HISTOMORPHOLOGICAL STUDY OF THYROID NEOPLASMS WITH SPECIAL REFERENCE TO PAPILLARY THYROID CARCINOMA AND ITS NEOPLASTIC HISTOLOGICAL MIMICKERS

Dissertation submitted in partial fulfilment of the requirements for the degree of

M.D. (PATHOLOGY)

BRANCH - III

INSTITUTE OF PATHOLOGY AND ELECTRON MICROSCOPY,

MADRAS MEDICAL COLLEGE,

CHENNAI – 600 003.

THE TAMIL NADU

DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI

APRIL 2012

CERTIFICATE

This is to certify that this dissertation titled **"HISTOMORPHOLOGICAL STUDY OF THYROID NEOPLASMS WITH SPECIAL REFERENCE TO PAPILLARY THYROID CARCINOMA AND ITS NEOPLASTIC HISTOLOGICAL MIMICKERS"** is a bonafide original work of **Dr. R. VIMAL CHANDER** under my direct guidance and supervision, in partial fulfilment of the requirement for M.D., (Branch III) in Pathology examination of the Tamil Nadu Dr. M.G.R Medical University to be held in April 2012.

DEAN:

Prof. Dr. V. KANAGASABAI, M.D.,
Dean,
Madras Medical College and
Government General Hospital,
Chennai – 600003.

DIRECTOR & GUIDE:

Prof. Dr. A. SUNDARAM, M.D.,
Director and Professor,
Institute of Pathology
and Electron Microscopy,
Madras Medical College,
Chennai – 600003.

DECLARATION

I, Dr. Vimal Chander, solemnly declare that this dissertation titled **"HISTOMORPHOLOGICAL STUDY OF THYROID NEOPLASMS WITH SPECIAL REFERENCE TO PAPILLARY THYROID CARCINOMA AND ITS NEOPLASTIC HISTOLOGICAL MIMICKERS"** is the bonafide work done by me under the expert guidance and supervision of **Prof. Dr. A. SUNDARAM, M.D.,** Director and Professor, Institute of Pathology and Electron Microscopy, Madras Medical College, Chennai – 3. This dissertation is submitted to the Tamil Nadu Dr. M.G.R Medical University towards partial fulfilment of requirement for the award of M.D., Degree (Branch III) in Pathology.

Place: Chennai

Date: **Dr. R. VIMAL CHANDER**

ACKNOWLEDGEMENT

I express my sincere thanks to Prof. Dr. **V. KANAGASABAI, M.D.**, Dean, Madras Medical College and Government General Hospital, for permitting me to utilize the facilities of the Institution.

I take this opportunity to express my heartfelt sincere gratitude to my respected teacher and esteemed guide, **Prof. Dr. A. SUNDARAM, M.D.,** Professor and Director of Institute of Pathology and Electron Microscopy, Madras Medical College, Chennai for his keen interest, constant encouragement, wholehearted support, expert guidance and valuable suggestions throughout the study.

I express my sincere thanks to **Prof. Dr. P. KARKUZHALI, M.D.**, Professor of Pathology, Institute of Pathology and Electron Microscopy, Madras Medical College for her advice, encouragement and suggestions during the study.

I express my heartfelt thanks to **Prof. Dr. SHANTHA RAVISANKAR, M.D.,** Professor of Neuropathology, Institute of Neurology, Madras Medical College for her valuable advice, timely suggestions and constant encouragement throughout the study.

I am truly thankful to **Prof. Dr. GEETHA DEVADAS, M.D., D.C.P.,** Professor of Pathology, Institute of Pathology and Electron Microscopy, Madras Medical College for her constant cheer, suggestions and support throughout the study.

I take the opportunity to express my thanks to **Prof. Dr. SUDHA VENKATESH, M.D.,** Professor of Pathology, Institute of Pathology and Electron Microscopy, Madras Medical College for her valuable opinions and encouragement throughout the study.

I am extremely thankful to **Prof. Dr. T. CHITRA, M.D.,** Professor of Pathology, Institute of Child Health, Madras Medical College, for her constant encouragement and valuable suggestions and aid during the study period.

I express my thanks to **Prof. Dr. M. P. KANCHANA, M.D.,** Professor of Pathology, Institute of Obstetrics & Gynecology, Madras Medical College for her constant encouragement and opinions about the study.

I convey my thanks to **Prof. Dr. K. RAMA, M.D.,** Professor of Pathology, Govt. Kasturba Gandhi Hospital, Madras Medical College for her suggestions and support during the period of study.

I express my thanks to **Prof. Dr. INDIRA, M.D.,** Professor of Pathology, Regional Institute of Ophthalmology, Madras Medical College, for her encouragement and suggestions during the study.

I express my sincere thanks to all Assistant Professors for their help and suggestions during the study.

I am thankful to all my Colleagues, Friends, Technicians and Staff of the Institute of Pathology and Electron Microscopy, Madras Medical College, Chennai for all their help and support they extended for the successful completion of this dissertation.

