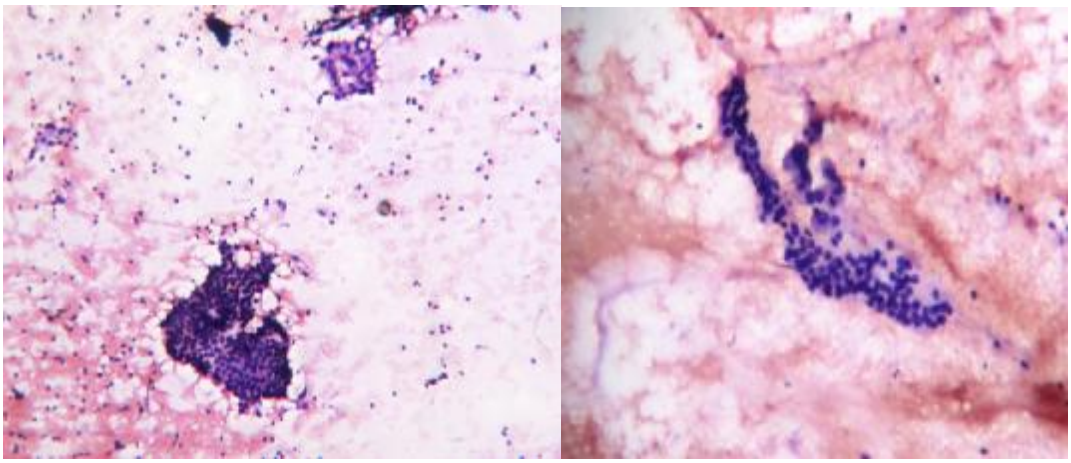

Fig 1: Monolayered sheets and poorly cohesive clusters of follicular epithelial cells and cyst macrophages – Nodular colloid Goiter. H&Ex10

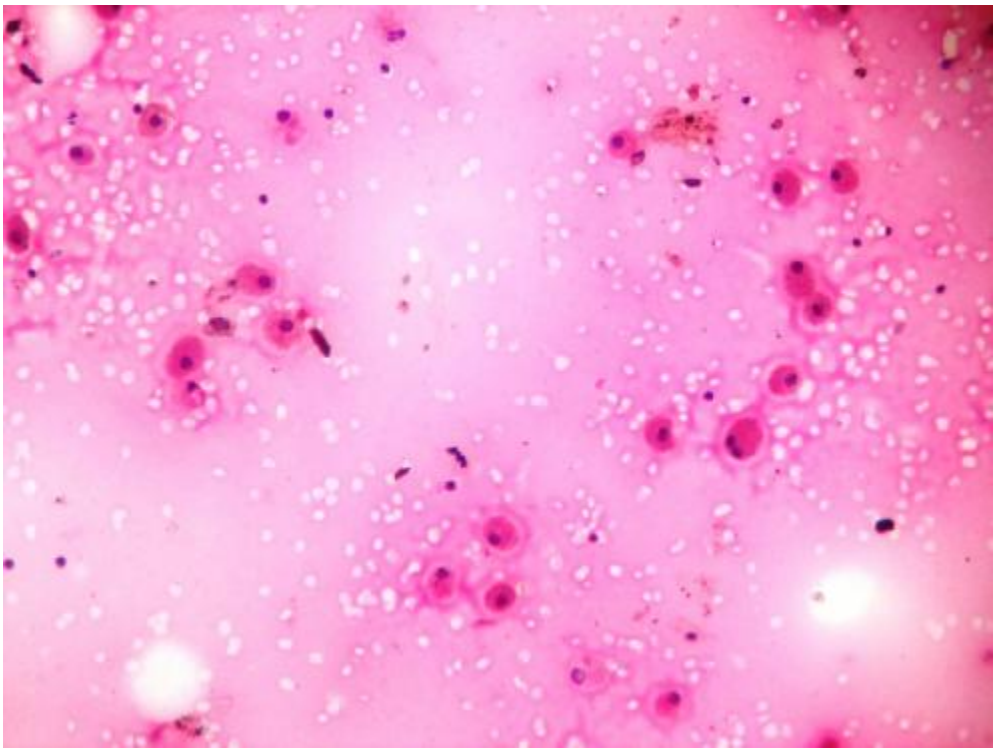

Fig 2: Cyst and Hemosiderin laden Macrophages in the background of thin colloid – Nodular colloid goiter with cystic degeneration. H&Ex10

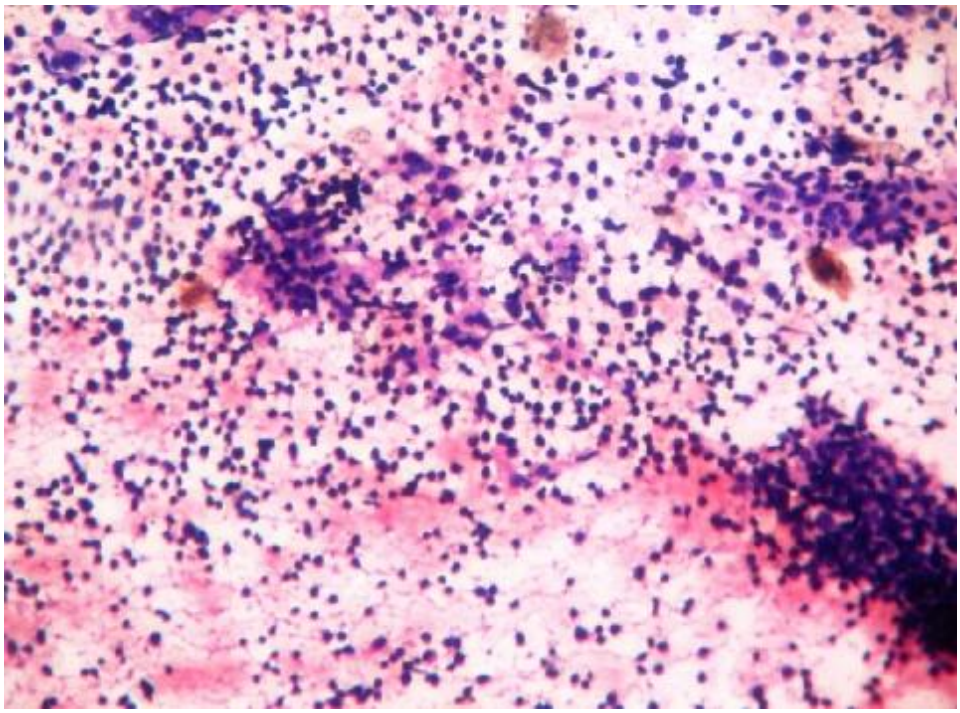

Fig 3: Hurthle cells and Lymphocytes in the background of colloid – Hashimoto Thyroiditis. H&E x 10

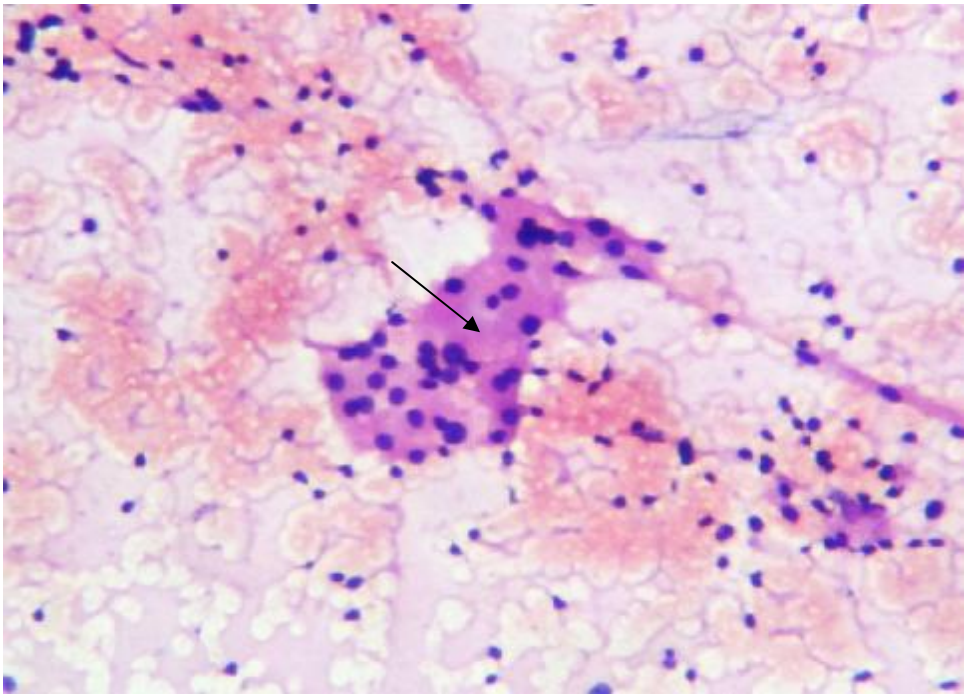

Fig 4: Hurthle cells – cells with abundant eosinophilic cytoplasm and anisocytosis of nucleus. H&E x10

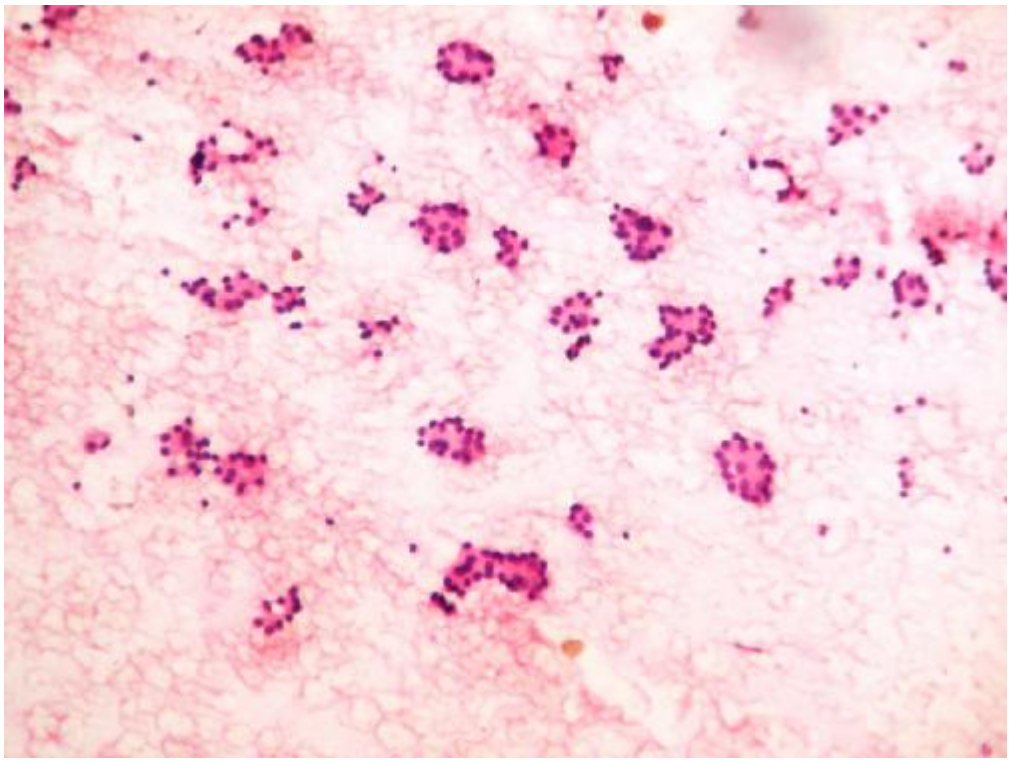

Fig 5: Repetitive thyroid follicular epithelial cells with scant colloid– Follicular Neoplasm. H&E x 4

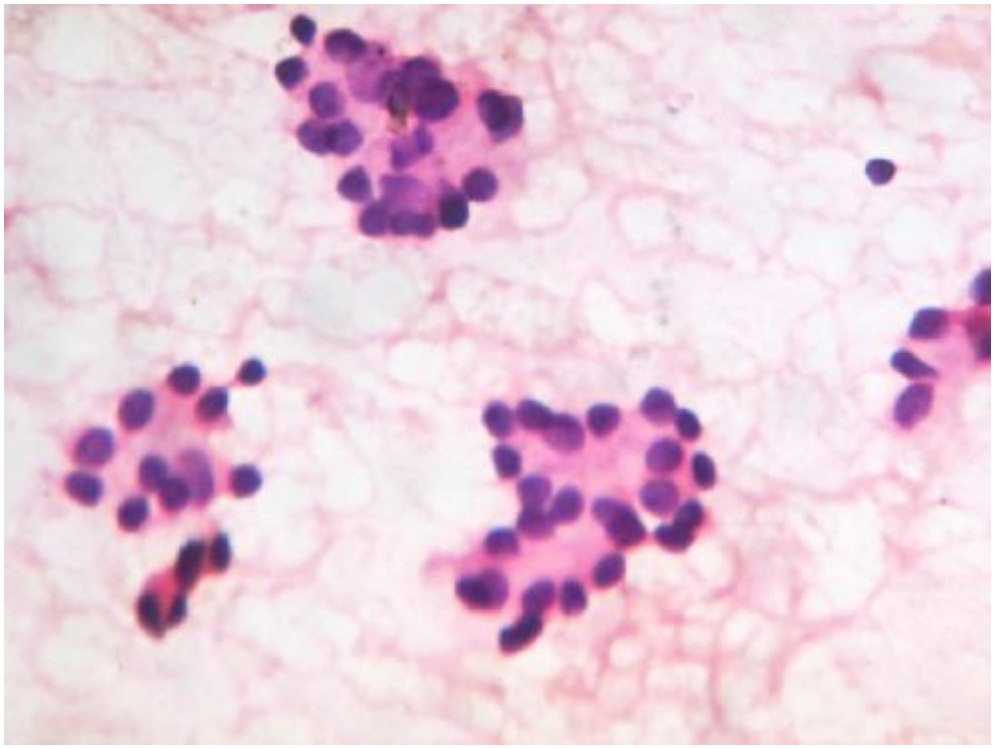

Fig 6: Microfollicular pattern with colloid–Follicular Neoplasm. H&E x 40

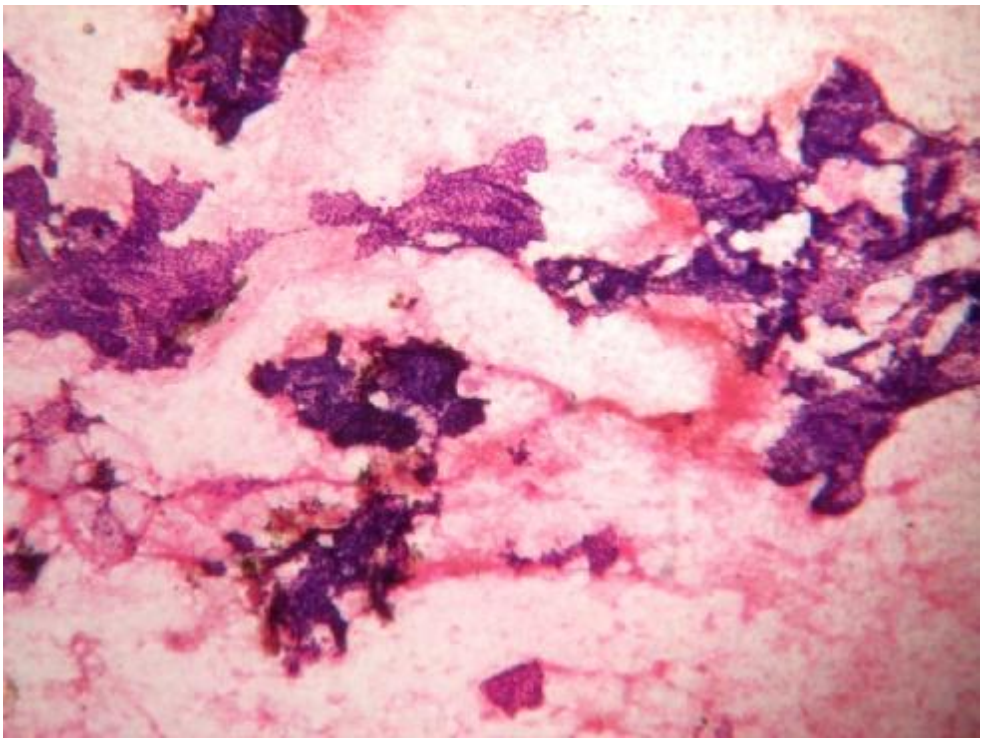

Fig 7: Sheats and Papillaroid fragments of Follicular epithelial cells – Papillary Carcinoma thyroid. H&E x 4

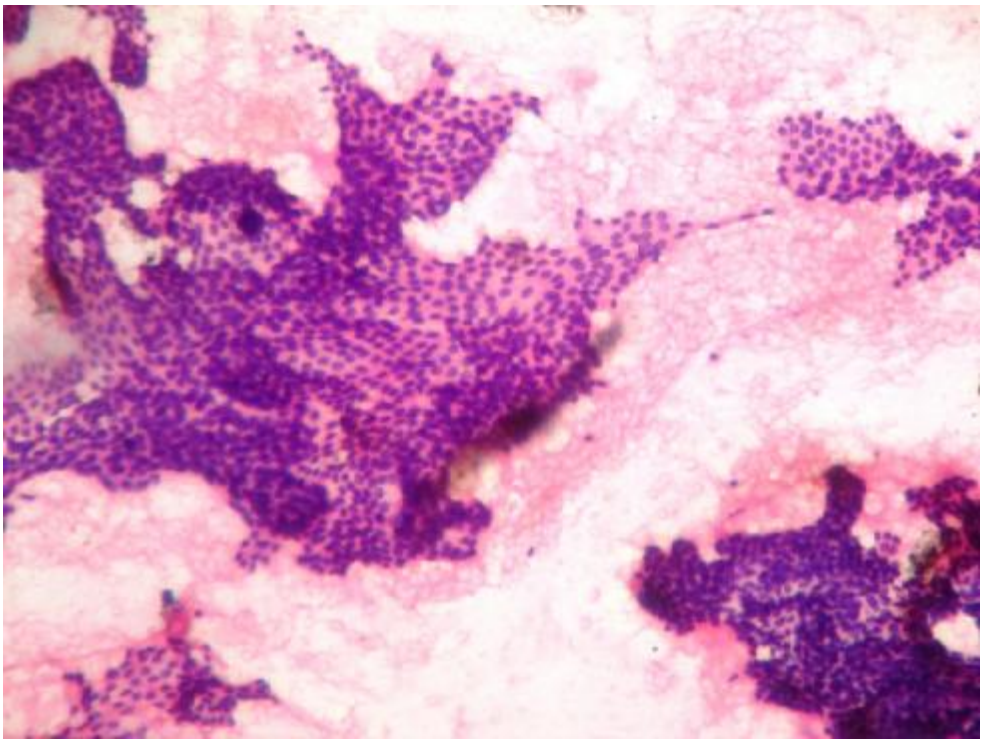

Fig 8: Nuclear crowding, overlapping in Papillary Carcinoma thyroid. H&E x 10

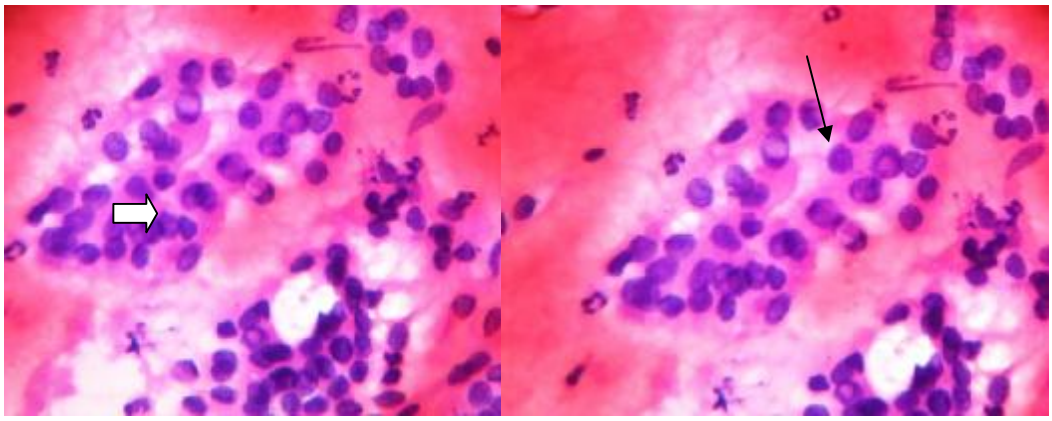

Fig 9: Nuclear Grooves and Intranuclear inclusions in Papillary Carcinoma Thyroid. H&E x 40

Fig 10: Total thyroidectomy specimen C/S – single nodule measuring 3cm diameter filled with colloid – Nodular Colloid goiter

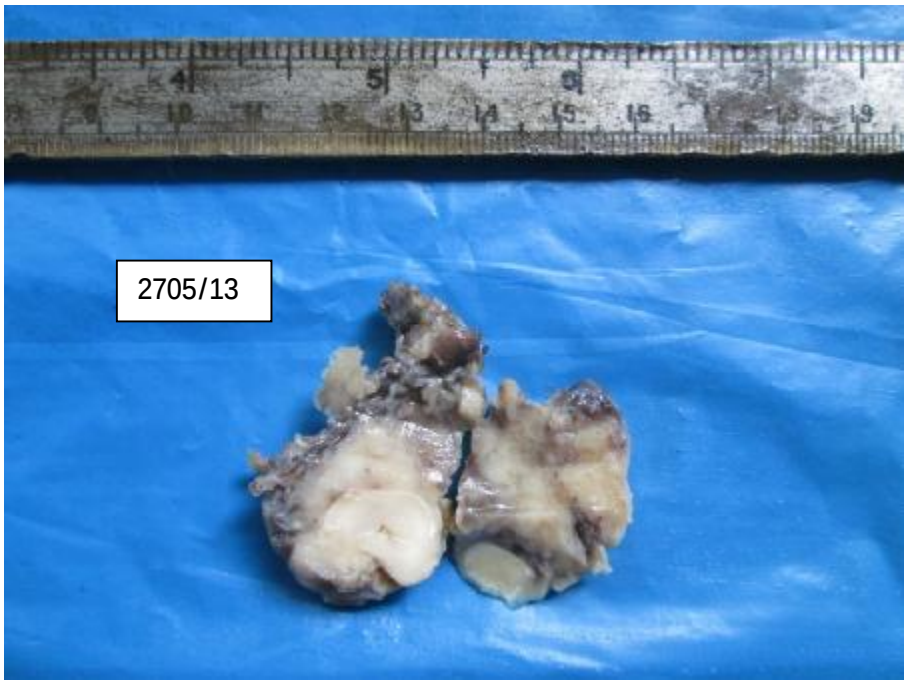

Fig 11: Total Thyroidectomy – C/S – greytan replacing entire thyroid parenchyma – Hashimoto thyroiditis

