CYTOKERATIN 19 AND GALECTIN – 3 IMMUNOHISTOCHEMISTRY IN THE DIFFERENTIAL DIAGNOSIS OF SOLITARY THYROID NODULES

Dissertation submitted in

partial fulfilment of the requirements for the degree of

M.D. (PATHOLOGY)

BRANCH - III

GOSCHEN INSTITUTE OF PATHOLOGY AND ELECTRON MICROSCOPY

MADRAS MEDICAL COLLEGE

CHENNAI – 600 003

THE TAMIL NADU

DR. M.G.R. MEDICAL UNIVERSITY

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APRIL 2017

CERTIFICATE

This is to certify that this Dissertation entitled **"CYTOKERATIN 19 AND GALECTIN – 3 IMMUNOHISTOCHEMISTRY IN THE DIFFERENTIAL DIAGNOSIS OF SOLITARY THYROID NODULES"** is the bonafide original work of **Dr.RAMESH BABU.C**, in partial fulfillment of the requirement for M.D., (Branch III) in Pathology examination of the Tamilnadu Dr.M.G.R Medical University to be held in April 2017.

Director and Guide

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DECLARATION

I, **Dr.RAMESH BABU.C,** solemnly declare that the dissertation titled"**CYTOKERATIN 19 AND GALECTIN – 3 IMMUNOHISTOCHEMISTRY IN THE DIFFERENTIAL DIAGNOSIS OF SOLITARY THYROID NODULES**" is the bonafide work done by me at Institute of Pathology, Madras Medical College under the expert guidance and supervision of **Prof.Dr.R,PADMAVATHI,** Director (I/C) and Professor of Pathology, Institute of pathology, Madras Medical College. The dissertation is submitted to the Tamilnadu Dr.M.G.R Medical University towards partial fulfillment of requirement for the award of M.D., Degree (Branch III) in Pathology.

Place: Chennai

Date: **Dr. C.RAMESH BABU**

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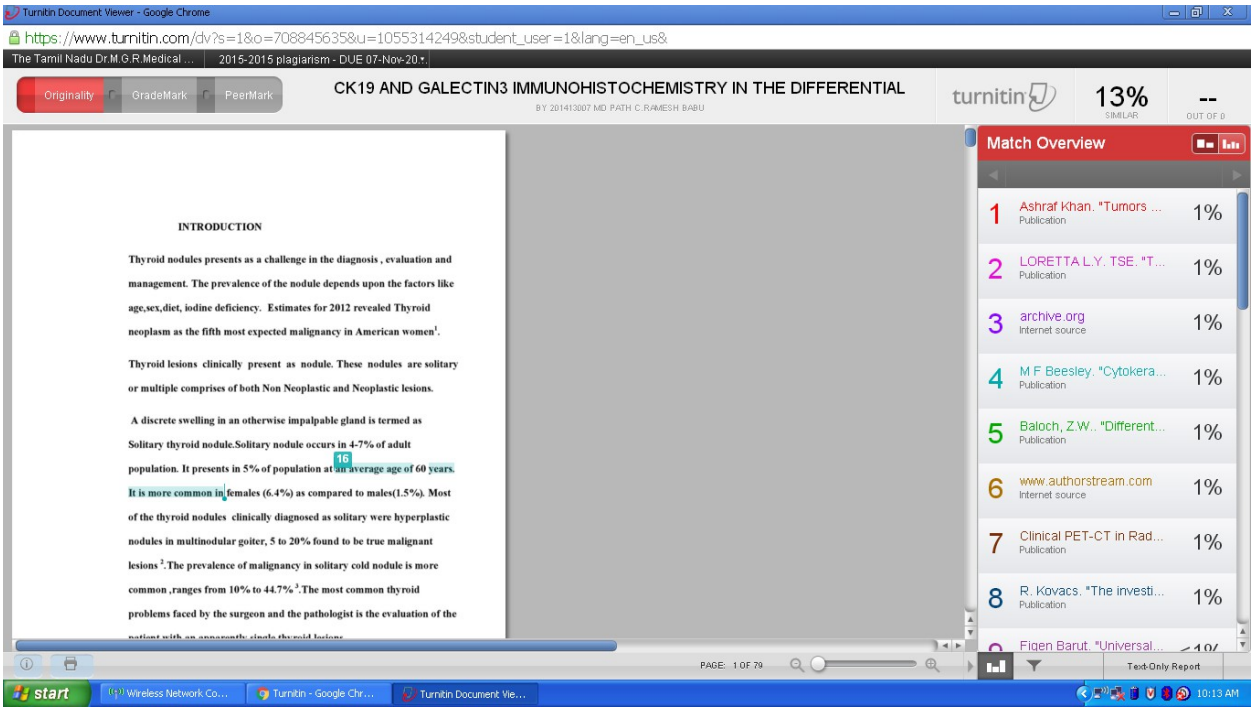
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INTRODUCTION
Thyroid nodules presents as a challenge in the diagnosis , evaluation and management. The prevalence of the nodule depends upon the factors like age,sex,diet, iodine deficiency. Estimates for 2012 revealed Thyroid neoplasm as the fifth most expected malignancy in American women[1].
Thyroid lesions clinically present as nodule. These nodules are solitary or multiple comprises of both Non Neoplastic and Neoplastic lesions.
A discrete swelling in an otherwise impalpable gland is termed as Solitary thyroid nodule.Solitary nodule occurs in 4-7% of adult population. It presents in 5% of population at an average age of 60 years. It is more common in females (6.4%) as compared to males(1.5%). Most of the thyroid nodules clinically diagnosed as solitary were hyperplastic nodules in multinodular goiter, 5 to 20% found to be true malignant lesions [2].The prevalence of malignancy in solitary cold nodule is more common ,ranges from 10% to 44.7% [3].The most common thyroid problems faced by the surgeon and the pathologist is the evaluation of the
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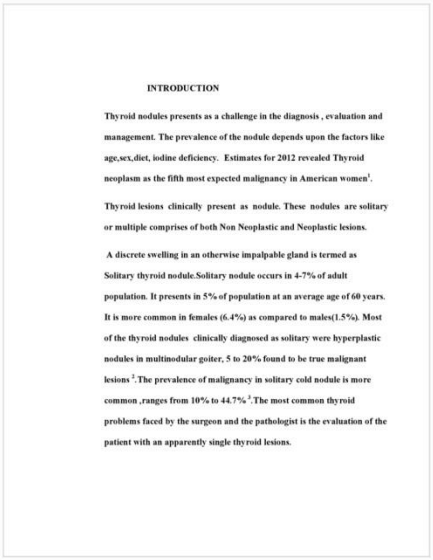

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CERTIFICATE OF APPROVAL

To
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Dear Dr.C.Ramesh babu,

The Institutional Ethics Committee has considered your request and approved your study titled " **CYTOKERATIN 19 AND GALECTIN – 3 IMMUNOHISTOCHEMISTRY IN THE DIFFERENTIAL DIAGNOSIS OF SOLITARY THYROID NODULES " - NO.23012016.**

The following members of Ethics Committee were present in the meeting hold on **05.01.2016** conducted at Madras Medical College, Chennai 3

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10.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
11.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

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ABBREVIATIONS

SNT	-	Solitary Nodule Thyroid
FNA	-	Fine Needle Aspiration
CK	-	CytoKeratin
HTA	-	Hyalinizing Trabecular Adenoma
PTC	-	Papillary Thyroid Carcinoma
IHC	-	ImmunoHistoChemistry
PDC	-	Poorly Differentiated Carcinoma
HBME-1	-	Hector BattiforaMEsothelial cell-1
CITED-1	-	Cbp/p300-Interacting Transactivator-1
FC	-	Follicular Carcinoma
FVPTC	-	Follicular Variant of Papillary Thyroid Carcinoma
PPV	-	Positive Predictive Value
NPV	-	Negative Predictive Value

CONTENTS

INTRODUCTION

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The incidence of malignancy was higher in men and young age or middle aged adults[4].The incidence of thyroid malignancy in SNT varies from 4.7%-18.3% [5].

Solitary nodule thyroid are common in 3rd and 5th decades, the youngest patient being 15 years old and older age being 65 years. SNT is found more common in right lobe(74%) than left lobe(26%)[6].

The first investigation of choice to differentiate benign and malignant is fine needle aspiration.Fine needle aspiration technique helps to prevent unwanted surgeries and therapeutic protocol.

Thyroid tumors are the most common endocrine neoplasms, originate mainly from follicular epithelial cells. The most common malignant neoplasm of thyroid is papillary carcinoma. The gold standard method of diagnosing thyroid nodules is histopathology. FNA lacks in differentiating follicular neoplasms. Diagnostic difficulties still persist in differentiating papillary hyperplasia vs encapsulated papillary carcinoma, follicular carcinoma vs follicular variant of papillary thyroid carcinoma, minimally invasive follicular carcinoma vs follicular adenoma.

IHC markers may aid in accurate diagnosis of thyroid neoplasms. My study aimed to evaluate the expression of CK 19 and Galectin3 in the differential diagnosis of solitary lesions of thyroid.

Ck19 is an intermediate filament protein belongs to the keratin family, responsible for the structural integrity of epithelial cells. Cytokeratin contains acidic proteins which are arranged in pairs of heterotypic keratin chains. It is a 40kDa protein, encoded by KRT 19 gene in humans. It has been used successfully in thyroid tumors to

recognize papillary thyroid carcinoma. It has a diagnostic utility in the differentiation of papillary carcinoma from its benign mimics.

Galectin 3 is a 30 kDa protein, encoded by LGAL S3 gene in humans,carbohydrate recognition-binding domain. Galectin 3 is a beta – galactosidase binding peptide on the cell surface glycoproteins and has been identified in nuclear and cytoplasmic compartment. Galectin 3 has been implicated in the regulation of normal cellular proliferation , apoptosis and promote angiogenesis. It helps in the differential diagnosis of solitary encapsulated follicular lesions, especially minimally invasive follicular carcinoma.

AIM AND OBJECTIVE

- To study the incidence of solitary thyroid nodule among surgical specimens at Madras Medical College and Rajiv Gandhi government general hospital,Chennai.
- Histomorphological study of solitary nodule of thyroid.
- To study the expression of immunohistochemical markers-CK 19 and Galectin3 in solitary nodular lesions of thyroid.
- Assess the value of IHC markers in differential diagnosis of solitary thyroid nodules.

REVIEW OF LITERATURE

ANATOMY OF THYROID GLAND

Thyroid is an endocrine gland which is placed anteriorly in the lower neck at the level of fifth cervical to the first thoracic vertebrae. It is highly vascular.

The thyroid gland composed of two lobes, connected by the median isthumus .It is ensheathed by the pretracheal layer of deep cervical fascia. It weighs about 25 gms.

Parathyroid glands are small , yellowish and ovoid structures .It is 4 in number, usually lying between the posterior border of thyroid and its capsule.

Liechy et al[7] study shown that right lobe is more commonly involved in cases of SNT.

HISTOLOGY OF THYROID GLAND

Thyroid gland is enveloped by a thin capsule of connective tissue, which extends into the glandular parenchyma and divides each lobe into irregularly shaped and sized lobules. The functional unit of the thyroid gland are follicles ,which are spheriodal structure contains a central homogeneous colloid core surrounded by a single layer of cuboidal epithelium bounded by a basement membrane. The cytoplasm is pale acidophilic or amphophilic staining quality. Colloid consists of an iodinated glycoprotein , iodothyroglobulin (stored form) , triiodothyronine (T3) and tetraiodothyronine or thyronine(T4).

FOLLICULAR CELLS

It vary from squamous to columnar epithelium ,depends on their level of activity ,which is controlled by circulating hypophysial thyroid –stimulating hormone(TSH). Resting follicles are large with abundant luminal follicle. Follicular cells with abundant granular acidophilic cytoplasm are referred to as Hurthle cells, Askanazy cells, Oxyphilic cells, Oncocytes.

PARAFOLLICULAR CELLS

The second type of endocrine cells with ultrastructural characteristic of neuroendocrine cells. They are the individual scattered cells in the follicle lining, or as clumps in the interstices between follicles. These cells secrete calcitonin, which is a physiological antagonist to parathormone . It lowers the blood calcium level by suppressing the osteoclastic resorption of bone.

ULTRASTRUCTURE

The ultrastructural features of follicular cells have

- Abundant granular endoplasmic reticulum
- A well formed golgi apparatus
- Lysosomes
- Numerous microvilli [8]

EVALUATION OF THE SOLITARY THYROID NODULE

Number: Solitary nodules are more likely to be malignant than the multiple ones. It should be kept in mind that approximately one third of the nodule thought to be solitary on palpation are shown to be multiple on scan.

Rate of growth: Most adenomas are very slow growing, but this is also true for most papillary or minimally invasive follicular carcinoma.

Rapid enlargement of the long standing nodule may signify an undifferentiated transformation or may be the development of hemorrhage within the nodule.

If the nodule is associated with ipsilateral lymphadenopathy, there is a strong clinical indicator of malignancy.

Nodules that are hyperfunctioning at the clinical level are less likely to be malignant.

Cystic nodules are less likely to be malignant than solid ones. These nodules are usually hypofunctioning[9].

The role of CT and MRI is relatively limited to thyroid lesions.MRI is said to be superior to CT for the evaluation of metastatic, retrotracheal, mediastinal lesions [10].

Needle biopsy provides the best means of determining the likelihood of malignancy of a thyroid nodule short of surgical excision and pathological examination[11].

NON NEOPLASTIC LESIONS OF THYROID

NODULAR GOITER

It is the most common form of thyroid disease. Due to the deficiency of thyroid hormone production leads to increased TSH secretion causes the hyperactive thyroid. Clinically the patients are euthyroid .

Grossly the thyroid gland is enlarged, one lobe being larger the other. The capsule is intact but the shape is distorted. Secondary changes in the form of hemorrhage, calcification and cystic changes are common.

Microscopically the hyperplastic nodule lacks a capsule.The follicles are lined by flattened epithelium. Some dilated follicles have a conglomerate of small active follicles called Sanderson polster. Some may have papillary projections facing the lumen of a cystic follicle, a feature that may lead to confusion with papillary thyroid carcinoma[12].

Chetan VR et al [6] study showed there was a higher incidence of colloid goiter in SNT,found to be 43.8% among 73 cases.

Bose et al [13] study revealed that only 50% of nodular goiter shows focal positivity for CK 19.

El-kateb et al[14] study stated that galectin 3 was negative in all the cases of nodular goiter.

NEOPLASTIC LESIONS OF THYROID

BENIGN NEOPLASM

FOLLICULAR ADENOMA

Follicular adenoma is the most common benign thyroid neoplasm. It occurs in 20 to 50 years of age, female preponderance with a ratio of 1:6. It is a benign encapsulated tumor with evidence of follicular cell differentiation, but lacks evidence of capsule, vascular invasion and nuclear features of papillary neoplasms. Clinically present as thyroid lump with increased thyroglobulin.

Grossly the lesion is solitary, encapsulated, variable in size range from 1-10cm. The cut surface appears solid, fleshy, tan to light brown.

Microscopy shows small to medium sized follicle with eosinophilic to amphophilic cytoplasm and uniform round nuclei. Mitosis are rare ,secondary degenerative changes are common. Focal thickening of the vessel wall in the capsule of the adenoma is referred as muscle cushion.

Some authors referred these tumors as papillary adenomas, exhibit papillary or pseudopapillary structures.

PATTERNS

1. Normofollicular pattern(Simple)
2. Macrofollicular pattern(Colloid)
3. Microfollicular pattern (Fetal)
4. Trabecular/Solid pattern (Embryonal)

VARIANTS

1. Follicular adenoma of oxyphilic cell type
2. Signet ring cell adenoma variant
3. Papillary variant of follicular adenoma
4. Lipoadenoma
5. Adenochondroma
6. Mucinous follicular adenoma
7. Clear cell follicular adenoma
8. Atypical adenoma
9. Hyperfunctionoing(toxic) adenoma
10. Follicular adenoma with bizarre nuclei

Elder S et al [15]study showed that the histomorphometrically gauged nuclear parameters of the tumor cells such as nuclear area, nuclear irregularity and diameter of the follicle may help in differentiation. These parameters helps in differentiating the benign and malignant categories.

Kishore et al[16] study evaluated the capsular collagen by picrosirius orange red staining technique (PSR) and found difference in

characteristics of the capsular collagen in follicular adenoma and follicular carcinoma which may help in differential diagnosis.

UzmaBukhari et al [69]study found that CK 19 was found negative in all cases of follicular adenoma.

HYALINIZING TRABECULAR TUMOR

It is the rare tumor of follicular origin with trabecular pattern of growth with intratrabecular hyalinization.

Carney et al[17] study on 11 encapsulated tumor shows polygonal and fusiform cells which are arranged in trabeculae separated by thin capillary network and hyalinized amyloid like stroma. The cells were negative for calcitonin staining.

Fonseca et al[18]have done a study in cytokeratin expression between papillary carcinoma and HTA.They found CK 19 was positive in both the tumors.

Hirokawa et al[19] showed that CK19 was positive in papillary carcinoma , but negative in HTA.

MALIGNANT NEOPLASM

Thyroid neoplasm is fairly common. According to GLOBOCAN 2008, the age-standardized annual incidence is 1 to 2.9 cases/100000 men and 3.4 to 9.1 per 1lakh women. The incidence was steadily increasing

,predominantly attributing to an increase in papillary thyroid carcinoma. 10 year survival rate in Papillary thyroid carcinoma is 98%,

Follicular carcinoma-92%

Medullary carcinoma-80%

Undifferentiated carcinoma-13%

FOLLICULAR CARCINOMA

Follicular carcinoma constitute about 10-20% of all thyroid neoplasm. More common in women (3:1) of older age group (40-60 years). Follicular carcinoma is more common in areas of iodine deficiency.Clinically presents as slowly enlarging painless nodules.

Grossly the tumor may be well circumscribed or widely infiltrative. Larger lesion can penetrate the capsule .On cut section they were gray to tan to pink in colour. Degenerative changes such as fibrosis and calcification may be seen.

The neoplasm is composed of closely packed follicles arranged in trabecular or solid sheets. The follicles are lined by cuboidal to low columnar epithelium, dark staining or pale staining round nuclei with inconspicuous nucleoli. Capsular and vascular invasion are characteristics, so distant metastasis is more common in bone, lung and liver. Regional lymph node involvement are very rare.

1. MINIMALLY INVASIVE CARCINOMA

It is a grossly encapsulated tumor. On cut surface shows solid and fleshy.The growth pattern resembles that of an adenoma. The diagnosis entirely depend on the vascular and capsule invasion[20]. The blood vessel should be of venous caliber, located inside or outside the capsule contains one or more tumor cells attached to the wall and protruding into the lumen.

Chernobyl group of thyroid pathologist [21]recommended the certain terminology

1. Follicular carcinoma- definite capsular invasion and no PTC-type nuclear changes.
2. Follicular tumor of uncertain malignant potential- questionable capsule invasion and absent PTC nuclear features.
3. Well differentiated tumor of uncertain malignant potential- questionable capsular invasion and nuclear features.

Thomson et al [22] study in a series of 95 minimally invasive follicular carcinoma, showed both capsular and vascular invasion with excellent survival rate.

IHC for actin and CD31 is more likely to be positive.

2. WIDELY INVASIVE FOLLICULAR CARCINOMA

It is the high risk counterpart of minimally invasive follicular carcinoma. Grossly the tumor shows invasion and necrosis. The tumor cells are arranged in solid or trabecular pattern with invasion into the surrounding thyroid parenchyma. High mitotic activity and areas of necrosis were seen.

The prognosis of this neoplasm is much worse than minimally invasive follicular carcinoma with a survival rate of 25-45% [23].

VARIANTS

1.Follicularcarcinoma,oncocytic variant

2.Clear cell variant

PAPILLARY CARCINOMA

Papillary carcinoma is a malignant neoplasm showing evidence of follicular cell differentiation, characterized by distinct nuclear features.It is the most commonest malignant neoplasm accounts for 75-85%.of all thyroid tumors. It occurs in any age group, with female preponderance.

Negri et al[24] study showed that PTC was 4 times more common in females than in males.

It is an indolent neoplasm, with an excellent long term prognosis, mortality rate-6.5%[5].

It invades locally and metastasize to regional lymph node. Local recurrence is common. Distant metastasis is uncommon,9-14%. Relapse may be delayed to 20-30 years after initial diagnosis.