ABBREVIATIONS

CASTLE	-	Carcinoma Showing Thymus Like Elements
CD	-	Cluster of Differentiation
CITED1	-	Cbp/p300-interacting transactivator-1
CK19	-	Cytokeratin 19
EFV	-	Encapsulated follicular variant
EMA	-	EMA – Epitlhelial Membrane Antigen
FA	-	Follicular adenoma
FNAC	-	Fine Needle Aspiration Cytology
FTC	-	Follicular thyroid carcinoma
FVPTC	-	Follicular variant of papillary thyroid carcinoma
HBME1	-	Hector Battifora MEsothelial cell-1
HMWCK	-	High Molecular Weight Cytokeratin
HPF	-	High Power Field
HTA	-	Hyalinising trabecular adenoma
HTT	-	Hyalinising trabecular tumour
MIFC	-	Minimally invasive follicular thyroid carcinoma
PDTC	-	Poorly differentiated thyroid carcinoma
PTC	-	Papillary thyroid carcinoma
RET/PTC	-	Rearranged in Transformation/Papillary Thyroid Carcinoma
SETTLE	-	Spindle Epithelial Tumor with Thymus-Like Elements
TCV	-	Tall Call Variant of Papillary thyroid carcinoma

CONTENTS

S. NO.	TITLE	PAGE NUMBER
1.	INTRODUCTION	1
2.	AIMS AND OBJECTIVES	2
3.	REVIEW OF LITERATURE	3
4.	MATERIALS AND METHODS	31
5.	OBSERVATION AND RESULTS	34
6.	DISCUSSION	60
7.	SUMMARY AND CONCLUSION	74
	BIBLIOGRAPHY	
	ANNEXURES	
	MASTER CHART	

INTRODUCTION

Thyroid neoplasms constitute the most common of all endocrine neoplasms and more than 95 % arise from follicular epithelial cells. They encompass a wide variety of benign and malignant tumours. The most common malignant tumour is papillary carcinoma with a frequency of 70 to 85 % with preponderance among young females.

Historically, the identification of papillary carcinoma relied on the presence of papillary architecture. The current accepted diagnosis is based on the nuclear features that include optical clearing, overlapping, nuclear grooves and pseudoinclusions. However, identification of these features remains, at times controversial and the distinction of papillary carcinoma from its histological mimickers such as follicular adenoma and follicular carcinoma may sometimes be difficult.[1]

Despite the propensity for lymphatic dissemination to the cervical lymph nodes, the majority of patients with these tumours, if appropriately treated, have an excellent long term prognosis compared to nonpapillary tumours. Hence it becomes mandatory to diagnose papillary carcinoma correctly for therapeutic purposes and for assessing the prognosis. Immunohistochemistry helps in the circumstances where cytological features do not suffice for differential diagnosis.[2]

The present study aims at histologically classifying all thyroid neoplasms and to study its histomorphological characteristics and to evaluate the expression of immunohistochemical markers such as Cytokeratin 19 and thyroglobulin in cases of papillary thyroid carcinoma and its histological mimickers.

AIMS AND OBJECTIVES

1. To record the incidence of thyroid neoplasms among surgical pathology specimens at Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai.

2. To study the histomorphological characteristics of these neoplasms and subtype them according to the established classification systems.

3. To compare the histomorphological profile of these cases with those reported in literature.

4. To study the expression of immunohistochemical markers – Cytokeratin 19 and thyroglobulin in thyroid neoplasms.

5. To determine the usefulness of immunohistochemistry in differentiating Papillary thyroid carcinoma and its variants from its histological mimickers.

REVIEW OF LITERATURE

Thyroid neoplasms constitute the most common type of endocrine neoplasms and more than 95% arise from follicular epithelial cells while a few arise from parafollicular C cells. The most common benign thyroid neoplasm is follicular adenoma.[3] Malignant tumours of the thyroid are less common but Papillary thyroid carcinoma is the most common type, though rarely other types also occur. The WHO classification of thyroid neoplasms is given in Annexure II.

BENIGN NEOPLASMS

FOLLICULAR ADENOMA

It is the most common thyroid neoplasm and is defined as a benign encapsulated tumour showing evidence of follicular cell differentiation.[4] It occurs most frequently in adults aged 20 to 50 years, more common in females than males.

Grossly, ranging from 1 to 3 cm, well demarcated with a thin intact fibrous capsule with homogenous gray white to red cut surface depending on cellular composition and colloid content.[5] Secondary changes like hemorrhage, calcification or cystic degeneration may be seen. Massive necrosis is sometimes seen as a complication of FNAC.

Microscopically, they are sub-classified according to the architectural differentiation of the follicle and colloid content within the neoplasms.

1. **Trabecular/Embryonal/Solid:** Little follicle formation with little or no colloid resembling the thyroid tissue during prefollicular embryonal stage of intra-uterine life.

2. **Fetal/Microfollicular:** Microfollicles with small amount of colloid.

3. **Simple/Normofollicular:** Well developed follicles with normal colloid content.

4. **Colloid/Macrofollicular:** Large follicles with excess colloid.

5. **Hurthle Cell:** Follicles are lined by Hurthle cells which are large cells with intense eosinophilic granular cytoplasm.

In most instances, more than one architectural patterns are seen in follicular adenoma. There is no clinical significance attributable to the different subtypes of follicular adenoma.

There is a single layer of lining follicular cells with eosinophilic to amphophilic cytoplasm, distinct cell borders, uniform round to oval nuclei. Mitosis is not usually seen.

Follicular adenomas have a complete fibrous capsule varying in thickness. In a study by Koren R et al,[6] utilizing picrosirius orange-red (PSR) staining techniques for the evaluation of the capsular collagen have found differences in the staining characteristics of capsular collagen in follicular adenoma and follicular carcinoma which may help in the differential diagnosis.

Hyperplastic changes in the form of papillary or pseudopapillary structures may be seen. They are short papillae with ill-defined fibrovascular core, with no cytological features of papillary carcinoma.