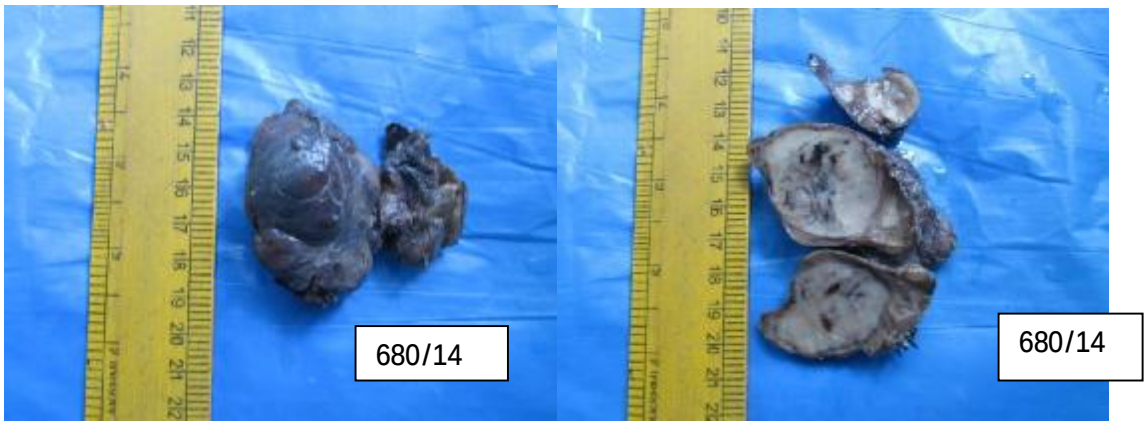

Fig 12: Total Thyroidectomy specimen C/S- shows a nodule measuring 3x2cm with peripheral compressed normal thyroid parenchyma – Follicular Adenoma

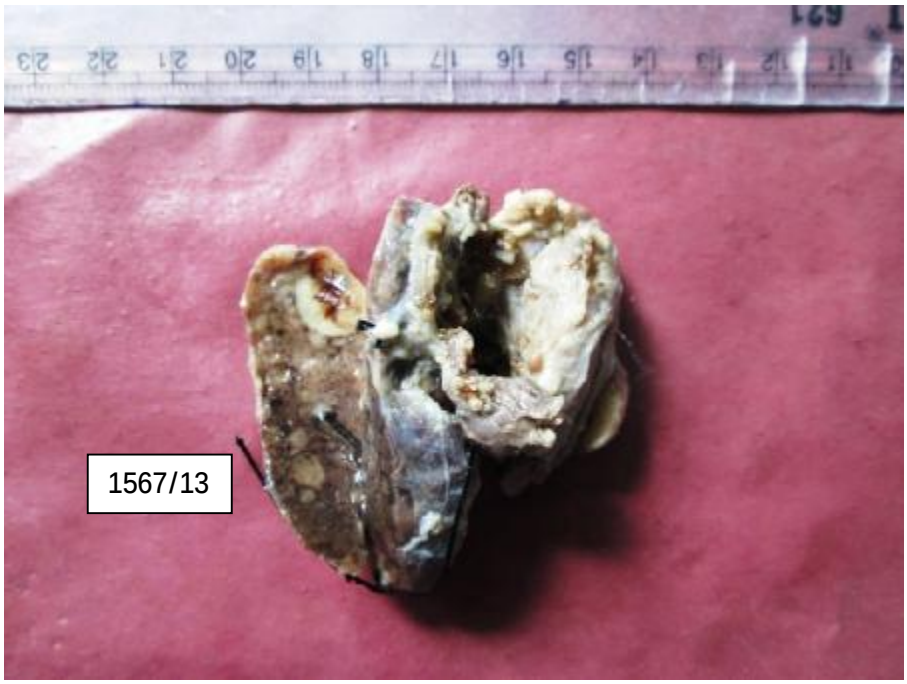

Fig 13: Total Thyroidectomy specimen C/S – Solid and cystic greywhite area – Papillary Carcinoma Thyroid

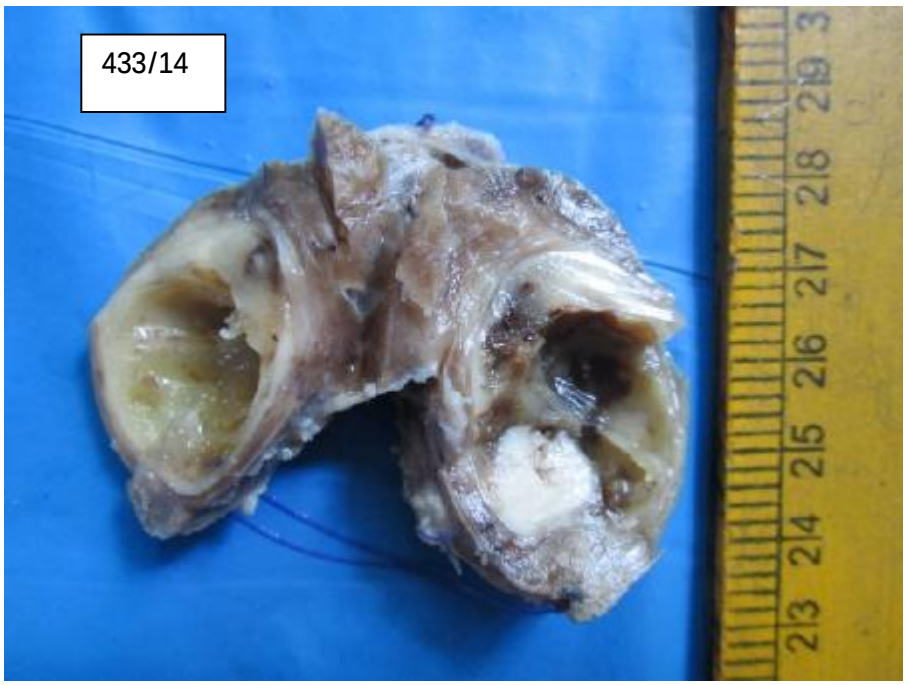

Fig 14: Total Thyroidectomy specimen C/S- Cyst with mural nodule- Papillary carcinoma thyroid

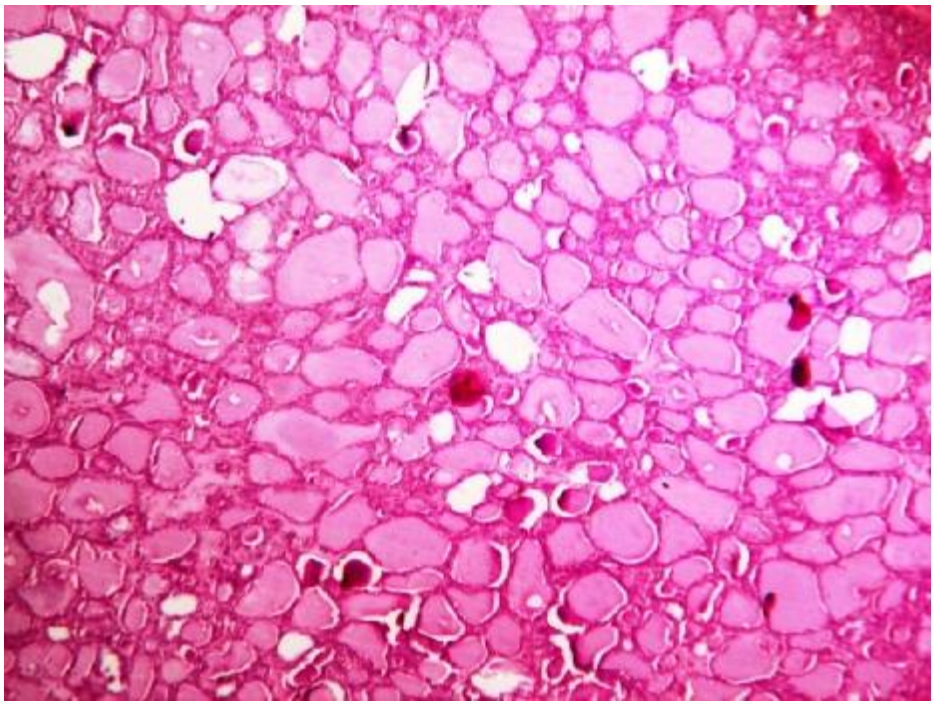

Fig 15: Follicles of varying sizes filled with colloid-Nodular colloid goiter. H&E x 4

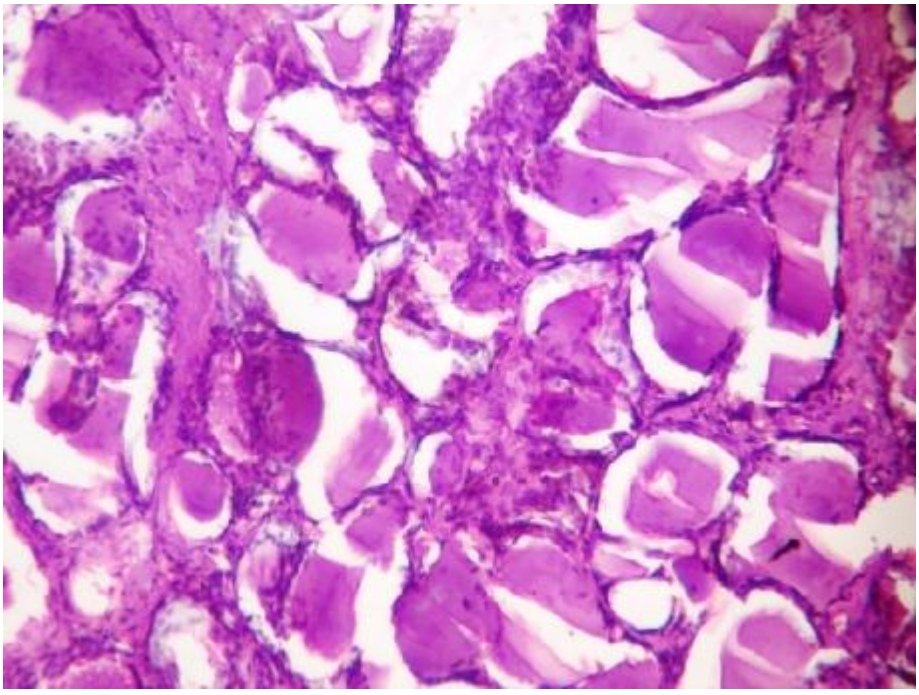

Fig 16: Follicles lined by flattened epithelial cell with colloid- Nodular colloid goiter. H&E x 10

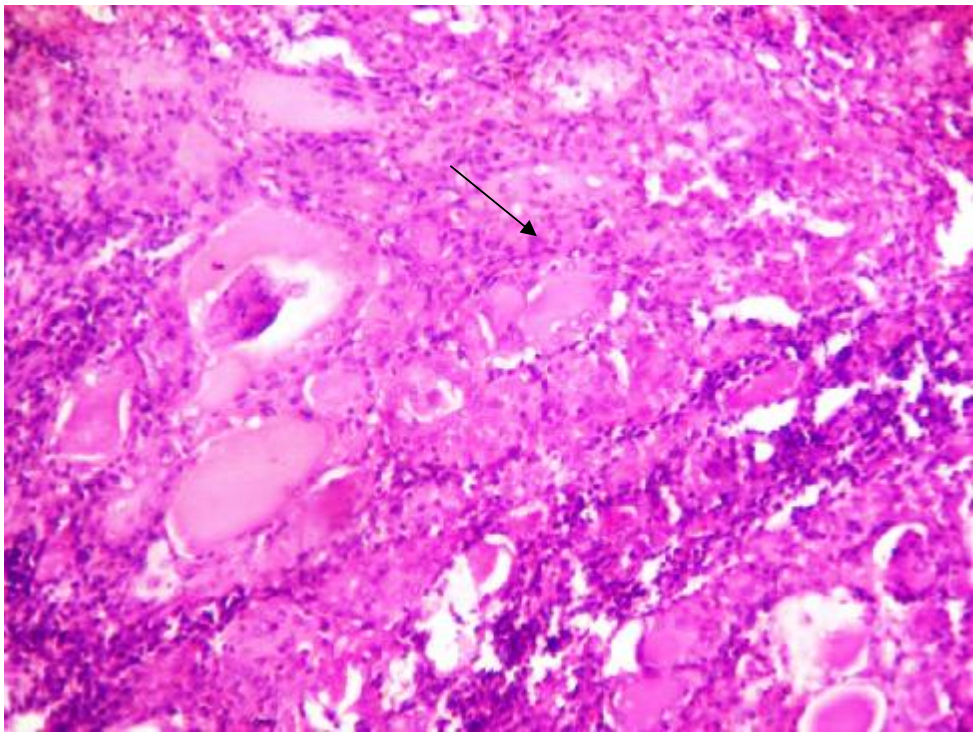

Fig 17: Hurthle cells with lymphocytes in the background - Hashimoto thyroiditis. H&E x 10

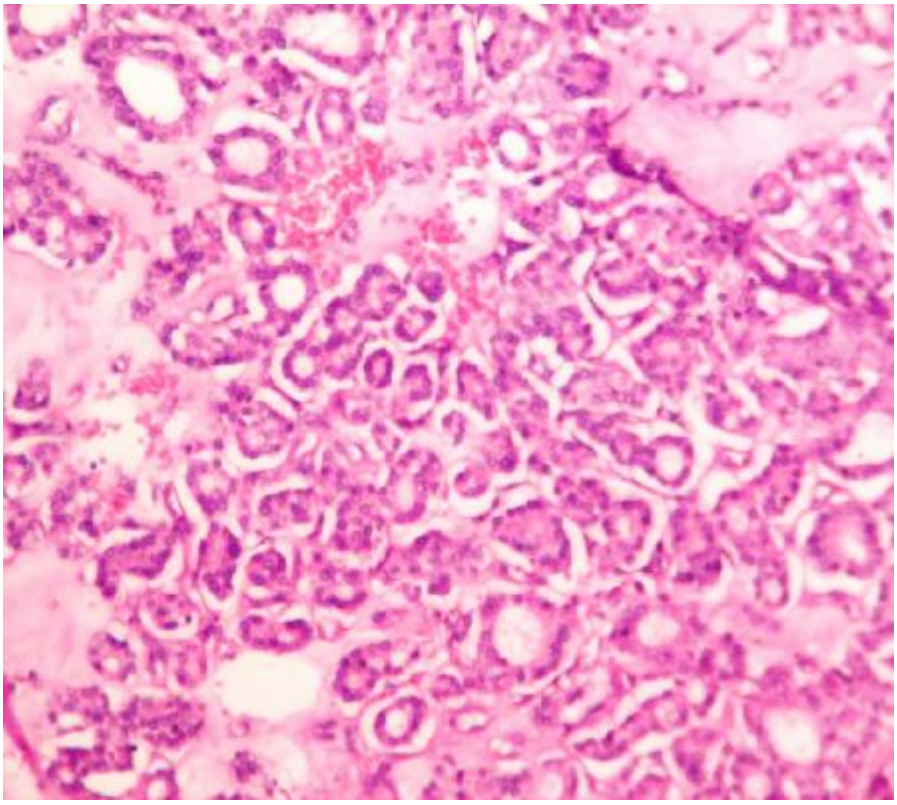

Fig 18: Encapsulated lesion showing microfollicles of varying sizes - Microfollicular adenoma. H&E x 10

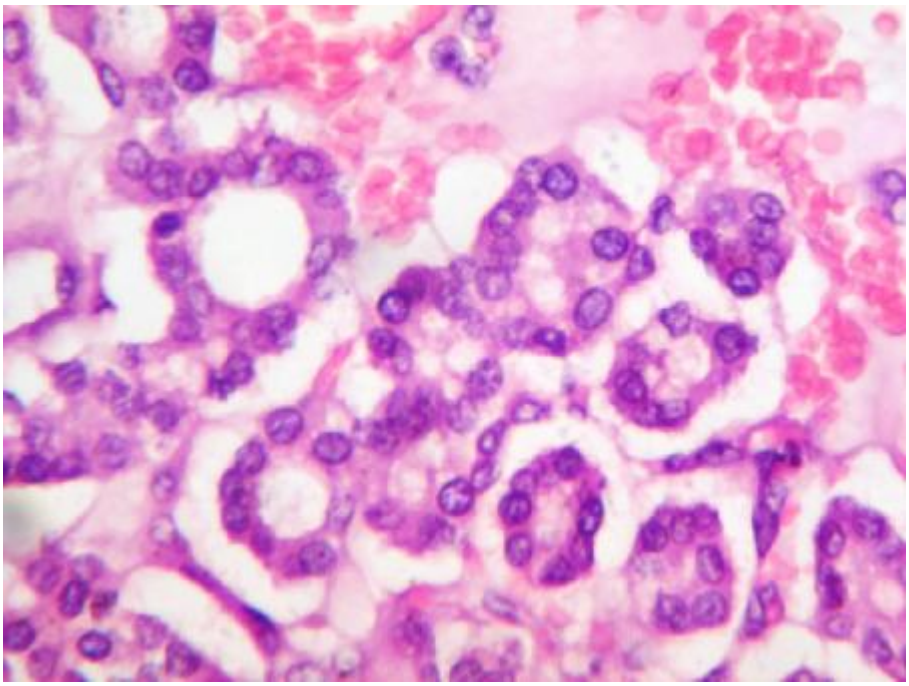

Fig 19: Uniform microfollicles lined by cuboidal follicular epithelial cells – Microfollicular adenoma. H&E x 40

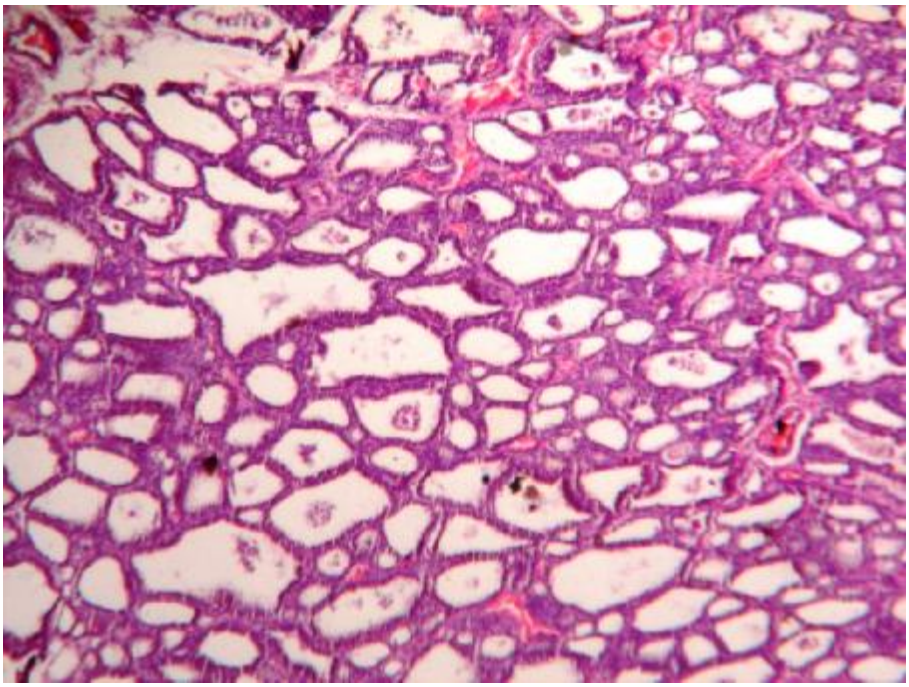

Fig 20: Circumscribed neoplasm showing Macrofollicles of varying sizes – Macrofollicular adenoma. H&E x 4

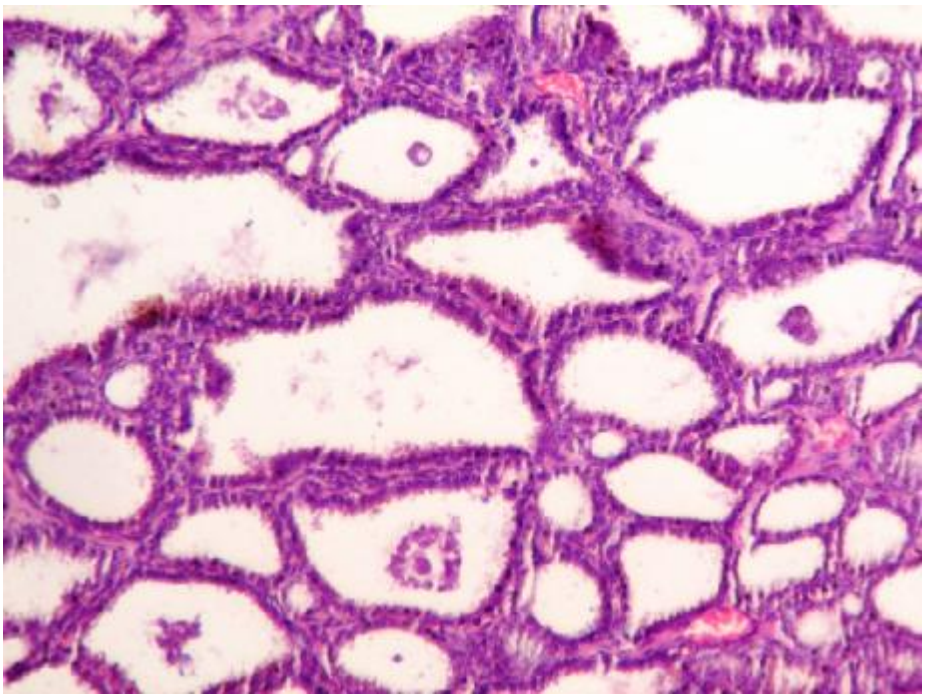

Fig 21: Macrofollicles lined by cuboidal epithelial cells with scant collid – Macrofollicular adenoma. H&E x 10