Grossly the tumor appears solid with irregular and illdefined borders. Hard in consistenency. Cut surface shows white to tan with granular texture which is due to the presence of papillae.The tumor may gritty to cut due to calcification and psammoma bodies. Some tumors are circumscribed or encapsulated.

CYTOLOGICAL FEATURES

The neoplasm composed of cells which are polygonal to cuboidal, but can be attenuated, dome shaped, hob nailed or columnar.The nucleus are large, crowded, ovoid “orphan Annie eye”, grooved with small distinct nucleoli and eosinophilic to amphophilic cytoplasm.

Ground glass change is the empty looking nuclei with scanty marginated dusty chromatin.

Nuclear groove is formed by the deep folding of nuclear membrane.

ARCHITECTURAL FEATURES

It is an infiltrative tumour, may be circumscribed , encapsulated. Papillae are arborizing with delicate fibrovascular core. Papillae can be broad with cores being formed by fibrocellular,odematous or hyalinised

tissue contains foamy macrophages ,adipose cells and small neoplastic follicles. Follicles are vary in size and contour. Stroma shows calcification, dense hyaline fibrosis and sclerotic. Luminal space of follicle and papillae contains multinucleated histiocyte with dark staining nucleus. Psammoma bodies are seen. Intrafollicular hemorrhage is common, resembles tubulopapillary pattern.

Other patterns were microglandular, cribriform, garland, anastomosing tubular, trabecular and solid.

The diagnosis of PTC is based on nuclear features such as nuclear clearing , overlapping, grooves and pseudo inclusions[23].

VARIANTS

1. Tall cell
2. Diffuse sclerosing
3. Columnar cell
4. Diffuse follicular
5. Solid
6. Trabecular
7. Hobnail
8. Micropapillary
9. Dedifferentiated

FOLLICULAR VARIANT

Follicular variant of Papillary carcinoma which is entirely composed of follicles. It grows in an infiltrative growth pattern or encapsulated(Lindsay tumor).Follicle are varying in size and shape, but elongated or irregular shaped with abortive papillary formation. Colloid is usually deep stained and scalloped. Typical nuclear features of papillary carcinoma are usually present. Psammoma bodies and sclerosis may be present.

In a study by Liu J et al[26]found that FVPTC with an infiltrative and non capsulated pattern showed significantly higher rate of regional lymph node metastasis(65% vs 5%), intramural fibrosis(88% vs 18%), extrathyroidal extension (65% vs 5%) and positive margins(50% vs 2%) compared to encapsulated tumor.

Types 1. Infiltrative- infiltrate into the thyroid parenchyma. Absent papillae. Presence of sclerosis

2.Encapsualted– encapsulated solid tumor surrounded by fibrous capsule with infrequent intratumoral sclerosis

SOLID VARIANT

Tumor constitute about more than 50% of solid sheets or trabecular pattern , traversed by delicate capillaries with characteristic nuclear features of papillary carcinoma

ENCAPSULATED VARIANT

It constitute about 4 to 14% of all papillary carcinoma of thyroid. It is common in younger age group. Tumor may or may not invade into the fibrous capsule, but lymph node metastasis can occur in 26%.

DIFFUSE FOLLICULAR VARIANT

It is a rare variant with aggressive nature. It commonly occurs in younger individual with a median age group of 21 years. Clinically present as diffuse enlargement of thyroid. On microscopy shows exclusively, predominantly follicular pattern of tumor cells without fibrosis along with the nuclear features of papillary carcinoma. It has a favourable outcome.

DIFFUSE SCLEROSING VARIANT

It occurs commonly in children and young adults.The features are

1. Diffuse involvement of one lobe or both lobes.
2. Sclerosis
3. Heavy lymphoplasmacytic infiltration
4. Abundant psammoma bodies.
5. Scattered small islands of papillary carcinoma with predominant squamous differentiation.

Diagnostic dilemma may arise when an encapsulated nodule with a follicular pattern of growth with grooves or dark staining colloid and

distinguishing follicular adenoma from encapsulated FVPTC becomes more difficult [27].

TALL CELL VARIANT

It commonly affects in older age(50-57 years). Tumour composed predominantly of cells whose heightareatleast 3 times with width.Higher frequency of BRAF mutation(80%). It is an aggressive tumour. Recurrence is common.

COLUMNAR CELL VARIANT

It is a rare and more aggressive tumor, M:F of 13:7. Tumor cells are arranged in papillary,complex glandular, cribriform,solid pattern. The papillae and glands are lined by tall columnar cells with pseudostratified hyperchromatic, oval or elongated nuclei. Subnuclear vacuolation and cytoplasmic clearing are also seen.

OXYPHILIC/ONCOCYTIC/HURTHLE CELL VARIANT

Tumor composed predominantly of cells with eosinophilic granular cytoplasm, partial or total cytoplasmic clearing.

WARTHIN LIKE VARIANT

The neoplastic cells are arranged in papillary pattern with broad papillae. Tumor cells have oxyphilic appearance.Lymphoplasmacytic infiltration is seen in the cores of papillae.

CLEAR CELL VARIANT

It is a rare variant. The tumor cells are oxyphilic with extensive cytoplasmic clearing. Clear cell changes were found in the apical portion of the cells.

TRABECULAR VARIANT

Tumor has more than 50% of trabecular growth pattern.The cells are columnar or cuboidal.

MACROFOLLICULAR VARIANT

Tumor contains larger follicles constitute more than 50% along with the nuclear features of papillary thyroid carcinoma.

CRIBRIFORM-MORULAR VARIANT

It is an uncommon variant.The tumor cells are arranged in cribriform pattern with interspersed squamoid islands, nuclei filled with light eosinophilic homogenous biotin.

PAPILLARY CARCINOMA WITH LIPOMATOUS STROMA

Adipose cells are interspersed within papillary thyroid carcinoma

VARIANTS WITH EXUBERANT NODULAR FASCIITIS –LIKE STROMA

It is a rare variant. Features of papillary thyroid carcinoma with adundant nodular fasciitis. The stroma shows spindle cells lying in vascularized fibromyxoid matrix with extravasated red cells.

VARIANTS WITH SPINDLE CELL METAPLASIA

The tumor contains bland looking spindle cell forms a short fascicles merges into the papillary carcinoma component.

HOBNAIL VARIANT

It is a rare,aggressive tumor. Tumor is multifocal with variable sized papillae covered by cells with apically placed nuclei that produce a surface bulge.

MICROPAPILLARY VARIANT

It is an uncommon variant with poor prognosis.Tumor constitute more than 5% of micropapillary pattern. It is characterized by group of neoplastic cells without fibrovascular cores lying in lacunar spaces.

ADENOID CYSTIC VARIANT

Abundant deposit of globular hyaline with reminiscent of the architectural features of adenoid cystic carcinoma.

DEDIFFERENTIATED CARCINOMA

Coexistence of papillary carcinoma with undifferentiated or poorly differentiated carcinoma. Features of papillary carcinoma and plump spindle cells with pleomorphic nuclei.

MICROCARCINOMA

Incidentally discovered papillary carcinoma with size less than 1 cm. It has excellent prognosis.

IHC: positive staining for pan CK,TTF1, Thyroglobulin, PAX-8

POORLY DIFFERENTIATED CARCINOMA

The group of tumors that shows morphology and behavior features intermediate between the well differentiated and undifferentiated carcinoma. It occurs in the older age group.

Grossly invasion can be made out. Cut surface shows solid and gray white areas with pushing border and areas of necrosis seen.

Microscopically the tumors cells are arranged in insular pattern, solid to microfollicular arrangement. The neoplastic cells have round to medium sized nuclei with a smooth contour and hyperchromasia with increased mitosis. Fresh tumor necrosis resulting in a peritheliomatous pattern.

Hiltzik et al[28] defined poorly differentiated carcinoma on the basis of mitosis(5 or more per 10HPF) and necrosis.

Turin[29] proposed a criteriafor poorly differentiated carcinoma.

1.Presence of solid/trabecular/insular growth pattern

2. Absence of nuclear features of PTC

3.Presence of atleast one of the following

A.convoluted nuclei

B.Mitotic activity 3 or more per 10 HPF

C.Tumor necrosis

PDC has an intermediate prognosis between well differentiated and undifferentiated thyroid neoplasm(siironen et al 2010)

ANAPLASTIC CARCINOMA

Anaplastic carcinoma is a rare, aggressive tumor accounts for 1.7% of all thyroid malignancies. Elderly age group are commonly affected. Clinically presents as a rapidly growing mass with hoarsness of voice, dysphagia and dysponea. Extrathyroidal extension is common at the initial diagnosis.

Grossly large portion of the thyroid is replaced by highly necrotic and hemorrhagic solid mass.

Microscopically there were 2 categories

1. Squamoid- The tumor does not have any papillae, trabecular or nesting pattern,with foci of keratinization [30].

2. Sarcomatoid pattern(spindle cell and gaint cell.)- The neoplastic cells were arranged in storiform or fasicular pattern with heavy neutrophilic infiltration, vascularization and divergent differentiation into bone, cartilage and skeletal muscle[31].

The most useful marker for confirming the epithelial nature of the tumor is keratin which should be expressed in 50-100% of the cases.

Thyroglobulin shows variable staining, ranging from 9-71%.

MEDULLARY CARCINOMA

Medullary carcinoma is the malignant tumor of thyroid with C cell differentiation.It constitute about 5-10% of all thyroid malignancies[23].Approximately 80% of medullary carcinoma were sporadic. Sporadic medullary carcinoma presents as a thyroid nodule. Bilaterality and multicentricity are common in familial cases.

Two forms of hereditary medullary carcinoma are sporadic and inherited. Sporadic form occurs in adult usually at the mean age of 45 years. It comprises about 80% of the cases and mostly solitary.

Grossly the tumor is solid, firm and non encapsulated but relatively well circumscribed. Cut surface shows gray to yellowish.

Microscopically the neoplasm composed of polygonal to spindle shaped cells arranged in nests, trabeculae and even follicles. The cells have granular amphophilic cytoplasm and medium sized nucleus, separated by highly vascularised stroma, hyalinised collagen and amyloid. Coarse calcification is common.

VARIANTS

1. Papillary/pseudopapillary variant
2. Follicular/glandular
3. Spindle cell
4. Gaint cell
5. Small cell
6. Paraganglioma like variant
7. Neuroblastoma like variant
8. Oncocytic variant
9. Clear cell variant
10. Angiosarcoma like variant
11. Squamous cell variant
12. Melanin producing variant
13. Carcinoid like variant

Immunohistochemically the tumor cells are reactive for epithelial markers such as keratin, TTF1, NSE, chromogranin, synaptophysin and calcitonin.

MEDULLARY MICROCARCINOMA

When the greatest diameter of the tumor is 1 cm or less, the tumor is described as Medullary Microcarcinoma.It constitutes about 0.15% of all thyroid malignancies.

MIXED MEDULLARY-FOLLICULAR CELL CARCINOMA

These tumors may represent another entity called collision tumor.

- Follicular carcinoma+ Medullary carcinoma
- Papillary carcinoma + Medullary carcinoma

Hales et al identified an unusual carcinoma showing predominant medullary carcinoma with areas of follicular differentiation[32].

IMMUNOHISTOCHEMISTRY

Immunohistochemistry is a technique for identifying cellular or tissue constitutents by means of antigen antibody interactions, the site of antibody binding being identified either by direct labeling of the antibody, or by use of a secondary labeling method.

CYTOKERATIN 19

CK 19 belongs to keratin family with 40kDa molecular protein. In human it is encoded by KRT 19 gene. The keratins are intermediate filament which is responsible for the structural integrity of epithelial cells. It is a type 1 cytokeratin consists of acidic proteins which are arranged in pairs of heterotypic keratin chain. They are clustered in a region of chromosome 17q12-21.

Cytokeratin 19 strong immunoreactivity in thyroid lesions favors the diagnosis of papillary thyroid carcinoma and may be useful in the identification of follicular variant of PTC. Conversely the negative

immunoreactivity for CK19 in areas of papillary hyperplasia in any lesion may help to avoid the misdiagnosis. It is best to use panel of other markers such as galectin-3, HBME1 and CITED1 to avoid misdiagnosis.

CK 19 immunoreactivity in follicular adenoma and follicular carcinoma is less intense. Normal thyroid follicular epithelium is often negative, although focal staining for CK19 is usually identified in compressed thyroid parenchyma surrounding nodule and in follicle cells within lymphocytic thyroiditis

CK19 expression was mainly found in the cell membrane and cytoplasm[41].

GALECTIN 3

Galectin 3 is a member of lectin family of 31 kDa molecular weight. It plays an important role in biological and pathological processes. It is a regulating component of cell cycle, cell-cell and cell matrix interaction, adhesion and migration[33]. Galectin 3 is expressed in various tissues and cell types in which it is localized in the nucleus and or cytoplasm[41].

Some authors in the prospective study proved that galectin 3 immunodetection of thyroid lesions concerning preoperative diagnostics had about 100% accuracy in differentiating benign and malignant lesions.

MATERIALS AND METHODS

This is a retrospective study includes 50 specimens, surgically removed solitary thyroid lesion. The clinical details, investigations, type of surgery were collected from the medical records of Institute of Pathology, Madras Medical College,Chennai between the period of June 2014-May 2016. Corresponding histopathological slides were made from formalin fixed, paraffin embedded tissue of resected thyroid specimens. H&E staining was done. Histological diagnosis of each was reviewed to confirm the diagnosis. The tumors were classified according to the WHO classification and grading of the thyroid tumors.(Annexure I and II) CK19 and Galectin 3 IHC markers were done .The step by step procedure of immunohistochemistry is given in Annexure III

ANTIGEN	**VENDOR**	**SPECIES**	**DILUTION**	**POSITIVE CONTROL**
CK19	Path in situ	Rabbit IgG	Ready to use	Colon
Galectin 3	Path in situ	Mouse IgG1	Ready to use	Papillary thyroid carcinoma

SCORING: CK19 AND GALECTIN 3

Depends on the Intensity of staining and percentage of positive cells.

0 - <10% Negative

>10- 25% Weak (1+)

26 – 50% Moderate (2+)

>50% Strong (3+)

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS program version 20.Comparison of qualitative variables was done using the Chi-square test. The sensitivity and the specificity for each marker and their combination in the diagnosis were calculated.

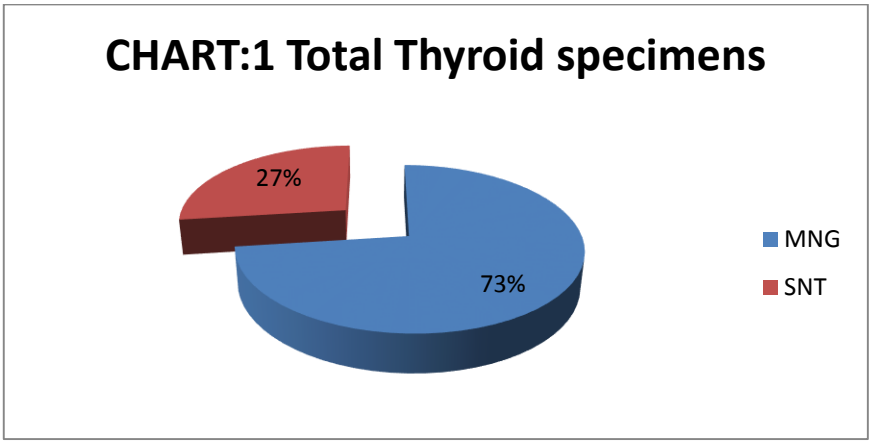
RESULTS

In our Institution(Institute of Pathology, Madras Medical College)643 surgically resected thyroid specimens were sent for histopathological examination during the study period from June 2014-May 2016. Among the 643 thyroid specimens,171 cases were clinically, radiologically diagnosed as solitary thyroid lesions.The incidence of solitary thyroid lesions was 13.29%

TABLE – 1

DISTRIBUTION OF TOTAL THYROID LESIONS

Total thyroid specimens	**643**	**100%**
MNG	472	73%
SNT	171	27%

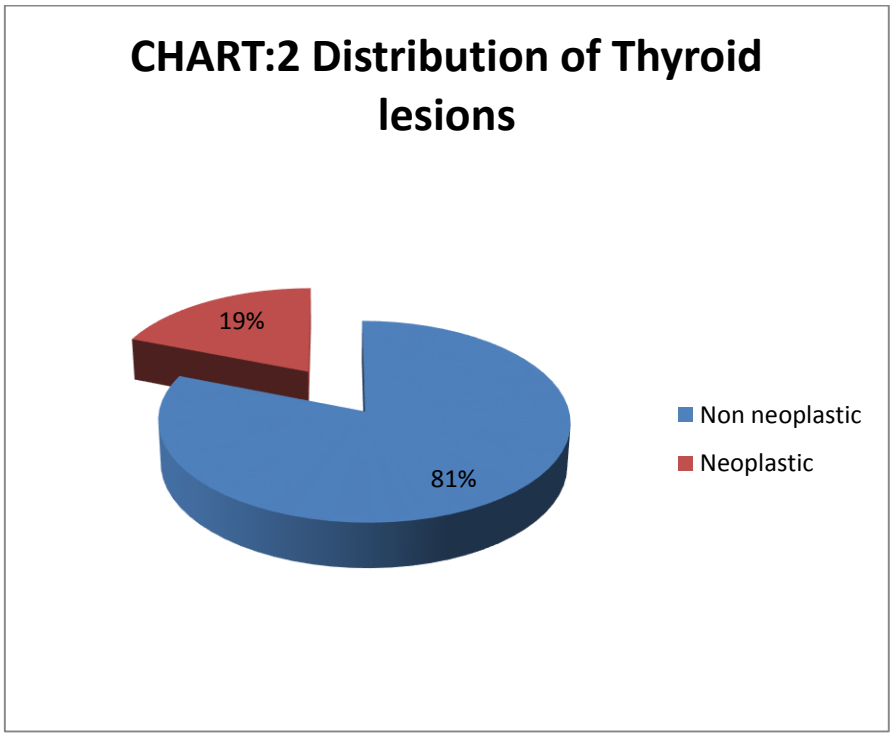


Out of 643 cases , Non -neoplastic lesions were 522 cases (81%) and Neoplastic lesions were 121 cases(19%)

TABLE -2

DISTRIBUTION OF THYROID LESIONS

Thyroid lesions	No.of cases	Percentage
Non neoplastic	522	81%
Neoplastic	121	19%
Total	643	100%

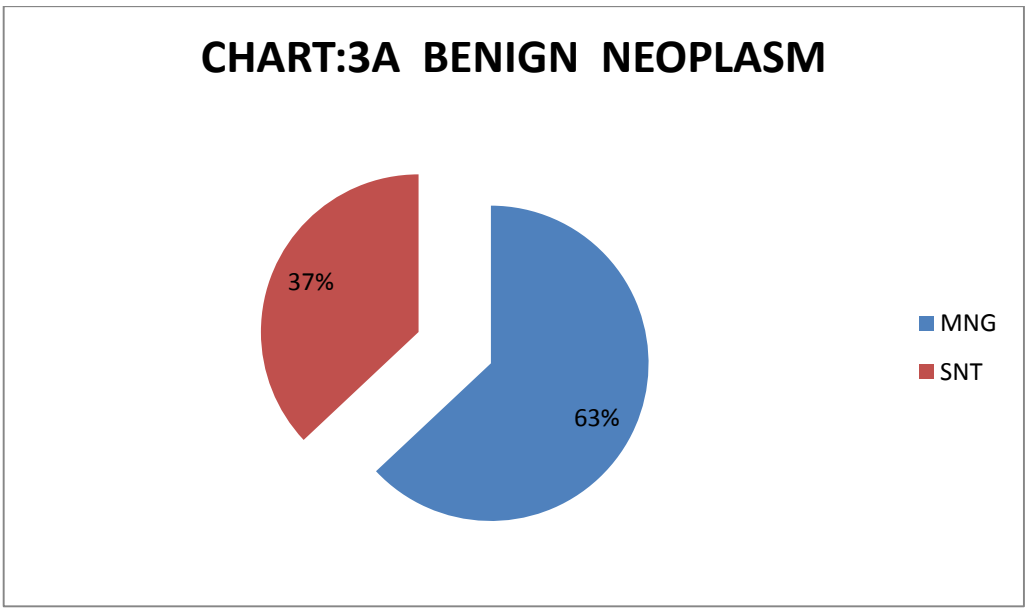


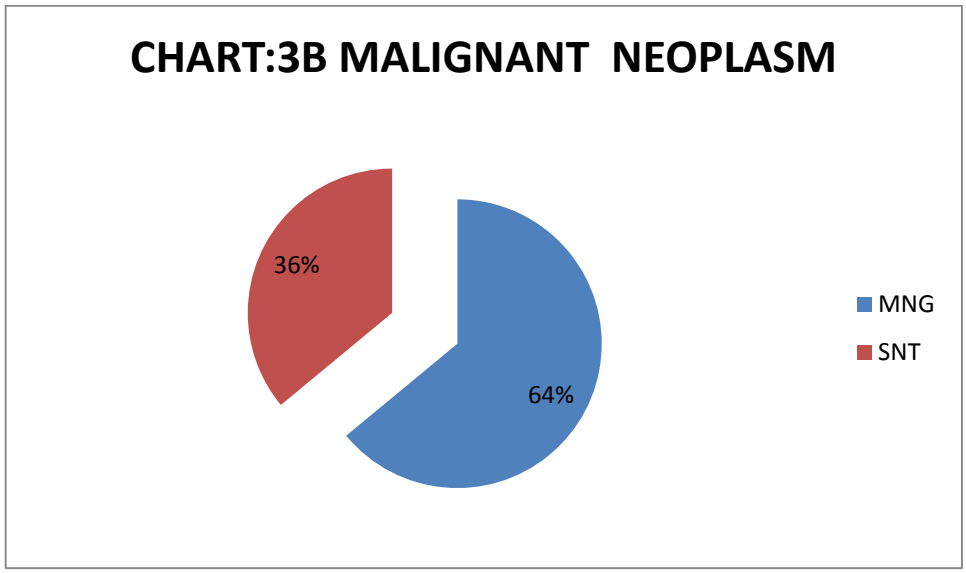
Out of 171 cases of Solitary Nodular lesions, Non Neoplastic lesions were 127 cases, Neoplastic lesions were 44 cases(benign-12, malignant-32)