Elder S et al[7] showed that histomorphometrically guaged nuclear parameters of the tumor cells such as the nuclear area, diameter, and nuclear irregularity factor of the follicle may help differentiation. In majority of cases the measurements of these parameters reliably allocated the tumor to benign versus malignant categories.

VARIANTS OF FOLLICULAR ADENOMA:

1. Follicular adenoma of Oxyphilic cell type (Oncocytic or Hurthle cell adenoma)

2. FA with papillary hyperplasia (Papillary variant of FA)

3. Signet-ring cell adenoma.

4. Mucinous follicular adenoma.

5. Lipoadenoma.

6. Adenochondroma.

7. Clear cell follicular adenoma.

8. Toxic (Hyperfunctioning) adenoma.

9. Atypical adenoma.

10. Follicular adenoma with bizarre nuclei.

HYALINISING TRABECULAR TUMOUR

It is a rare tumour of follicular origin with a trabecular pattern of growth and marked intratrabecular hyalinisation.

Carney et al.[8] in 1987 first coined the term hyalinizing trabecular adenoma (HTA) while describing a series of 11 encapsulated tumors microscopically showing polygonal and fusiform cells arranged in trabeculae separated by thin capillary network and hyalinized amyloid-like stroma which is often calcified. The cells are negative for calcitonin. This pattern is similar to that of a paraganglioma (Paraganglioma like adenoma of the thyroid).

The cells within the trabecular islands occasionally show longitudinal nuclear grooves, nuclear pseudoinclusions, psammoma bodies, and paranuclear yellow cytoplasmic bodies.[9] In view of these nuclear features, which resemble papillary carcinoma, Cheung CC et al[10] suggested that HTA may a variant of papillary carcinoma since RET/PTC rearrangement has been reported in HTA which suggests its similarity to PTC at the molecular level.

A study by Fonseca E et al[12] showed similarities in cytokeratin immunoprofile between papillary carcinoma and HTA, especially CK19 which was positive in both.[11] But the study by Hirokawa et al. showed that HTAs were all CK-19 negative, while papillary carcinomas were positive. A study by Galgano MT et al[13] reported lack of CK 19 and HBME-1 immunoreactivity in all their HTAs compared to diffuse positive staining noted in all papillary carcinomas.

In view of the nuclear features which resemble papillary thyroid carcinoma along with some studies reporting similar immunophenotype and the presence of RET/PTC gene rearrangement in HTA, WHO in 2004 reclassified these tumors as HTT, which clearly emphasizes the uncertain biologic behavior of these tumors.[3]

Gowrishankar S et al[14] reported a case of hyalinizing trabecular carcinoma presenting as lung metastasis with evidence of vascular invasion and showing some nuclear groves and rare pseudoinclusions. The tumor was negative for CK19.

MALIGNANT NEOPLASMS

PAPILLARY CARCINOMA OF THYROID

Papillary carcinoma is defined as a malignant epithelial tumour showing evidence of follicular cell differentiation, and characterised by distinctive nuclear features.[3]

It is the most common form of thyroid malignancy comprising 75 to 85 % of all malignant thyroid tumours, with male to female ratio of 2:1, occurring at any age, mean being 40 years. They tend to be biologically indolent and have excellent prognosis.[15,16] These tumours metastasize via lymphatics; vascular invasion can also be seen.

Gross: They typically present as firm to hard white-tan tumors with invasive borders with a granular cut surface resulting from the presence of papillae. The presence of psammoma bodies can impart a gritty sensation while cutting. Tumors with

predominantly follicular architecture are often tan-brown and fleshy, similar to follicular neoplasms. Some tumors can be encapsulated. Cystic change can occur. Multifocal disease is common in about 65% of cases.[17]

Microscopic features: Microscopically, the diagnosis is based together on characteristic cytological and architectural features.

Cytological features:

Nuclear features of follicular cells are important in diagnosing Papillary carcinoma. The nuclei are typically large, crowded, ovoid, ground glass (Orphan Annie eyed) and grooved with small distinct nucleoli and nuclear pseudoinclusions.

Orphan Annie eyed nuclei refers to the empty looking nuclei with scanty marginated dusty chromatin seen as an artefact in paraffin sections in more than 80% of cases. The chromatin material is apposed to the inner surface of the nuclear membrane, which looks thickened with an irregular inner contour. However this feature is not pathognomonic, since benign lesions such as nodular hyperplasia, follicular adenoma, Graves disease and Hashimoto's thyroiditis can exhibit clear nuclei focally.[18]

The ***nuclear groove***, formed by deep infolding of the nuclear membrane along the longitudinal axis of the oval nucleus, is found in almost all cases of papillary carcinoma, at least focally. Yet, nuclear grooving is not pathognomonic since it can also be observed in solid cell nests, follicular neoplasms, hyalinizing trabecular adenomas, poorly differentiated thyroid carcinomas and adenocarcinomas of non-thyroid origin.[19,20]

Nuclear pseudoinclusions, representing intranuclear cytoplasmic herniation pockets, are typical but not pathognomonic, are found only in a minority of tumor cells.[21]

In some cases, the nuclear features may not be well developed or occur only focally. In such cases, the diagnosis depends on the architectural features or identification of foci showing the typical nuclear features.

The neoplastic cells are polygonal to cuboidal with lightly eosinophilic to amphophilic cytoplasm but can be oxyphilic or clear.[22,23] Stroma may show calcification or ossification.[24] Cytoplasmic mucin can be demonstrated in a proportion of cases by histochemical stains.[25] Focal squamous differentiation is seen in some cases and such foci usually do not exhibit the characteristic nuclear features of papillary carcinoma.