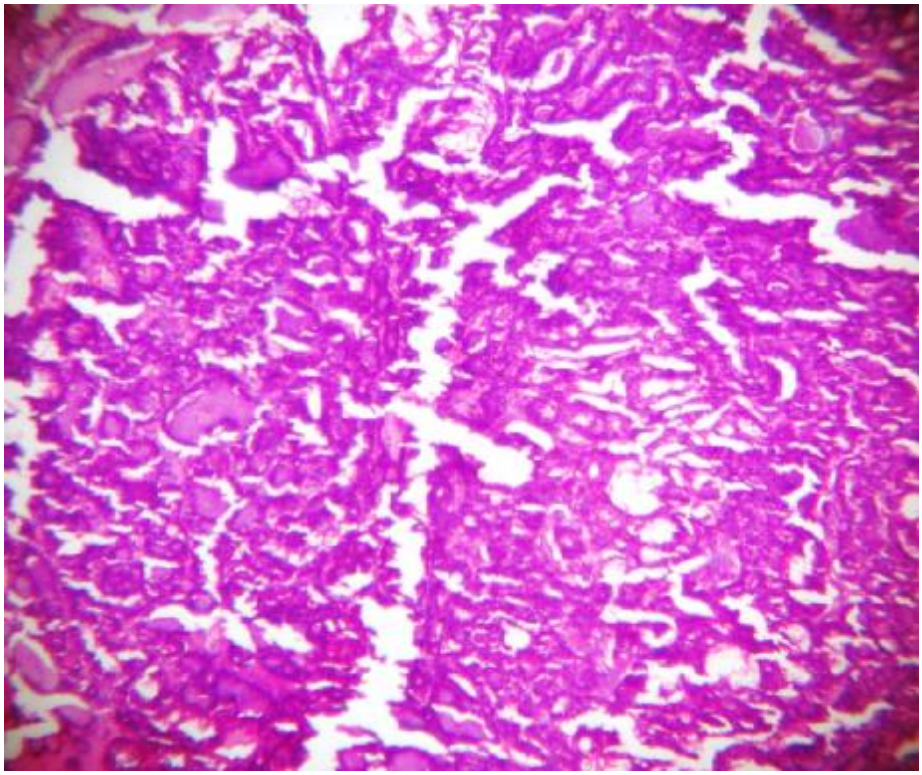

Fig 22: Nodular colloid goiter with foci of micropapillary carcinoma. H&E x 4

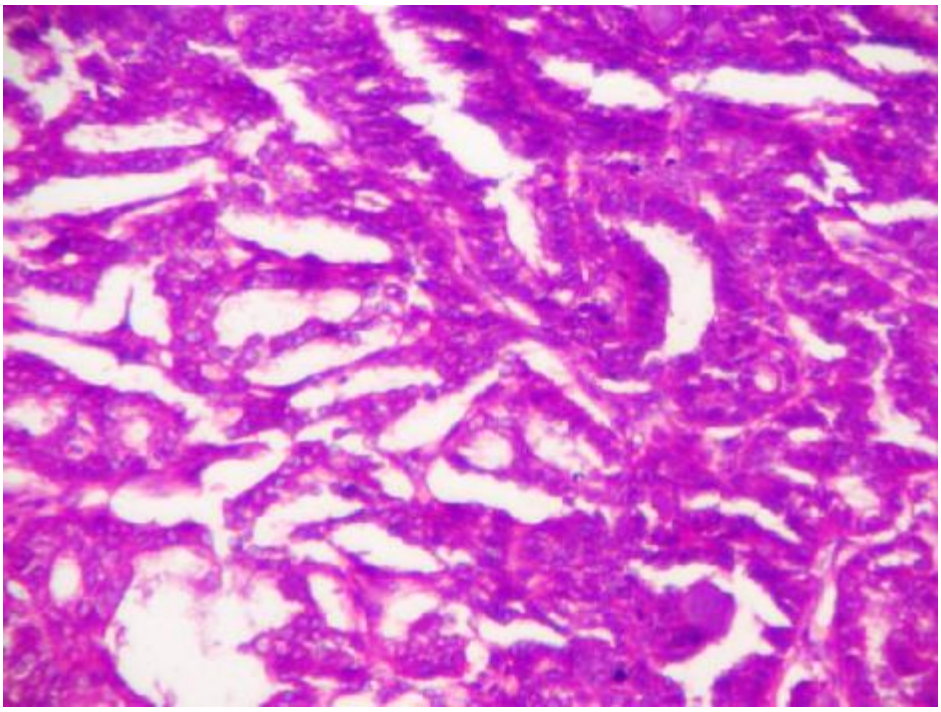

Fig 23: Micropapillary carcinoma. H&E x 10

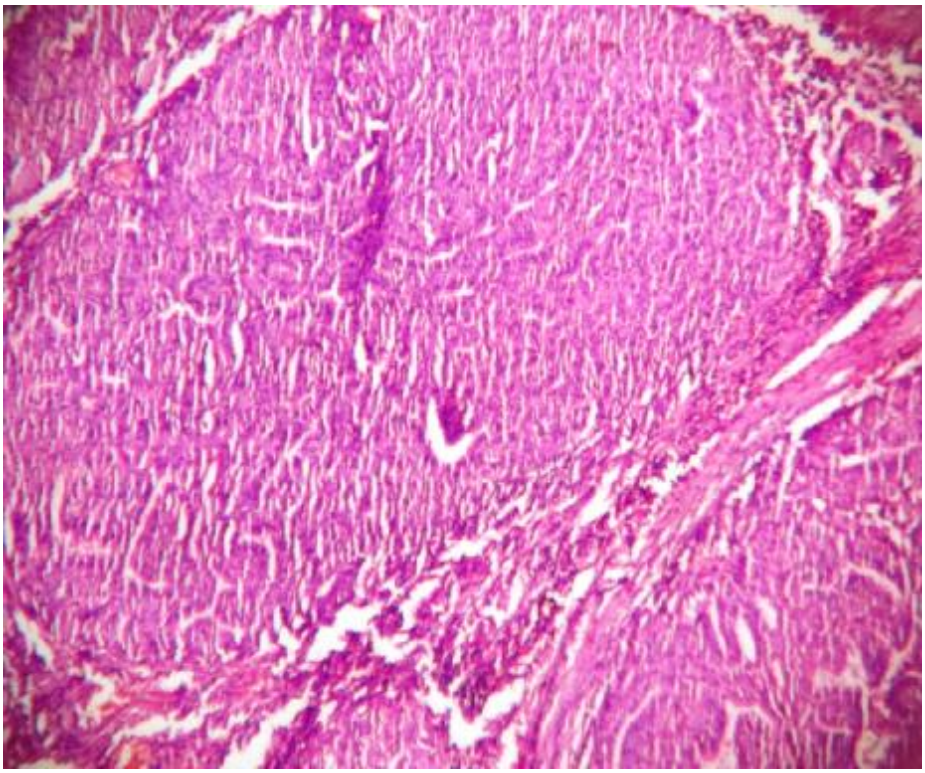

Fig 24: Encapsulated papillary carcinoma thyroid. H&E x 4

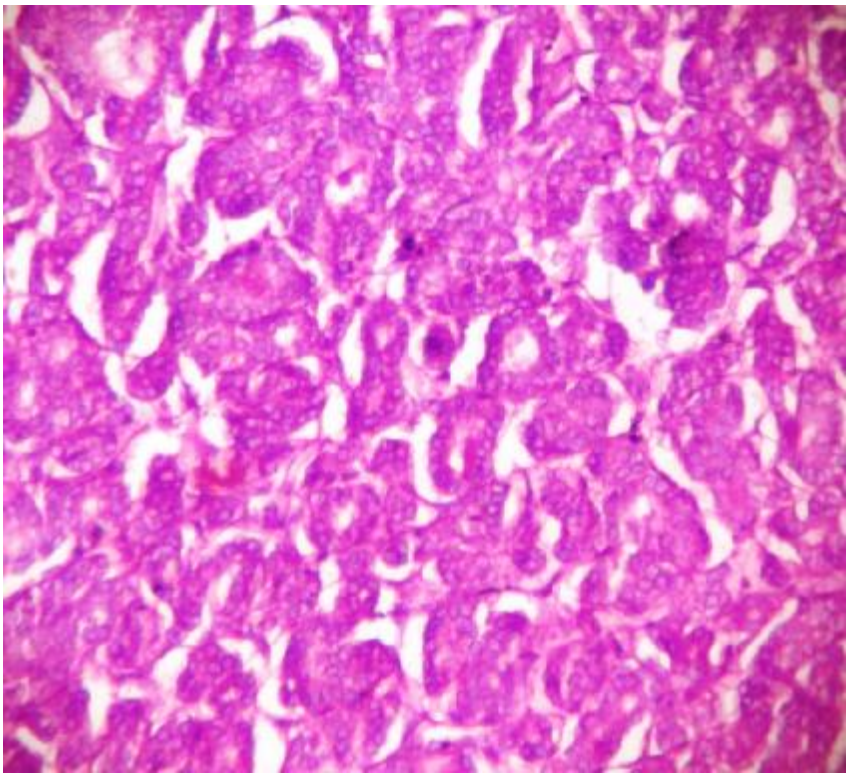

Fig 25: Follicular variant of papillary carcinoma thyroid. H&E x 10

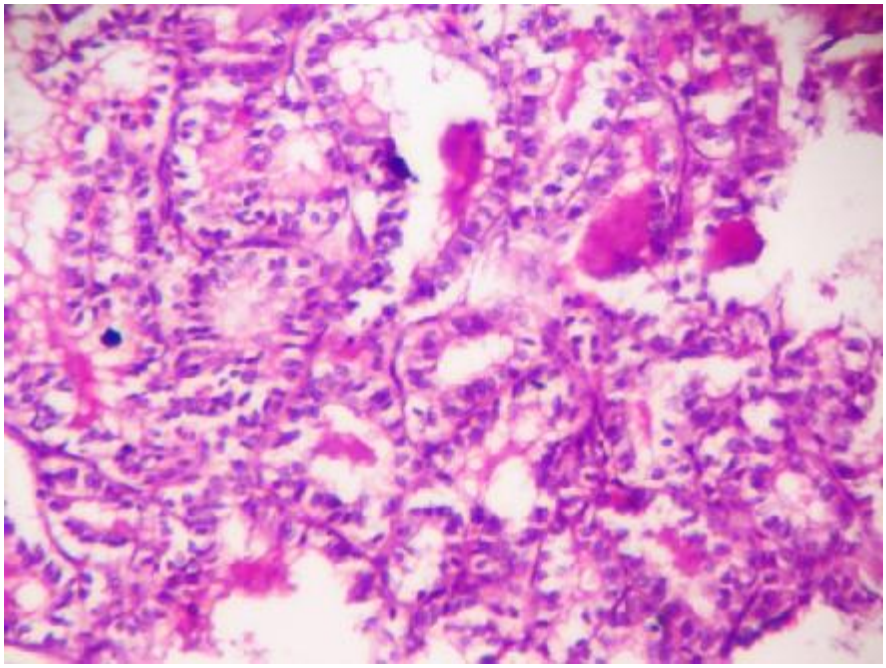

Fig 26: Clear cell change in papillary carcinoma thyroid. H&E x 10

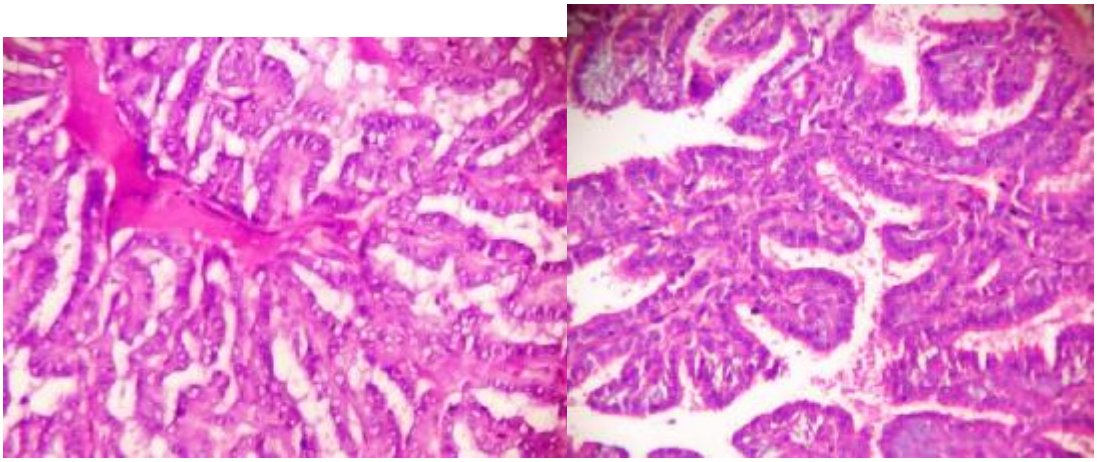

Fig 27: Papillae with prominent fibrovascular core in papillary carcinoma thyroid. H&E x 10

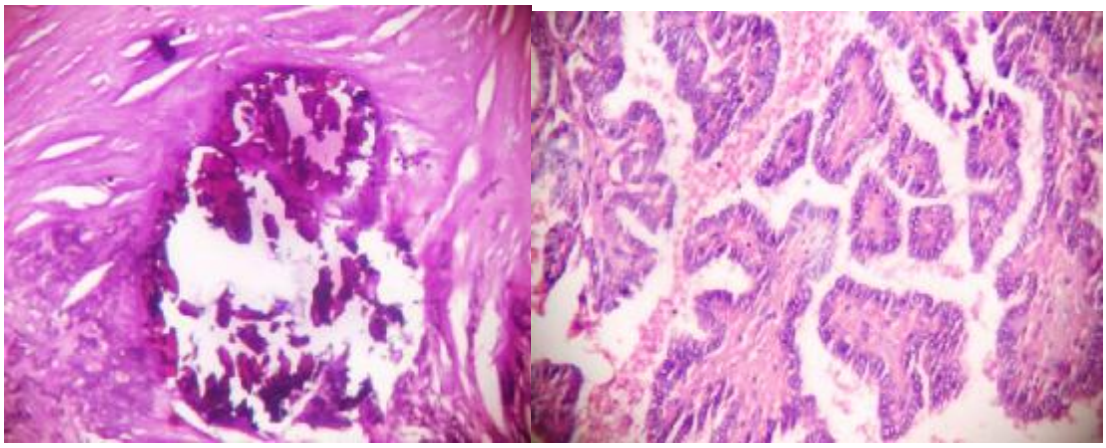

Fig 28: Psammoma bodies and orphan annie eye nucleus in papillary carcinoma thyroid

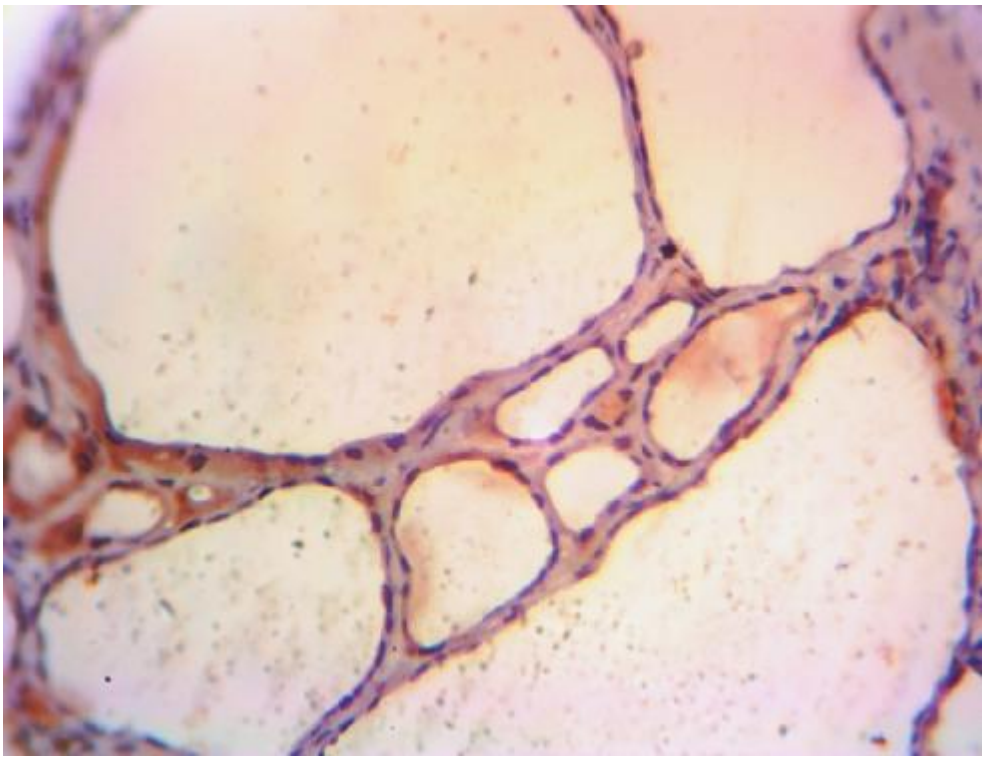

Fig 29: Multinodular goiter showing 1% of Ki-67 expression. x 40

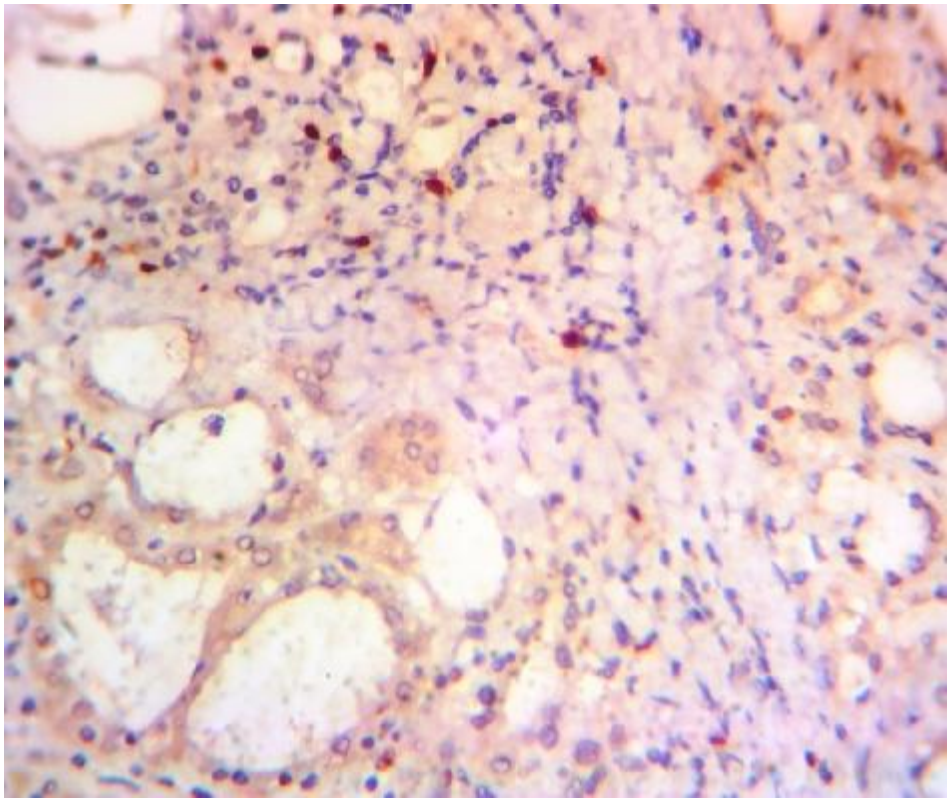

Fig 30: Hashimoto thyroiditis showing 2-5% of Ki- 67 expression. X 40

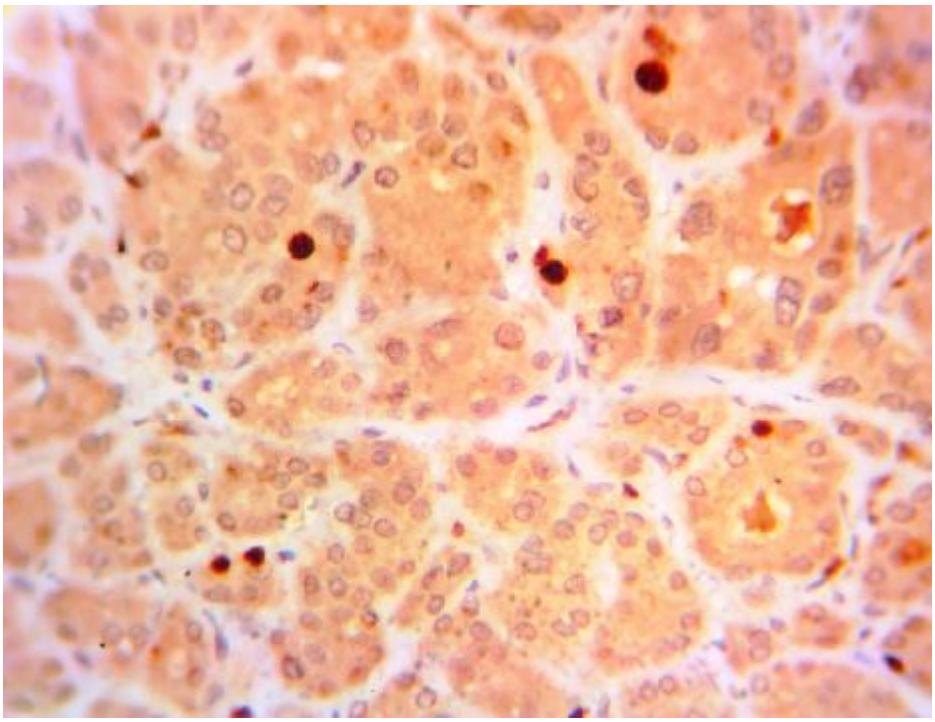

Fig 31: 6-10% of nuclear positivity of Ki-67 expression in Follicular adenoma. x 40