TABLE -3

DISTRIBUTION OF THYROID LESIONS

MNG			SNT		
NON NEOPASTIC	NEOPLASTIC		NON NEOPLASTIC	NEOPLASTIC	
	BENIGN	MALIGNANT		BENIGN	MALIGNANT
395	20	57	127	12	32
83.69%	4.24%	12.07%	74.27%	7.01%	18.72%





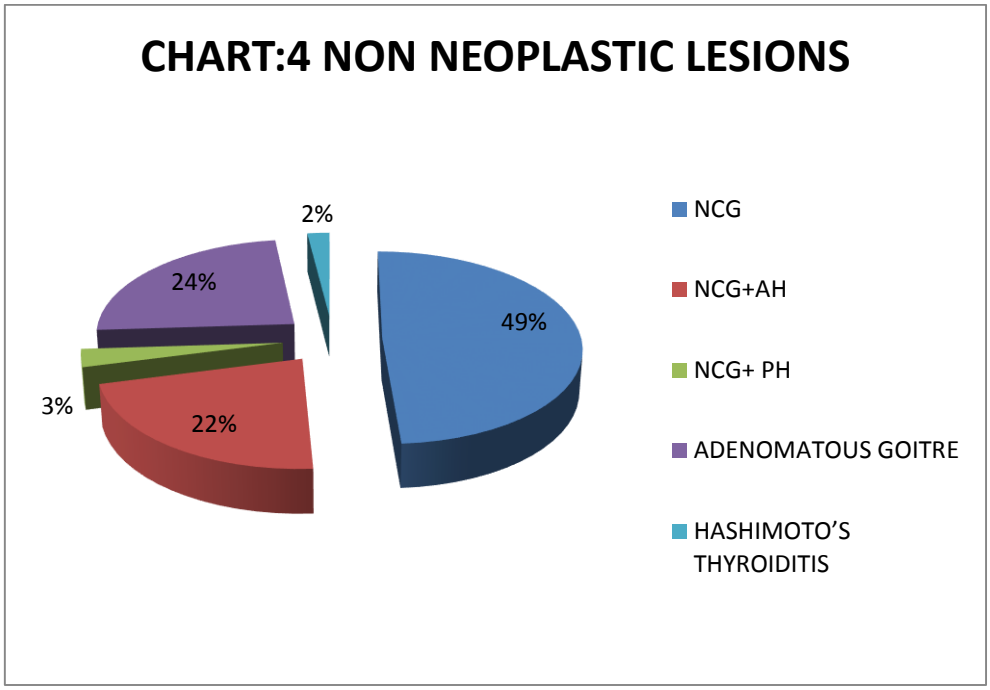
NON NEOPLASTIC LESIONS

Out of 127 cases of Non Neoplastic lesions, 62 (49%)cases wereNodular colloid goiter, Adenomatous goitre / Nodular colloid goiter with adenomatous hyperplasia were 59 cases(46%), nodular colloid goiter with papillary hyperplasia were 4 cases (3%),Hashimoto's thyroiditis were 2 cases (2%)

TABLE – 4

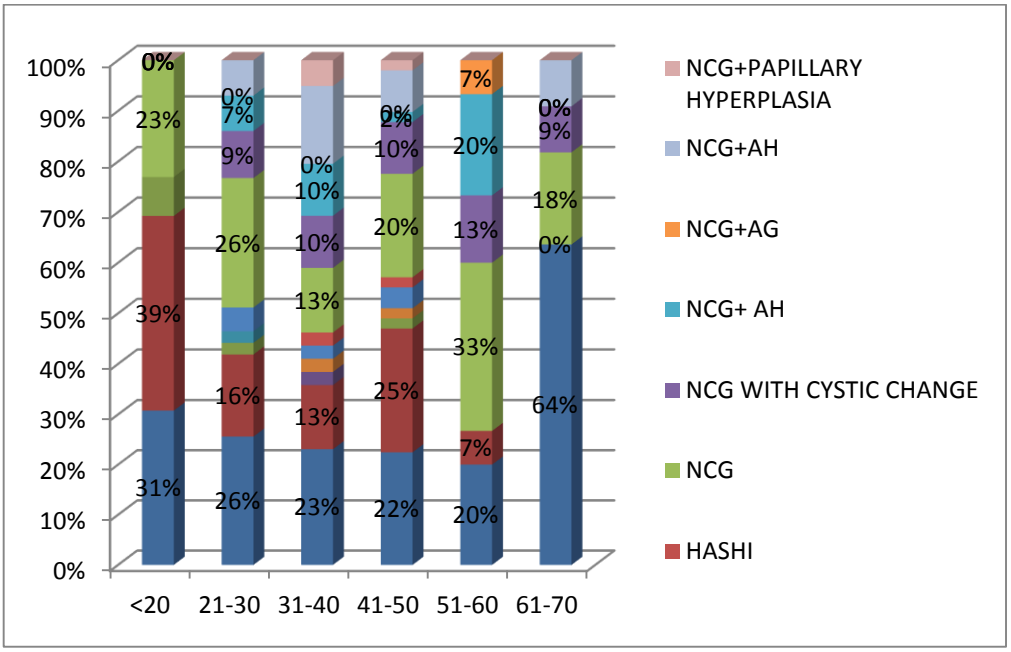
DISTRIBUTION OF NON NEOPLASTIC LESION OF SNT

Non Neoplastic lesions	No of cases	Percentage
NCG	62	49%
NCG+AH	28	22%
NCG+ PH	4	3%
ADENOMATOUS GOITRE	31	24%
HASHIMOTO'S THYROIDITIS	2	2%
Total cases	127	100%



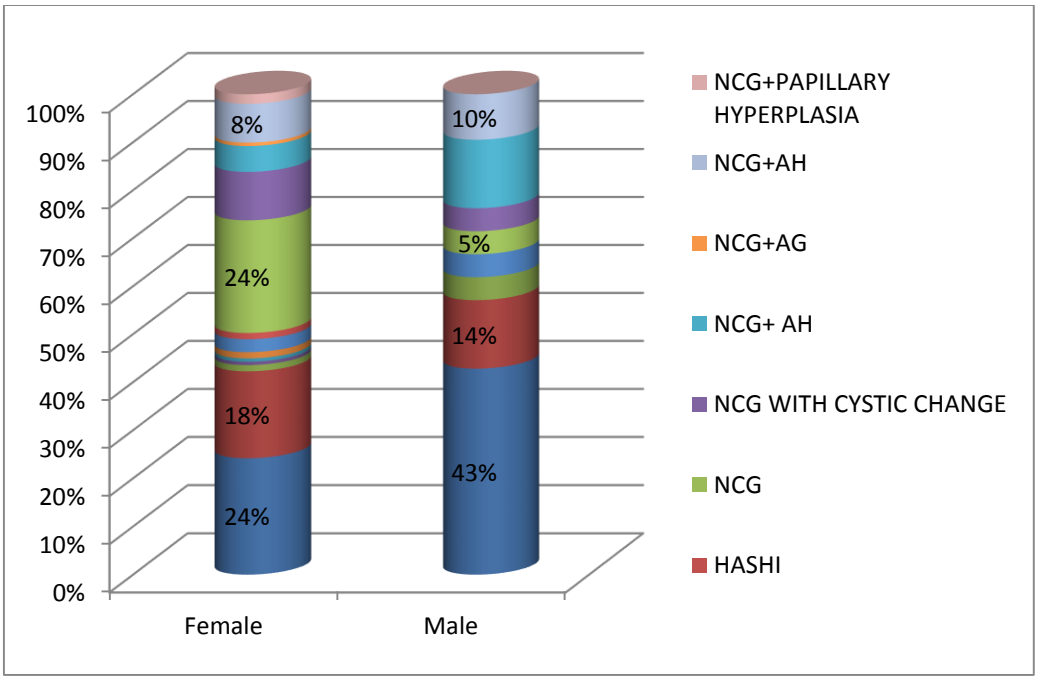
AGE DISTRIBUTION

The non neoplastic lesions were common in 3rd to 6th decade



SEX DISTRIBUTION

The non neoplastic lesions were common in females than males.



NEOPLASM

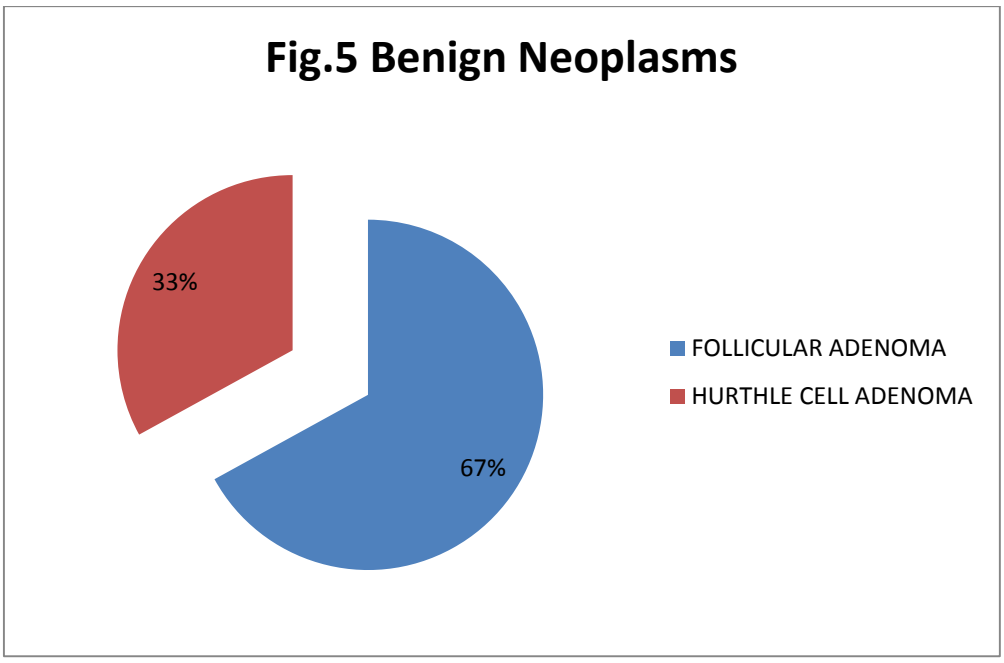
BENIGN NEOPLASM

Out of 12 benign neoplasms of SNT, Follicular adenoma were 8 cases(67%),Hurthle cell adenoma were 4 cases(33%).

TABLE – 5

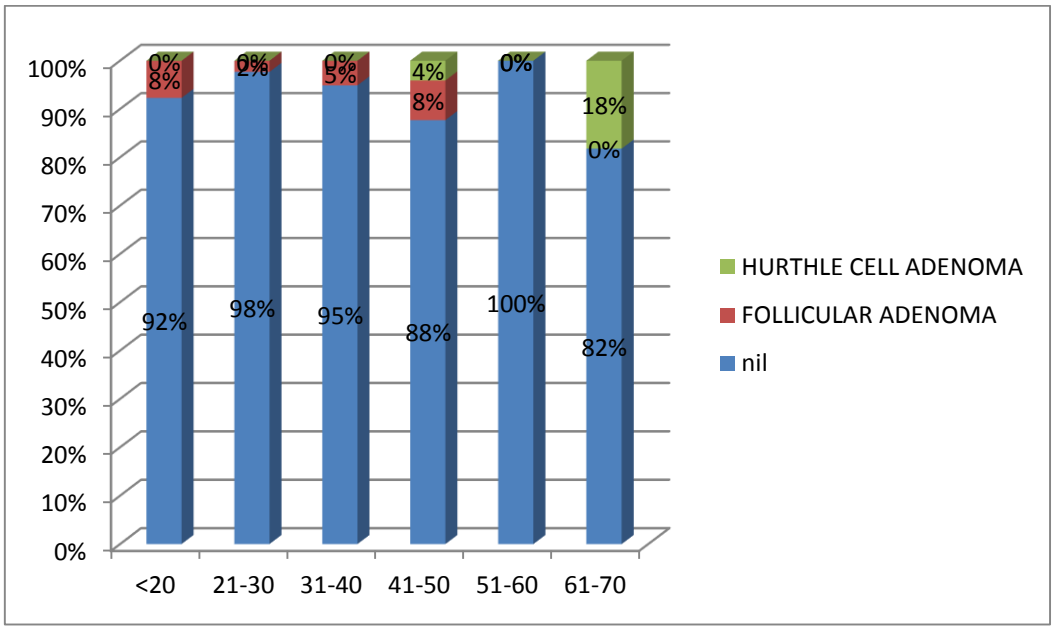
DISTRIBUTION OF BENIGN NEOPLASMS

BENIGN NEOPLASM	NO OF CASES	PERCENTAGE
FOLLICULAR ADENOMA	8	67%
HURTHLE CELL ADENOMA	4	33%
TOTAL	12	100%



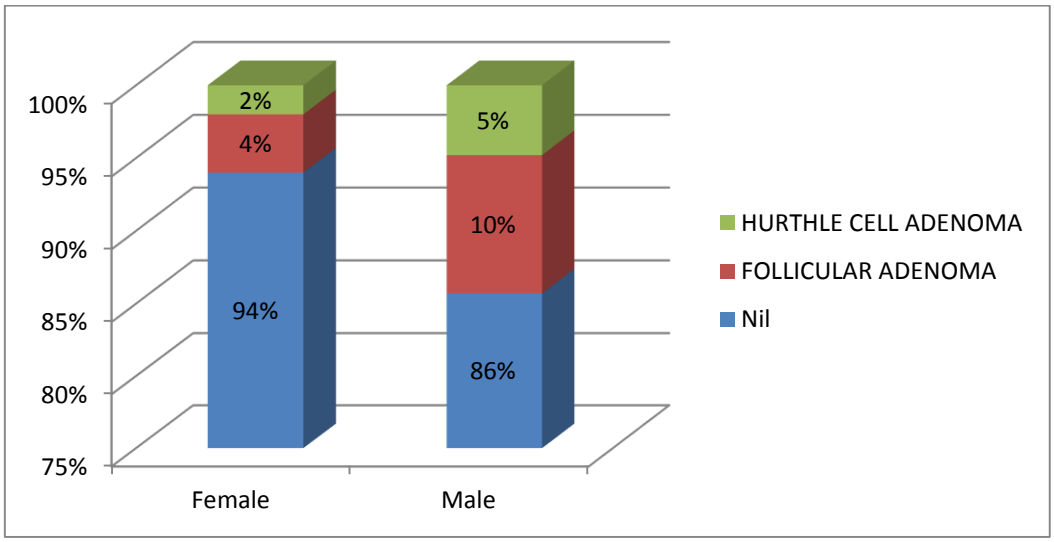
AGE DISTRIBUTION

The peak age incidence was 20-50 years for follicular adenoma and 6th decade for Hurthle cell adenoma



SEX DISTRIBUTION

Adenoma was found to be common in males. Male to female ratio of 2.5:1

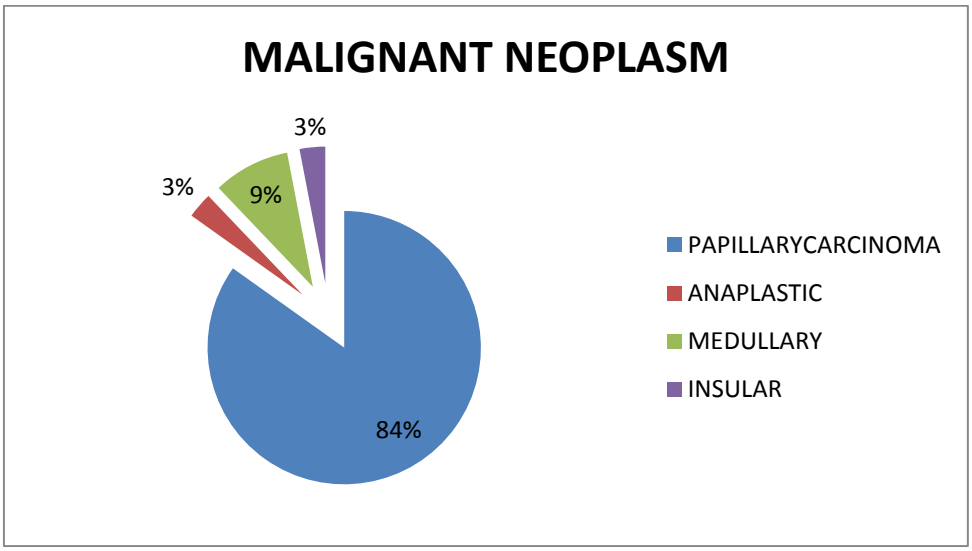


MALIGNANT NEOPLASM

Out of 32 malignant neoplasms, there were 27 cases of papillary carcinoma (85%),1 case of anaplastic carcinoma(3%), 3 cases of medullary carcinoma(9%),1 case of insular carcinoma(3%). Papillary carcinoma constitutes about 67.5% of all thyroid neoplasms

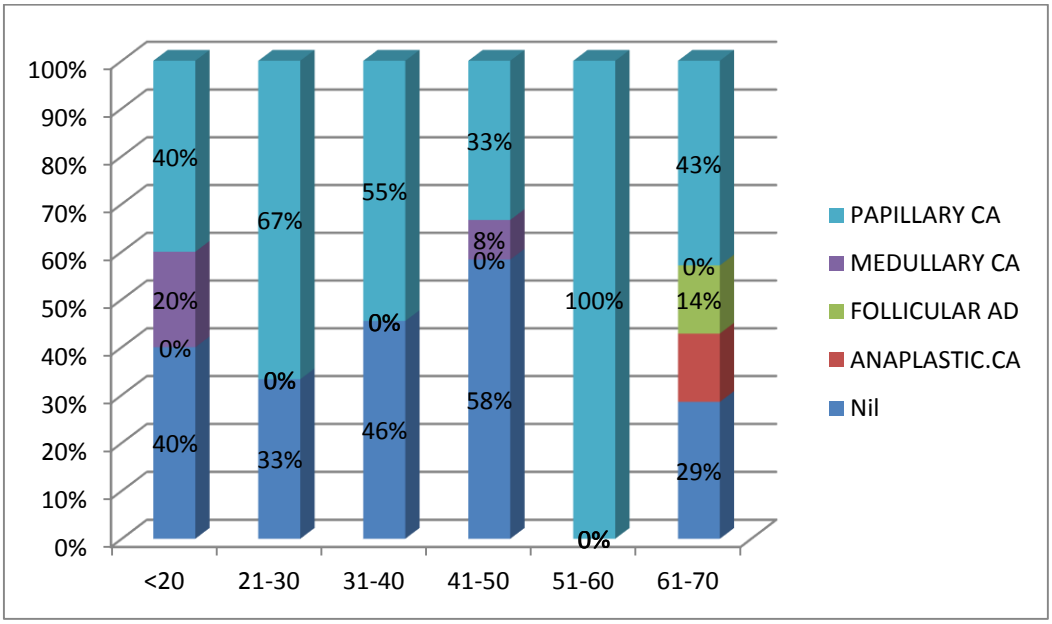
DISTRIBUTION OF MALIGNANT NEOPLASM

Malignant neoplasm	Cases	Percentage
Papillarycarcinoma	27	85%
Anaplastic carcinoma	1	3%
Medullary carcinoma	3	9%
Insular carcinoma	1	3%
Total	32	100%



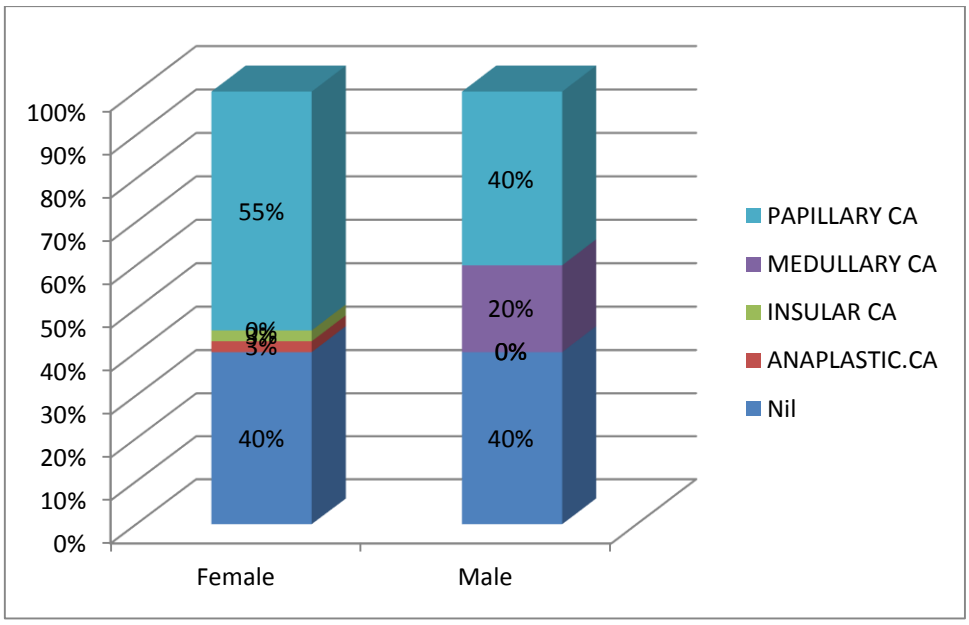
AGE DISTRIBUTION

The malignant neoplasms were common in 3rd to 5th decade.