Psammoma bodies are seen in about 25% of cases. They are roughly spherical, basophilic, non-birefringent, concentrically layered calcium deposits and are located in the epithelium covering the stalks of the papillary tumors and in the sessile masses of epithelium that form the lining of cystic spaces in these growths. At times, they are seen in the core of the papillary stalk and are occasionally free in colloid lakes.

Architectural features:

The characteristic feature is a complex branching papillary pattern with a well defined stalk and delicate fibrovascular stroma lined by neoplastic epithelial cells.

The papillae seen in nodular goiter and follicular adenoma with papillary hyperplasia are usually broad with follicles in the cores. The lining cells appear columnar with regular, non crowded, basally situated, dark, round nuclei resembling

beads on string which is in striking contrast to the crowded and haphazardly oriented pale nuclei of papillary carcinoma.

The papillae in thyrotoxicosis, Hashimoto's thyroiditis and toxic follicular adenoma are non branching short, stubby projections that protrude into the follicular lumen and without well defined fibrovascular cores. In Hashimoto's thyroiditis well developed nuclear features of papillary carcinoma are lacking although focal nuclear clearing may be seen.

Hurthle cell adenoma/carcinoma may have a minor papillary component. The papillae are usually non arborizing and the cells do not show nuclear crowding. However occasional nuclear grooves may be present.

The majority of papillary carcinomas contain some portion of follicular elements or purely follicular elements. The mixture of follicular structures does not alter the biological behaviour or prognosis of neoplasm.

Other common patterns include complex tubulopapillary, microglandular, cribriform, anastomosing tubular, trabecular and solid patterns.

VARIANTS OF PAPILLARY CARCINOMA

While the characteristic nuclear features are common to all histological types of papillary carcinoma, there are a number of variants which have been described on the basis of the size or architectural patterns of the tumour. The diagnosis of some of these variants is important since some may behave in a more aggressive fashion compared to the conventional papillary carcinoma

.

TABLE 1: VARIANTS OF PAPILLARY CARCINOMA

	PTC VARIANT	DEFINING MORPHOLOGIC FEATURES	MIMICKERS	CLINICAL SIGNIFICANCE
Less aggressive (Better prognosis) variants				
1.	Papillary microcarcinoma[26]	Incidentally discovered small papillary carcinoma <1 cm size	Fibrosing thyroiditis Hyperplastic adenomatoid nodule	Highly favorable prognosis[27,28]; unfavorable outcome when lymphadenopathy >3 cm and a nonencapsulated type of primary lesion[29]
2.	Encapsulated follicular variant	Encapsulated tumor composed almost exclusively of follicles	Follicular adenoma Follicular carcinoma	Highly favorable prognosis: no tumor relapse after excision
Variants with behaviour similar to the conventional type				
3.	Follicular variant	Composed almost exclusively of follicles, with abortive papillae; colloid often dark-staining	Follicular adenoma Follicular carcinoma	No prognostic implications
4.	Macrofollicular variant	Presence of many large-sized follicles in >50% of tumour[30]	Nodular goiter	No prognostic implications
5.	Solid variant	>50% of tumor showing solid growth pattern[31,32] often traversed by delicate fibrovascular septa	Poorly differentiated (insular) carcinoma Medullary carcinoma	Slightly higher frequency of distant metastasis and less favourable prognosis compared with conventional PTC

	PTC VARIANT	DEFINING MORPHOLOGIC FEATURES	MIMICKERS	CLINICAL SIGNIFICANCE
6.	Oxyphil cell (Oncocytic, Hürthle cell) variant	>50% of tumor cells with abundant oxyphilic cytoplasm[33]	Hürthle cell adenoma Hürthle cell carcinoma	No prognostic implications
7.	Clear cell variant	Extensive cytoplasmic clearing of tumour cells (accumulation of glycogen)[34]	Intrathyroidal parathyroid tumor	No prognostic implications
8.	Cribriform morular variant	Intricate admixture of cribriform pattern, small follicles, papillae & squamoid morules; colloid usually absent	Columnar cell carcinoma Tall cell variant of papillary carcinoma	Familial adenomatous polyposis should be excluded;[35,36] by itself, it has no prognostic implications[37]
9.	Warthin tumor–like variant[38]	Broad papillae lined by oxyphilic neoplastic cells, with the cores packed with lymphoplasmacytic infiltrates	Hashimoto's thyroiditis	No prognostic implications[39]
10.	Variant with exuberant nodular fasciitis like stroma[40]	Presence of abundant nodular fasciitis like or fibromatosis like reactive stroma amidst the papillary carcinoma component	Nodular fasciitis Fibromatosis Benign mesenchymal neoplasm	No prognostic implications[41]

	PTC VARIANT	DEFINING MORPHOLOGIC FEATURES	MIMICKERS	CLINICAL SIGNIFICANCE
11.	Papillary carcinoma with lipomatous stroma	Adipose cells found within the papillary carcinoma[42]	—	No prognostic implications
12.	Variant with spindle cell metaplasia	Component of short fascicles of bland looking spindled tumor cells merging into the papillary carcinoma component[43]	Dedifferentiated papillary carcinoma	—
More aggressive (Worse prognosis) variants				
13.	Diffuse follicular variant	Diffuse involvement of entire thyroid without formation of discrete tumor nodules and composed entirely of follicles	Colloid goiter	More aggressive Frequent lymph node and distant metastases[44]
14.	Trabecular variant	>50% of tumor showing a trabecular growth pattern	Follicular adenoma or carcinoma, trabecular (embryonal) type	Less favourable outcome
15.	Tall cell variant[18]	Composed predominantly of cells whose heights are at least three times their widths; tumor cells often with oxyphilic cytoplasm	Columnar cell carcinoma	More aggressive Larger tumors More frequent extrathyroidal extension Higher recurrence rate Higher mortality