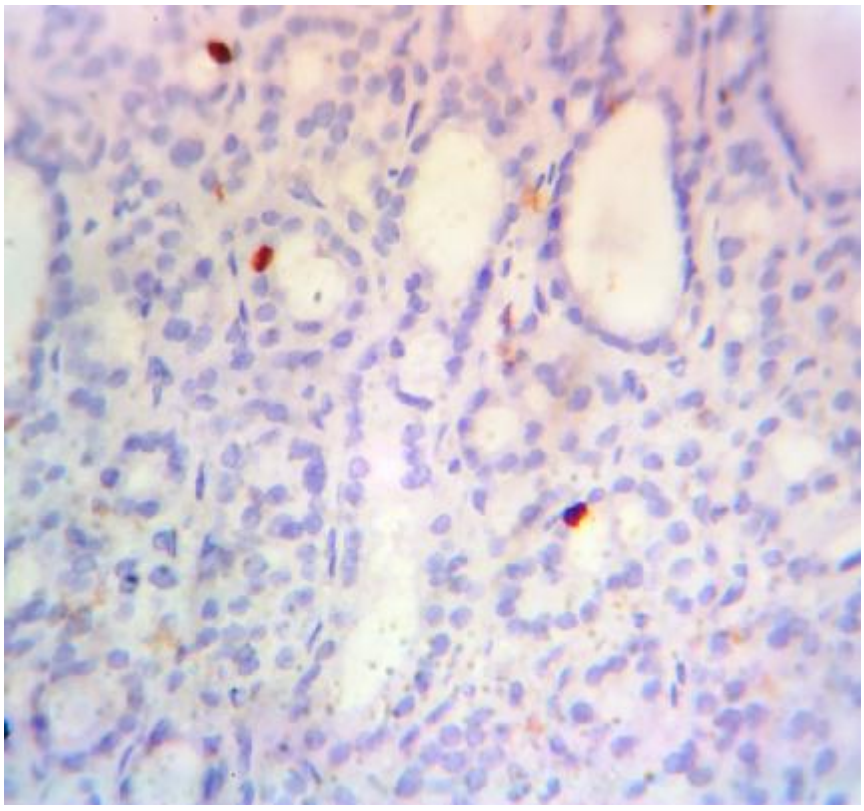

Fig 32: 2-5% Ki-67 expression in Follicular adenoma. x 40

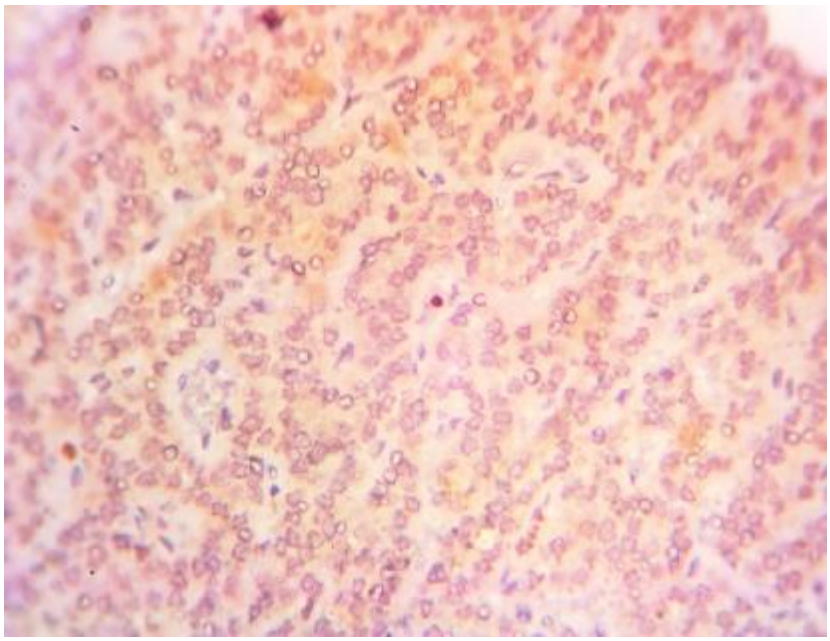

Fig 33: Papillary carcinoma thyroid showing 2- 5% Ki-67 expression. x 40

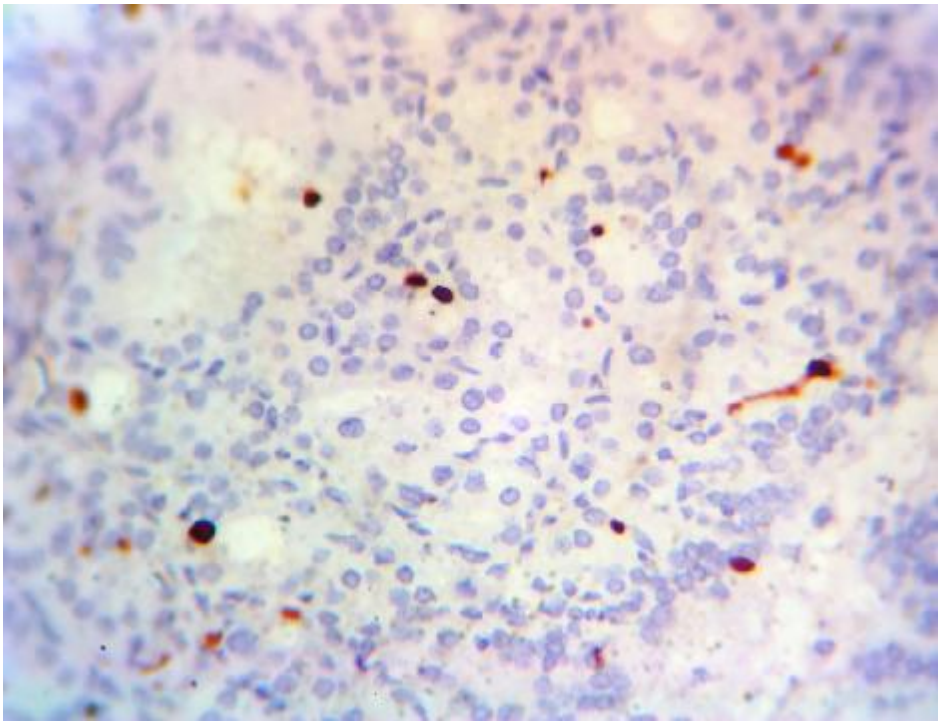

Fig 34:6-10%Ki-67expression in papillary carcinoma thyroid.x40

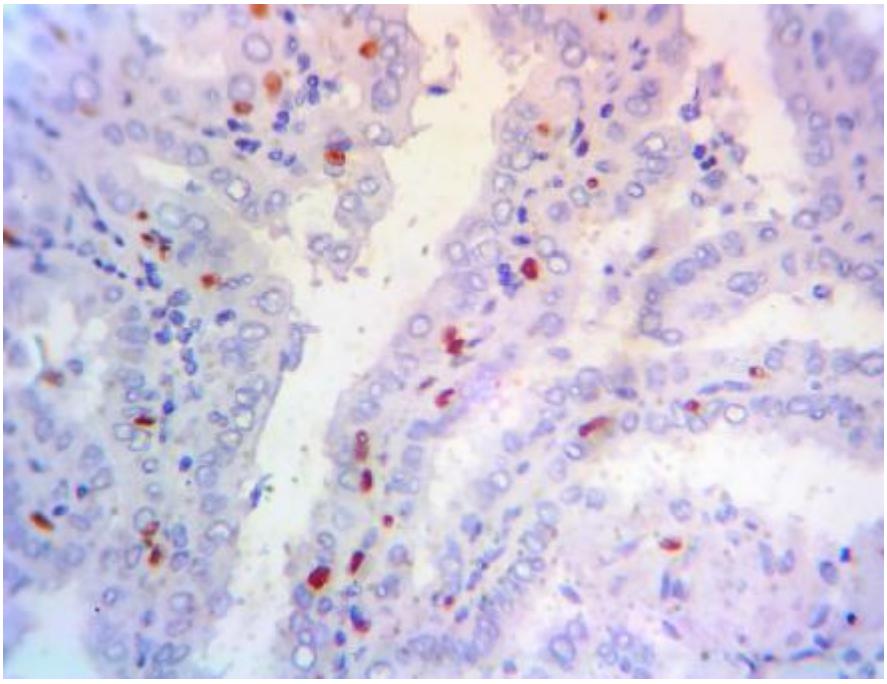

Fig 35: >10% expression of Ki-67 in Papillary carcinoma thyroid- x40

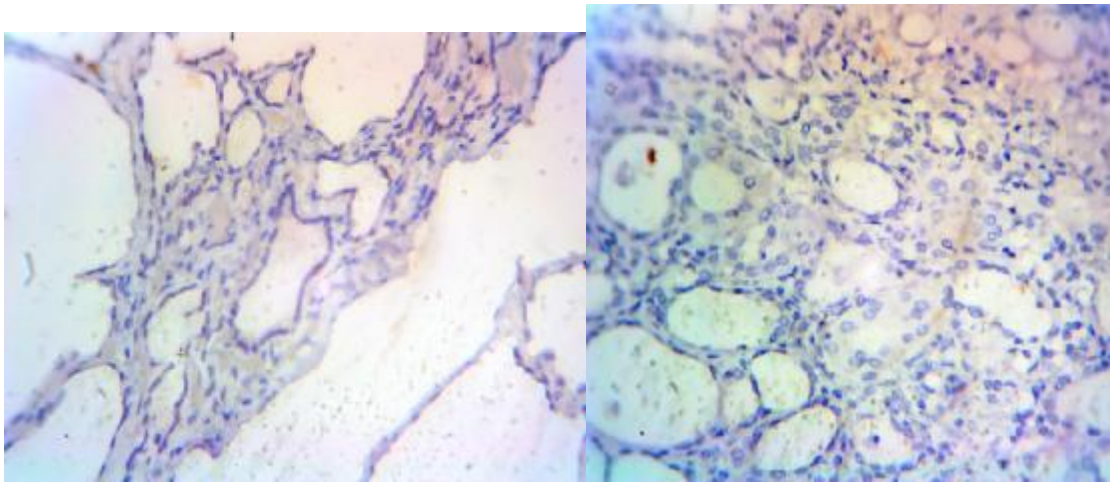

Fig 36: 100% negative staining of p53 in Nodular colloid goiter and Hashimoto thyroiditis. x40

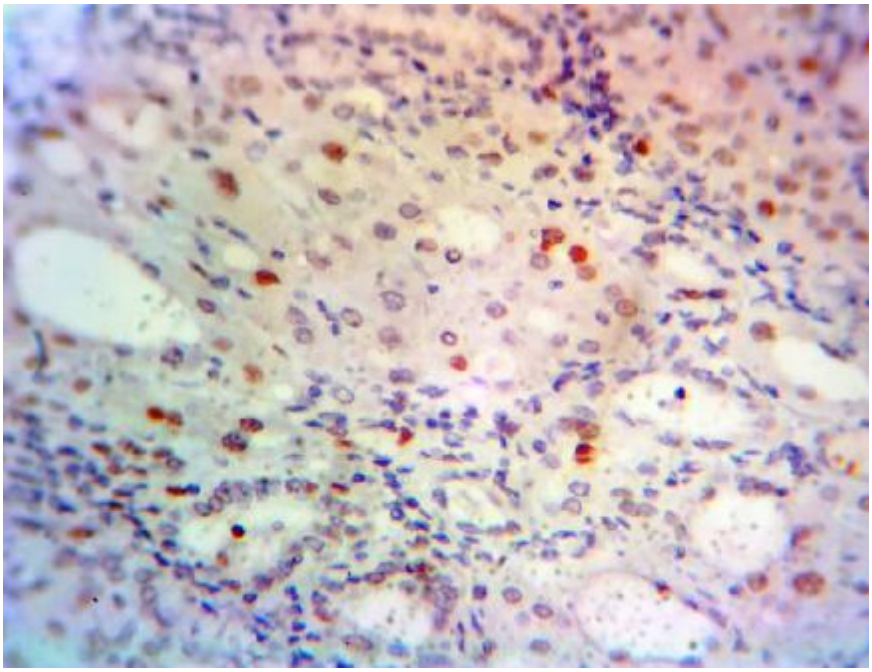

Fig 37: Weak positivity(<25%) of p53 in Hashimoto throiditis. x 40

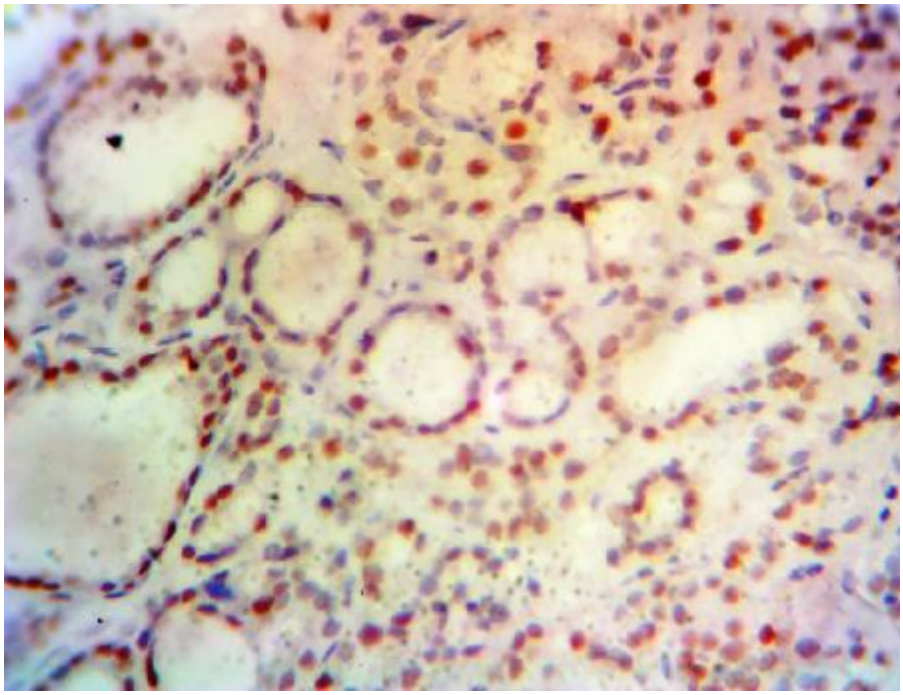

Fig 38: Moderate staining(26-50%) of p53 in Follicular adenoma. x40

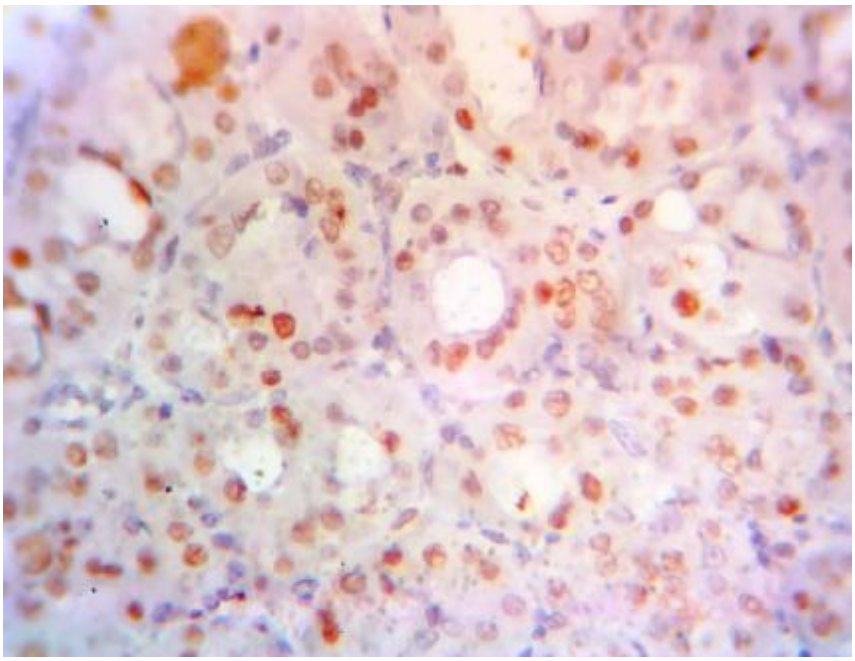

Fig 39: Strong nuclear positivity(>50%) of p53 in Hurthle cell adenoma. x40

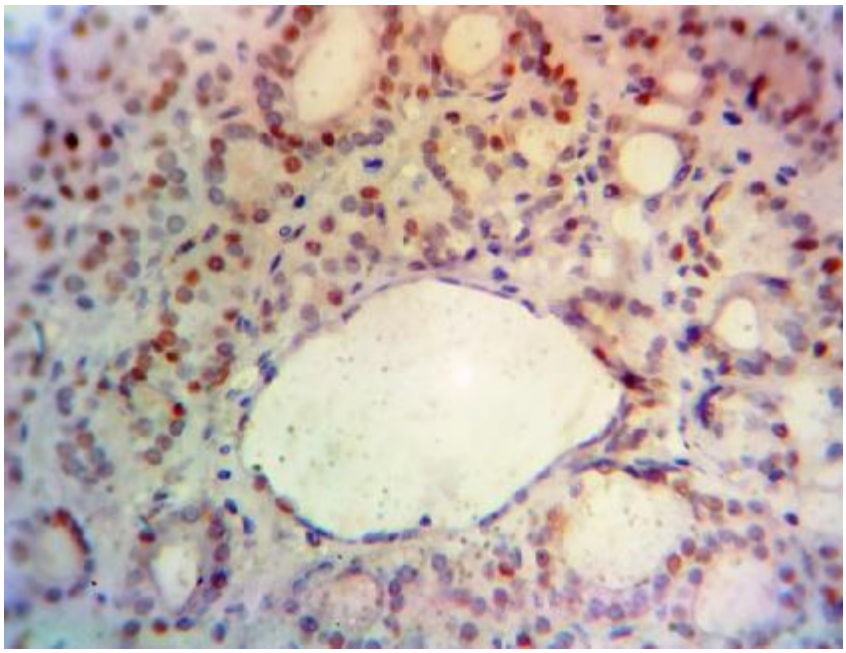

Fig 40: Moderate nuclear positivity(26-50%) of p53 in Papillary carcinoma thyroid. x40

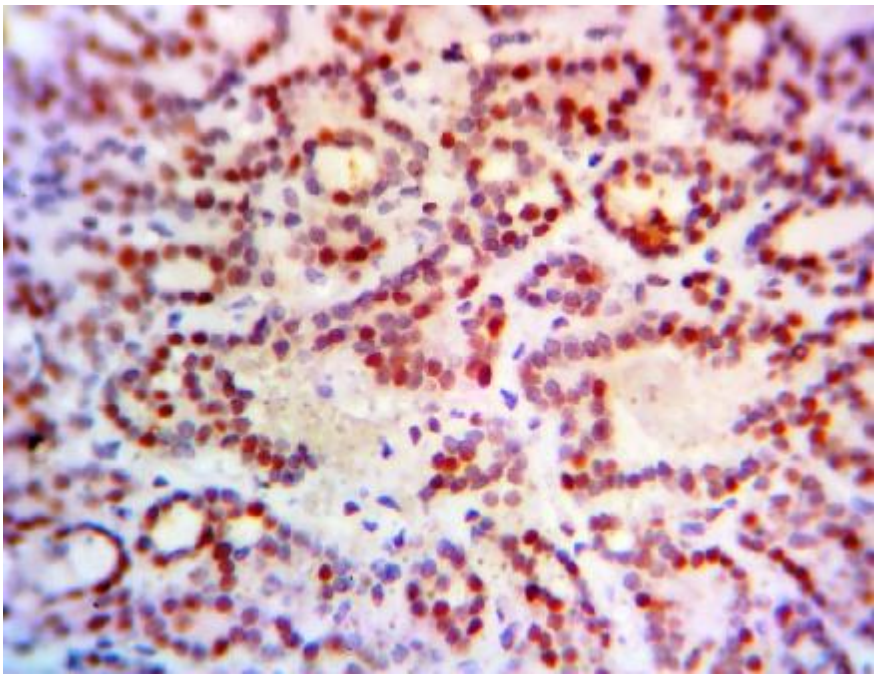

Fig 41: Strong nuclear positivity(>50%) of p53 in Papillary carcinoma thyroid. x40

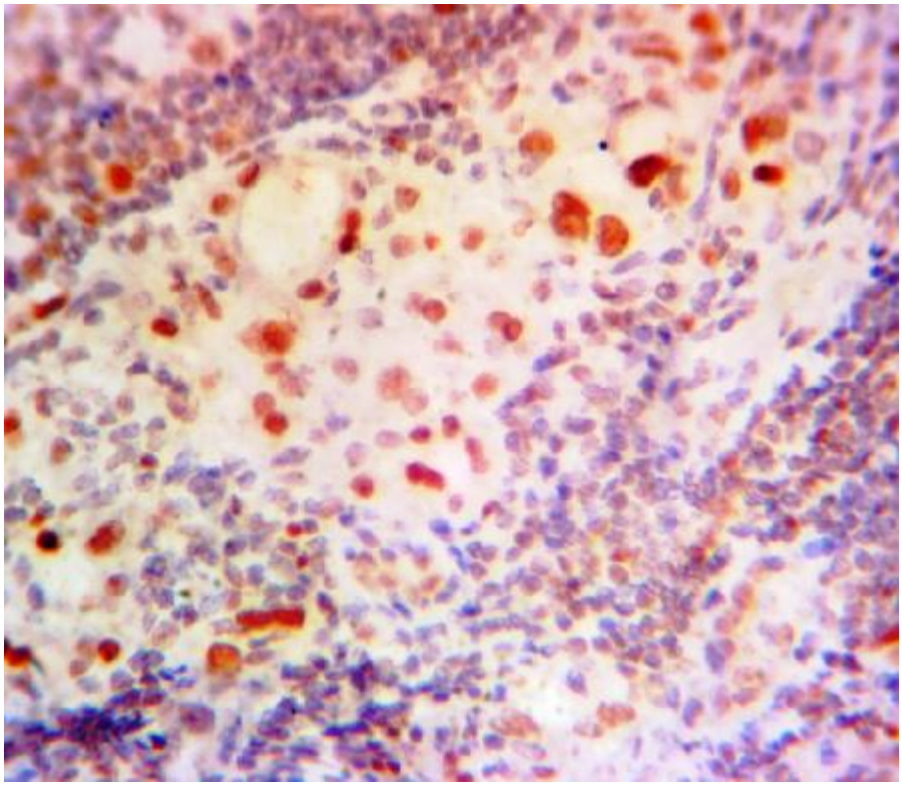

Fig 42: Strong Nuclear positivity(>50%) in Papillary carcinoma thyroid in background of Hashimoto thyroiditis. x40

OBSERVATIONS AND RESULTS

TABLE 1

INCIDENCE OF THYROID LESIONS IN HEAD AND NECK

Duration of Study	Total No. of Specimens	Total No of Cases in Head & Neck	Total No of cases in Thyroid	Total No of Thyroid Malignancies
JUNE 2010 to JUNE 2014	20937	1540	200	21

The total numbers of specimens received during the period of June 2010 to June 2014 were 20937. Out of the 20937 specimens 1540 specimens were from Head and neck region, of which 200 cases were from thyroid and 21 were thyroid tumours.