SEX DISTRIBUTION

The malignant neoplasms were common in males.

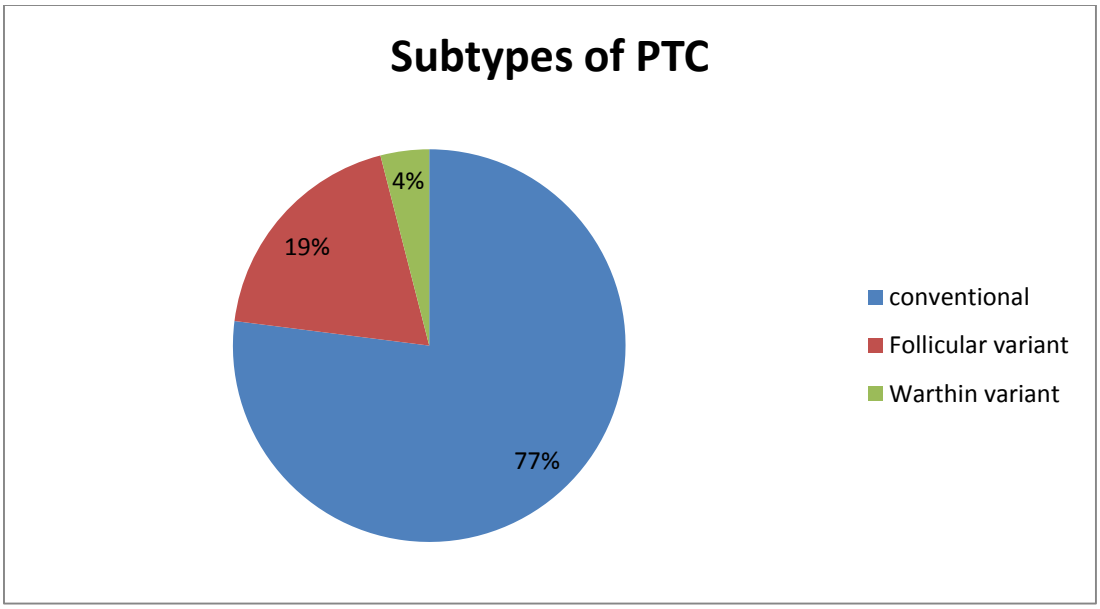


PAPILLARY CARCINOMA

Out of 27 cases of Papillary carcinoma of thyroid, 21 cases were conventional, 5 cases Follicular variant of papillary carcinoma, 1 case of warthin variant of papillary carcinoma.

VARIANTS

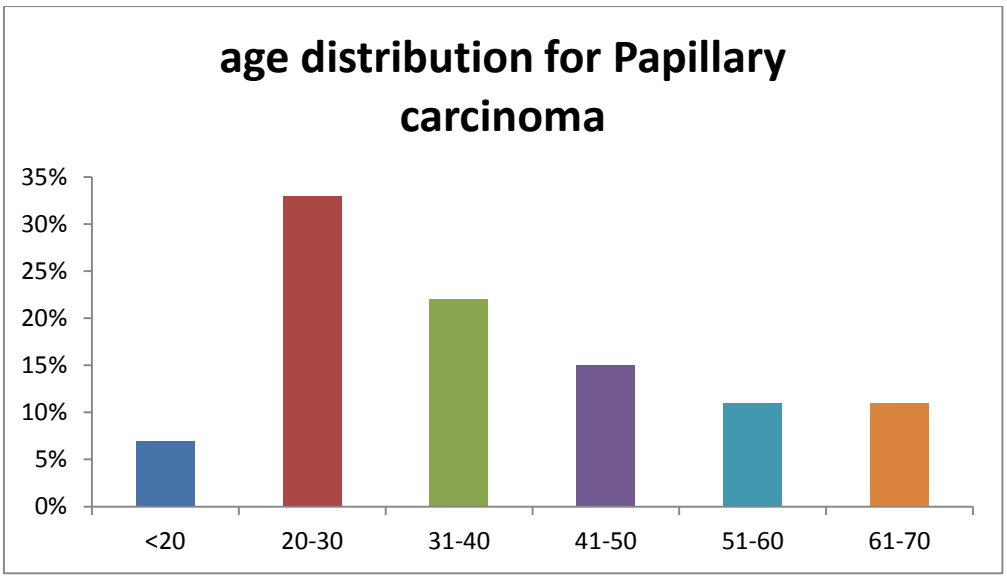
Subtypes of PTC	No.of cases	Percentage
Conventional	21	77%
Follicular variant	5	19%
Warthin Like variant	1	4%
Total	27	100%



AGE DISTRIBUTION

Maximum age incidence of papillary carcinoma of thyroid ,during 3rd and 4th decade of life .

Age	Frequency	Percent
<20	2	7.4
20-30	9	33.3
31-40	6	22.2
41-50	4	14.8
51-60	3	11.1
61-70	3	11.1
Total	27	100.0

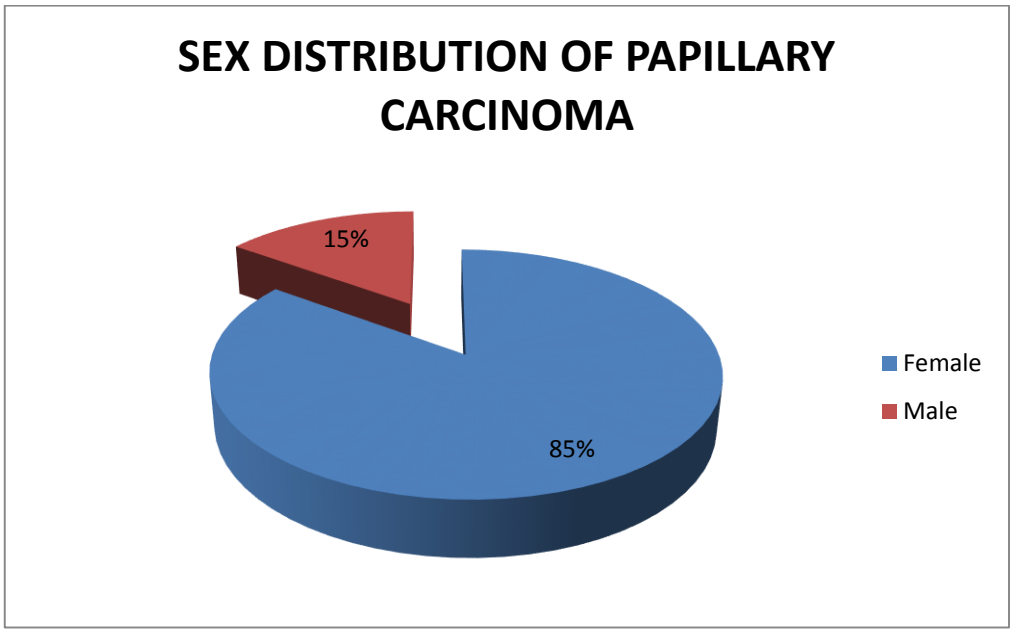


SEX DISTRIBUTION

Among the sex,the females are more affected.Male:female ratio was 1:8

SEX DISTRIBUTION OF PAPILLARY CARCINOMA

SEX	CASES	PERCENT
Female	24	85%
Male	3	15%
Total	27	100%



MEDULLARY CARCINOMA

Among the malignant neoplasm, there were 3 cases of medullary carcinoma. Male to female ratio of 2:1(2 cases were male of 17 years and 44 years. 1 case was 25 year female.)

ANAPLASTIC CARCINOMA

Only one case of anaplastic carcinoma was reported, female with age of 70 years

POORLY DIFFERENTIATED CARCINOMA

Only one case of insular carcinoma was reported, female with age of 68 years.

IHC

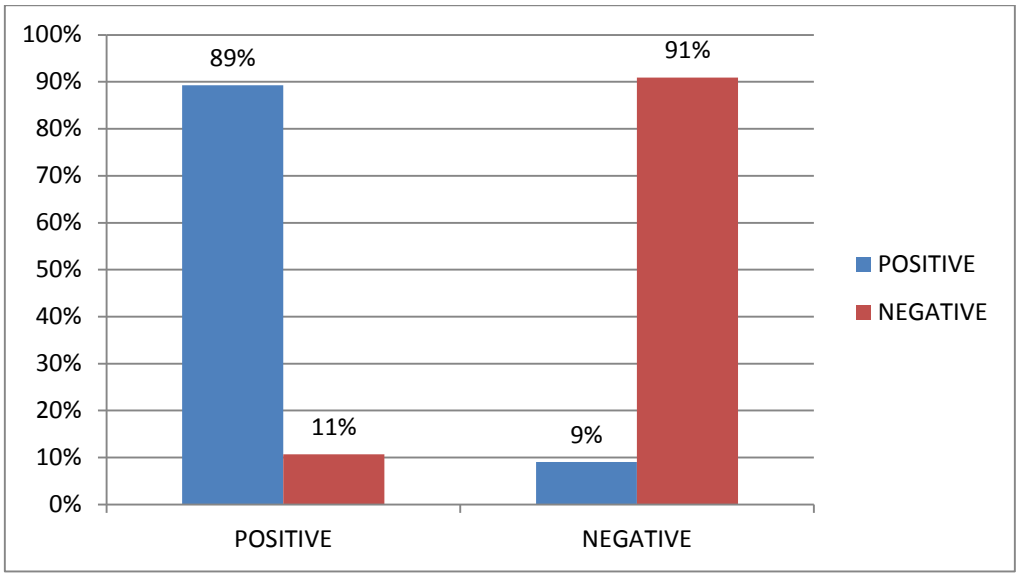
Immunohistochemistry was done for 50 cases,of which 26 cases of papillary carcinoma,2 cases of medullary carcinoma,1 case of anaplastic carcinoma,1 case of insular carcinoma,8 cases of follicular adenoma,4 cases of hurthle cell adenoma, 6 cases of adenomatous goiter, 1 case of adenomatous goitre with papillay hyperplasia, 1 case of adenomatous goiter with hyperplasia. Among 26 cases of papillary carcinoma, 20 cases of conventional type ,5 cases of follicular variant of papillary carcinoma, 1 case of warthin variant of papillary carcinoma.

PAPILLARY CARCINOMA

Among the PTC, CK19 expression was found to be strongly positive in 19 cases(95%) in conventional type. In cases of FVPTC showed strong positivity in 3 cases(67%) and moderate positivity in 2 cases(33%). Warthin like variant of PTC was negative for CK 19 expression. Positive and negative were tabulated below

CK 19 was positive in 89% of papillary carcinoma, where as it is positive in 9% of the mimickers and this difference is statistically significance with P<0.001.

PAPILLARY CARCINOMA	**POSITIVE**	**NEGATIVE**	**TOTAL**	
POSITIVE	25	2	27	CHI SQUARE =31.897 P<0.001
NEGATIVE	3	20	23	
	28	22	50	



For a diagnosis of papillary carcinoma of thyroid, CK19 had a sensitivity of 89.29% and specificity of 90.91%. The positive predictive value of 92.59% and negative predictive value of 86.96% while the false positive rate was 9.09% and false negative rate was 10.71%. The diagnostic accuracy was found to be 90%

CK 19 IN THE DIAGNOSIS OF PAPILLARY CARCINOMA

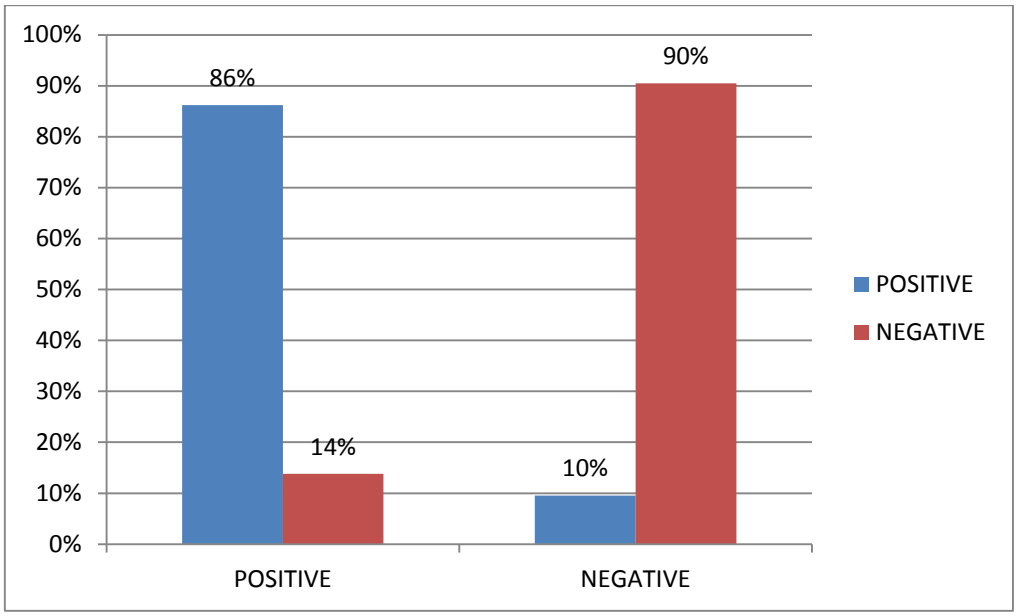
SENSITIVITY	89.29%
SPECIFICITY	90.91%
POSITIVE PREDICTIVE VALUE	92.59%
NEGATIVE PREDICTIVE VALUE	86.96%
DISEASE PREVALENCE	56.00%
DIAGNOSTIC ACCURACY	90
FALSE POSITIVITY RATE	9.09%
FALSE NEGATIVITY RATE	10.71%

GALECTIN 3 EXPRESSION IN PAPILLARY CARCINOMA

Among the 20 cases of papillary carcinoma,conventional type 12 cases showed 3+,strong positivity and 8 cases showed moderate positivity. In follicular variant of papillary carcinoma(5 cases), galectin 3 showed strong positivity in 1 case and moderate positivity in 4 cases.Warthin variant was found to be negative for galectin 3 expression.

Galectin 3 was found to be positive in 86% of papillary carcinoma which is statistically significant with P <0.001.

PAPILLARY CARCINOMA	**POSITIVE**	**NEGATIVE**	**TOTAL**	
POSITIVE	25	2	27	CHI SQUARE =28.333 P<0.001
NEGATIVE	4	19	23	
TOTAL	29	21	50	



For a diagnosis of papillary carcinoma, Galectin 3 has a sensitivity of 86.21%, specificity of 90.48%. the positive predictive value of 92.5%, negative predictive value of 82.61%. The diagnostic accuracy was 88%.

GALECTIN 3 IN THE DIAGNOSIS OF PAPILLARY CARCINOMA

PARAMETER	PERCENTAGE
SENSITIVITY	86.21%
SPECIFICITY	90.48%
POSTIVE PREDICTIVE VALUE	92.59%
NEGATIVE PREDICTIVE VALUE	82.61%
DISEASE PREVALENCE	58.00%
DIAGNOSTIC ACCURACY	88
FALSE POSITIVITY RATE	9.52%
FALSE NEGATIVITY RATE	13.79%

MEDULLARY CARCINOMA

Among the 2 cases of Medullary carcinoma, CK 19 expression was found to be strong positivity in 1 case and other case showed moderate positivity.

Galectin 3 expression was found to be moderate positivity in one case and weak positivity in other among the 2 cases of Medullary carcinoma

ANAPLASTIC CARCINOMA

CK 19 expression was found to be strongly positive in 1 case of Anaplastic carcinoma and Galectin 3 expression found to be moderate positive intensity.

INSULAR CARCINOMA

Both CK 19 and Galectin 3 were found to be negative

BENIGN NEOPLASM

FOLLICULAR ADENOMA

Ck19 expressionwas detected in 2 of 8 cases of follicular adenoma. Both the cases showed moderate staining and intensity .Other 5 cases were negative for CK 19 expression

Galectin 3 expression was found in 1 of 8 cases of follicular adenoma. One case showed only weak staining..other 7 cases were negative.

HURTHLE CELL ADENOMA

Among the 4 cases of Hurthle cell adenoma , 1 case showed weak staining 1+, 2 cases showed moderate positivity and other 1 case was found to be negative for CK19 expression.

Galectin3 was found to be weak staining 1 of 4 cases of Hurthle cell adenoma. All the other 3 cases were negative for galectin 3 expression.

NONNEOPLASTIC LESION

8 cases of non neoplastic lesions were subjected to CK19 and Galectin 3 expression. Out of 8 cases, 6 cases were adenomatous goiter, 1 case of adenomatous goiter with papillary hyperplasia And 1 case of nodular colloid goiter with adenomatous hyperplasia.

CK19 and galectin 3 was negative in all the 6 cases of adenomatous goiter. In 1 case of papillary hyperplasia and 1 case of adenomatous hyperplasia showed moderate positivity. Galection 3 expression was negative in all the cases.