	PTC VARIANT	DEFINING MORPHOLOGIC FEATURES	MIMICKERS	CLINICAL SIGNIFICANCE
16.	Diffuse sclerosing variant	Diffuse extensive involvement of one or both lobes with sclerosis and lymphoplasmacytic infiltration; tumor islands often small and dispersed, commonly showing squamous metaplasia and prominent psammoma body formation	Thyroiditis, especially because of the diffuse nature of the process and frequent presence of serum antithyroglobulin or antimicrosomal antibodies	More aggressive Frequent lymph node and distant metastases[45]
17.	Dedifferentiated papillary carcinoma	Coexistence of PTC with undifferentiated or poorly differentiated carcinoma indicating transformation to higher grade neoplasm	—	Worse prognosis High mortality rate

*All variants show the typical nuclear characteristics of papillary carcinoma, at least in some area of the tumor.

In a study by Roti E et al,[28] tumor size more than 0.8 cm was associated with more aggressive disease. However, in a recent meta-analysis study by Elio R et al,[29] significant risk factors for recurrence included younger age group, clinically overt tumor, multifocality, and lymph node involvement at diagnosis; tumor size was not associated with recurrence.

Follicular variant, the most common variant of papillary carcinoma, has generated a lot of controversy in its diagnosis. While PTC with a recognised follicular pattern was observed as early as 1953, the term FVPTC was first proposed by Lindsay in 1960,[46] and was, at that time, still regarded as a type of follicular carcinoma. In 1974, the WHO recognized the entity as Follicular variant of papillary carcinoma in its histological classification of thyroid tumors.

In a study by Liu J and Singh B et al, FVPTC with an infiltrative and noncapsulated pattern showed significantly higher rate of regional lymph node metastasis (65% vs. 5%), intratumoral fibrosis (88% vs. 18%), exrathyroidal extension (65% vs. 5%), and positive margins (50% vs. 2%) compared to encapsulated tumors.[47]

One of the most challenging and controversial diagnoses in thyroid pathology may be the identification of focal nuclear changes of PTC in encapsulated follicular patterned lesions[48] with a tendency to overdiagnose FVPTC.[49]

As the nuclear changes may not be diffuse, they can sometimes be misdiagnosed as follicular adenoma. The nuclear changes are most often seen in the subcapsular region of the tumor.[50] The importance of diagnosing these lesions as encapsulated FVPTC is important since these tumors may later present with bone metastases some even 15–17 years after initial diagnosis justifying their appropriate treatment at the time of presentation.[51] In view of this difficulty in their diagnosis, some have suggested that encapsulated follicular lesions with doubtful nuclear changes should be diagnosed as well differentiated tumor of uncertain malignant potential (WDTUMP).[48]

PROGNOSTIC FACTORS IN PAPILLARY CARCINOMA

The overall 5 year survival rate for papillary thyroid carcinoma is 96 to 97% with a 10 year survival rate of 93%.[52] For a more specific prognosis for individual cases, there are at minimum 13 known scoring systems for prognosis;[53] among the more often used are given in Annexure IV.

FOLLICULAR CARCINOMA

Follicular carcinoma is a malignant tumor of the thyroid follicular cells showing a follicular architecture and without the characteristic nuclear features of PTC.[3] Comprising 5 to 10 % of all thyroid cancers, it is more aggressive than PTC, occurs in a slightly older age group and less common in children.[5]

Capsular and vascular invasion are characteristic and so, distant metastasis is common. Lung, bone, liver, bladder and skin are the potential sites of distant spread. Lymph nodes are less commonly involved.

(a) Minimally invasive follicular carcinoma[54,55]

This is a grossly encapsulated tumor with a pattern of growth resembling that of an adenoma. The diagnosis of malignancy depends entirely on the demonstration of blood vessel invasion and or capsular invasion on histology. The vessel should be of venous caliber and located immediately outside the capsule and should contain one or more clusters of malignant cells attached to the wall and protruding into the lumen.[3] The tumor expands in a mushroom like fashion in the adjacent area of capsular breach

with an occasional formation of second capsule in the advancing edge of the tumor. WHO defines capsular invasion as penetration through the capsule unassociated with previous FNAC.[3]

In situations of questionable capsular breach, the terms "*Follicular tumor of uncertain malignant potential (FT-UMP)*" is used when the characteristic nuclear changes of papillary carcinoma are absent[48] and "*Well differentiated tumor of uncertain malignant potential*" is used when the changes are questionable. Thomson et al.[56] in a series of 95 cases of minimally invasive follicular carcinoma, which included cases both with capsular and/or vascular invasion, showed excellent survival.

Distant metastases are seen more often in tumors with vascular invasion, thus it may be best to regard this as a distinct group when evaluating the prognosis.[57] The differential diagnosis includes other follicular patterned lesions such as follicular adenoma, FVPTC, and hyperplastic colloid nodule.