In our study, the incidence of thyroid lesions over period of four years was 0.1% and incidence of thyroid tumours among head and neck lesions was 1.36%.

CHART - 1

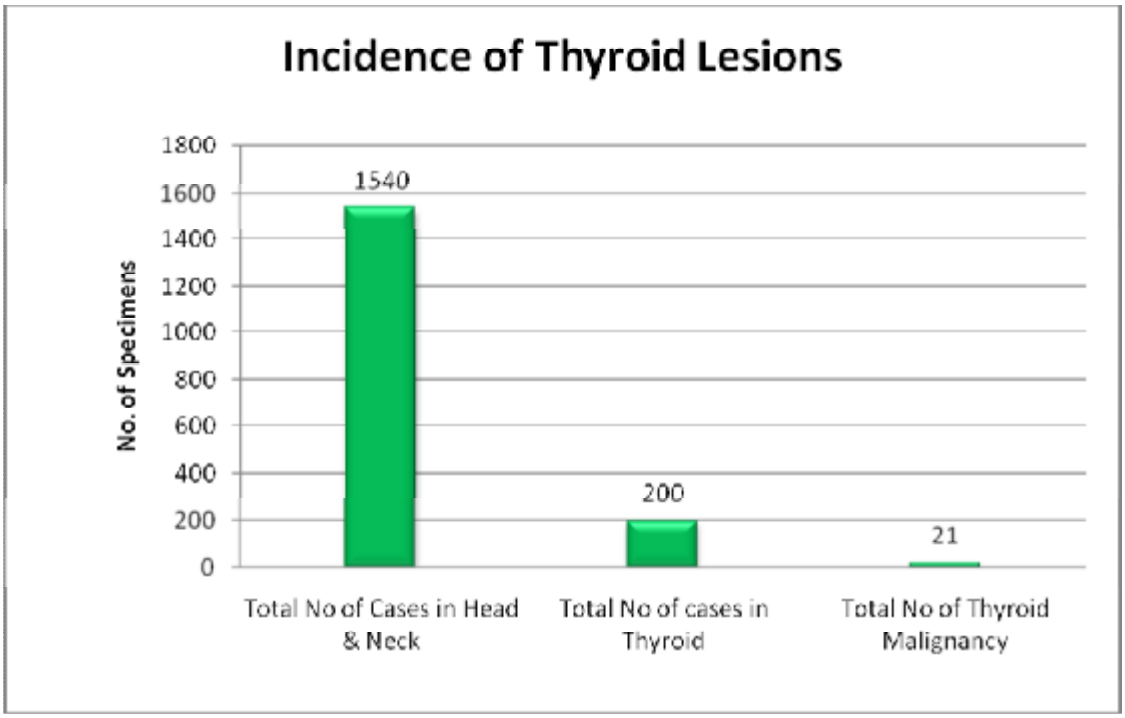

TABLE 2

AGE DISTRIBUTION OF THYROID LESIONS

Age Group (in years)	No of Cases	Percentage (%)
0 – 9	0	0.00
10 – 19	5	2.50
20 – 29	45	22.50
30 – 39	56	28.00
40 – 49	53	26.50
50 – 59	30	15.00
60 – 69	8	4.00
70 – 79	2	1.00
80 – 89	1	0.50
Total	200	100

Table 2 and chart 2 shows the incidence of thyroid lesions in different age groups. In our study, the youngest person reported was 10yrs and the eldest one was 84yrs. The maximum number of cases (28%) reported was between 30-39 yrs of age followed by 40-49yrs of age (26%). About 54.5% of cases were more than 30yrs with median age of presentation being 39yrs.

CHART 2

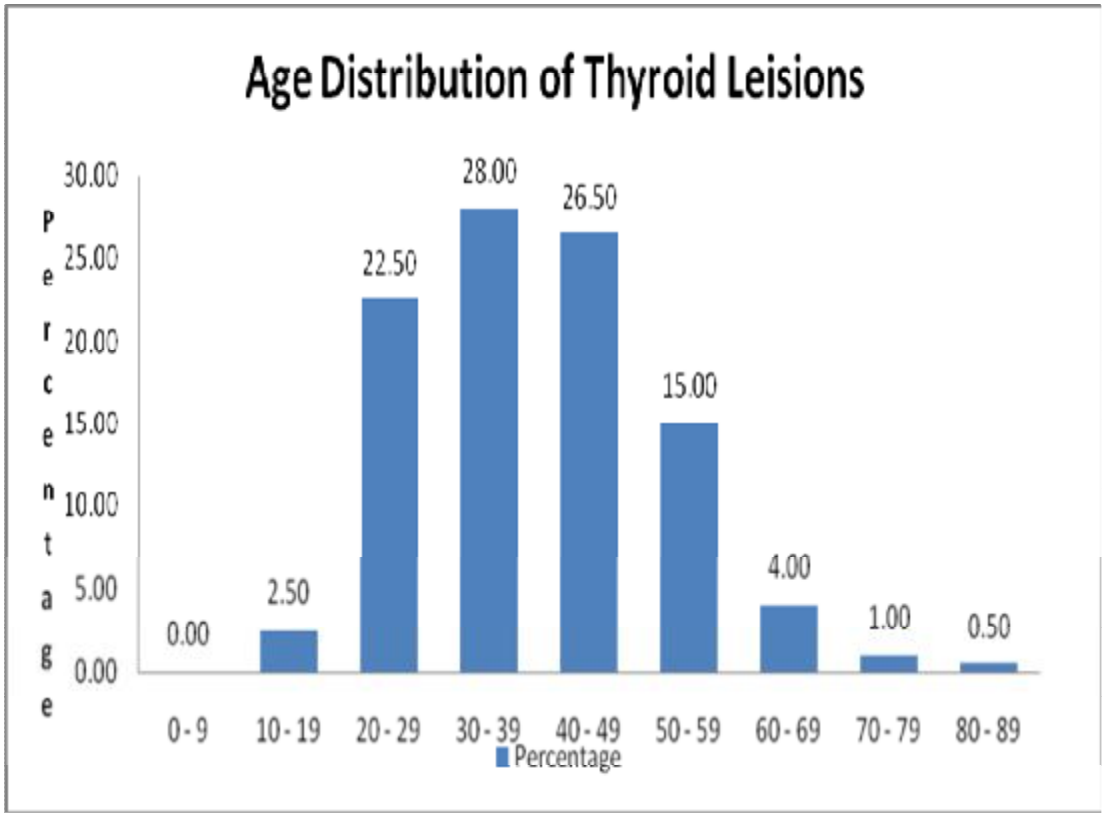

TABLE - 3

GENDER DISTRIBUTION OF THYROID LESIONS

Gender	No of Cases	Percentage (%)
Male	18	9
Female	182	91
Total	200	100

In our study, the occurrence of thyroid lesions was more common in females when compared to males. Among 200 specimens, 182 specimens belonged to female patients and 18 specimens were from male patients, as evident from table 3 and chart 3.

Thus the incidence of thyroid lesions was higher in females with 91%. The observed male : female ratio is 1:10.1.

CHART 3

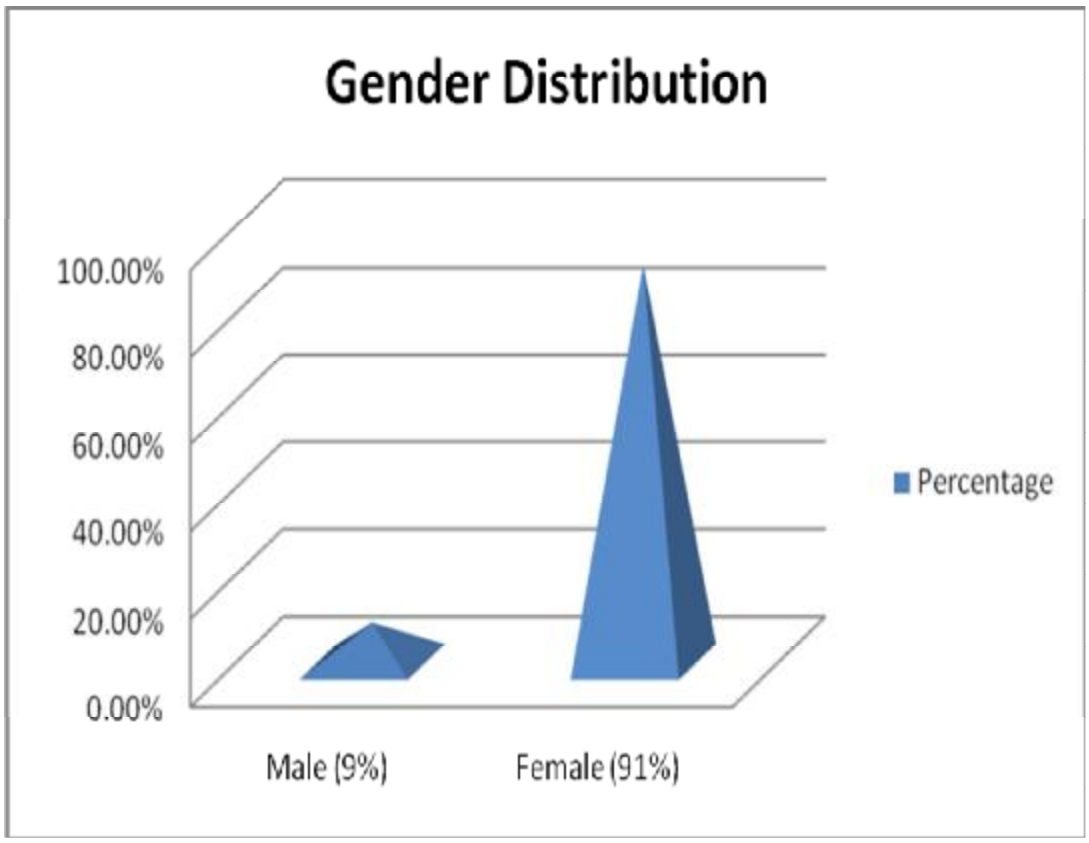

TABLE 4

FNAC & BIOPSY CORRELATION

FNAC	Correlation	Correlation Percentage
Positive	125	74
Negative	44	26
Total	**169**	**100**

Table 4 and chart 4 indicates total number of cases correlated. Out of 200 cases, 31 cases FNAC was not done, remaining 169cases were taken into consideration for correlation. Out of 169 cases 125 cases (74%) were positively correlated and 44 cases (26%) were negatively correlated.

CHART 4

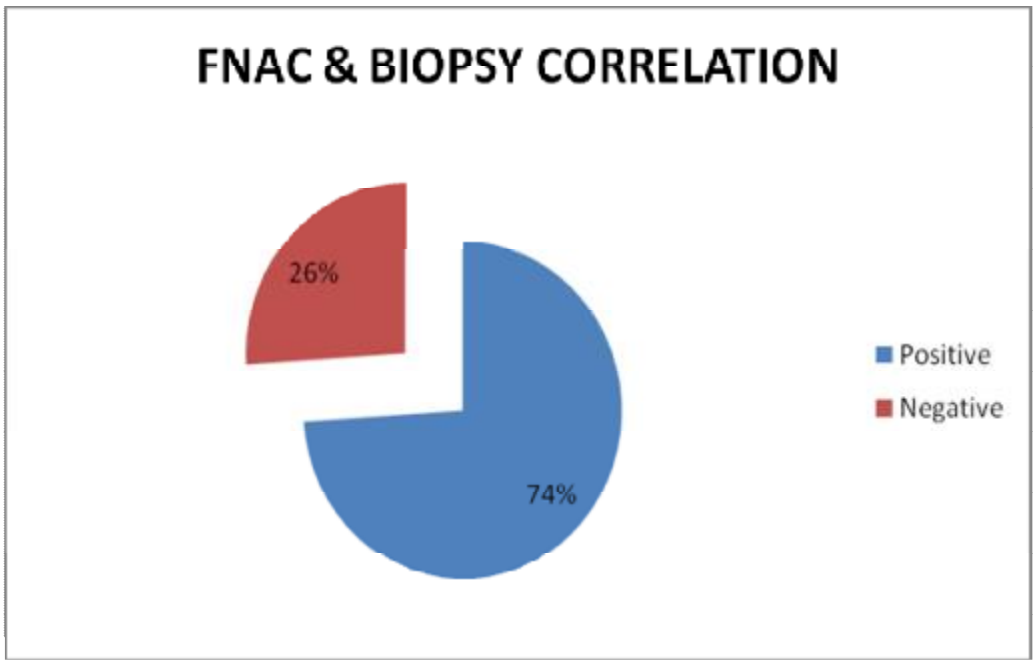

TABLE 5

COMPARISON OF TYPE OF SPECIMEN RECEIVED

Specimen Distribution	No of Specimens	Percentage (%)
Sistrunk Operation	6	3.00
Hemithyroidectomy	72	36.00
Subtotal Thyroidectomy	28	14.00
Neartotal Thyroidectomy	3	1.50
Total Thyroidectomy	91	45.50
Total	**200**	**100**

Among 200 thyroid specimens, total thyroidectomy was more common, constituting about 91 specimens(45%) followed by hemithyroidectomy constituting about 72 specimens(36%).

CHART 5

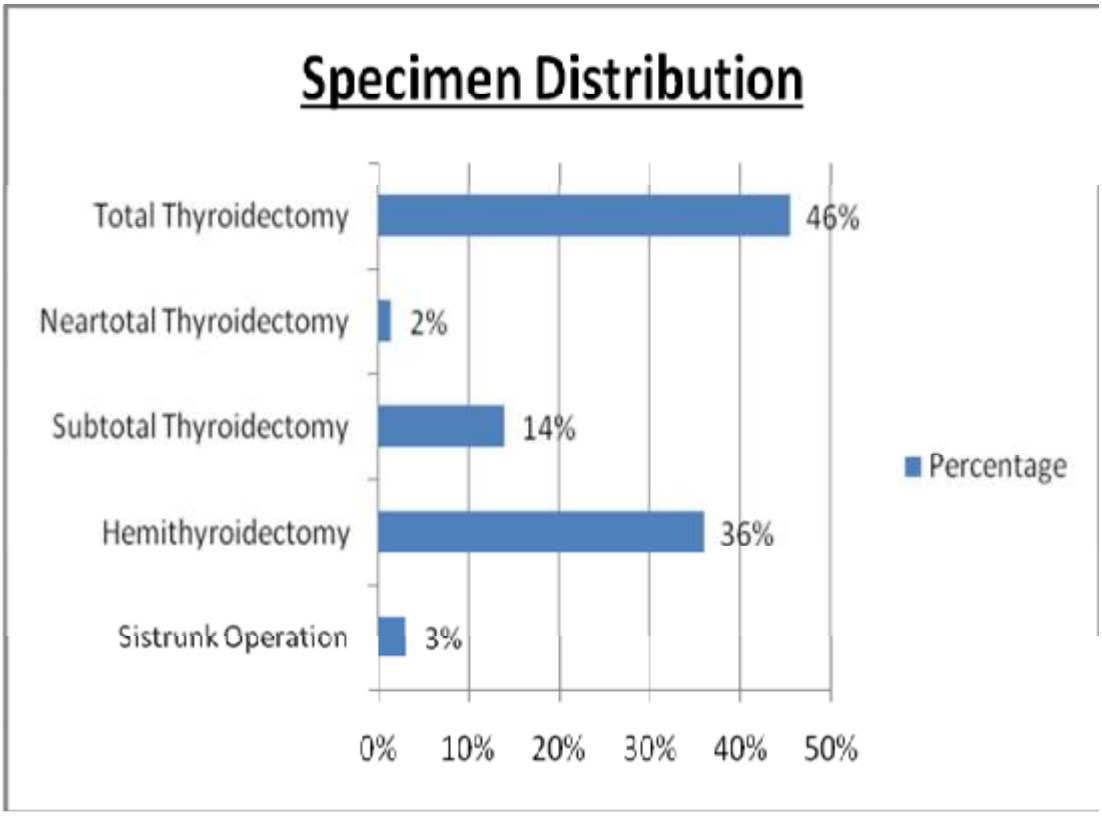

TABLE 6

DISTRIBUTION OF NEOPLASTIC AND NON NEOPLASTIC LESIONS IN CYTOLOGY

S.No	Lesions	No of Cases	Percentage (%)
1	Neoplastic	23	14
2	Non Neoplastic	146	86
	Total	**169**	**100**

In the present study, non neoplastic lesions were commonly encountered than neoplastic lesions. Out of 169 cases, non neoplastic were 146 cases (86%) and neoplastic were 23 cases (14%) with ratio of about 6.34:1.

CHART 6

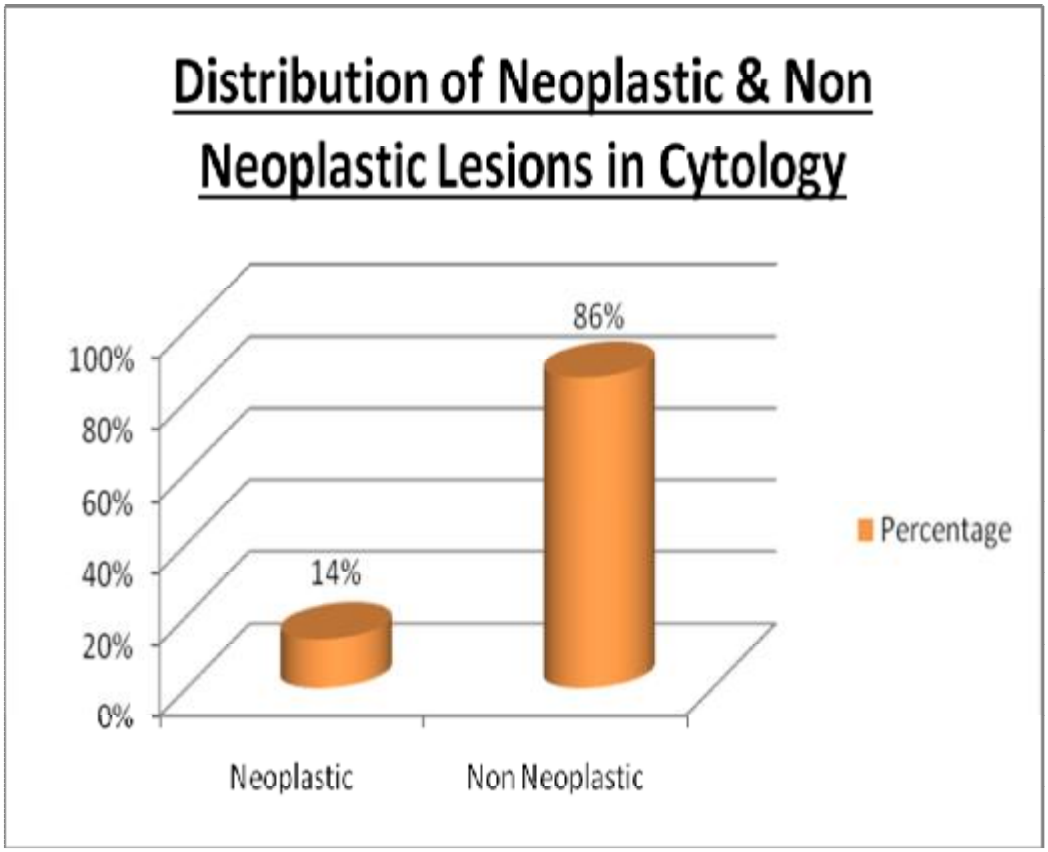

TABLE 7

DISTRIBUTION OF THYROID LESIONS BASED ON CYTOLOGY

Thyroid Lesions	Total no. of cases	Incidence (%)
Benign	16	9
Inflammatory	12	7
Malignant	7	4
Non Neoplastic	134	79
Total	**169**	**100**

In our study, non neoplastic lesions are more commonly encountered than neoplastic lesions. The lesions in present study were broadly classified into non neoplastic, benign, inflammatory and malignant. Out of 169 cases, 134(79%) cases were non neoplastic, 16 (9%) cases were benign, 12cases (7%) were inflammatory and 7(4%) were malignant.

CHART 7

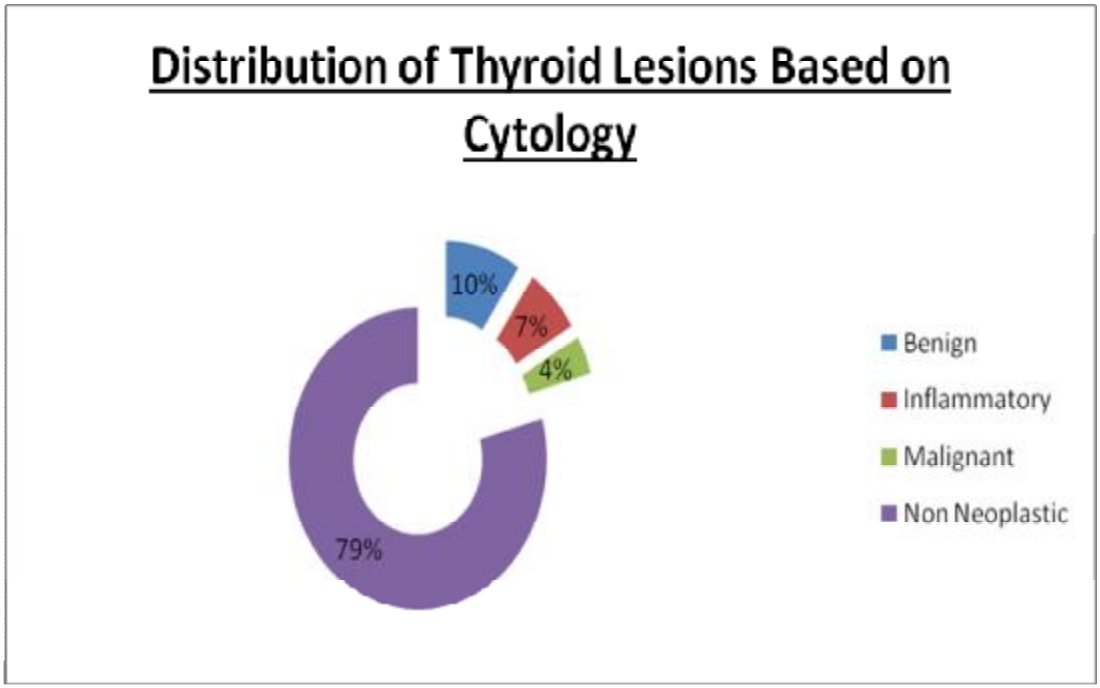

TABLE 8

DISTRIBUTION OF INDIVIDUAL THYROID LESIONS BASED ON CYTOLOGY

Diagnosis	No of cases	Incidence (%)
Hashimoto Thyroiditis	12	7
Thyroglossal Cyst	5	3
Nodular Goiter	129	76
Follicular Neoplasm	16	9
Papillary Carcinoma Thyroid(PTC)	7	4
Total	**169**	**100**

As shown in the Table 8 and chart 8, nodular goiter was the commonly encountered thyroid lesion. Out of 169 cases, 129(76%) cases were nodular goiter, 12 cases (7%) were Hashimoto thyroiditis, 16(9%) cases were follicular neoplasm, 7(4%) cases were papillary carcinoma thyroid (PTC) and 5(3%) cases were thyroglossal cyst.