CK 19 EXPRESSION IN SNT

	CASES	**0**	**1+**	**2+**	**3+**
PTC	20			1(5%)	19 (95%)
FVPTC	5			2(33%)	3(67%)
warthin variant of PTC	1	1 (100%)	0	0	0
Medullary Ca	2	0	0	1(50%)	1(50%)
Anaplastic	1	0	0	0	1(100%)
Insular	1	1			
Follicular adenoma	8	5		2	
Hurthle cell adenoma	4	1(25%)	2(50%)	1(25%)	
Adenomatous goiter	6	6(100%)			
AG+PH	1			1(100%)	
NCG +AH	1			1(100%)	

GALECTIN 3 EXPRESSION IN SNT

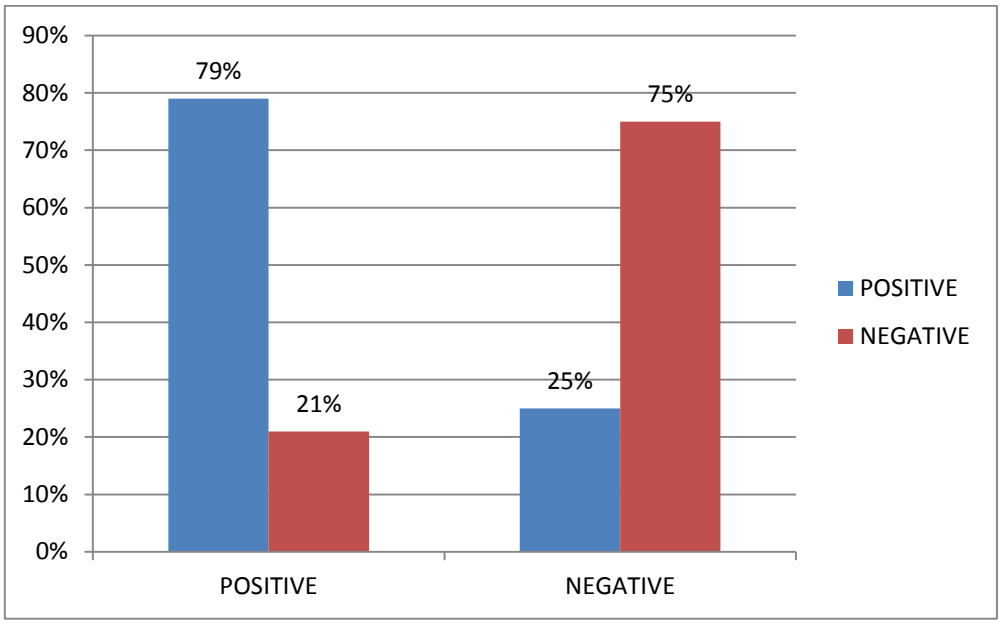
			0	**1+**	**2+**	**3+**
	CASES	%				
PTC	20	40%			8(40%)	12(60%)
FVPTC	5	10%			4(80%)	1(20%)
WARTHIN	1	2%	1(100%)			
MEDULLARY	2	4%		1(50%)	1(50%)	
ANAPLASTIC	1	2%			1(100%)	
INSULAR	1	2%	1(100%)			
FA	8	16%	7(88%)	1(12%)		
HA	4	8%	3(75%)	1(25%)		
AG	6	12%	6(100%)			
AG+PH	1	2%	1(100%)			
NCG+AH	1	2%	1(100%)			

Focal CK 19 expression was found in the normal thyroid follicles of all the cases. But Galectin expression was negative in normal thyroid follicles.

CK19 and Galectin 3 expression in all the cases of present study has been tabulated below.

Crosstab

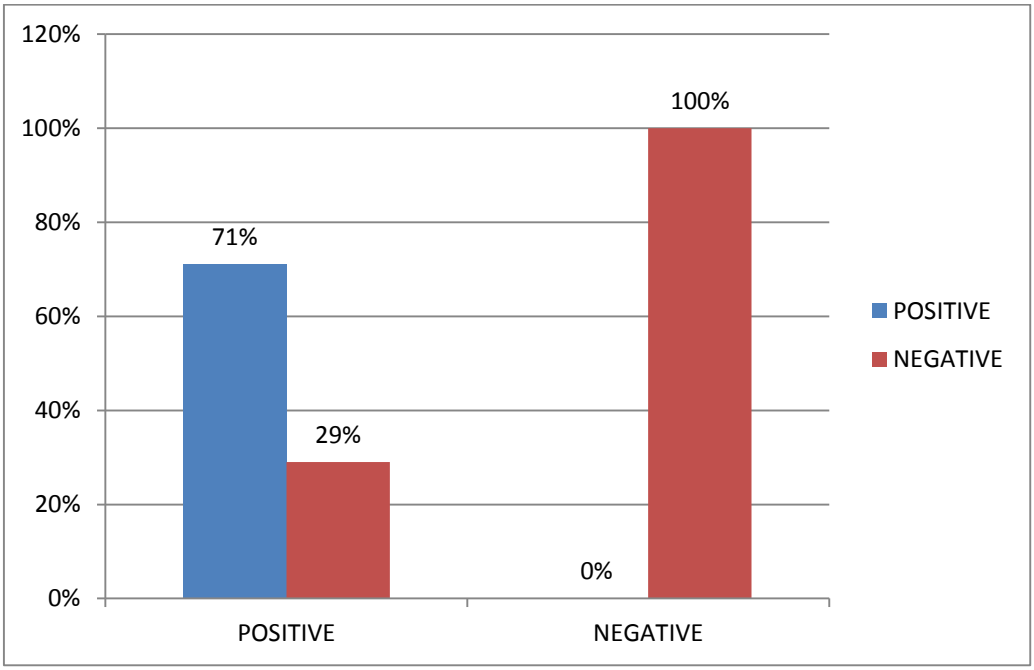
			disease		Total	
			positive	negative		
ck19	positive	Count	33	2	35	chi square =9.184* p=0.002
		% within disease	78.6%	25.0%	70.0%	
	negative	Count	9	6	15	
		% within disease	21.4%	75.0%	30.0%	
Total		Count	42	8	50	
		% within disease	100.0%	100.0%	100.0%	



SENSTIVITY	78.57%
SPECIFICITY	75.00%
POSTIVE PREDICTIVE VALUE	94.29%
NEGATIVE PREDICTIVE VALUE	40.00%
DISEASE PREVALENCE	84.00%
DIAGNOSTIC ACCURACY	78.00%
FALSE POSITIVITY RATE	25.00%
FALSE NEGATIVITY RATE	21.43%

GALECTIN 3 EXPRESSION IN ALL THE CASES OF PRESENT STUDY

			Disease		Total	
			positive	negative		
Gal3	positive	Count	30	0	30	chi square =14.286 * p<0.001
		% within disease	71.4%	0.0%	60.0%	
	negative	Count	12	8	20	
		% within disease	28.6%	100.0%	40.0%	
Total		Count	42	8	50	
		% within disease	100.0%	100.0%	100.0%	



SENSITIVITY	71.43%
SPECIFICITY	100.00%
POSTIVE PREDICTIVE VALUE	100.00%
NEGATIVE PREDICTIVE VALUE	40.00%
DISEASE PREVALENCE	84.00%
DIAGNOSTIC ACCURACY	76.00%
FALSE POSITIVITY RATE	0.00%
FALSE NEGATIVITY RATE	28.57%

DISCUSSION

The incidence of solitary thyroid nodule is common among the 4-7% of adult population. Solitary nodule were more common in females . The malignancy incidence is more common in males. The ultimate aim in evaluation of the solitary nodule is to differentiate benign hyperplasia from the true malignancy.

Currently available modalities to evaluate the solitary lesions are FNAC, diagnostic imaging, serology, histopathology technique and immunohistochemistry.

Out of 643 resected thyroid specimens,171 cases were solitary nodular lesions. In 171 cases,127 were non neoplastic and 44 cases were neoplastic(benign-12, malignant-32). Among the 171 solitary thyroid lesions,50 thyroid lesions were evaluated with CK 19 and Galectin3 to assess the potential in the diagnosis. 26 cases of papillary carcinoma,1 case of anaplastic carcinoma,2cases of medullary carcinoma, 1 case of insular carcinoma, 8 cases of follicular adenoma,3 cases of hurthle cell adenoma, 8 cases of non neoplasm.

Chetan V R et al [6]studied among 73 cases of SNT, colloid goitre-32 cases,43.8%, FA 24 cases-32.9%, PTC 9 cases -12.3%, follicular carcinoma-3 cases,4.1%, MNG 3 cases-4.1%. Incidence of malignant lesions (12)16.5% and benign (61) 83.5%. Among the malignant cases 8/12 were males(66.6%), 4/12 were females (33.3%) .

A.Ravi kamal kumar et al[33] in a study of 126 cases of SNT found the incidence of benign lesion was 85.17% { FA-52.38% (66 cases), colloid goiter- 24.60%(31 cases), cyst-4.76%(6), hashimoto's thyroiditis - 3.96%(5)} malignant lesions of 14.29% {PTC-77.78%(14 cases), FC-22.22% (4cases)}. Among the malignant cases 11.11%males(6/18), and 33.33% females(12/108).

In our study the highest age incidence of SNT is between 20 -49 years of age.

COMPARATIVE AGE INCIDENCE OF SNT

Age	Fenn et al[61]	Nagori et al[55]	Ananthakrishnan et al[36]	Ravikamal kumar[33]	Present study
<20	18	11	39	5	12
20-29	81	25	167	50	42
30-39	122	29	150	56	39
40-49	74	21	81	10	47
50-59	38	8	46	5	16
>60	9	6	20	0	15
Total	342	100	503	126	170

Out of 32 malignant cases, 10 cases lies between the age group of 21-30 years. Female outnumbered the males with a ratio of 7.5:1

The percentage of benign and malignant cases in our study is benign (81.28%) and malignant-18.72%. The present study results are similar to that of Chetan et al [6]study. The other studies has been tabulated below.

	Psarras et al[34]	Nagori et al[35]	Ananthakrishnan et al[36]	Khadhikar et al[37]	Tsegaye et al[38]	Chetan et al[6]	Ravikamalkumar et al[33]	Present study
Benign	88.3%	89%	84.7%	79%	91.8%	83.5%	85.7%	81.28%
Malignant	11.7%	11%	15.3%	21%	8.2%	16.5%	14.29 %	18.72%

MALIGNANT NEOPLASM

PAPILLARY CARCINOMA

Papillary carcinoma is the common malignant neoplasm of thyroid. The incidence of papillary carcinoma was 31.25% of all malignant thyroid neoplasm.Among the SNT the incidence was 84.5%.It is the highest incidence among the other studies ,which has been tabulated below

COMPARATIVE STUDY OF INCIDENCE OF PTC

	Anandhakrishnan et al[36]	Tsegaye et al[38]	Khadilkar et al[37]	Ravikamal kumar et al[33]	Chetan et al[6]	Present study
PTC	46.8%	76.6 %	38.29%	77.78%	28.7%	84.5%

In our study the peak age incidence of PTC in the 3rd to 5th decade (22 /32 cases).

Out of 26 cases of papillary carcinoma, 20 cases were conventional, 5 cases were follicular variant of papillary thyroid carcinoma, 1 case of warthin variant.

CK19 showed strong positivity (3+) in 19/20 cases of conventional papillary carcinoma, 1 case showed moderate staining 2+. Out of 5 cases of FVPTC 2 cases showed 2+ positivity,3 cases showed strong positivity. Warthin like variant was negative for CK19 expression.

Baloch et al [39] study in warthin like variant of papillary carcinoma shows strong and diffuse positivity with CK19, which is controversial in present study.

In the comparative study , CK 19 expression is positive in PTC , moderate to strong intensity in FVPTC.

CK 19 EXPRESSION IN PAPILLARY CARCINOMA- DIFFERENT STUDIES

study	**Cases**	**0**	**1+**	**2+**	**3+**
Beesley[40]	26			2	24
Lei gong et al[41]	38			12	26
Theresa et al[38]	49				49
Qingbin et al[42]	441	16			425
Dunderovic et al [43]	87				75
Carol[44]	138				91
Bose et al[13]	22				22
Saleh et al[45]	32				27
Hanen[46]	22			6	16
Present study	26	1		3	22

Galectin 3 showed strong positivity in 12 cases and 8 cases showed moderate positivity in 4 cases, strong positivity in 1 case. Warthin like variant was negative .

As compared to the other studies, the present study was near to the El katebet al[14] study.

COMPARATIVE STUDY OF GALECTIN 3 EXPRESSION IN PAPILLARY CARCINOMA

	Cases	**0**	**1+**	**2+**	**3+**
Beesley[40]	26	4	3	1	18
Gong et al[41]	38	1	1	22	14
El kateb et al[14]	15	0	1	1	12
Theresa et al[38]	78			73	
Qingbin et al[42]	441	14		427	
Dunderovic et al[43]	87			80	
Rita et al[47]	20			1	19
Marie et al[48]	12				10
Saleh et al[45]	46			1	18
Hanen[46]	22		1	3	18
Present study	26			12	13

In all the literatures reviewed showed CK 19 is strongly expressed in papillary carcinoma and its variants.

Galectin3 expression showed moderate to strong intensity in all the cases of papillary carcinoma. Galectin 3 expression is slightly more when compared with the literature.

In present study there was a weak staining in normal thyroid. But according to Beesley[40] study, neither CK 19 nor Galectin 3 were expressed in normal thyroid.

Fonseca et al[49] identified that there was a weakly staining in normal thyroid.

Dockhorn –Dworniczak[50] found, that there was a focal staining in normal thyroid.

MEDULLARY CARCINOMA

Anandhakrishnan et al[36], Taegaye et al [38],Khadikar et al[37], found that the incidence of medullary carcinoma was 5.2%,1.5%,2.94% respectively. Present study shows the incidence of 6.81%.

COMPARATIVE STUDY OF INCIDENCE IN MEDULLARY CARCINOMA

	Anandhkrishnan et al	Tsegaye et al	Khadikar et al	Present study
Medullary carcinoma	5.2	1.5	2.94	6.81%

In present study Male to female ratio is 2:1. Kishore et al[51] study showed the male to female ratio of 1:2.

CK19 expression in medullary carcinoma of present study is similar to that of Beesley[40] study

COMPARATIVE STUDY OF CK19 EXPRESSION IN MEDULLARY CARCINOMA

	Cases	**0**	**1+**	**2+**	**3+**
Beesley[40]	2			1	1
Our study	2			1	1

COMPARATIVE STUDY OF GALECTIN3 EXPRESSION IN MEDULLARY CARCINOMA

	Cases	**0**	**1+**	**2+**	**3+**
Beesley[40]	2	1			1
Elkateb et al[14]	6	2		2	2
Rita et al[47]	5	1		1	3
Cvejic et al[52]	20	4	7	7	2
Present study	2		1	1	

CK 19 expression in medullary carcinoma in our study is similar to that of the literature.

Galectin 3 expression is slightly higher than reviewed in the literature.

ANAPLASTIC CARCINOMA

Anaplastic carcinoma constitute about 5-10% of all thyroid malignancies. Anandhakrishnanet al[36] and kishore et al [51]noticed about 3.9% and 3.27% respectively.

CK19 expression was found to be strong positive (3+) in the Anaplastic carcinoma. When compared with the literature CK 19 expression was same as that of present study.

COMPARATIVE STUDY OF CK 19 EXPRESSION IN ANAPLASTIC CARCINOMA

	Cases	**0**	**1+**	**2+**	**3+**
Beesley[40]	1				1
Carol[44]	2	2			
Lam et al[53]	4				4
Present study	1				1

Galectin 3 expression in present study was strongly positive staining in anaplastic carcinoma. It was similar to the studies condutedby Cvejic et al [52] (10/10cases), Gasbarri et al[54] (5/5),Inhora et al [55] (3/4) showed strong positivity for Galectin 3 expression.

GALECTIN 3 EXPRESSION IN ANAPLASTIC CARCINOMA

	Cases	0	1+	2+	3+
Beesley[40]	1	1			
El kateb et al [14]	2			2	
Fernandez et al[56]	5				5
Prasad et al[57]	4			4	
Bartolazzi et al[58]	20			18	
Our study	1			1	

INSULAR CARCINOMA

Pilotti et al [59] and Volante et al[60] found the incidence of 4% and 6.3% respectively, mean age of 53 years and 57 years in Insular carcinoma. In our study the age was 68 year, female.

CK 19 andGalectin 3 was found to be negative in present study.

COMPARATIVE STUDY OF CK 19 EXPRESSION IN INSULAR CARCINOMA

	Cases	0	1+	2+	3+
Carol[44]	6	3		3	
Our study	1	1			

COMPARATIVE STUDY OF GALECTIN 3 EXPRESSION IN INSULAR CARCINOMA

	Cases	0	1+	2+	3+
El kateb et al[14]	2			2	
Fernandez et al[56]	3			2	
Bartolazzi et al [58]	20			13	
Our study	1	1			

BENIGN NEOPLASM

Out of 12 cases,8 cases were follicular adenoma, 4 cases were Hurthle cell adenoma.

Incidence of benign neoplasm is less in present study when compared with the literature.

COMPARATIVE INCIDENCE OF ADENOMA

	Fenn et al[61]	Nagori et al[55]	Anantha krishnan et al[36]	Kadhikar et al[37]	Chetan et al[6]	Ravikamal kumar[33]	Present study
Adenoma	54.97 %	44%	53.3%	13%	32.9%	52.38%	18.72 %

FOLLICULAR ADENOMA

Out of 8 cases CK 19 expression was negative in 5 cases and 2 cases showed 2+ positivity. Galectin3 expression was found in 1/8 cases. Weak positivity in that case.

Beesley M F, K.M. Mc Laren[40] study showed CK 19 positivity in 5/20 cases, the remaining 15 cases were negative. 2 Cases showed positivity in scattered cells in areas of normal thyroid tissue.

Galectin 3 expression was found in 2/20 cases. One case showed strong positivity,it was confined to the neoplasm, but it was distributed focally.

HURTHLE CELL ADENOMA

Out of 4 cases , 2 cases showed moderate positivity, 1 case showed weak staining and the other one case was negative.

Dunderovic et al [43] study found that ,out of 10 cases ofhurthle cell adenoma, CK19 expresion was found in 6 cases (60%). Galectin 3 expression in 5 cases (50%)

CK19 EXPRESSION IN FOLLICULAR ADENOMA

	Cases	**0**	**1+**	**2+**	**3+**
Beesley[40]	20	15	1	2	2
Theresa et al[38]	49			7	
Qingbin et al[42]	54	41	13		
Dunderovic et al[43]	27			6	
Carol et al[44]	35			6	1
Saleh et al[45]	46			23	
Hanan[46]	7	3	1	3	
Our study	8	5		2	

GALECTIN 3 EXPRESSION IN FOLLICULAR ADENOMA

	Cases	0	1+	2+	3+
Beesley[40]	20	18	1		1
El kateb et al[14]	10	6			
Theresa et al[38]	49		9		
Qingbin et al[42]	54	28	26		
Dunderovic et al[43]	27		11		
Rita et al[47]	19	15	4		
Marie et al[48]	12		4		
Bose et al[13]	8	2	6		
Present study	8	7	1		

PAPILLARY HYPERPLASIA

In present study of 2 cases showed moderate staining with CK 19 and negative in Galectin 3 expression.

Gong et al [41] study found that ,out of 12 cases of papillary hyperplasia, 1 case showed weak staining 1+. CK19. The positive rate was only 9.1%. All the other 11 cases were negative.

Galectin3 expression was weak in1/12 cases of papillary hyperplasia. Positive rate of 16.7%.

Kovacs et al [62]study on 3 cases of papillary hyperplasia, all were negative for galectin3 expression.

HBME-1 may be the useful marker in distinguising papillary hyperplasia from papillary carcinoma[63].

CK19 positive rate in papillary carcinoma was 9.5% and Galectin 3 was 16.7%[41].

ADENOMATOUS GOITRE

In present study 6 cases of adenomatous goiter were found to be negative for CK 19 and Galectin 3 expression.

Marie et al[48]study 12 cases of adenomatous goitre expressed galectin 3 in less than 75% of cells.

In the Present study, Ck19 has a sensitivity of 78.7%, specificity of 75%,PPV-94.29%,NPV-40%. The diagnostic accuracy was found to be 78%. This difference was statistically significant with $P<0.002$ which was in accordance with other studies in the literature.

Galectin3 has a sensitivity of 71.43%, specificity of 100%,PPV-100%,NPV-40%. The diagnostic accuracy was 76%. Statistically significant P <0.001.

CK19 staining in papillary carcinoma has sensitivity of 89.29%, specificity of 90.91%,PPV of 92.59%, NPV of 86.96%, diagnostic accuracy of 90%. Galectin 3 staining in papillary carcinoma shows sensitivity of 86.21%, specificity of 90.48%, PPV-92.59%,NPV-82.61%, diagnostic accuracyof 88%. Both are statistically significant P value of<0.001.