(b) Widely invasive follicular carcinoma[54,55]

Macroscopically, the tumor has widely invasive edges with necrotic foci. Microscopy shows a follicular tumor, usually with solid or trabecular areas with invasion of the surrounding thyroid parenchyma, high mitotic rate and necrosis. There are complete or multifocal areas of capsular invasion, and vascular invasion. These tumors spread to distant organs through blood vessels and up to 80% can develop systemic metastases. The prognosis being much worse than MIFC, the 10 year survival is 25 to 45% as opposed to 70 to 100% in the MIFC group.[3]

VARIANTS OF FOLLICULAR CARCINOMA

(a) Follicular carcinoma, oncocytic variant (Hurthle cell carcinoma)

It is a rare thyroid malignancy representing fewer than 5% of all differentiated thyroid carcinomas.[58] The male to female ratio is 1:7 and mean age is 52.6 years. In the WHO classification, this is classified as a subtype of follicular carcinoma. Now, many authors consider this as a distinct clinical entity, which is histologically in the group of well-differentiated carcinomas since they have a different oncogenic expression than follicular carcinomas.[59]

Grossly, the tumor may be solitary or multiple solid tan, well-vascularised, well encapsulated or lobulated unencapsulated. Microscopically, tumors show patterns like solid or trabecular. They are composed predominantly of oxyphil cells. The diagnosis of malignancy is reliably based on histologic evidence of capsular or vascular invasion, extrathyroidal local tissue invasion and nodal or distant metastasis.

Hurthle cell carcinomas do show some differences from conventional follicular carcinoma.[60] They appear to be more aggressive and show a higher tendency to metastatize to regional lymph nodes. They generally take up radioactive iodine less satisfactorily. Thyroglobulin immunoreactivity is weak and patchy.

The ***differential diagnosis*** includes Hurthle Cell adenoma, Oncocytic variant of PTC and Oncocytic variant of Medullary Thyroid carcinoma.

TABLE 2: IHC MARKERS IN HURTHLE CELL CARCINOMA AND MTC

IHC MARKERS[61]	HURTHLE CELL CARCINOMA	MEDULLARY CARCINOMA
Cytokeratin, CEA & TTF-1	+	+
Thyroglobulin	+	-
Calcitonin	-	+
Synaptophysin & Chromogranin	-	+
S100, HMB45 & EMA	+	-

(b) Clear cell variant of follicular carcinoma

It is a rare variant with predominant clear cells that contain glycogen, mucin, lipid or dilated mitochondria. Vascular and/or capsular invasion is the only criteria to distinguish it from clear cell variant of follicular adenoma. Differential diagnosis includes metastatic renal cell carcinoma in which there are multiple nodules, clear cytoplasm, sinusoidal blood vessels or fresh hemorrhage.

POORLY DIFFERENTIATED THYROID CARCINOMA

It shows histologic and biologic features intermediate between well differentiated thyroid carcinomas and undifferentiated carcinomas. It is more common in women and in patients older than 50 years. Some of these tumours arise from pre-existing papillary and follicular thyroid carcinomas, others most likely arise de novo.

Gross Features: Most are more than 3 cm diameter and are solid and gray white with frequent foci of necrosis and pushing borders and rarely a thick capsule and rarely,

satellite nodules may be seen. Extrathyroidal spread is less common compared to undifferentiated carcinomas.[3]

Microscopic features: Three different histologic patterns (insular, trabecular and solid) are seen with infiltrative pattern of growth, necrosis and vascular invasion.[62]

The ***insular pattern*** is characterised by well defined nests of tumour cells surrounded by thin fibrovascular septa with artefactual clefts. Tumour cells are small uniform with round hyperchromatic or vesicular nucleus with indistinct nucleoli with increased mitotic figures.

The ***trabecular pattern*** is characterised by tumour cells in cords or ribbons.

The ***solid pattern*** shows large sheets of tumour cells occasionally showing small abortive follicles or colloid droplets.

Hiltzik et al. defined PDTC on the basis of mitosis (5 or more per 10 HPF) and necrosis and found those criteria to identify a more aggressive subtype of thyroid carcinoma independent of the growth pattern.[63]

Turin proposal[64] for the diagnosis of Poorly differentiated thyroid carcinoma:

- Presence of solid/trabecular/insular growth pattern
- Absence of nuclear features of PTC
- Presence of at least one of the following:
    - Convoluted nuclei
    - Mitotic activity of 3 or more per 10 HPF
    - Tumor necrosis

ANAPLASTIC (UNDIFFERENTIATED) THYROID CARCINOMA

Anaplastic carcinoma, a highly aggressive and rare thyroid tumor, accounts for 1.7% of all thyroid malignancies.[3]

The patients are usually elderly in their seventh or eighth decade of life with a female preponderance of around 2.5:1 and presenting with rapidly enlarging thyroid mass or a metastatic tumour in the cervical lymph nodes or distant sites with frequent pressure symptoms such as dysphagia, hoarseness, and stridor.

Grossly, the tumour is usually large, fleshy and often replacing the entire thyroid with areas of necrosis and hemorrhage with frequent infiltration of perithyroidal soft tissues.

Microscopically, highly pleomorphic large polygonal, ovoid or spindle shaped tumour cells in diffuse sheets, irregular islands and cords with high mitiotic rate and necrosis with tendency to infiltrate and replace the walls of vessels obliterating the lumen. They are commonly admixed with neutrophils. A component of papillary, follicular or poorly differentiated thyroid carcinoma may be found in 50% of cases suggesting that anaplastic carcinoma may arise through a process of dedifferentiation.

Thyroglobulin staining is variable ranging from 9 to 71% cases and is usually focal and weak; Thyroid transcription factors 1 and 2, two other markers of thyroid differentiation, may also be variable, and in the study by Nonaka D et al,[65] were positive in 18 and 7%, respectively.[65] The prognosis is extremely poor with 5-year survival ranging from 0 to 14%.