Out of 169 cases, the most common non neoplastic lesion was nodular goiter (76%) followed by Hashimoto thyroiditis (7%) and most common neoplastic lesion was Follicular neoplasm(9%) followed by Papillary Carcinoma thyroid(4%).

The various lesions like cystic lesion of thyroid, colloid nodule, adenomatous goiter, toxic goiter, dominant nodule of nodular colloid goiter, hyperplastic nodule are grouped under the spectrum of nodular colloid goiter.

Lymphocytic thyroiditis and thyroiditis are grouped under hashimoto thyroiditis.

CHART 8

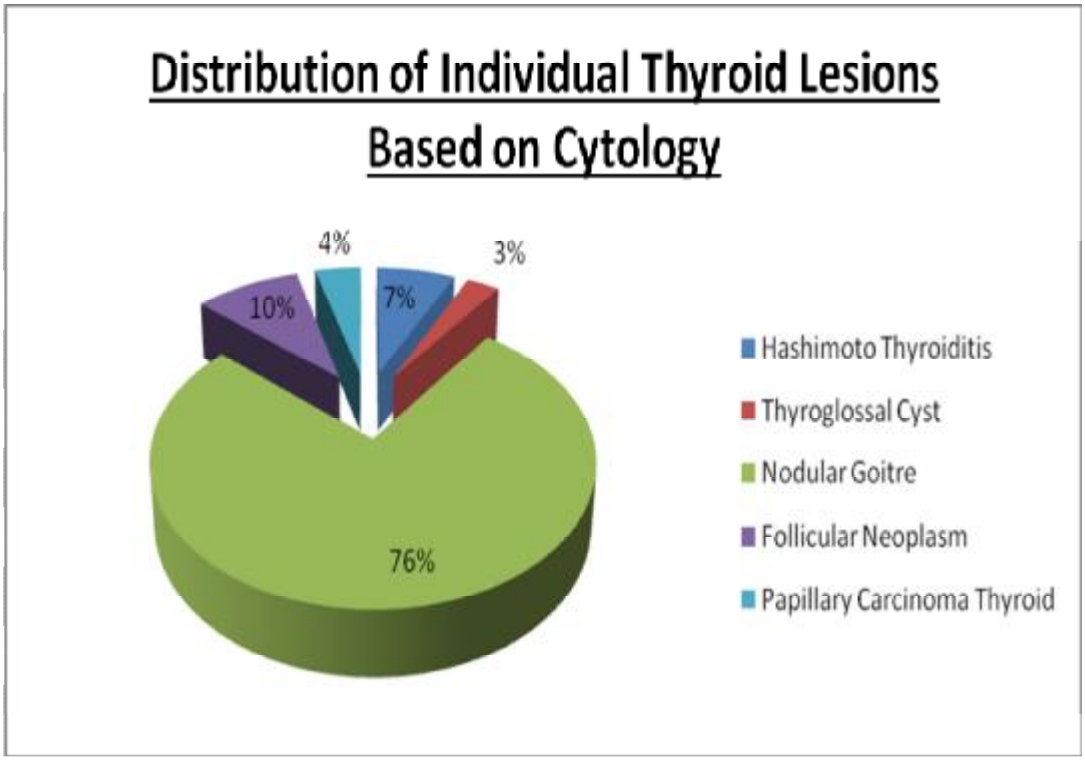

TABLE 9

DISTRIBUTION OF THYROID LESIONS BASED ON HISTOPATHOLOGY

Thyroid lesions	**HPE Frequency (%)**
Benign	46
Inflammatory	20
Malignant	21
Non Neoplastic	113
Total	**200**

Table 9 and chart 9 denotes distribution of lesions in total number of biopsy specimens received. Out of 200 cases, non neoplastic was more common constituting about 113(57%) specimens followed by benign cases(23%), malignant(10%) and inflammatory(10%) cases.

CHART 9

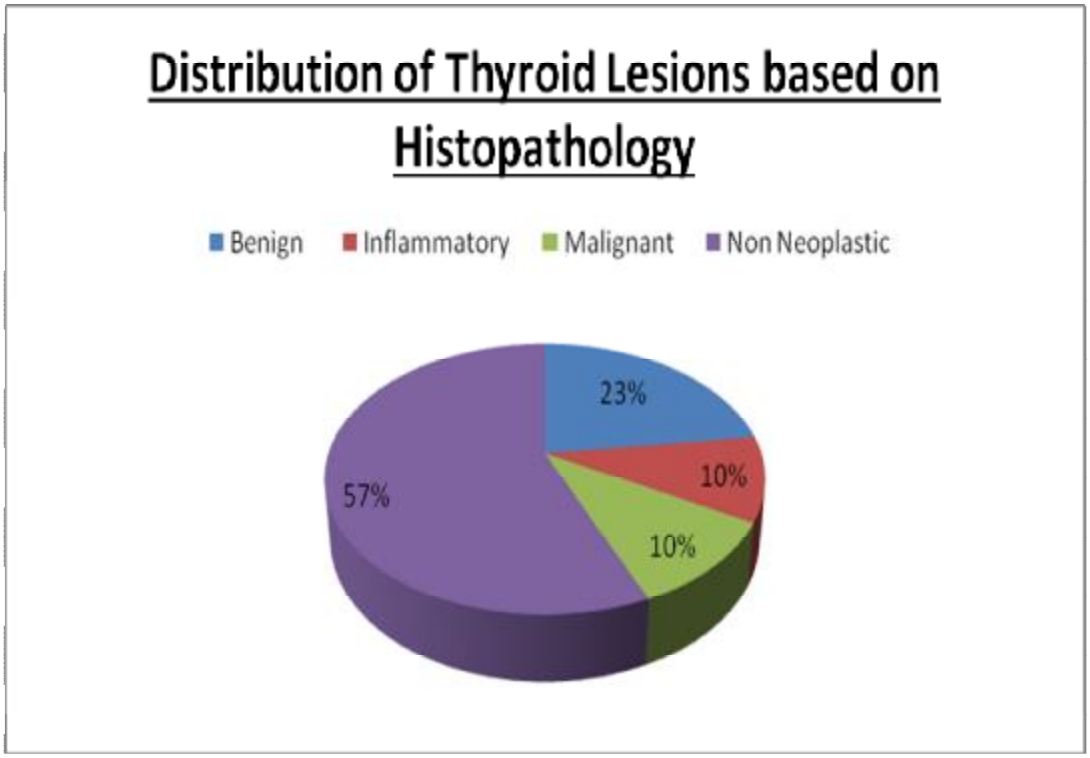

TABLE 10

DISTRIBUTION OF INDIVIDUAL THYROID LESIONS BASED ON HISTOPATHOLOGY

Diagnosis	No of Cases	Incidence (%)
Hashimoto Thyroiditis	17	10
Thyroglossal Cyst	5	3
Nodular Goiter	103	61
Follicular Adenoma	22	13
Hurthle Cell Adenoma	1	1
Hyalinising Trabecular Adenoma	1	1
Papillary Carcinoma Thyroid(PTC)	20	12
Total	**169**	**100**

Table 10 and chart 10, denotes individual case distribution in histopathology which has correlated with cytology. Out of 169 cases, nodular goiter (61%) was more common followed by follicular adenoma(13%), PTC(12%), Hashimoto thyroiditis(10%), thyroglossal cyst(3%) and hurthie cell adenoma(1%) and hyalinising trabecular adenoma(1%).

The lesions like multinodular goiter, adenomatous goiter, nodular goiter with micropapillary hyperplacia are grouped under spectrum of nodular goiter. Some of the variants reported in papillary carcinoma of thyroid are micropapillary variant and encapsulated variant.

CHART 10

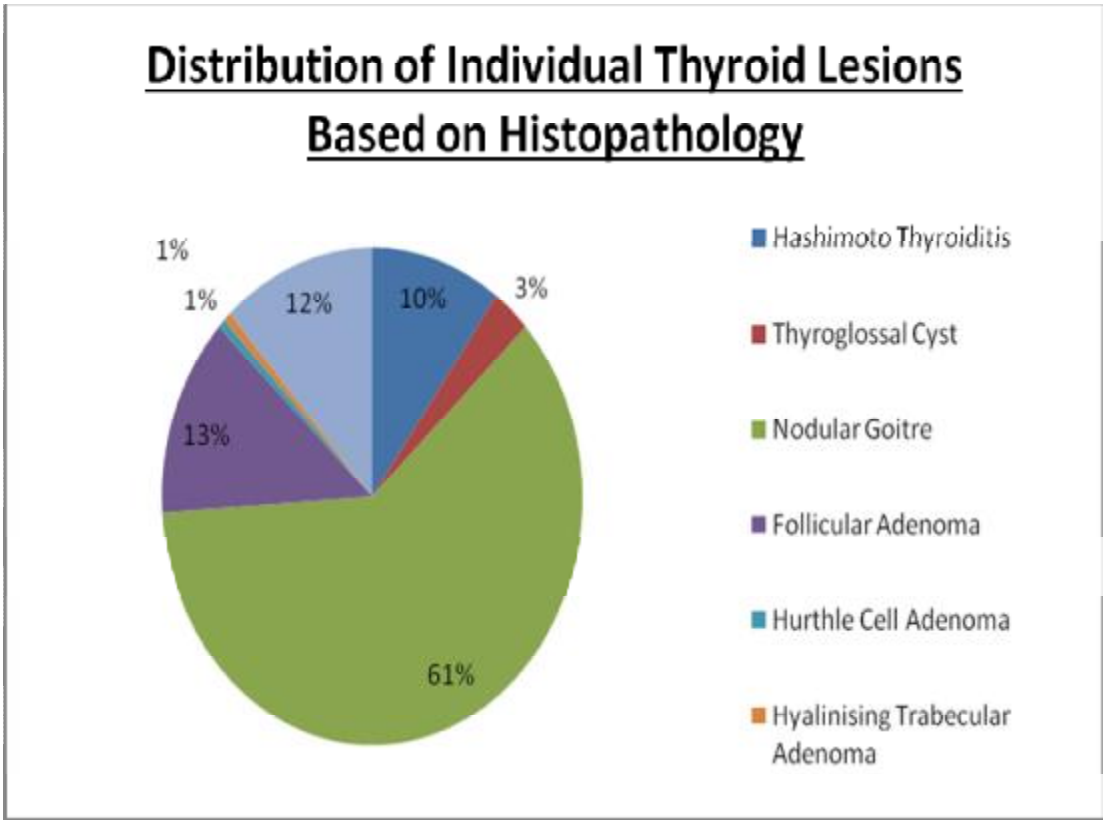

TABLE 11

AGE WISE DISTRIBUTION OF INDIVIDUAL THYROID LESIONS

Age	Hashimoto Thyroiditis	Thyroglossal Cyst	Nodular Goiter	Follicular Adenoma	Papillary Carcinoma	Total
0 - 9	-	-	-	-	-	0
10 - 19	1	-	2	1	1	5
20 - 29	5	3	22	8	3	41
30 - 39	5	2	35	9	8	59
40 - 49	8	-	36	4	7	55
50 - 59	2	1	22	3	1	29
60 - 69	-	-	5	2	1	8
70 - 79	-	-	2	-	-	2
80 - 89	-	-	-	-	1	1
				Total Sample Size		200

Table 11 shows that the most affected age group in nodular goiter is 40 – 49 years. Out of 55 total cases in this category 36 cases (65%) were diagnosed for nodular goiter. Also the most affected age group in follicular adenoma and papillary carcinoma thyroid is 30 – 39 years. Out of 59 cases 9 cases(15%) belongs to follicular adenoma and 8 Cases (14%) belongs to papillary carcinoma.

TABLE 12

AGE & SEX WISE DISTRIBUTION OF INDIVIDUAL THYROID LESIONS

Age	Hashimoto Thyroiditis		Thyroglossal Cyst		Nodular Goiter		Follicular Adenoma		Papillary Carcinoma		Total
	M	F	M	F	M	F	M	F	M	F	
0 - 9	-	-	-	-	-	-	-	-	-	-	0
10 - 19	-	1	-	-	-	2	1	-	-	1	5
20 - 29	-	5	1	2	-	22	2	6	1	2	41
30 - 39	-	5	-	2	1	34	-	9	2	6	59
40 - 49	-	8	-	-	3	33	-	4	-	7	55
50 - 59	-	2	-	1	3	19	1	2	-	1	29
60 - 69	-	-	-	-	2	3	-	2	-	1	8
70 - 79	-	-	-	-	1	1	-	-	-	-	2
80 - 89	-	-	-	-	-	-	-	-	-	1	1
						Total Sample size					200

In the study females are more commonly affected than males. Among females nodular goiter are more common followed by follicular adenoma and papillary carcinoma thyroid.

In 10 -19 yrs of age category, 2 cases out of 5 cases (40%) are diagnosed for nodular goiter in female.

In 20 – 29 yrs of age category, 22 cases out of 41 cases (54%) are diagnosed for nodular goiter in female.

In 30 – 39 yrs of age category, 34 cases out of 59 cases (58%) are diagnosed for nodular goiter in female.

In 40 – 49 yrs of age category, 33 cases out of 55 cases (60%) are diagnosed for nodular goiter in female.

In 50 – 59 yrs of age category, 19 cases out of 29 cases (66%) are diagnosed for nodular goiter in female.

TABLE 13

CYTOHISTOPATHOLOGICAL CORRELATION OF THYROID LESIONS

TEST		HPE				
		Benign	**Inflammatory**	**Malignant**	**Non Neoplastic**	**Total**
FNAC	**Benign**	12	0	1	3	**16**
	Inflammatory	0	10	0	2	**12**
	Malignant	0	0	7	0	**7**
	Non Neoplastic	29	6	11	88	**134**
	Total	**41**	**16**	**19**	**93**	**169**

Table 13 shows distribution of cases in histopathology followed by cytological aspiration. Out of 16 cases which was reported as benign in cytology, 12(75%) cases turned out to be benign, 1(6.25%) case reported to be malignant and 3(18.75%) cases turned out to be non neoplastic. Out of 12 cases reported as inflammatory in cytology, 10(83.33%) correlated with histopathology, 2(16.66%) cases turned out to be non neoplastic.

All cases which were reported as malignant(100%) in cytology correlated well with histopathology. Out of 134 cases reported as non neoplastic in cytology, 29(21.64%) cases were benign, 6(4.47%) cases inflammatory, 11(8.20%) cases malignant and 88(65.67%) cases non neoplastic in histopathology.

TABLE 14

CYTOHISTOPATHOLOGICAL CORRELATION OF INDIVIDUAL THYROID LESIONS

Test		FNAC SPECIFIC					
		Follicular Neoplasm	**Hashimoto thyroiditis**	**Nodular colloide goiter**	**Papillary Carcinoma Thyroid**	**Thyro glossal Cyst**	**Total**
HPE SPECIFIC	**Follicular Adenoma**	5	0	17	0	0	22
	Hashimoto thyroiditis	0	10	7	0	0	17
	Hurthle cell adenoma	0	0	1	0	0	1
	Hyalinising trabecular adenoma	1	0	0	0	0	1
	Nodular colloid goiter	8	2	92	0	1	103
	Papillary Carcinoma Thyroid	1	0	12	7	0	20
	Thyroglossal Cyst	0	0	1	0	4	5
	Total	15	12	130	7	5	169

Table 14 indicates individual case distribution in cytology and its correlation in histopathology. Out of 15 cases of follicular neoplasm, 5 cases (33.33%) were follicular adenoma, 1(6.66%) case HTA, 8 cases (53.33%) nodular colloid goiter and 1 case (6.66%) PTC.

Out of 12 cases in Hashimoto thyroiditis in cytology, 2 (16.66%) cases turned out to be nodular colloid goiter. Out of 130 cases of nodular colloid goiter, 17 (13.07%) cases were Follicular Adenoma, 12 (9.23%) cases were PTC,7 (5.38%) were Hashimoto thyroiditis and 1(0.76%) case Hurthle cell Adenoma. Out of 5 cases reported as thyroglossal cyst, 1(20%) case turned out to be nodular colloid goiter.

Significant agreement was observed between FNAC and histopathology as indicated by kappa(0.41)

TABLE 15

CYTOHISTOPATHOLOGICAL CORRELATION OF PAPILLARY CARCINOMA THYROID

PTC		FNAC		
		Positive	**Negative**	**Total**
HPE	**Positive**	7	13	20
	Negative	0	149	149
	Total	7	162	169

Table 15 denotes the sensitivity and specificity of FNAC in Papillary Carcinoma Thyroid. In our study, FNAC is 100% sensitive, 91.98% specific for diagnosins Papillary carcinoma thyroid with accuracy of 92.31%.

TABLE 16

CYTOHISTOPATHOLOGICAL CORRELATION OF FOLLICULAR NEOPLASM

Follicular neoplasm		FNAC		
		Positive	**Negative**	**Total**
HPE	**Positive**	5	17	22
	Negative	10	137	147
	Total	15	154	169

In our study, FNAC is 33% sensitive,88.96% specific in diagnosing follicular adenoma with accuracy of 84.02%.

TABLE 17

CYTOHISTOPATHOLOGICAL CORRELATION OF NODULAR COLLOID GOITER

Nodular colloid goiter		FNAC		
		Positive	**Negative**	**Total**
HPE	**Positive**	92	11	103
	Negative	38	28	66
	Total	130	39	169

In our study, FNAC was 71% sensitive, 71.79% specific in diagnosing Nodular Colloid Goiter with accuracy of 71.01%.

TABLE 18

CYTOHISTOPATHOLOGICAL CORRELATION OF HASHIMOTO THYROIDITIS

Hashimoto thyroiditis		FNAC		
		Positive	**Negative**	**Total**
HPE	**Positive**	10	7	17
	Negative	2	150	152
	Total	12	157	169

In our study FNAC is 83% sensitive, 95.54% specific in diagnosing Hashimoto thyroiditis with diagnostic accuracy of about 94.67%.

TABLE 19

IMMUNOHISTOCHEMICAL EXPRESSION OF Ki-67 IN THYROID LESIONS

LESIONS	0 < 2 %	1 3% - 5%	2 6% - 10%	3 > 10%	Total Cases
Papillary Carcinoma Thyroid	1	5	11	4	21
Follicular Adenoma	11	2	3	0	16
Hurthle Cell Adenoma	0	2	0	0	2
Hyalinising Trabecular Adenoma	0	0	1	0	1
Nodular Goiter	5	1	2	0	8
Hashimoto Thyroiditis	1	1	0	0	2

Out of 21 cases in PTC, Ki-67 expression was maximum in 6-10%. Out of 16 cases of follicular adenoma, Ki-67 expression was maximum in < 2%. Out of 8 cases in nodular goiter 6 cases(75%) were below < 5%.

Significant difference was observed between neoplastic and benign/non neoplastic thyroid lesions($P < 0.005$)

TABLE 20

IMMUNOHISTOCHEMICAL EXPRESSION OF p53 IN THYROID LESIONS

LESIONS	0	1	2	3	Total Cases
Papillary Carcinoma Thyroid	1	10	8	2	21
Follicular Adenoma	1	12	3	0	16
Hurthle Cell Adenoma	0	1	1	0	2
Hyalinising Trabecular Adenoma	0	0	1	0	1
Nodular Goiter	2	4	2	0	8
Hashimoto Thyroiditis	1	1	0	0	2

Out of 21 cases of PTC, p53 expression was maximum in grade 1 followed by grade 2. Out of 16 cases of follicular adenoma p53 expression was in grade 1 as with papillary carcinoma thyroid.

Statistically significant difference was observed between neoplastic and benign/ non neoplastic thyroid lesions (P 0.001)

DISCUSSION

Thyroid enlargement, either diffuse or nodular leads to array of investigations mainly to rule out a neoplasm or thyroiditis. The main aim of cytological or histopathological examination is to guides the clinicians for appropriate management of patients. FNAC, as first line of investigation aids for the categorical management, followed by other modes of investigations like Ultrasonography, thyroid scan, TFT and level of antibodies.

After obtaining ethical committee clearance, the study was conducted in the department of pathology at Kilpauk Medical College and hospital. A total of 200 specimens of thyroid have been received over the period from June 2010 to June 2014 which were analysed for cytohistopathological and immunohistochemical studies.

INCIDENCE

Carcinoma of the thyroid is rather uncommon with wide geographical variation in its incidence. In the UK, the annual incidence of thyroid malignancy is about between 2-3/100,000 population[60]. In USA an average of 11000 cases of thyroid malignancy are reported every year and more than 1 person die each year[61]. In India thyroid malignancy constitute about 1% of all Head and Neck cancers.

In our study the incidence of thyroid cancers among Head and neck lesions is about 1.36% which is in concordance with the other studies. The incidence of papillary carcinoma thyroid is 10.50%.

INCIDENCE OF CARCINOMA

Study	Year	Percentage (%)
Wagana et al	2002	16.00
Rehman et al	2009	11.47
Suresh et al	2012	10.60
Present Study	2014	10.50

AGE

In the previous studies by Quari[86] et al and Talepoor[84] et al in 2005, the mean age at presentation was 36.7yrs and 38.6yrs respectively. Khurshid Anwar in 2012 reported mean age at presentation as 37yrs. In the present study the mean age at presentation is found to be 39yrs with the range between 10 yrs and 84yrs which correlates with other studies. The median age of presentation for PTC in our study is 39yrs. Most of the studies correlated with our study having the average age at initial diagnosis between 30-49yrs.

Mean Age at Presentation

AUTHORS	MEAN AGE IN YEARS
Cheung et al[90] (2007)	46
Khurshid Anwar et al[89] (2012)	37
Rajesh S et al[82] (2013)	32.5
Suresh et al (2013)	37.24
Present Study	39

SEX DISTRIBUTION

In the previous studies done by Dorairajan et al(1996), Rajesh et al(2013) and Suresh(2013) the sex ratio was 1:9, 1:5 and 1:8.16 respectively, which correlates with our present study with ratio of 1:10.1.