SPECIFICITY AND SENSITIVITY OF CK 19 AND GALECTIN 3 IN NEOPLASM

STUDY	**Markers**	**Sensitivity**	**Specificity**
Wu et al [64]	CK19	92.7%	89.2%
	Galectin3	81.9%	92.3%
Dunderovic et al[43]	CK 19	75%	71%
	Galectin 3	88.52%	65%
Saussez et al [65]	Galectin 3	11%	100%
Zu x et al [66]	CK19	79%	74%
	Galectin 3	86%	66%
Barut F[67]	CK19	92%	78%
	Galectin 3	94%	96%
Beesley[40]	CK19	83%	75%
	Galectin3	85%	82%
Rossi ED et al[68]	CK19	86%	97%
	Galectin3	88%	100%
Present study	CK19	78%	75.7%
	Galectin3	71%	100%

SUMMARY AND CONCLUSION

A total of 643 thyroid specimens, 171 cases were solitary nodule thyroid during the study period from june 2014 to may 2016 were subjected to histopathology and were classified according to the WHO classification.

The incidence of solitary thyroid lesion was 13.29% with an age incidence of 3rd to 5th decade. Females are more commonly affected, but male has the higher incidence for malignancy. Right lobe is more commonly affected.

Among the solitary thyroid lesions, benign neoplasm constitutes about 18.72%, malignant lesions were 88.28%.The commonest malignant neoplasm was papillary carcinoma constitute about 84.5%.

Immunohistochemical analysis of cytokeratin 19 and galectin3 was done in 50 cases of SNT. The following cases were selected for IHC. 20 cases of papillary carcinoma,variants of PTC were 5 cases, 2 cases of medullary carcinoma, 1 case of anaplastic carcinoma, 1 case of insular carcinoma. Benign cases were 8 cases of follicular adenoma,4 cases of hurthle cell adenoma , 6 cases of adenomatous goiter, 1 case of papillary hyperplasia and 1 case of adenomatous hyperplasia.

CK19 was found strongly positive in PTC. Moderate to strong positivity in FVPTC.Warthin variant was negative.Galectin 3 expression

was also found to show moderate to strong positivity in papillary carcinoma. It was found to be negative in all the benign conditions.

CK19 has a sensitivity of 78.7%, specificity of 75%,PPV-94.29%,NPV-40%. The diagnostic accuracy was found to be 78%. This difference was statistically significant with P<0.002 which was in accordance with other studies in the literature.

Galectin3 has a sensitivity of 71.43%, specificity of 100%,PPV-100%,NPV-40%. The diagnostic accuracy was 76%. Statistically significant P<0.001.

CK19 staining in papillary carcinoma has sensitivity of 89.29%, specificity of 90.91%,PPV of 92.59%, NPV of 86.96%, diagnostic accuracy of 90%. Galectin 3 staining in papillary carcinoma shows sensitivity of 86.21%, specificity of 90.48%, PPV-92.59%,NPV-82.61%, diagnostic accuracyof 88%. Both are statistically significant with a P value of <0.001.

So CK 19 favours the diagnosis of papillary carcinoma of thyroid and follicular variant. A lesion with follicular architecture without nuclear features of papillary carcinoma is best assessed by Galectin 3. Galectin 3 serve as a marker for recognition of follicular carcinoma. Galectin 3 helps in differentiating the benign and malignant neoplasm.

ANNEXURE I

WHO HISTOLOGICAL CLASSIFICATION OF THYROID NEOPLASMS

(A) Thyroid adenoma and related tumors

- Follicular adenoma
- Hyalinizing trabecular tumor

(B) Thyroid carcinomas

- Papillary carcinoma
- Follicular carcinoma
- Poorly differentiated carcinoma
- Undifferentiated (anaplastic) carcinoma
- Squamous cell carcinoma
- Mucoepidermoid carcinoma
- Sclerosing mucoepidermoid carcinoma with eosinophilia
- Mucinous carcinoma
- Medullary carcinoma
- Mixed medullary and follicular carcinoma
- Spindle cell tumor with thymus-like differentiation
- Carcinoma showing thymus-like differentiation

(C) Other thyroid tumors

- Teratoma
- Primary lymphoma and plasmacytoma
- Ectopic thymoma
- Angiosarcoma
- Smooth muscle tumors
- Peripheral nerve sheath tumors

- Paraganglioma
- Solitary fibrous tumor
- Follicular dendritic cell tumor
- Langerhans cell histiocytosis

(D) Secondary tumors

ANNEXURE II

TNM CLASSIFICATION OF THYROID CARCINOMAS

PRIMARY TUMOR (T)

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤2 cm greatest dimension, limited to the thyroid
T2	Tumor >2 cm but not >4 cm, limited to the thyroid
T3	Tumor >4 cm in greatest dimension, limited to the thyroid; or Any tumor with minimal extrathyroid extension (e.g., extension to sternothyroid muscle or perithyroid soft tissues)
T4a	Tumor of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve
T4b	Tumor invades prevertebral fascia or encases carotid artery or mediastinal vessels

All anaplastic carcinomas are considered T4 tumors

T4a	Intrathyroidal anaplastic carcinoma– surgically resectable
T4b	Extrathyroidal anaplastic carcinoma– surgically unresectable

REGIONAL LYMPH NODES (N)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1a	Metastasis to Level VI (pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes
N1b	Metastasis to unilateral, bilateral, or contralateral cervical or superior mediastinal lymph nodes

DISTANT METASTASIS (M)

MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

ANNEXURE III
IMMUNOHISTOCHEMISTRY PROCEDURE

1. 4μm thick sections are cut from formalin fixed paraffin embedded tissue samples and transferred on to gelatin-chrome alum coated slides.

2. The sections are deparaffinized in xylene for 30 minutes x 2 changes.

3. The sections are dehydrated with absolute alcohol for 5 minutes x 2 changes.

4. The sections are washed in tap water for 10 minutes.

5. The slides are then immersed in distilled water for 5 minutes.

6. The slides are then kept in citrate buffer solution for 5 to 10 minutes.

7. Heat induced antigen retrieval is done using microwave oven with citrate buffer solution for 20 minutes.

8. The slides are then cooled to room temperature and washed in running tap water for 5 minutes.

9. The slides are then rinsed in distilled water for 5 minutes.

10. The slides are then washed with phosphate buffer solution for 5 minutes x 2 changes.

11. ***PEROXIDE BLOCK*** (to quench endogenous peroxidise in the tissue) is applied over the sections for 10 minutes.

12. The slides are washed in phosphate buffer solution for 5 minutes x 2 changes.

13. The sections are covered with ***POWER BLOCK*** (to block nonspecific antigen – antibody reactions) for 15 minutes.

14. The sections are drained (without washing) and appropriate ***PRIMARY ANTIBODY*** applied over the sections and incubated for 45 minutes.

15. The slides are washed in phosphate buffer for 5 minutes x 2 changes.

16. The slides are covered with ***SUPER ENHANCER*** for 30 minutes (which increases the sensitivity of antigen – antibody reaction thereby enhancing the final reaction product).

17. The slides are washed in phosphate buffer for 5 minutes x 2 changes.

18. The slides are covered with ***SS LABEL*** (Secondary antibody from goat with tagged horse radish peroxidase enzyme) for 30 minutes.

19. The slides are washed in phosphate buffer for 5 minutes x 2 changes.

20. ***DAB*** substrate solution (prepared by diluting 1 drop of Diamino benzidine chromogen to 1 ml of DAB buffer) is then applied on the sections for 8 minutes. (DAB is cleaved by the enzyme to give the colored product at antigen sites)

21. The slides are washed with phosphate buffer solution for 5 minutes x 2 changes.

22. The slides are washed well in running tap water for 5 minutes.

23. The sections are counterstained with Hematoxylin stain for 2 seconds (1 dip).

24. The slides are washed in running tap water for 3 minutes.

25. The slides are air dried, cleared with xylene and mounted with DPX.

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MASTER CHART 1

S.NO	B.NO	AGE	SEX	DIAG	PROCEDURE	NON-NEOPLASTIC	BENIGN	MALIGNANT	VARIANTS	GRADE	FNAC	USG	CK 19	GAL 3
1	6292/14	30	F	SNT -R	HEMITHYROIDECTOMY			PAPILLARY CA	CONV-UNICENT	LOW		SNT	3+	3+
2	6346/14	44	F	SNT	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE					NCG			
3	6518/14	17	F	SNT	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE						SNT-L		
4	8325/14	37	F	SNT-L	HEMITHYROIDECTOMY	NCG+ AH								
5	8378/14	40	F	SNT-L	HEMITHYROIDECTOMY	NCG+ AH								
6	8458/14	57	F	SNT-R	TOTAL THYROIDECTOMY	NCG+ AH								
7	9189/14	25	F	SNT-L	HEMITHYROIDECTOMY	ADENOMATOUS GOITRE								
8	9535/14	42	F	SNT-L	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE								
9	9616/14	54	F	SNT-R	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE								
10	9619/14	52	F	SNT-R	TOTAL THYROIDECTOMY	NCG+ AH								
11	9884/14	26	F	SNT-R	TOTAL THYROIDECTOMY	NCG								
12	10018/14	30	F	SNT-L	TOTAL THYROIDECTOMY	NCG+ AH								
13	10027/14	45	F	SNT-R	TOTAL THYROIDECTOMY	NCG								
14	10441/14	40	F	SNT-L	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE								
15	10459/14	69	M	SNT	HEMITHYROIDECTOMY			PAPILLARYCA	CONV-UNI	LOW			3+	3+
16	10579/14	47	F	SNT-L	HEMITHYROIDECTOMY	NCG								
17	10558/14	59	F	SNT-L	TOTAL THYROIDECTOMY	NCG								
18	10665/14	34	F	SNT-L	TOTAL THYROIDECTOMY			PAPILLARY CA	CONV-UNI	LOW			3+	2+
19	10828/14	38	F	SNT	TOTAL THYROIDECTOMY	NCG								
20	11205/14	30	M	SNT	TOTAL THYROIDECTOMY	NCG+ AH								
21	11382/14	38	F	SNT	TOTAL THYROIDECTOMY			PAPILLARY CA	CON-UNI	LOW			3+	2+
22	11777/14	18	F	SNT-L	HEMITHYROIDECTOMY	ADENOMATOUS GOITRE								
23	11812/14	38	F	SNT	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE								
24	11828/14	34	F	SNT	TOTAL THYROIDECTOMY	NCG+ AH								
25	11979/14	21	F	SNT	TOTAL THYROIDECTOMY	NCG+ AH								
26	106/15	45	F	SNT	TOTAL THYROIDECTOMY	NCG								
27	126/15	50	F	SNT	TOTAL THYROIDECTOMY	NCG								
28	235/15	30	F	SNT	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE								
29	484/15	28	F	SNT-R	TOTAL THYROIDECTOMY	NCG					NCG	SNT		
30	490/15	44	M	SNT-L	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE					PAP	SNT		
31	645/15	25	F	SNT-R	TOTAL THYROIDECTOMY	NCG								
32	859/15	55	F	SNT	HEMITHYROIDECTOMY	NCG+ AH								
33	930/15	30	F	SNT-L	TOTAL THYROIDECTOMY	NCG WITH CYSTIC CHANGE					NCG WITH	SNT		
34	**1416/15**	**44**	**M**	**SNT**	**TOTAL THYROIDECTOMY**			**MEDULLARY CA**			**?FOLLICU**	**LAR CARC**	**2+**	**1+**
35	1432/15	53	F	SNT-L	HEMITHYROIDECTOMY	NCG								
36	1463/15	44	F	SNT-R	TOTAL THYROIDECTOMY	NCG+PAPILLARY HYPERPLASIA								
37	1484/15	26	F	SNT	HEMITHYROIDECTOMY	NCG								
38	1629/15	34	M	SNT	TOTAL THYROIDECTOMY	NCG+ AH								
39	1763/15	44	F	SNT	TOTAL THYROIDECTOMY	HASHI								
40	**1928/15**	**67**	**M**	**SNT-R**	**TOTAL THYROIDECTOMY**		**HURTHLE CELL ADENOMA**				**HURTHLE**	**CELL NEO**	**1+**	**1+**
41	2009/15	27	F	SNT-R	TOTAL THYROIDECTOMY			PAPILLARY CA	CONV-MULTI	LOW	PAP	SNT		
42	2315/15	48	M	SNT	HEMITHYROIDECTOMY	NCG+ AH								
43	2332/15	37	F	SNT-L	HEMITHYROIDECTOMY	ADENOMATOUS GOITRE								
44	2334/15	67	F	SNT-L	TOTAL THYROIDECTOMY	NCG WITH CYSTIC CHANGE								
45	**2490/15**	**65**	**F**	**SNT**	**TOTAL THYROIDECTOMY**		**HURTHLE CELL ADENOMA**						**NEGETIVE**	**NEGATIVE**
46	**2708/15**	**34**	**F**	**SNT**	**TOTAL THYROIDECTOMY**			**PAPILLARY CA**	**FOLLICULAR**		**PAP**	**SNT**	**3+**	**3+**
47	2751/15	35	F	SNT	TOTAL THYROIDECTOMY	NCG+AH								
48	2904/15	33	F	SNT-L	TOTAL THYROIDECTOMY			PAPILLARY CA	CONV	LOW			3+	3+
49	2987/15	65	F	SNT-R	TOTAL THYROIDECTOMY			PAPILLARY CA	CONV-UNI	LOW	S/O PAP	SNT	3+	3+
50	3114/15	59	F	SNT	TOTAL THYROIDECTOMY	NCG								
51	3155/15	45	M	SNT-L	TOTAL THYROIDECTOMY			PAPILLARY CA	CONV	LOW			3+	3+
52	**3162/15**	**50**	**F**	**SNT**	**TOTAL THYROIDECTOMY**		**HURTHLE CELL ADENOMA**						**2+**	**NEGATIVE**
53	3166/15	65	F	SNT-R	TOTAL THYROIDECTOMY	NCG+AH								
54	3216/15	20	F	SNT	HEMITHYROIDECTOMY	NCG								
55	3300/15	35	F	SNT-R	TOTAL THYROIDECTOMY	NCG								
56	3315/15	38	F	SNT-L	TOTAL THYROIDECTOMY	NCG								
57	3363/15	42	F	SNT-L	TOTAL THYROIDECTOMY		FOLLICULAR ADENOMA				NCG		NEGATIVE	NEGATIVE

58	3571/15	50	F	SNT-R	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE								
59	**3618/15**	**24**	**F**	**SNT**	**TOTAL THYROIDECTOMY**			**PAPILLARY CA**	**FOLLICULAR**	**LOW**	**?FA**		**3+**	**2+**
60	3672/15	30	F	SNT-R	HEMITHYROIDECTOMY	NCG								
61	3964/15	45	M	SNT-R	TOTAL THYROIDECTOMY	NCG+AH								
62	3983/15	14	F	SNT-R	HEMITHYROIDECTOMY	NCG								
63	4164/15	43	M	SNT-R	TOTAL THYROIDECTOMY			PAPILLARY CA	CONV	LOW	PAP	SNT-R	3+	3+
64	4566/15	32	F	SNT	TOTAL THYROIDECTOMY	COLLOID NODULE								
65	4688/15	20	F	SNT-R	TOTAL THYROIDECTOMY			PAPILLARY CA	CON-MULTI	LOW	PAP	SNT-R	3+	2+
66	**4872/15**	**17**	**M**	**SNT-L**	**TOTAL THYROIDECTOMY**			**MEDULLARY CA**			**NCG**	**SNT-L**	**3+**	**2+**
67	4921/15	58	F	SNT-L	HEMITHYROIDECTOMY	NCG								
68	5255/15	31	F	SNT-R	TOTAL THYROIDECTOMYNCG									
69	5342/15	53	F	SNT-R	TOTAL THYROIDECTOMY	NCG+AG								
70	5351/15	30	F	SNT-R	TOTAL THYROIDECTOMY	NCG								
71	5655/15	19	F	SNT-R	HEMITHYROIDECTOMY	ADENOMATOUS GOITRE								
72	5896/15	70	F	SNT-R	TOTAL THYROIDECTOMY	NCG								
73	5906/15	25	M	SNT-R	TOTAL THYROIDECTOMY	COLLOID NODULE								
74	5910/15	50	M	SNT-R	TOTAL THYROIDECTOMY	ADENOMATOUS HYPERPLASIA								
75	5911/15	47	F	SNT-R	HEMITHYROIDECTOMY	NCG								
76	5985/15	29	F	SNT-R	TOTAL THYROIDECTOMY	ADENOMATOUS HYPERPLASIA								
77	5994/15	15	F	SNT-R	TOTAL THYROIDECTOMY			PAPILLARY CA			ADENOMA	SNT	3+	2+
78	6156/15	20	F	SNT-L	TOTAL THYROIDECTOMY	NCG								
79	6246/15	25	F	SNT-L	TOTAL THYROIDECTOMY			MEDULLARY CA			NCG	SNT		
80	6394/15	27	F	SNT-L	HEMITHYROIDECTOMY	NCG+AH								
81	6435/15	44	F	SNT-L	HEMITHYROIDECTOMY	COLLOID NODULE								
82	6715/15	20	F	SNT-R	TOTAL THYROIDECTOMY	ADENOMATOUS HYPERPLASIA								
83	6857/15	35	F	SNT-R	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE							NEGATIVE	NEGATIVE
84	6907/15	57	F	SNT-L	TOTAL THYROIDECTOMY	NCG WITH CYSTIC CHANGE								
85	6908/15	30	F	SNT-R	HEMITHYROIDECTOMY	NCG+AH								
86	7405/15	28	F	SNT	TOTAL THYROIDECTOMY	NCG+AH								
87	7582/15	26	F	SNT-R	HEMITHYROIDECTOMY	NCG								
88	7591/15	34	F	SNT-R	TOTAL THYROIDECTOMY	NCG							NEGATIVE	NEGATIVE
89	7655/15	35	F	SNT-L	TOTAL THYROIDECTOMY	NCG+AH								
90	7697/15	33	F	SNT	TOTAL THYROIDECTOMY	NCG WITH CYSTIC CHANGE					NCG WITH	CYSTIC CH	ANGE	
91	7826/15	48	F	SNT-R	TOTAL THYROIDECTOMY	NCG+AH								
92	**7894/15**	**24**	**F**	**SNT-R**	**TOTAL THYROIDECTOMY**			**PAPILLARY CA**	**CONV-UNI**	**LOW**	**PAP.CA**	**CA.THYRO**	**3+**	**2+**
93	7990/15	40	F	SNT-R	HEMITHYROIDECTOMY	NCG WITH CYSTIC CHANGE					NCG			
94	8126/15	19	F	SNT-R	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE							NEGATIVE	NEGATIVE
95	8375/15	50	F	SNT-R	TOTAL THYROIDECTOMY	COLLOID NODULE								
96	8382/15	43	F	SNT-L	HEMITHYROIDECTOMY	NCG								
97	8562/15	45	F	SNT-L	HEMITHYROIDECTOMY	NCG								
98	8587/15	22	F	SNT-L	TOTAL THYROIDECTOMY	NCG WITH CYSTIC CHANGE								
99	**8592/15**	**24**	**F**	**SNT**	**TOTAL THYROIDECTOMY**	**AG+PAP.HYPERPLASIA**							**2+**	**NEGATIVE**
100	8678/15	36	F	SNT-R	TOTAL THYROIDECTOMY	NCG WITH CYSTIC CHANGE								
101	8721/15	25	F	SNT-R	TOTAL THYROIDECTOMY	NCG WITH CYSTIC CHANGE								
102	8723/15	21	F	SNT-R	HEMITHYROIDECTOMY	NCG					NCG			
103	8727/15	41	F	SNT-L	TOTAL THYROIDECTOMY	NCG WITH CYSTIC CHANGE					NCG			
104	**8766/15**	**57**	**F**	**SNT**	**TOTAL THYROIDECTOMY**			**PAPILLARY.CA**	**WARTHIN**		**NCG**	**SNT**	**NEGATIVE**	**NEGATIVE**
105	8929/15	40	F	SNT-R	TOTAL THYROIDECTOMY	ADENOMATOUS NODULE								
106	9150/15	40	F	SNT	TOTAL THYROIDECTOMY	NCG+AH								
107	9215/15	45	F	SNT-L	TOTAL THYROIDECTOMY	NCG WITH CYSTIC CHANGE								
108	9229/15	40	F	SNT-L	TOTAL THYROIDECTOMY	NCG+AH					?FOLLICUL	SNT		
109	9363/15	28	F	SNT-R	HEMITHYROIDECTOMY	NCG								
110	9435/15	40	M	SNT	TOTAL THYROIDECTOMY			**PAPILLARY.CA**	CON	LOW	PAP	SNT	3+	3+
111	**9472/15**	**66**	**F**	**SNT**	**TOTAL THYROIDECTOMY**			**PAPILLARY.CA**	**CON-MULTI**	**LOW**	**PAP**	**CA**	**3+**	**2+**
112	9514/15	30	F	SNT	TOTAL THYROIDECTOMY	NCG					S/O MALI			
113	9618/15	51	F	SNT-L	TOTAL THYROIDECTOMY	NCG					NCG			
114	9661/15	60	F	SNT-R	TOTAL THYROIDECTOMY			**PAPILLARY.CA**	CONV-MULTI	LOW	PAP.CA	SNT	3+	2+
115	9717/15	47	F	SNT-R	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE								
116	9751/15	50	F	SNT-R	TOTAL THYROIDECTOMY		HURTHLE CELL ADENOMA						1+	NEGATIVE
117	9989/15	48	M	SNT-L	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE					PAP	SNT		