MEDULLARY THYROID CARCINOMA

It is defined as a malignant thyroid tumor showing evidence of C-cell differentiation. It comprises 5 to 10 % of all cases of thyroid malignancies.[3]

Approximately 80% of the medullary carcinomas occur sporadically.[66] Most are unilateral with no associated C-cell hyperplasia in the rest of the gland.

In the familial form, the tumor often develops at an earlier age, multicentric and often bilateral. There is usually an associated background of C-cell hyperplasia.[67]

Gross features

It usually lacks a capsule, but well demarcated, with lobulated outer contour and shows bulging, gray white or tan cut surface. Some are ill defined, hard and sclerotic with radiating contours. Older lesions may show calcification, bone formation, necrosis and hemorrhage. It affects the middle third of the lateral lobe where the C-cell density is highest. Rarely a thick fibrous capsule may sometimes be seen and may sometimes be associated with cystic and papillary change.[68]

Microscopic features

It is composed of sheets, nests or trabeculae of polygonal or plump spindle cells characteristically traversed by delicate fibrovascular septae, whorling or pseudopapillary pattern can be observed. Cellular dehiscence is common. The nuclei are round or oval and typically possess finely stippled chromatin and indistinct nucleoli. The cytoplasm is finely granular and often argyrophilic. Cytoplasmic mucin is demonstrable in 40-50% of cases.

Occasionally tumor cells may assume signet-ring appearance. Amyloid deposition is seen in 15 - 20% of cases as pink-staining amorphous material in the form of globules, may show calcification and foreign body giant cell reaction.

Medullary carcinoma variants include the following:[3]

1. Papillary/Pseudopapillary variant
2. Follicular/Glandular variant
3. Giant cell variant
4. Spindle cell variant
5. Small cell variant
6. Neuroblastoma like variant
7. Paraganglioma 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

Presence of all these variants makes medullary carcinoma the great mimicker of other thyroid carcinoma; therefore, immunohistochemistry should be performed in all cases when the diagnosis is in doubt or some atypical features are present.

Immunohistochemical staining reveals positivity for calcitonin, chromogranin, whereas S-100 and HMB-45 was only positive in pigmented cells and negative for thyroglobulin. It is associated with RET point mutation which may sometimes behave as a dominant oncogene for thyroid follicular cells which may explain association of MTC with papillary thyroid carcinoma in some cases.[69]

MEDULLARY MICROCARCINOMA

Medullary carcinoma measuring less than 1 cm is called Medullary microcarcinoma. They are rare lesions comprising 0.15% of all thyroid carcinomas. Most often clinically latent, an elevated calcitonin levels helps in early diagnosis. Familial forms are common which are usually associated with C-cell hyperplasia.

Nodular C-cell hyperplasia should be differentiated from microcarcinoma. Extension of C-cells through defects in the follicular based lamina and the infiltration of the thyroid interstitium are regarded as criteria to diagnose malignancy.

MIXED MEDULLARY - FOLLICULAR CELL CARCINOMA

Hales et al,[69] in 1982, described an unusual carcinoma of thyroid that showed predominant medullary carcinoma admixed with areas of follicular differentiation. Both patterns prevailed at the primary site and also at the lymphnode metastasis.

These tumors may represent another entity-collision tumor, which can occur in two forms:

1. Follicular carcinoma + Medullary carcinoma

2. Papillary carcinoma + Medullary carcinoma

The two components are either side by side or are intermingled. Each primary tumor exhibits only one line of cell differentiation, however, the metastatic deposits in lymphnode contain both elements abutting each other and resemble mixed tumor. This apparent dual differentiation in the metastasis should also be regarded as a collision phenomenon. A common tumorigenic stimulus which triggers the neoplastic transformation of both C-cells and follicular epithelial cells could be a possible explanation for such a phenomenon.

RARE TYPES OF THYROID CARCINOMAS

COLUMNAR CELL CARCINOMA

It is a rare aggressive thyroid neoplasm, characterised by mixed papillary, complex glandular, cribriform and solid patterns. The papillae and glands are lined by, tall columnar cells with pseudostratified hyperchromatic oval or elongated nuclei. Subnuclear vacuoles and cytoplasmic clearing may be seen.

It differs from the tall cell variant of papillary carcinoma by greater height of the cells, nuclear pseudostratification, nuclear hyperchromasia and lack of oxyphilic change in the cytoplasm.[17]

MUCOEPIDERMOID CARCINOMA

It is a rare low grade malignant non-circumscribed tumor with islands of cells in a sclerotic background with areas of squamoid and mucin secretion. Areas of cribriform pattern, with elongated lumina containing colloid-like material are seen. Occasional papillae may be found. Mild to moderate nuclear pleomorphism with pale nuclei will be seen. Comedo-type necrosis and psammoma bodies may be seen.[17]

SCLEROSING MUCOEPIDERMOID CARCINOMA WITH EOSINOPHILIA

It is rare, low grade malignant tumor occurring in a background of Hashimoto thyroiditis, possibly arising from metaplastic squamous epithelium.

MUCINOUS CARCINOMA

Primary mucinous carcinoma of thyroid is extremely rare and is identical to mucinous/colloid carcinoma of other sites.