AUTHORS	SEX RATIO (M:F)
Gupta et al[85] (2001)	1:5
Rajesh S et al[82] (2013)	1:5
Suresh et al (2013)	1:8.6
Dorai Rajan et al[83] (1996)	1:9
Raafat A et al[21] (2013)	7:10
Present Study	1:10.1

Because of fluctuations in hormonal status in females as in puberty, menstrual cycle, pregnancy, menopause, the chances of formation of thyroid nodule in females are high when compared to males.

FNAC AS DIAGNOSTIC TOOL

Percentage of failure in making cytological diagnosis is not an uncommon feature. Present study shows failure rate of around 26% of cases. It makes distinct difference for surgeons to approach different investigation modalities for appropriate management. Present study was compared with previous studies conducted by various authors shown in table:

Comparison of Value of FNAC as Diagnostic Tool

Study (Year)	No of Study Cases	Positive Correlation (%)
Kessler et al[79] (2005)	170	80%
Gupta et al[80] (2006)	75	84%
P Pandey et al[81] (2012)	112	81%
Rajesh et al[82] (2013)	142	89%
Present Study	169	74%

In our study total of 74% cases in cytology have shown positive correlation in histopathology which correlates well with other studies.

26% of cases show negative correlation. The probable reasons for this negative correlation are

- Faulty biopsy technique – too much or too little suction while aspiration
- Sampling error – biopsy needle in the tissue surrounding the nodule
- Long standing cysts with calcification – inadequate material
- Thick fibrous calcified capsule
- Highly vascular and sclerotic lesions

DISTRIBUTION OF THYROID LESIONS IN CYTOLOGY

In our study, non neoplastic lesions were common in cytological diagnosis when compared to neoplastic lesions which includes adenomas and malignancies. The ratio of non neoplastic lesions to neoplastic lesions is 6.34:1 is same when compared to other studies shown in table below

Distribution of Non Neoplastic & Neoplastic Lesions Diagnosed by FNAC

Authors	Non Neoplastic	Neoplastic	Ratio
Talepoor M et al[84] (2005)	325	70	4.33:1
Naggada et al[88] (2006)	51	18	2.83:1
Chao CT et al[87] (2007)	276	264	1.04:1
Suresh et al (2013)	36	19	1.89:1
Present Study	146	23	6.34:1

CYTOHISTOPATHOLOGICAL CORRELATION

Sensitivity of thyroid FNAC varies from 78-92% and specificity varies from 74-99%[62,63,64]. In our study, the sensitivity in detecting neoplastic lesion is 82%, specificity 78% which is similar to other studies shown in table. Sensitivity for detecting Papillary carcinoma thyroid in our study is 100%, with specificity of 91.98% and diagnostic accuracy of about 92.31%. This shows FNAC is more sensitive in diagnosing thyroid malignancy. The diagnostic accuracy for detecting neoplastic lesions and papillary carcinoma thyroid are 97% and 92.31% respectively which correlates well with other studies.

Comparison with previous studies

Authors	Sensitivity (%)	Specificity (%)	Accuracy (%)
Bagga & Mahajan[76] (2010)	66	100	96.2
Likhar et al[77] (2013)	100	70	77.78
Sarma Usha[78] (2014)	95	95	92
Present Study	100	91.98	92.31

IMMUNOHISTOCHEMISTRY

Various studies have been published on immunohistochemical expression of Ki-67 and p53 in thyroid lesions to till date. Most of the studies conclude that Ki-67 and p53 can act as useful marker for differentiating benign and malignant thyroid lesions.

Ki-67 in thyroid:

In our study, Ki-67 labelling index of 6-10% was observed maximally in papillary carcinoma thyroid in 52.38% of cases whereas follicular adenoma and nodular goiter show low proliferative activity of < 2%. These findings are in close agreement with Erichson et al[65]. However

in present study there is significant difference in mean values between benign/non neoplastic and malignant lesions, but cut-off value for differentiating these cannot be given due to small sample size. Kjellman et al[66] in his study suggested a cut off value of 1.9% or more for differentiating benign and malignant thyroid lesions. This is in concordant with our study as both benign and non neoplastic cases express < 2%.

The mean and range of Ki-67 labelling index for papillary carcinoma thyroid in our study are 9.33 and 1.63-17.03 respectively and for benign/non neoplastic lesions are 4.66 and 4.28-13.6. This observation is concordant with other studies of Singh et al[59], Yoshida et al[71] and Basolo et al[72], but in contrast to the study conducted by Wallin et al[67] were the observed Ki-67 LI was 0.1-1% in non neoplastic lesions, 0.3-1% in benign and 0.2-3.9% in malignant lesions.

Out of 6 cases in nodular goiter, one case has micropapillary hyperplasia area which shows strong positivity in Ki-67 LI when compared to other cases. Hashimoto thyroiditis and nodular goiter shows weak positivity with Ki-67 LI, but some areas shows increased staining due to presence of lymphocytes which normally show nuclear positivity

p53 in thyroid

In studies related to p53 antibody in thyroid lesions, the p53 expression was generally negative in well differentiated tumors, but strongly positive in anaplastic carcinomas[70]. Donghi et al[75] and Fagin et al[50] in their studies reported that p53 mutation is seen 5 out of 7 undifferentiated carcinomas and 5 out of 6 ATCs respectively. In present study all the malignant cases reported are papillary carcinoma thyroid. The positive staining was achieved in 48% of papillary carcinoma, 75% of follicular adenoma and 50% of nodular goiter.

In the present study all 21 malignant cases reported was Papillary carcinoma thyroid with p53 expression seen maximally in grade 1(<25%). This low positivity of p53 expression in thyroid tumours may probably be due to lack of undifferentiated tumours in present study. It has been proposed in other studies that p53 detection in immunohistochemistry may rarely be positive in early tumours and appear only as a late event. Our observations are in agreement with previous studies of Pollina et al[73] and Okayasu et al[74].

Out of 21 cases in papillary carcinoma thyroid, one case show no staining at all, this may be due to defective processing. There are also

variation in intensity of staining among malignant cases which is due to loss of heterogenecity of tumour and defective antigen retrieval.

LIMITATIONS OF THE STUDY

Because of small sample size, lack of undifferentiated tumours and limited number of cases in benign and malignant cases in the study, a definite cut-off value for differentiating these thyroid lesions could not be ascertained. Larger sample sizes are needed to confirm this observation.

SUMMARY AND CONCLUSION

Thyroid lesions are common in surgical practice with incidence of 4-7% of the population[82]. The incidence of thyroid malignancy is 1% with papillary carcinoma of thyroid being the most common comprising about 84% of thyroid malignancies.

The salient features observed in the study were:

1. Thyroid lesions constitute about 12.98% of head and neck lesions.
2. Thyroid tumours constitute about 1.36% of head & neck lesions.
3. The incidence of papillary carcinoma of thyroid is 10.5%
4. The common age group affected was 30-39yrs.
5. The median age of presentation of papillary carcinoma thyroid was 39yrs.
6. Females were commonly affected with male female ratio of about 1:10.1.
7. 74% of thyroid FNAC had positive correlation with histopathology
8. Non neoplastic lesions were more common than neoplastic lesions in thyroid with a incidence of 86%
9. Nodular goiter was more common among non neoplastic lesions in both cytology and histopathology with a incidence of 76% and 61% respectively.

10. Follicular adenoma was the most common neoplastic lesion in both cytology and histopathology with a incidence of 9% and 13% respectively.
11. The sensitivity, specificity and diagnostic accuracy of FNAC in detecting neoplastic and non neoplastic lesions was 82%, 78% and 97% respectively.
12. The sensitivity, specificity and accuracy of FNAC for detecting papillary carcinoma of thyroid was 100%,91.98% and 92.31%
13. Ki-67 staining was seen in 52.38% in PTC, 68.75% in follicular adenoma, 62.5% in nodular goiter
14. p53 staining was seen in 47.62% in PTC, 75% in follicular adenoma and 50% in nodular goiter. Both these markers were statistically significant in differentiating non neoplastic and neoplastic lesions.

In conclusion, FNAC is a safe, simple, rapid, cost effective and accurate method in diagnosing thyroid lesions with high sensitivity, specificity and efficacy. It can be used as an initial investigation in the management of thyroid diseases and avoid unnecessary surgery.

Most of the thyroid neoplasms are diagnosed based on their well characterised histological features. However there are certain subsets of tumours with follicular architecture that lack equivocal features of malignancy, thus posing diagnostic difficulty. In such cases, the use of ancillary techniques like Immunohistochemistry and molecular analysis can significantly improve the accuracy of diagnosis.

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PROFORMA

NAME:

AGE:

SEX:

PERSONAL H/O:

PAST H/O:

H/O IRRADIATION:

CLINICAL HISTORY:

FNAC:

HPE:

DIAGNOSIS:

IHC PANEL:

CONCLUSION:

Master Chart

S.No.	name	Age /Sex	Clinical Diagnosis	Procedure Done	FNAC No	Diagnosis	Biopsy No	Diagnosis	Ki 67	P53			
										0	1	2	3
1	Nagammal	46/F	Multinodular Goitre	Total Thyroidectomy	F 742/10	Hashimoto Thyroiditis	1018/10	Hashimoto Tyroiditis					
2	Meera	40/F	Solitary thyroid Nodule	Hemithyroidectomy	F 322/10	Nodular Goitre	1072/10	Adenomatous Goitre					
3	jayakumari	32/F	Multinodular Goitre	Subtotal Thyroidectomy	F 842/10	Lymphocytic thyoiditis	1081/10	Lymphocytic Thyroiditis					
4	Kanagi	40/F	Multinodular Goitre	Total Thyroidectomy	F 800/10	Nodular Goitre	1124/10	Papillary Carcinoma Thyroid	5 %	70 %	30 %	_	_
5	Guruvammal	50/F	Multinodular Goitre	Total Thyroidectomy	-	-	1186/10	Multinodular goitre					
6	Jayamary	54/F	Multinodular Goitre	Subtotal Thyroidectomy	-	-	1187/10	Multinodular goitre					
7	Nalini	45/F	Throid Nodule	Hemithyroidectomy	-	-	1259/10	Multinodular goitre					
8	Maheshwari	33/F	Thyroglossal Cyst	Sistrunk Operation	-	-	1260/10	Thyroglossal Cyst					
9	Parveena	26/F	thyroid Nodule	Subtotal Thyroidectomy	F 940/10	Nodular Goitre	1362/10	Hashimoto Tyroiditis					
10	Parameshwari	42/F	Multinodular Goitre	Subtotal Thyroidectomy	F1120/10	Multinodular Goitre	1380/10	Nodular Colloid goitre					
11	Alamelu	42/F	Multinodular Goitre	Subtotal Thyroidectomy	F1062/10	Hashimoto Thyroiditis	1442/10	Toxic Goitre					
12	Nagamani	37/F	Solitary thyroid Nodule	Hemithyroidectomy	F 1226/10	Nodular Goitre	1594/10	Multinodular goitre					
13	Dhanalakshmi	56/F	Multinodular Goitre	Total Thyroidectomy	F 1216/10	Follicular Neoplasm	1762/10	Follicular Adenoma					
14	Shanthi	35/F	Solitary thyroid Nodule	Total Thyroidectomy	F 1269/10	Nodular Goitre	1791/10	Adenomatous Goitre					
15	Loganayagi	55/F	Multinodular Goitre	Subtotal Thyroidectomy	-	-	1880/10	Hashimoto Tyroiditis					
16	Manjula	35/F	Multinodular Goitre	Subtotal Thyroidectomy	F1212/10	Nodular Goitre	1951/10	Nodular Colloid goitre					
17	Saraswathi	38/F	Solitary thyroid Nodule	Hemithyroidectomy	-	-	1986/10	Colloid Nodule					

18	Chellammal	43/F	Multinodular Goitre	Neartotal Thyroidectomy	F1507/10	Nodular Goitre	2026/10	Multinodular goitre					
19	Krishnaveni	58/F	Solitary thyroid Nodule	Hemithyroidectomy	F1573/10	Cystic Lesion of Thyroid	2125/10	Multinodular goitre					
20	Gomathi	22/F	Adenoma Thyroid	Hemithyroidectomy	-	-	49/11	Adenomatous Goitre					
21	Anthony Ammal	22/F	Multinodular Goitre	Subtotal Thyroidectomy	F20/11	Nodular Goitre	63/11	Multinodular goitre					
22	Amritha	46/F	Multinodular Goitre	Total Thyroidectomy	F40/11	Follicular Neoplasm	171/11	Multinodular goitre					
23	Lalitha	40/F	Solitary thyroid Nodule	Hemithyroidectomy	F307/11	Nodular Goitre	470/11	Multinodular goitre					
24	Gnanammal	35/F	Thyroglossal Cyst	Sistrunk Operation	F384/11	Thyroglossal Cyst	514/11	Thyroglossal Cyst					
25	Gunasundari	29/F	Multinodular Goitre	Subtotal Thyroidectomy	F382/11	Thyroiditis	545/11	Multinodular goitre					
26	Mohan	54/M	Multinodular Goitre	Total Thyroidectomy	-	-	552/11	Multinodular goitre					
27	Pushpa	25/F	Thyroglossal Cyst	Sistrunk Operation	F442/11	Colloid Nodule	639/11	Thyroglossal Cyst					
28	Singari	41/F	Multinodular Goitre	Subtotal Thyroidectomy	F435/11	Colloid Nodule	748/11	Papillary Carcinoma Thyroid	10%	30%	35%	30%	5%
29	Dhanalakshmi	25/F	Solitary thyroid Nodule	Hemithyroidectomy	-	-	846/11	Nodular Colloid goitre					
30	Revathy	25/F	Solitary thyroid Nodule	Hemithyroidectomy	F1265/10	Colloid Nodule	892/11	Multinodular goitre					
31	Kannammal	38/F	Solitary thyroid Nodule	Hemithyroidectomy	F562/11	Nodular Goitre	902/11	Nodular Colloid goitre					
32	Chitra	40/F	Multinodular Goitre	Subtotal Thyroidectomy	F676/11	Nodular Goitre	919/11	Multinodular goitre					
33	Kanchana	36/F	Solitary thyroid Nodule	Subtotal Thyroidectomy	F626/11	Nodular Goitre	953/11	Multinodular goitre					
34	Amutha	37/F	Solitary thyroid Nodule	Hemithyroidectomy	F760/11	Nodular Goitre	993/11	Multinodular goitre					
35	Devi	28/F	Solitary thyroid Nodule	Hemithyroidectomy	F714/11	Nodular Goitre	995/11	Multinodular goitre					
36	Geetha	37/F	Nodular Goitre	Total Thyroidectomy	F384/11	Infected Thyroglossal cyst	1034/11	Multinodular goitre					
37	Rajam	45/F	Solitary thyroid Nodule	Hemithyroidectomy	-	-	1064/11	Multinodular goitre					
38	Amul	38	Solitary	Hemithyroide	F412	Nodular	1103/	Multinodular					

		/F	thyroid Nodule	ctomy	/11	Colloid Goitre	11	goitre					
39	Ramalakshmi	24/F	Multinodular Goitre	Subtotal Thyroidectomy	F802/11	Nodular Goitre	1107/11	Adenomatous Goitre					
40	Saraswathi	41/F	Solitary thyroid Nodule	Total Thyroidectomy	-	-	1140/11	Papillary Carcinoma Thyroid	10%	50%	20%	20%	10%
41	Meenakshi	25/F	Solitary thyroid Nodule	Hemithyroidectomy	F858/11	Nodular Goitre	1147/11	Adenomatous Goitre					
42	Ramu	40/M	Solitary thyroid Nodule	Hemithyroidectomy	F851/11	Nodular Goitre	1175/11	Adenomatous Goitre					
43	Vijayan	58/M	Solitary thyroid Nodule	Neartotal Thyroidectomy	F667/11	Follicular Neoplasm	1184/11	Follicular Adenoma					
44	Kannagi	24/F	Solitary thyroid Nodule	Hemithyroidectomy	-	-	1245/11	Hurthle cell adenoma	4%	30%	20%	20%	20%
45	Nalini	53/F	Solitary thyroid Nodule	Hemithyroidectomy	F828/11	Nodular Colloid Goitre	1260/11	Multinodular goitre					
46	Ammu	28/F	Solitary thyroid Nodule	Hemithyroidectomy	F903/11	Nodular Colloid Goitre	1261/11	Adenomatous Goitre					
47	Samboranam	29/F	Thyroglossal Cyst	Sistrunk Operation	F801/11	Infected Thyroglossal cyst	1289/11	Thyroglossal Cyst					
48	Zarina	35/F	Solitary thyroid Nodule	Hemithyroidectomy	-	-	1304/11	Hashimoto Tyroiditis					
49	Ranganayaki	55/F	Solitary thyroid Nodule	Hemithyroidectomy	F966/11	Nodular Goitre	1326/11	Multinodular goitre					
50	Sugunamma	45/F	Multinodular Goitre	Total Thyroidectomy	F955/11	Colloid Nodule	1566/11	Multinodular goitre					
51	Nagammal	55/F	Solitary thyroid Nodule	Total Thyroidectomy	F1114/11	Follicular Neoplasm	1575/11	Adenomatous Goitre	10%	50%	40%	5%	5%
52	Mariammal	60/F	Papillary Carcinoma Thyroid	Total Thyroidectomy	F1250/11	Papillary Carcinoma Thyroid	1723/11	Papillary Carcinoma Thyroid	10%	50%	20%	20%	10%
53	Sundhambal	60/F	Solitary thyroid Nodule	Subtotal Thyroidectomy	F971/11	Nodular Colloid Goitre	1724/11	Multinodular goitre					
54	Ponnulakshmi	25/F	Solitary thyroid Nodule	Hemithyroidectomy	F1251/11	Nodular Goitre	1753/11	Adenomatous Goitre					
55	Ganesan	55/M	Solitary thyroid Nodule	Subtotal Thyroidectomy	F1239/11	Colloid Nodule	1758/11	Multinodular goitre					
56	Kanthammal	60/F	Solitary thyroid Nodule	Hemithyroidectomy	F1252/11	Follicular Neoplasm	1766/11	Hyalinising Trabecular Adenoma	10%	20%	20%	20%	30%
57	Gowri	50/F	Solitary thyroid	Hemithyroidectomy	F1302/11	Follicular Neoplasm	1870/11	Multinodular goitre					

			Nodule										
58	Mohana priya	21 /F	Solitary thyroid Nodule	Neartotal Thyroidectomy	F1260/11	Nodular Goitre	1875/11	Hashimoto Tyroiditis					
59	Sangeetha	21 /F	Multinodular Goitre	Total Thyroidectomy	F1270/11	Colloid Nodule	1955/11	Hashimoto Tyroiditis					
60	Ponkumari	42 /F	Multinodular Goitre	Subtotal Thyroidectomy	F1298/11	Nodular Goitre	1996/11	Multinodular goitre					
61	Anuradha	36 /F	Multinodular Goitre	Total Thyroidectomy	F1300/11	Colloid Nodule	2047/11	Multinodular goitre					
62	Malathi	45 /F	Multinodular Goitre	Subtotal Thyroidectomy	F1415/11	Nodular Colloid Goitre	2058/11	Adenomatous Goitre					
63	Kokila	25 /F	Multinodular Goitre	Subtotal Thyroidectomy	F1314/11	Nodular Colloid Goitre	2452/11	Hashimoto Tyroiditis					
64	Kumari	40 /F	Solitary thyroid Nodule	Hemithyroidectomy	F1500/11	Nodular Colloid Goitre	2197/11	Multinodular goitre					
65	Muniyammal	27 /F	Solitary thyroid Nodule	Hemithyroidectomy	F1564/11	Follicular Neoplasm	2290/11	Follicular Adenoma					
66	Varatharajan	65 /M	Solitary thyroid Nodule	Hemithyroidectomy	F1550/11	Colloid Nodule	2308/11	Multinodular goitre					
67	Revathy	45 /F	Multinodular Goitre	Total Thyroidectomy	F1659/11	Nodular Colloid Goitre	2431/11	Multinodular goitre					
68	Punitha	22 /F	Solitary thyroid Nodule	Hemithyroidectomy	F1582/11	Nodular Colloid Goitre	2435/11	Adenomatous Goitre	2 %	70 %	30 %	-	_
69	Mohan	32 /M	Cystic Nodular Goitre	Total Thyroidectomy	F910/11	Colloid Nodule	234/12	Papillary Carcinoma Thyroid	1 %	90 %	5 %	5 %	
70	Chennammal	47 /F	Multinodular Goitre	Subtotal Thyroidectomy	F31/12	Nodular Goitre	326/12	multinodular goitre					
71	Chakravarthy	62 /M	Multinodular Goitre	Hemithyroidectomy	_	_	859/12	Nodular Goitre					
72	Muniyammal	60 /F	Multinodular Goitre	Total Thyroidectomy	F542/12	Nodular Goitre	979/12	Adenomatous Goitre					
73	Mumtaj	48 /F	Solitary thyroid Nodule	Hemithyroidectomy	F536/12	Nodular Goitre	1020/12	Follicular Adenoma					
74	Dharani	40 /F	Multinodular Goitre	Total Thyroidectomy	F565/12	Nodular Goitre	1130/12	Multinodular goitre					
75	Yesurathinam	30 /M	Solitary thyroid Nodule	Hemithyroidectomy	F311/12	Colloid Nodule	1269/12	Adenomatous Goitre					
76	Suguna	26 /F	Adenoma Thyroid	Hemithyroidectomy	F751/12	Adenomatous Goitre	1282/12	Follicular Adenoma	1 %	100 %	_	_	_