118	10238/15	28	F	SNT-R	TOTAL THYROIDECTOMY			**PAPILLARY.CA**	UNI	LOW	PAP	SNT-R	2+	2+
119	10376/15	25	F	SNT-R	TOTAL THYROIDECTOMY	COLLOID NODULE								
120	10497/15	25	F	SNT-R	TOTAL THYROIDECTOMY			**PAPILLARY.CA**	CONV-MULTI	LOW	S/O MALI		3+	3+
121	10532/15	50	M	SNT-L	TOTAL THYROIDECTOMY	NCG+AH								
122	**10626/15**	**46**	**F**	**SNT-R**	**TOTAL THYROIDECTOMY**			**PAPILLARY.CA**	**CONV-UNI**	**LOW**	**PAP**	**SNT**	**3+**	**3+**
123	**10776/15**	**30**	**F**	**SNT-L**	**TOTAL THYROIDECTOMY**			**PAPILLARY.CA**	**CONV-MULTI**				**3+**	**3+**
124	10807/15	35	F	SNT-L	TOTAL THYROIDECTOMY	NCG+PAPILLARY HYPERPLASIA								
125	10847/15	45	F	SNT-L	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE								
126	**10864/15**	**68**	**F**	**SNT**	**TOTAL THYROIDECTOMY**			**INSULAR CA**	**MULTICENTRIC**				**NEGATIVE**	**NEGATIVE**
127	11103/15	44	F	SNT-R	TOTAL THYROIDECTOMY	NCG+AH								
128	11127/15	40	F	SNT-L	TOTAL THYROIDECTOMY	NCG+PAPILLARY HYPERPLASIA								
129	**11268/15**	**19**	**M**	**SNT-L**	**TOTAL THYROIDECTOMY**		**FOLLICULAR ADENOMA**						**2+**	**NEGATIVE**
130	65/16	35	M	SNT-R	HEMITHYROIDECTOMY	NCG WITH CYSTIC CHANGE								
131	504/16	38	F	SNT	TOTAL THYROIDECTOMY	COLLOID GOITRE								
132	781/16	50	F	SNT-R	TOTAL THYROIDECTOMY	NCG WITH CYSTIC CHANGE								
133	834/16	45	F	SNT	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE								
134	963/16	44	F	SNT-R	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE								
135	985/16	35	F	SNT	TOTAL THYROIDECTOMY	NCG+AH								
136	1018/16	31	F	SNT	HEMITHYROIDECTOMY	ADENOMATOUS GOITRE								
137	1065/16	60	F	SNT-L	TOTAL THYROIDECTOMY	NCG WITH CYSTIC CHANGE								
138	1072/16	21	F	SNT-L	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE								
139	1212/16	27	F	SNT	TOTAL THYROIDECTOMY	NCG								
140	1229/16	20	F	SNT-R	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE								
141	1323/16	32	F	SNT	HEMITHYROIDECTOMY	NCG								
142	**1566/16**	**41**	**F**	**SNT**	**TOTAL THYROIDECTOMY**	**ADENOMATOUS GOITRE**							**NEGATIVE**	**NEGATIVE**
143	1567/16	46	F	SNT	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE								
144	**1603/16**	**70**	**F**	**SNT-R**	**TOTAL THYROIDECTOMY**			**ANAPLASTIC.CA**	**MULTICENTRIC**		**FOLLICULAR NEOPL**		**3+**	**2+**
145	**1644/16**	**29**	**F**	**SNT**	**TOTAL THYROIDECTOMY**	**ADENOMATOUS GOITRE**							**NEGATIVE**	**NEGATIVE**
146	1712/16	26	F	SNT-R	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE								
147	1809/16	38	F	SNT	TOTAL THYROIDECTOMY	HASHI								
148	2012/16	42	F	SNT	TOTAL THYROIDECTOMY	NCG WITH CYSTIC CHANGE								
149	2073/16	45	F	SNT-R	HEMITHYROIDECTOMY	NCG								
150	2142/16	43	F	SNT	TOTAL THYROIDECTOMY	COLLOID GOITRE								
151	2145/16	61	M	SNT	TOTAL THYROIDECTOMY	NCG								
152	**2168/16**	**27**	**F**	**SNT-R**	**HEMITHYROIDECTOMY**			**PAPILLARY CA**	**CONV-MULTI**			**SNT**	**3+**	**3+**
153	2279/16	30	F	SNT-L	HEMITHYROIDECTOMY	ADENOMATOUS GOITRE								
154	**2282/16**	**58**	**F**	**SNT**	**TOTAL THYROIDECTOMY**			**PAPILLARY.CA**	**FOLLICULAR**		**NCG**		**2+**	**2+**
155	2363/16	45	F	SNT-L	TOTAL THYROIDECTOMY	NCG WITH CYSTIC CHANGE								
156	2366/16	50	F	SNT-R	TOTAL THYROIDECTOMY	NCG								
157	2477/16	43	F	SNT-L	TOTAL THYROIDECTOMY	NCG								
158	2600/16	41	F	SNT-R	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE								
159	**2704/16**	**35**	**F**	**SNT-L**	**TOTAL THYROIDECTOMY**		**FOLLICULAR ADENOMA**				**FOLLICUL**	**?FOLLICU**	**NEGATIVE**	**NEGATIVE**
160	**2809/16**	**46**	**F**	**SNT**	**TOTAL THYROIDECTOMY**		**FOLLICULAR ADENOMA**						**NEGATIVE**	**NEGATIVE**
161	**3011/16**	**37**	**F**	**SNT-R**	**TOTAL THYROIDECTOMY**	**NCG+AH**							**2+**	**NEGATIVE**
162	**3189/16**	**50**	**F**	**SNT**	**TOTAL THYROIDECTOMY**			**PAPILLARY.CA**	**FOLLICULAR**				**2+**	**2+**
163	**3361/16**	**37**	**F**	**SNT**	**TOTAL THYROIDECTOMY**		**FOLLICULAR ADENOMA**						**NEGATIVE**	**NEGATIVE**
164	**3446/16**	**50**	**F**	**SNT-R**	**TOTAL THYROIDECTOMY**		**FOLLICULAR ADENOMA**						**NEGATIVE**	**NEGATIVE**
165	3448/16	27	F	SNT-R	TOTAL THYROIDECTOMY	NCG WITH CYSTIC CHANGE								
166	**3570/16**	**46**	**M**	**SNT**	**TOTAL THYROIDECTOMY**		**FOLLICULAR ADENOMA**						**2+**	**1+**
167	**3629/16**	**22**	**M**	**SNT**	**TOTAL THYROIDECTOMY**	**ADENOMATOUS GOITRE**							**NEGATIVE**	**NEGATIVE**
168	**3685/16**	**30**	**F**	**SNT**	**TOTAL THYROIDECTOMY**		**FOLLICULAR ADENOMA**						**NEGATIVE**	**NEGATIVE**
169	**5702/16**	**30**	**F**	**SNT-R**	**TOTAL THYROIDECTOMY**			**PAPILLARY.CA**	**CONV-UNI**	**LOW**	**NCG**	**SNT**	**3+**	**3+**
170	**7004/16**	**35**	**F**	**SNT-R**	**TOTAL THYROIDECTOMY**			**PAPILLARY.CA**	**FOLLICULAR**		NCG		3+	2+

MASTER CHART 2

S.NO	B.NO	AGE	SEX	DIAG	PROCEDURE	NON-NEOPLASTIC	BENIGN	MALIGNANT	VARIANTS	GRADE	FNAC	USG	CK 19	GAL 3
1	6292/14	30	F	SNT -R	HEMITHYROIDECTOMY			PAPILLARY CA	CONV-UNI	LOW		SNT	3+	3+
2	10459/14	69	M	SNT	HEMITHYROIDECTOMY			PAPILLARYCA	CONV-UNI	LOW			3+	3+
3	10665/14	34	F	SNT-L	TOTAL THYROIDECTOMY			PAPILLARY CA	CONV-UNI	LOW			3+	2+
4	11382/14	38	F	SNT	TOTAL THYROIDECTOMY			PAPILLARY CA	CONV-UNI	LOW			3+	2+
5	1416/15	44	M	SNT	TOTAL THYROIDECTOMY			MEDULLARY CA			?FOLLICULAR CARCIN		2+	1+
6	1928/15	67	M	SNT-R	TOTAL THYROIDECTOMY		HURTHLE CELL ADENOMA				HURTHLE CELL NEOPL		1+	1+
7	2490/15	65	F	SNT	TOTAL THYROIDECTOMY		HURTHLE CELL ADENOMA						NEGATIVE	NEGATIVE
8	2708/15	34	F	SNT	TOTAL THYROIDECTOMY			PAPILLARY CA	FOLLICULAR		PAP.CA	SNT	3+	3+
9	2904/15	33	F	SNT-L	TOTAL THYROIDECTOMY			PAPILLARY CA	CONV-UNI	LOW			3+	3+
10	2987/15	65	F	SNT-R	TOTAL THYROIDECTOMY			PAPILLARY CA	CONV-UNI	LOW	S/O PAP	SNT	3+	3+
11	3155/15	45	M	SNT-L	TOTAL THYROIDECTOMY			PAPILLARY CA	CONV-UNI	LOW			3+	3+
12	3162/15	50	F	SNT	TOTAL THYROIDECTOMY		HURTHLE CELL ADENOMA						2+	NEGATIVE
13	3363/15	42	F	SNT-L	TOTAL THYROIDECTOMY		FOLLICULAR ADENOMA				NCG		NEGATIVE	NEGATIVE
14	3618/15	24	F	SNT	TOTAL THYROIDECTOMY			PAPILLARY CA	FOLLICULAR	LOW	?FA		3+	2+
15	4164/15	43	M	SNT-R	TOTAL THYROIDECTOMY			PAPILLARY CA	CONV-MULTI	LOW	PAP.CA	SNT-R	3+	3+
16	4688/15	20	F	SNT-R	TOTAL THYROIDECTOMY			PAPILLARY CA	CONV-MULTI	LOW	PAP.CA	SNT-R	3+	2+
17	4872/15	17	M	SNT-L	TOTAL THYROIDECTOMY			MEDULLARY CA			NCG	SNT-L	3+	2+
18	5994/15	15	F	SNT-R	TOTAL THYROIDECTOMY			PAPILLARY CA			ADENOMA	SNT	3+	2+
19	6857/15	35	F	SNT-R	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE							NEGATIVE	NEGATIVE
20	7591/15	34	F	SNT-R	TOTAL THYROIDECTOMY	NCG							NEGATIVE	NEGATIVE
21	7894/15	24	F	SNT-R	TOTAL THYROIDECTOMY			PAPILLARY CA	CONV-UNI	LOW	PAP.CA	CA.THYROI	3+	2+
22	8126/15	19	F	SNT-R	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE							NEGATIVE	NEGATIVE
23	8592/15	24	F	SNT	TOTAL THYROIDECTOMY	AG+PAP.HYPERPLASIA							2+	NEGATIVE
24	8766/15	57	F	SNT	TOTAL THYROIDECTOMY			PAPILLARY.CA	WARTHIN		NCG	SNT	NEGATIVE	NEGATIVE
25	9435/15	40	M	SNT	TOTAL THYROIDECTOMY			PAPILLARY.CA	CONV-UNI	LOW	PAP.CA	SNT	3+	3+
26	9472/15	66	F	SNT	TOTAL THYROIDECTOMY			PAPILLARY.CA	CONV-MULTI	LOW	PAP.CA	CA	3+	2+
27	9661/15	60	F	SNT-R	TOTAL THYROIDECTOMY			PAPILLARY.CA	CONV-MULTI	LOW	PAP.CA	SNT	3+	2+
28	9751/15	50	F	SNT-R	TOTAL THYROIDECTOMY		HURTHLE CELL ADENOMA						1+	NEGATIVE
29	10238/15	28	F	SNT-R	TOTAL THYROIDECTOMY			PAPILLARY.CA	CONV-UNI	LOW	PAP.CA	SNT-R	2+	2+
30	10497/15	25	F	SNT-R	TOTAL THYROIDECTOMY			PAPILLARY.CA	CONV-MULTI	LOW	S/O MALI		3+	3+
31	10626/15	46	F	SNT-R	TOTAL THYROIDECTOMY			PAPILLARY.CA	CONV-UNI	LOW	PAP.CA	SNT	3+	3+
32	10776/15	30	F	SNT-L	TOTAL THYROIDECTOMY			PAPILLARY.CA	CONV-MULTI				3+	3+
33	10864/15	68	F	SNT	TOTAL THYROIDECTOMY			INSULAR CA	MULTICENTRIC				NEGATIVE	NEGATIVE
34	11268/15	19	M	SNT-L	TOTAL THYROIDECTOMY		FOLLICULAR ADENOMA						2+	NEGATIVE
35	1566/16	41	F	SNT	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE							NEGATIVE	NEGATIVE
36	1603/16	70	F	SNT-R	TOTAL THYROIDECTOMY			ANAPLASTIC.CA	MULTICENTRIC		FOLLICULAR NEOPLAS		3+	2+
37	1644/16	29	F	SNT	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE							NEGATIVE	NEGATIVE
38	2168/16	27	F	SNT-R	HEMITHYROIDECTOMY			PAPILLARY CA	CONV-MULTI			SNT	3+	3+
39	2282/16	58	F	SNT	TOTAL THYROIDECTOMY			PAPILLARY.CA	FOLLICULAR		NCG		2+	2+
40	2704/16	35	F	SNT-L	TOTAL THYROIDECTOMY		FOLLICULAR ADENOMA				FOLLICULA	?FOLLICUL	NEGATIVE	NEGATIVE
41	2809/16	46	F	SNT	TOTAL THYROIDECTOMY		FOLLICULAR ADENOMA						NEGATIVE	NEGATIVE
42	3011/16	37	F	SNT-R	TOTAL THYROIDECTOMY	NCG+AH							2+	NEGATIVE
43	3189/16	50	F	SNT	TOTAL THYROIDECTOMY			PAPILLARY.CA	FOLLICULAR				2+	2+
44	3361/16	37	F	SNT	TOTAL THYROIDECTOMY		FOLLICULAR ADENOMA						NEGATIVE	NEGATIVE
45	3446/16	50	F	SNT-R	TOTAL THYROIDECTOMY		FOLLICULAR ADENOMA						NEGATIVE	NEGATIVE
46	3570/16	46	M	SNT	TOTAL THYROIDECTOMY		FOLLICULAR ADENOMA						2+	1+
47	3629/16	22	M	SNT	TOTAL THYROIDECTOMY	ADENOMATOUS GOITRE							NEGATIVE	NEGATIVE
48	3685/16	30	F	SNT	TOTAL THYROIDECTOMY		FOLLICULAR ADENOMA						NEGATIVE	NEGATIVE
49	5702/16	30	F	SNT-R	TOTAL THYROIDECTOMY			PAPILLARY.CA	CONV-UNI	LOW	NCG	SNT	3+	3+
50	7004/16	35	F	SNT-R	TOTAL THYROIDECTOMY			PAPILLARY.CA	FOLLICULAR		NCG		3+	2+

KEY TO MASTER CHART

SNT	SOLITARY NODULE THYROID
SNT-R	SOLITARY NODULE THYROID-RIGHT LOBE
SNT-L	SOLITARY NODULE THYROID -LEFT LOBE
M	MALE
F	FEMALE
NCG	NODULAR COLLOID GOITRE
AH	ADENOMATOUS HYPERPLASIA
PH	PAPILLARY HYPERPLASIA
AG	ADENOMATOUS GOITRE
CA	CARCINOMA
CONV	CONVENTIONAL
UNI	UNICENTRIC
MULTI	MULTICENTRIC
FNAC	FINE NEEDLE ASPIRATION CYTOLOGY
USG	ULTRASONOGRAM
1+	WEAK STAINING
2+	MODERATE
3+	STRONG
PAP.CA	PAPILLARY CARCINOMA
FA	FOLLICULAR ADENOMA

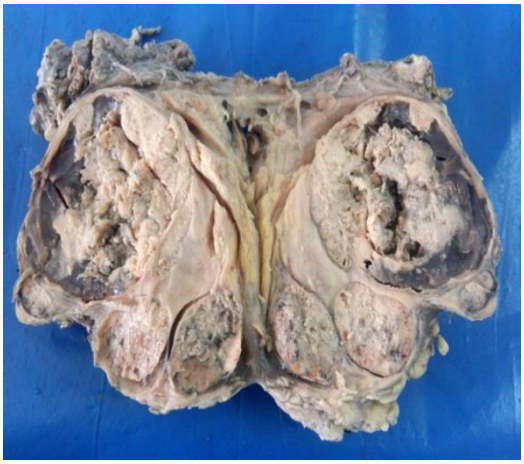

Fig.1 Gross appearance of Papillary Carcinoma

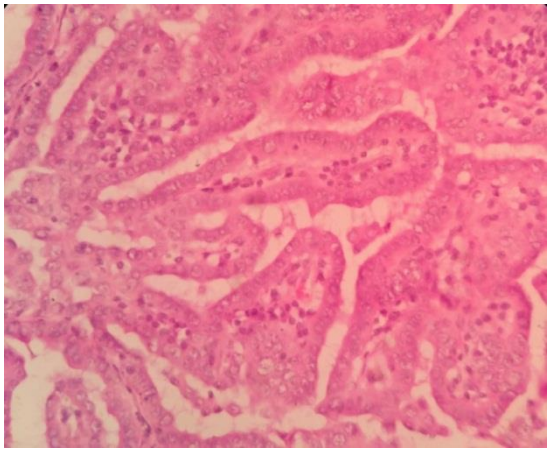

Fig.2 Conventional type of PTC with arborizing papillary process (H&E,100x)

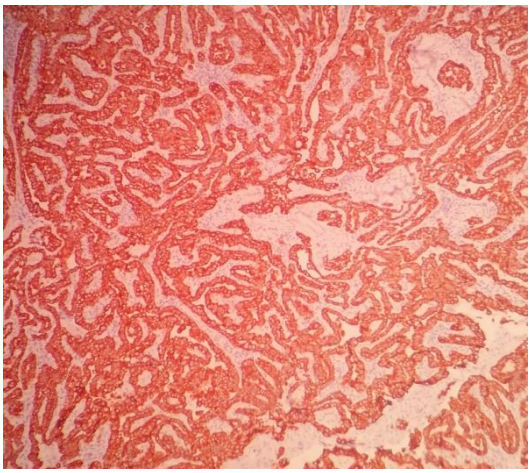

Fig.3 CK19 strong immunoreactivity in conventional type of PTC (40x)

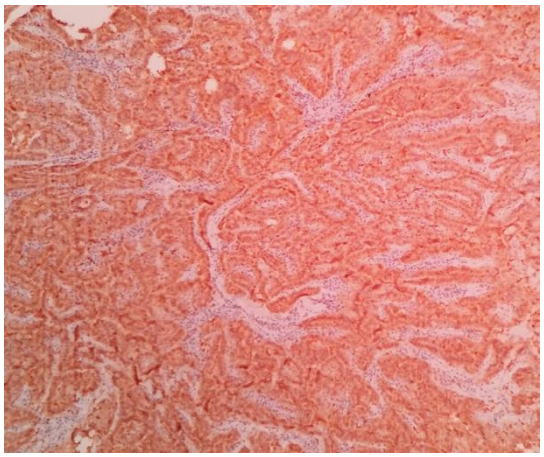

Fig.4 Galectin3 strong immunoreactivity in conventional type of PTC (40x)