77	Priya	37 /F	Solitary thyroid Nodule	Hemithyroidectomy	F730 /12	Nodular Goitre	1288/ 12	Follicular Adenoma	2 %	90 %	5 %	5 %	_
78	Senbagam	35 /F	Solitary thyroid Nodule	Hemithyroidectomy	F839 /12	Nodular Colloid Goitre	1435/ 12	Nodular Colloid goitre with Micropapillary Hyperplasia					
79	Jaya	40 /F	Solitary thyroid Nodule	Hemithyroidectomy	F968 /12	Nodular Goitre	1648/ 12	Multinodular goitre					
80	Pooja	42 /F	Cystic Nodular Goitre	Hemithyroidectomy	F999 /12	Nodular Colloid Goitre	1666/ 12	Multinodular goitre					
81	Panjali	40 /F	Hyperthyroid	Subtotal Thyroidectomy	-	-	1805/ 12	Hashimoto Tyroiditis					
82	Poongothai	65 /F	Multinodular Goitre	Total Thyroidectomy	F600 /12	Colloid Nodule	1902/ 12	Hurthle cell adenoma	5 %	20 %	30 %	20 %	30 %
83	Shanthi	28 /F	Multinodular Goitre	Total Thyroidectomy	F855 /12	Colloid Nodule	1965/ 12	Nodular Goitre					
84	Selvi	31 /F	Follicular Adenoma	Hemithyroidectomy	F1160/12	Follicular Neoplasm	2020/ 12	Follicular Adenoma					
85	Sasikala	50 /F	Multinodular Goitre	Subtotal Thyroidectomy	F1202/12	Nodular Colloid Goitre	2080/ 12	Nodular Colloid Goitre					
86	Mariya	47 /F	Multinodular Goitre	Total Thyroidectomy	F1123/12	Nodular Goitre	2126/ 12	Nodular Colloid Goitre					
87	Pangajam	40 /F	Multinodular Goitre	Subtotal Thyroidectomy	-	-	2138/ 12	Multinodular goitre					
88	suganthi	32 /F	Multinodular Goitre	Total Thyroidectomy	F1267/12	Hashimoto Thyroiditis	2180/ 12	Hashimoto Tyroiditis					
89	Senthil	20 /M	Thyroglossal Cyst	Sistrunk Operation	F1243/12	Thyroglossal Cyst	2265/ 12	Thyroglossal Cyst					
90	Chellammal	70 /F	Solitary thyroid Nodule	Hemithyroidectomy	F1182/12	Nodular Colloid Goitre	2274/ 12	Adenomatous Goitre					
91	Kumari	38 /F	Papillary Carcinoma Thyroid	Total Thyroidectomy	F1208/12	Papillary Carcinoma Thyroid	2291/ 12	Papillary Carcinoma Thyroid	5 %	40 %	30 %	20 %	10 %
92	Jagathambal	58 /F	Multinodular Goitre	Subtotal Thyroidectomy	F1364/12	Nodular Colloid Goitre	2306/ 12	Nodular Colloid Goitre					
93	Chellammal	50 /F	Multinodular Goitre	Total Thyroidectomy	F1301/12	Colloid Nodule	2323/ 12	Multinodular goitre with Encapsulated Papillary Carcinoma	15 %	10 %	40 %	20 %	30 %
94	Purushothaman	41 /M	Multinodular Goitre	Subtotal Thyroidectomy	-	-	2373/ 12	Nodular colloid Goitre with Micropapillary Hyperplasia	5 %	20 %	20 %	40 %	20 %
95	Anjalai	40	Papillary	Total	F143	Papillary	2441/	Papillary	10	10	5	2	2

		/F	Carcinoma Thyroid	Thyroidectomy	1/12	Carcinoma Thyroid	12	Carcinoma Thyroid	%	%	0 %	0 %	0 %
96	Devagi	45 /F	Papillary Carcinoma Thyroid	Total Thyroidectomy	F148 2/12	Papillary Carcinoma Thyroid	2559/ 12	Papillary Carcinoma Thyroid	5 %	30 %	30 %	30 %	10 %
97	Kalavathi	32 /F	Solitary thyroid Nodule	Hemithyroidectomy	F148 5/12	Nodular Colloid Goitre	2651/ 12	Nodular colloid Goitre					
98	Poornima	27 /F	Solitary thyroid Nodule	Hemithyroidectomy	F157 9/12	Colloid Nodule	2674/ 12	Follicular Adenoma	2 %	50 %	20 %	5 %	5 %
99	Lourthsamy	30 /m	Solitary thyroid Nodule	Hemithyroidectomy	F134 1/12	Nodular Colloid Goitre	66/13	Papillary Carcinoma Thyroid	10 %	10 %	40 %	30 %	20 %
100	pushpavalli	39 /F	Solitary thyroid Nodule	Hemithyroidectomy	F163 3/12	Cystic Colloid nodule	108/13	Nodular Colloid Goitre					
101	Unnamalai	61 /F	Multinodular Goitre	Total Thyroidectomy	-	-	192/13	Nodular Colloid Goitre					
102	syed jeelani	24 /M	Solitary thyroid Nodule	Hemithyroidectomy	-	-	354/13	Follicular Adenoma					
103	Vijiyalakshmi	48 /F	Multinodular Goitre	Total Thyroidectomy	F122 /13	Colloid Nodule	384/13	Nodular Goitre					
104	Manjula	38 /F	Colloid Goitre	Total Thyroidectomy	F176 /13	Nodular Goitre	444/13	Nodular Colloid Goitre					
105	Girija	51 /F	Multinodular Goitre	Total Thyroidectomy	F6/13	Nodular Colloid Goitre	475/13	Nodular Colloid Goitre					
106	Mugundhani	20 /F	Multinodular Goitre	Total Thyroidectomy	-	-	498/13	Hashimoto Tyroiditis					
107	Sandhiya	20 /F	Solitary thyroid Nodule	Hemithyroidectomy	F206 /13	Nodular Colloid Goitre	500/13	Follicular Adenoma					
108	Uma	46 /F	Multinodular Goitre	Total Thyroidectomy	F199 /13	Hashimoto Thyroiditis	526/13	Hashimoto Tyroiditis					
109	Muniyammal	50 /F	Multinodular Goitre	Total Thyroidectomy	-	-	547/13	Multinodular Goitre					
110	Murugamma	42 /F	Nodular Goitre	Total Thyroidectomy	-	-	638/13	Nodular Colloid Goitre					
111	Parimala	48 /F	Multinodular Goitre	Total Thyroidectomy	-	-	652/13	Nodular Colloid Goitre					
112	Maheshwari	37 /F	Papillary Carcinoma Thyroid	Total Thyroidectomy	F359 /13	Papillary Carcinoma Thyroid	659/13	Papillary Carcinoma Thyroid	10 %	10 %	40 %	30 %	20 %
113	Kalaiselvi	29 /F	Solitary thyroid Nodule	Subtotal Thyroidectomy	F318 /13	Nodular Colloid Goitre	675/13	Follicular Adenoma	10 %	40 %	30 %	20 %	10 %
114	Malliga	39 /F	Solitary thyroid	Total Thyroidectom	F385 /13	Nodular Colloid Goitre	693/13	Nodular colloid Goitre					

			Nodule	y									
115	Antony	42 /F	Multinodular Goitre	Total Thyroidectomy	F326 /13	Nodular Colloid Goitre	726/13	Hashimoto Tyroiditis					
116	Thilagavathy	46 /F	Multinodular Goitre	Total Thyroidectomy	-	-	795/13	Nodular Colloid Goitre					
117	Padmini	37 /F	Multinodular Goitre	Total Thyroidectomy	F477 /13	Nodular Colloid Goitre	980/13	Nodular Colloid goitre					
118	Subbulakshmi	34 /F	Multinodular Goitre	Total Thyroidectomy	-	-	993/13	Adenomatous Goitre	10 %	58 %	20 %	10 %	2 %
119	Jayapriya	16 /F	Multinodular Goitre	Total Thyroidectomy	F551 /13	Nodular Colloid Goitre	999/13	Hashimoto Tyroiditis					
120	Kamsala	46 /F	Multinodular Goitre	Total Thyroidectomy	F479 /13	Nodular Colloid Goitre	1005/13	Nodular Colloid Goitre					
121	Rani	55 /F	Multinodular Goitre	Total Thyroidectomy	F369 /13	Nodular Colloid Goitre	1119/13	Nodular colloid goitre					
122	Nathiya	25 /F	Multinodular Goitre	Total Thyroidectomy	F511 /13	Follicular Neoplasm	1128/13	Adenomatous Goitre	< 1 %	100 %	_	_	_
123	Devika	38 /F	Solitary thyroid Nodule	Hemithyroidectomy	f632 /13	Hyperplastic nodular Goitre	1135/13	Nodular Colloid Goitre					
124	Saraswathi	30 /F	Solitary thyroid Nodule	Hemithyroidectomy	F530 /13	Follicular Neoplasm	1137/13	Adenomatous Goitre					
125	Pushpa	84 /F	Papillary Carcinoma Thyroid	Total Thyroidectomy	F519 /13	Papillary Carcinoma Thyroid	1160/13	Papillary Carcinoma Thyroid	15 %	5 %	45 %	20 %	30 %
126	Anitha	38 /F	Solitary thyroid Nodule	Hemithyroidectomy	F597 /13	Nodular Colloid Goitre	1165/13	Nodular colloid goitre					
127	Usha	44 /F	Solitary thyroid Nodule	Hemithyroidectomy	F659 /13	Nodular Colloid Goitre	1243/13	Nodular colloid goitre					
128	Kalaiselvi	41 /F	Multinodular Goitre	Total Thyroidectomy	F743 /13	Hashimoto Thyroiditis	1249/13	Hashimoto Tyroiditis					
129	Mohana	33 /F	Multinodular Goitre	Total Thyroidectomy	F578 /13	Nodular Colloid Goitre	1258/13	Follicular Adenoma	5 %	50 %	40 %	5 %	5 %
130	Ellizebeth	51 /F	Multinodular Goitre	Total Thyroidectomy	-	-	1369/13	Nodular colloid goitre					
131	Jothi	35 /F	Multinodular Goitre	Total Thyroidectomy	F610 /13	Hashimoto Thyroiditis	1408/13	Hashimoto Tyroiditis					
132	Devi	23 /F	Solitary thyroid Nodule	Total Thyroidectomy	f630 /13	Follicular Neoplasm	1439/13	Adenomatous Goitre	1 %	40 %	10 %	10 %	40 %
133	Sudha	32 /F	Familial thyroid Disease	Total Thyroidectomy	F678 /13	Hyperplastic nodular Goitre	1557/13	Nodular colloid goitre					

134	Ansarbee	28/F	Multinodular Goitre	Total Thyroidectomy	F654/13	Dominant nodule of Colloid Goitre	1565/13	Nodular colloid goitre					
135	Revathy	26/F	Papillary Carcinoma Thyroid	Total Thyroidectomy	-	-	1576/13	Papillary Carcinoma Thyroid	15%	55%	20%	15%	10%
136	Uma	21/F	Multinodular Goitre	Total Thyroidectomy	F963/13	Nodular Colloid Goitre	1620/13	Nodular colloid goitre					
137	Devaki	52/F	Multinodular Goitre	Total Thyroidectomy	F119/13	Dominant nodule of Colloid Goitre	1689/13	Nodular colloid goitre					
138	Malarkodi	36/F	Multinodular Goitre	Total Thyroidectomy	F1021/13	Nodular Colloid Goitre	1695/13	Papillary Carcinoma Thyroid	5%	55%	20%	20%	5%
139	Prema	47/F	Solitary thyroid Nodule	Hemithyroidectomy	F443/13	Nodular Colloid Goitre	1710/13	Follicular Adenoma	10%	40%	10%	20%	30%
140	Manjula	38/F	Multinodular Goitre	Total Thyroidectomy	F171/13	Nodular Colloid Goitre	1734/13	Nodular colloid goitre					
141	Natarajan	70/M	Solitary thyroid Nodule	Total Thyroidectomy	F1097/13	Nodular Colloid Goitre	1808/13	Nodular colloid goitre					
142	Andal	40/F	Multinodular Goitre	Total Thyroidectomy	F1096/13	Nodular Colloid Goitre	1840/13	Nodular colloid goitre					
143	Devaki	42/F	Recurrant Multinodular Goitre	Total Thyroidectomy	F564/13	Hyperplastic nodular Goitre	1186/13	Multinodular goitre with Encapsulated Papillary Carcinoma	10%	10%	40%	20%	30%
144	Papammal	52/F	Multinodular Goitre	Total Thyroidectomy	F1419/13	Nodular Colloid Goitre	2359/13	Nodular colloid goitre					
145	Jayanthi	53/F	Multinodular Goitre	Total Thyroidectomy	F1464/13	Nodular Colloid Goitre	2491/13	Nodular colloid goitre					
146	Shanthakumari	37/F	Multinodular Goitre	Total Thyroidectomy	F1743/13	Nodular Colloid Goitre	2705/13	Nodular colloid goitre					
147	Lakshmi	33/F	Solitary thyroid Nodule	Hemithyroidectomy	F1580/13	Nodular Colloid Goitre	2750/13	Follicular Adenoma	2%	20%	30%	40%	10%
148	Shantha	43/F	Multinodular Goitre	Total Thyroidectomy	F1744/13	Nodular Colloid Goitre	2751/13	Papillary Carcinoma Thyroid	10%	10%	30%	30%	30%
149	Nirmala	31/F	Multinodular Goitre	Total Thyroidectomy	F1621/13	Nodular Colloid Goitre	2840/13	Nodular colloid goitre					
150	Eswari	41/F	Multinodular Goitre	Total Thyroidectomy	F1671/13	Nodular Colloid Goitre	2842/13	Nodular colloid goitre					
151	Maheshwari	52/F	Solitary thyroid Nodule	Total Thyroidectomy	F1784/13	Nodular Colloid Goitre	2860/13	Nodular colloid goitre					
152	Azhagimeena	57/F	Solitary thyroid	Hemithyroidectomy	F1837/13	Follicular Neoplasm	2882/13	Follicular Adenoma					

			Nodule										
153	lilly	31 /F	Multinodular Goitre	Total Thyroidectomy	F1842/13	Follicular Neoplasm	2943/13	Nodular colloid goitre					
154	vatchala	48 /F	Multinodular Goitre	Total Thyroidectomy	-	-	2953/13	Nodular colloid goitre					
155	Malliga	50 /F	Thyroglossal Cyst	Sistrunk Operation	-	-	2990/13	Thyroglossal Cyst					
156	Kala	38 /F	Multinodular Goitre	Total Thyroidectomy	F1870/13	Nodular Colloid Goitre	2999/13	Nodular colloid goitre					
157	Velangani	46 /F	Multinodular Goitre	Total Thyroidectomy	F1727/13	Nodular Colloid Goitre	66/14	Nodular colloid goitre					
158	Chandra kumar	53 /M	Colloid Goitre	Hemithyroidectomy	-	-	235/14	Nodular colloid goitre					
159	Doloros a	37 /F	Solitary thyroid Nodule	Hemithyroidectomy	-	-	265/14	Colloid Goitre with Papillary Microcarcinoma	10 %	10 %	10 %	20 %	60 %
160	Priya	30 /F	Solitary thyroid Nodule	Total Thyroidectomy	F1820/13	Nodular Colloid Goitre	377/14	Papillary Carcinoma Thyroid	10 %	20 %	10 %	40 %	30 %
161	valarmathi	45 /F	Multinodular Goitre	Total Thyroidectomy	f155 /14	Cystic Nodular Goitre	395/14	Nodular colloid goitre					
162	Datchayani	39 /F	Solitary thyroid Nodule	Hemithyroidectomy	F118 /14	Cystic Nodular Goitre	433/14	Papillary Carcinoma Thyroid	5 %	10 %	40 %	30 %	20 %
163	Selvi	22 /F	Solitary thyroid Nodule	Hemithyroidectomy	F1950/13	Follicular Neoplasm	455/14	Adenomatous Goitre					
164	Devi	23 /F	Solitary thyroid Nodule	Hemithyroidectomy	F294 /14	Nodular Colloid Goitre	490/14	Nodular colloid goitre					
165	Krishnaveni	42 /F	Multinodular Goitre	Total Thyroidectomy	F30/ 14	Hashimoto Thyroiditis	516/14	Hashimoto Tyroiditis	25	80 %	20 %	_	_
166	Lakshmi	55 /F	Solitary thyroid Nodule	Hemithyroidectomy	F45/ 14	Colloid Nodule	551/14	Nodular colloid goitre	2 %	65 %	20 %	10 %	5 %
167	Devi	26 /F	Multinodular Goitre	Total Thyroidectomy	F359 /14	Nodular Colloid Goitre	590/14	Nodular colloid goitre					
168	Shanthi	28 /F	Multinodular Goitre	Total Thyroidectomy	F203 /14	Cystic Nodular Goitre	603/14	Nodular Colloid Goitre					
169	Navamani	32 /F	Multinodular Goitre	Subtotal Thyroidectomy	F312 /14	Nodular Colloid Goitre	680/14	Follicular Adenoma	10 %	20 %	20 %	20 %	40 %
170	Rani	50 /F	Multinodular Goitre	Total Thyroidectomy	F478 /14	Nodular Colloid Goitre	686/14	Nodular colloid goitre					
171	Devi	33 /F	Multinodular Goitre	Total Thyroidectomy	F472 /14	Nodular Colloid Goitre	687/14	Nodular colloid goitre					

172	Priya	30 /F	Completion Thyoidecto my	Total Thyroidectom y	F470 /14	Nodular Colloid Goitre	724/1 4	Nodular colloid goitre					
173	Bakkiya m	38 /F	Solitary thyroid Nodule	Hemithyroide ctomy	F410 /14	Nodular Colloid Goitre	730/1 4	Nodular colloid goitre					
174	Bharathi	39 /F	Multinodul ar Goitre	Total Thyroidectom y	F431 /14	Nodular Colloid Goitre	734/1 4	Nodular colloid goitre	1 %	10 0 %	_	_	_
175	Alagara m	52 /F	Multinodul ar Goitre	Total Thyroidectom y	F506 /14	Hashimoto Thyroiditis	748/1 4	Hashimoto Tyroiditis	5 %	10 0 %	_	_	_
176	Vijaya	40 /F	Multinodul ar Goitre	Total Thyroidectom y	F427 /14	Nodular Colloid Goitre	798/1 4	Nodular colloid goitre					
177	Ruby	39 /F	Colloid Goitre	Total Thyroidectom y	F435 /14	Nodular Colloid Goitre	921/1 4	Nodular colloid goitre					
178	Raghupa thy	28 /M	Solitary thyroid Nodule	Hemithyroide ctomy	F616 /14	Nodular Colloid Goitre	946/1 4	Follicular Adenoma	5 %	60 %	2 0 %	1 0 %	1 0 %
179	Dhanala kshmi	25 /F	Solitary thyroid Nodule	Hemithyroide ctomy	F630 /14	Colloid Nodule	967/1 4	Nodular Colloid Goitre					
180	Inkersal	45 /M	Solitary thyroid Nodule	Total Thyroidectom y	F700 /14	Colloid Nodule	993/1 4	Nodular Colloid Goitre					
181	Vijaya	45 /F	Multinodul ar Goitre	Total Thyroidectom y	F557 /14	Colloid Nodule	1009/ 14	Hashimoto Tyroiditis					
182	Bhavani	37 /F	Solitary thyroid Nodule	Hemithyroide ctomy	F697 /14	Colloid Nodule	1044/ 14	Follicular Adenoma	2 %	80 %	1 0 %	1 0 %	0
183	Sushila	45 /F	Solitary thyroid Nodule	Hemithyroide ctomy	F627 /14	Nodular Colloid Goitre	1053/ 14	Follicular Adenoma	1 %	40 %	1 0 %	3 0 %	2 0 %
184	Selvi	36 /F	Solitary thyroid Nodule	Hemithyroide ctomy	F691 /14	Nodular Colloid Goitre	1072/ 14	Nodular Colloid Goitre					
185	Ramabai	49 /F	Multinodul ar Goitre	Total Thyroidectom y	F542 /14	Hashimoto Thyroiditis	1090/ 14	Hashimoto Tyroiditis					
186	Selvi	31 /F	Multinodul ar Goitre	Total Thyroidectom y	F780 /14	Hashimoto Thyroiditis	1126/ 14	Hashimoto Tyroiditis					
187	Vanitha	14 /F	Solitary thyroid Nodule	Hemithyroide ctomy	F714 /14	Colloid Nodule	1134/ 14	Nodular Colloid Goitre					
188	Gowri	38 /F	Solitary thyroid Nodule	Hemithyroide ctomy	F623 /14	Nodular Colloid Goitre	1156/ 14	Nodular Colloid Goitre					
189	Suguna	34 /F	Multinodul ar Goitre	Total Thyroidectom y	-	-	1190/ 14	Follicular Adenoma	2 %	90 %	5 %	5 %	_
190	Udhaya	36 /F	Solitary thyroid Nodule	Hemithyroide ctomy	F520 /14	Nodular Colloid Goitre	1221/ 14	Follicular Adenoma	2 %	50 %	2 5 %	2 0 %	5 %
191	Jansi	10	Multinodul	Total	F270	Follicular	1239/	Papillary	15	10	2	2	5

		/F	ar Goitre	Thyroidectomy	1/14	Neoplasm	14	Carcinoma Thyroid	%	%	0 %	0 %	0 %
192	pandidurai	12 /M	Multinodular Goitre	Hemithyroidectomy	F655 /14	Colloid Nodule	1262/ 14	Follicular Adenoma	2 %	60 %	20 %	10 %	10 %
193	Lakshmi	30 /F	Solitary thyroid Nodule	Hemithyroidectomy	F186 5/13	Colloid Nodule	1276/ 14	Follicular Adenoma	1 %	80 %	10 %	10 %	_
194	Alamelu	25 /F	Solitary thyroid Nodule	Hemithyroidectomy	F915 /14	Nodular Colloid Goitre	1310/ 14	Nodular Colloid Goitre					
195	Rajeswari	37 /F	Multinodular Goitre	Subtotal Thyroidectomy	F809 /14	Colloid Nodule	1380/ 14	Nodular Colloid Goitre					
196	Sadaiyammal	48 /F	Multinodular Goitre	Subtotal Thyroidectomy	-	-	1392/ 14	Nodular Colloid Goitre					
197	Selvambal	42 /F	Multinodular Goitre	Total Thyroidectomy	F983 /14	Colloid Nodule	1419/ 14	Follicular Adenoma	2 %	70 %	10 %	10 %	10 %
198	Jayaseela	23 /F	Solitary thyroid Nodule	Hemithyroidectomy	F901 /14	Nodular Colloid Goitre	1455/ 14	Nodular Colloid Goitre					
199	Kasif	25 /m	Multinodular Goitre	Hemithyroidectomy	F102 8/14	Benign Cystic Lesion	1542/ 14	Papillary Carcinoma Thyroid	10 %	10 %	40 %	30 %	20 %
200	Beula	16 /F	Solitary thyroid Nodule	Hemithyroidectomy	_	_	1567/ 14	Nodular Goitre					