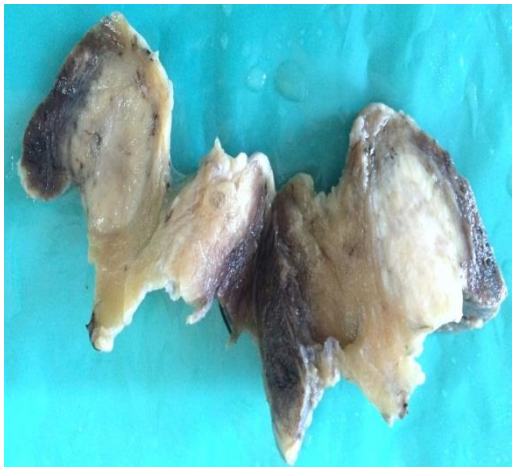

Fig.5 Macroscopic appearance of follicular variant of PTC

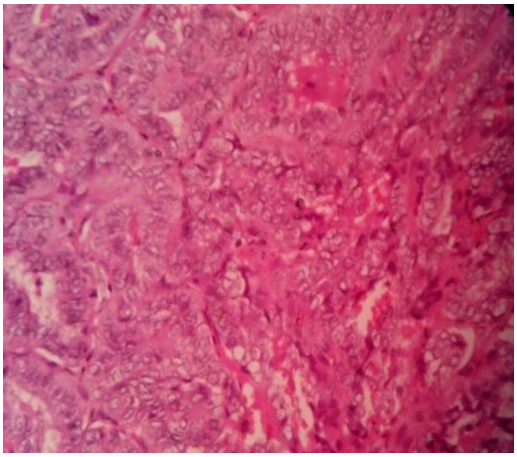

Fig.6 Microscopy showing predominantly follicular pattern (H&E, 100x)

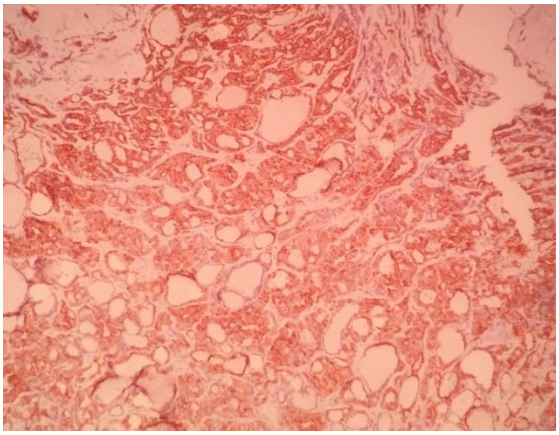

Fig.7 CK19 strong positivity in FVPTC (40x)

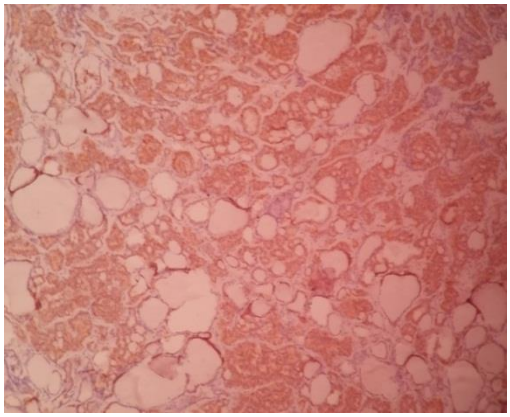

Fig.8 Galectin3 moderate positivity in FVPTC (40x)

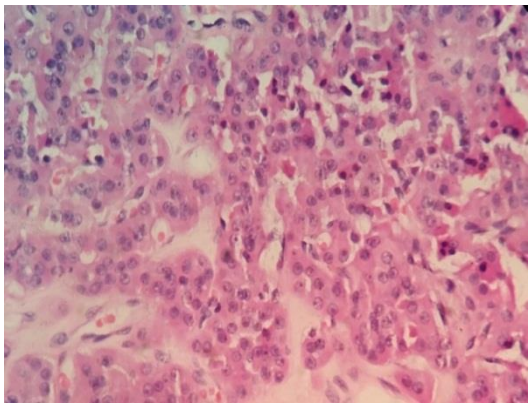

Fig. 9 Microscopic appearance of warthin variant of papillary carcinoma(H&E,100X)

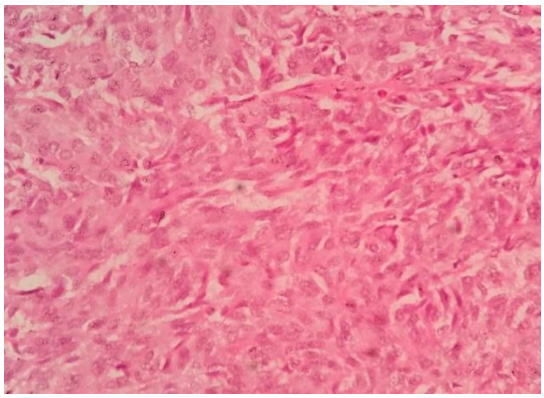

Fig.12. Medullary carcinoma showing sheets of polygonal to spindle cells (H&E,100X)

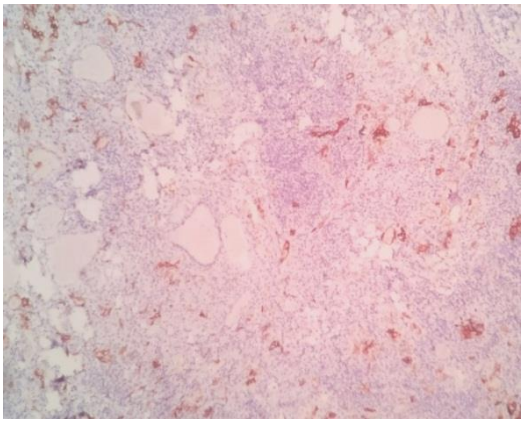

Fig. 10 CK19 negativity in warthin variant of papillary carcinoma (40x)

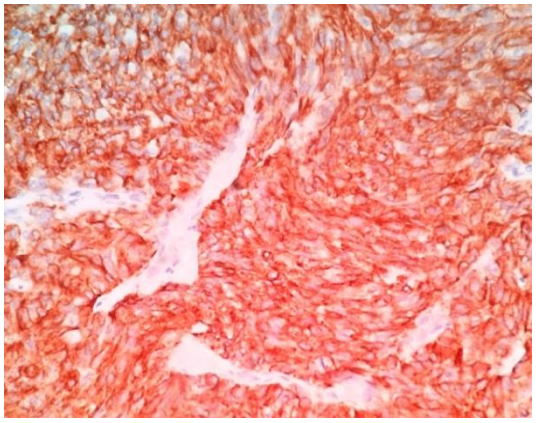

FIG.13.CK19 strong immunoreactivity in medullary carcinoma(40x)

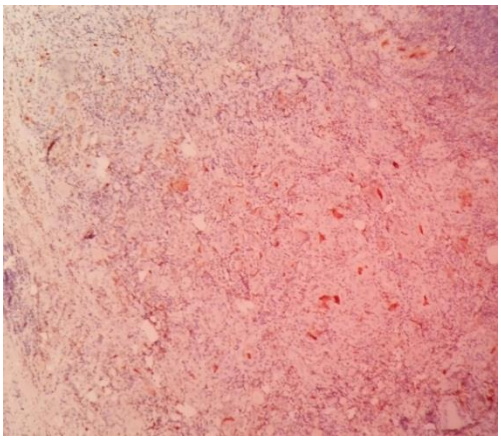

Fig. 11 Galectin3 negativity in warthin variant of papillary carcinoma (40x)

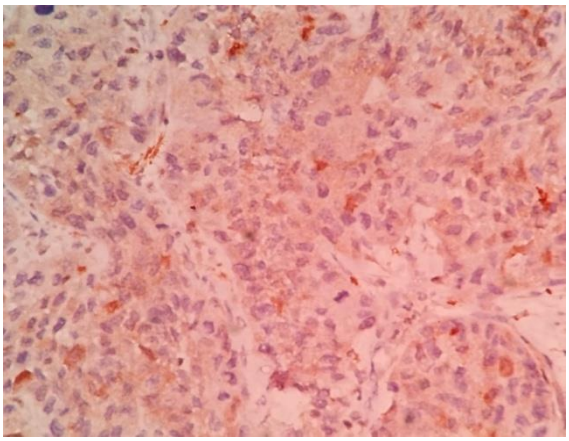

Fig.14 Galectin 3 moderate immunoreactivity in Medullary carcinoma(100x)

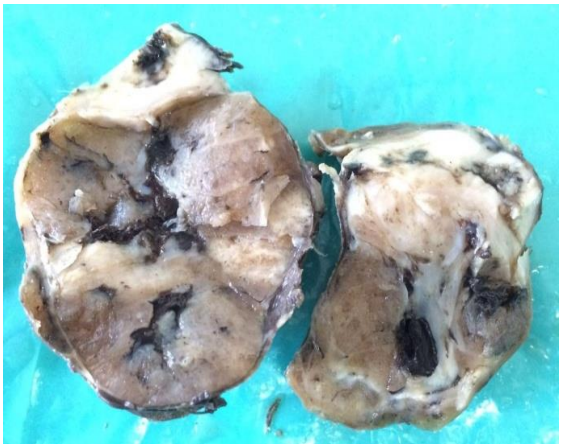

Fig.15. Gross appearance of Anaplastic carcinoma

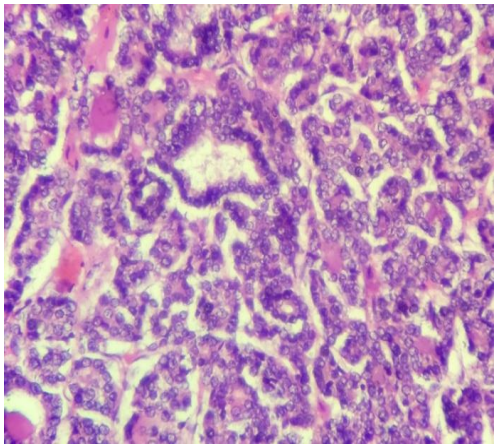

Fig.16. Microscopic appearance of Anaplastic carcinoma (100x)

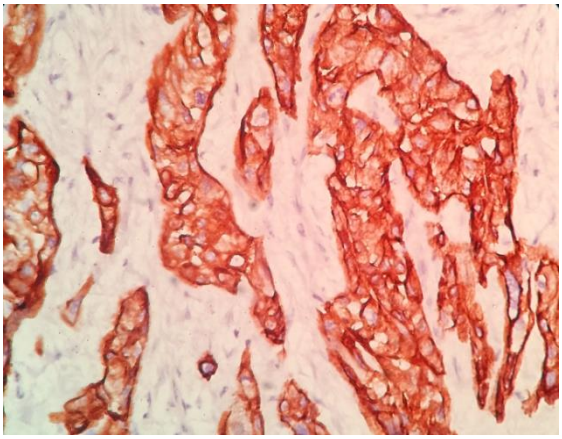

Fig.17.CK19 strong immunoreactivity in Anaplastic carcinoma(100x)

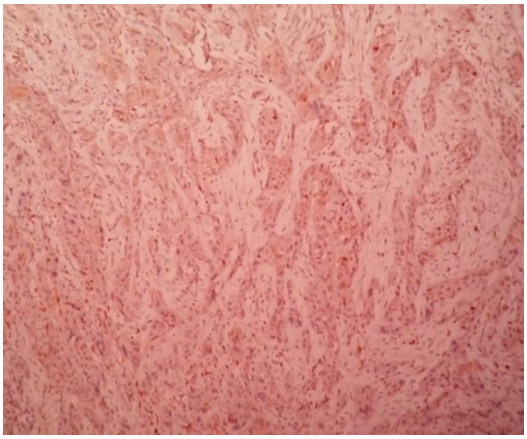

Fig.18. Galectin 3 moderate immunoreactivity in Anaplastic carcinoma(40x)

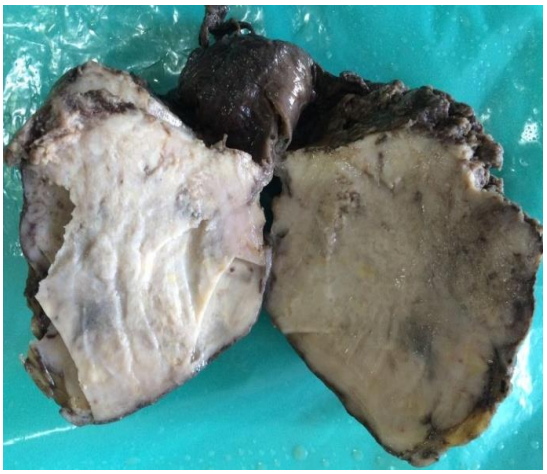

FIG.19.Gross appearance of insular carcinoma

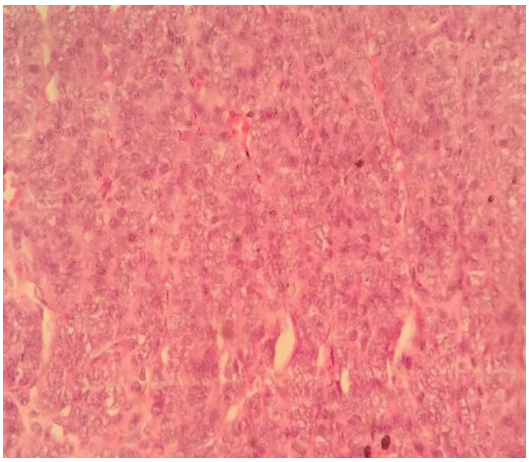

Fig.20. microscopic appearance of insular carcinoma(H&E,100X)

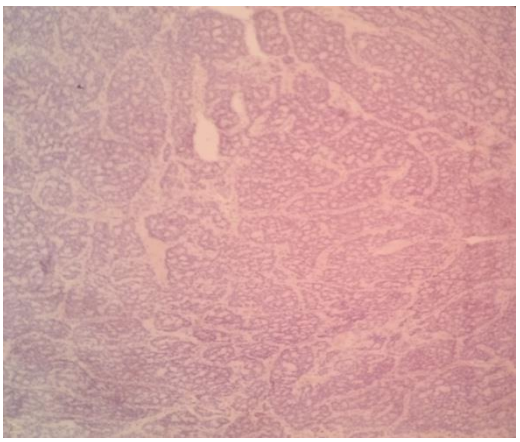

FIG.21.CK19 negativity in insular carcinoma (40x)

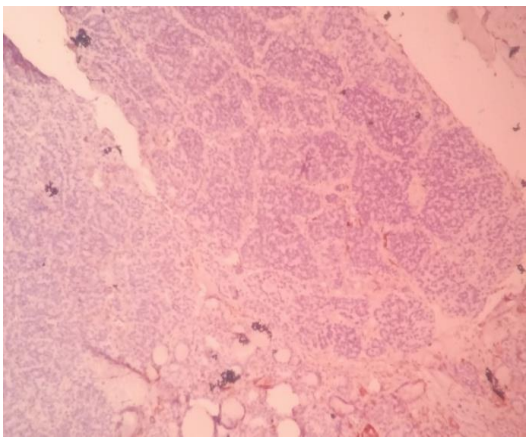

Fig.22 Galectin 3 negativity in insular carcinoma (40x)

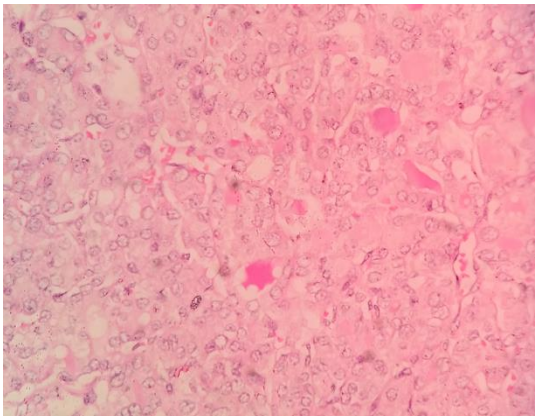

Fig.23. microscopic appearance of adenomatous hyperplasia (H&E,100X)

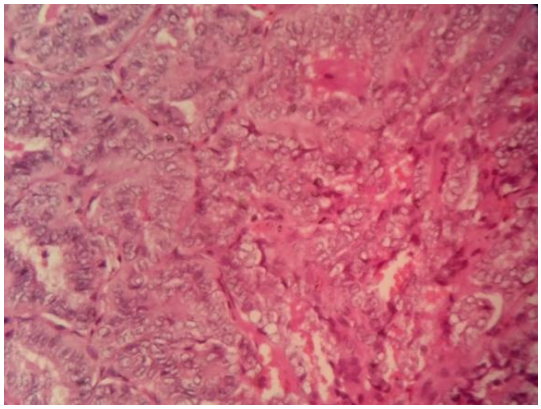

Fig.26.Microscopic Appearance of papillary hyperplasia (H&E,100X)

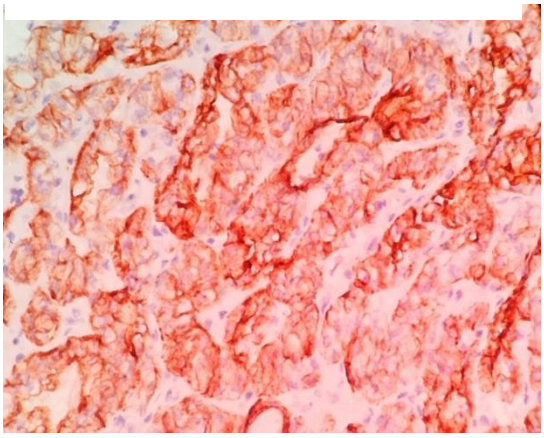

FIG.24. CK19 strong immunoreactivity in adenomatous hyperplasia(100x)

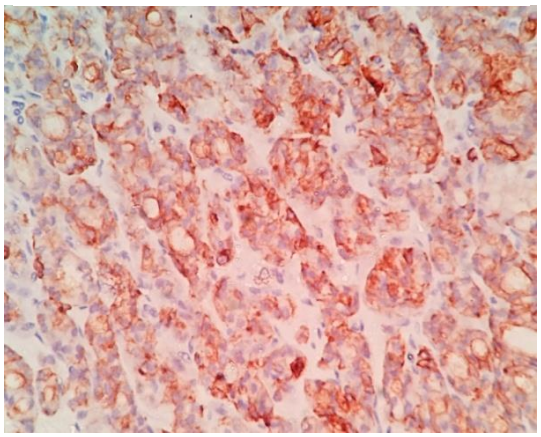

FIG.27.CK19 MODERATE immunoreactivity in papillary hyperplasia(100x)

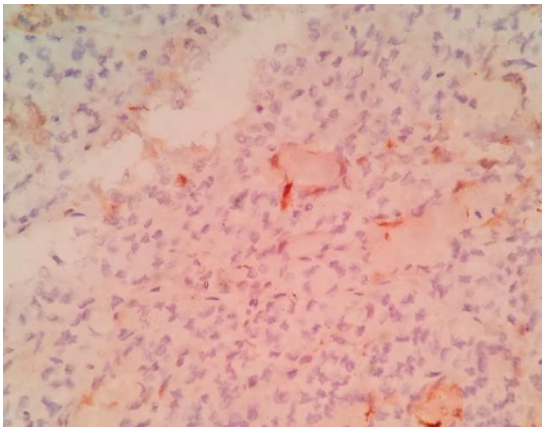

Fig.25.Galectin3 negativity in Adenomatous hyperplasia(100x)

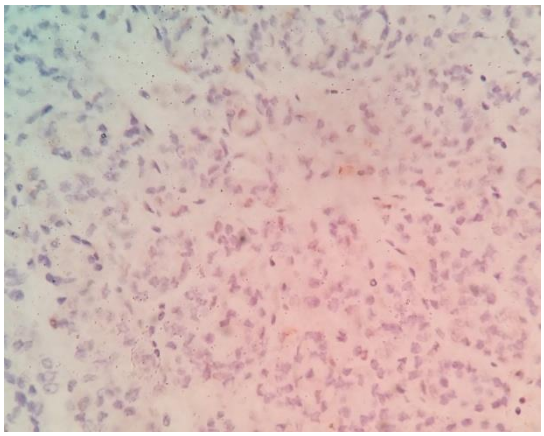

Fig.28. Galectin 3 negativity in papillary hyperplasia (100x)