SPINDLE EPITHELIAL TUMOR WITH THYMUS-LIKE DIFFERENTIATION (SETTLE)

Also known as intrathyroid spindle cell tumour with mucous cysts, it is a rare tumour thought to be derived from ectopic thymus or branchial pouch remnant. The tumor cells stain positive with cytokeratin and muscle specific actin while they are negative for thyroglobulin and calcitonin.[70]

CARCINOMA SHOWING THYMUS LIKE ELEMENTS (CASTLE)

Histologically identical to thymic carcinoma, it usually involves the lower pole of thyroid and adjacent extrathyroidal tissues with regional lymph node metastasis in about one third of the cases. The neoplastic cells are immunoreactive for cytokeratin and p63, but not thyroglobulin, calcitonin or TTF-1. Like thymic carcinomas, CD5 and CD117 are always expressed.[17]

NONEPITHELIAL TUMOURS

Non epithelial tumours of the thyroid gland include:

1. Primary lymphoma of thyroid
2. Plasmacytoma
3. Angiosarcoma
4. Solitary fibrous tumour
5. Smooth muscle tumours
6. Paraganglioma

METASTATIC CARCINOMA

Metastases to thyroid from another primary source are infrequent; tumors that most commonly spread to the thyroid include kidney, breast, and lung carcinoma. Metastatic carcinoma has to be considered in the differential diagnosis of poorly differentiated carcinoma especially when there is non-insular pattern, and clinicopathological correlation and thyroglobulin immunostaining may be of help in these situations.[17]

IMMUNOHISTOCHEMISTRY

Immunohistochemistry is used to determine the expression of a particular antigen and its microanatomic location in the tissue. It involves binding of primary antibody to the antigen of interenst in the tissueand then, the detection of the bound antibody using a chromogen. The differences in the immunoreactivity for particular antigens help to identify the lineage or the differentiation of the cells.

Thyroglobulin

It is the primary product synthesised in the thyroid and is a highly sensitive histogenetic marker for follicular cell origin. Staining may be patchy in the less well differentiated tumours. It is expressed in tumours of follicular cell origin and is absent in medullary carcinoma.

Cytokeratin 19

It is a type I intermediate filament protein and is the smallest known keratin and is unique that, compared to other keratins, it does not have a designated partner for the formation of filaments, implying that the regulation of its expression is different from other keratin encoding genes.[71]

Immunohistochemical diagnosis of Papillary carcinoma and its mimics

Until today, the gold standard for the diagnosis of follicular lesions particularly PTC is histology. Some of the ancillary studies such as immunohistochemistry and molecular techniques may be helpful, but none of them is conclusive.[71]

Papillary carcinoma typically stains for thyroglobulin and TTF-1. Expression of a variety of markers such as HMWCK (34βE12), CK19, Galectin 3, HBME1, Leu7 (CD57), CITED 1, fibronectin 1, CD15 (LeuM1) or CD44, singly or in combination, has been suggested to be of value in the diagnosis of papillary carcinoma versus benign thyroid lesions or other thyroid tumours, but these markers are not totally specific, and the staining can be patchy and weak even in classical PTC.

CK19 has been shown to be a sensitive marker for PTC, usually resulting in diffuse positivity in 80 to 100% of cases.[1] Since CK19 detection in FA and FTC is often absent or less intense and weaker than in PTC, this has become one of the most commonly used marker to investigate thyroid lesions. Several authors emphasize the importance of the distribution and intensity of CK19 staining as the most critical aspects of accurate interpretation. The finely dispersed positivity seen in the cells of PTC is distinctive. Although this feature is usually diffuse throughout the lesion, focal staining for CK19 does not rule out a diagnosis of PTC, particularly in nodules with nuclear features of PTC that are seen focally.

CK19 is also considered by many investigators to be a useful ancillary tool for the diagnosis of PTC in FNAC and in cell block preparation, especially in cytologically suggestive but indeterminate cases. The reported sensitivity and specificity using CK19 as a single marker is as high as 92% and 97% respectively. A panel of markers including CK19 and Galectin-3 was reported as reaching 100% of both specificity and sensitivity in the diagnosis of PTC.[72]

Mustafa Kosem et al,[2] in their immunohistochemical study showed that HBME-1 and CK19 are more valuable in the differential diagnosis of papillary carcinoma. The high sensitivity and specificity of HBME-1 makes it a good marker for the diagnosis of papillary thyroid carcinoma.

Michel R Nasr et al[73] suggested that a combination of HBME1 and CK19 attains a high sensitivity and specificity for the diagnosis of PTC. Raphael SJ et al[74] concluded that HMWCK and CK19 are useful in the distinction of PTC from FA, FTC and nodular hyperplasia.

Dina El Demellawy et al[71] found that a panel of CD56, CK19 and P63 is of value in the distinction of Papillary thyroid carcinoma from other thyroid follicular lesions. P63 is a specific but less sensitive marker for papillary thyroid carcinoma than CK19. CD56 is a more specific and sensitive marker than CK19, however it is a negative rather than a positive marker for PTC. E-cadherin is of no value in the diagnosis of thyroid follicular lesions/tumours.

MATERIALS AND METHODS

SOURCE OF DATA

Cases of thyroid neoplasms reported in thyroid specimens received in the Institute of Pathology, Madras Medical College, Chennai from January 2009 to April 2011 formed the material for this study.

INCLUSION CRITERIA

All cases of thyroid neoplasms and few cases of nonneoplastic lesions mimicking papillary carcinoma histologically irrespective of the age and sex were included for the study.

EXCLUSION CRITERIA

Nonneoplastic lesions of thyroid except for the cases histologically mimicking papillary carcinoma.

Cases with inadequate material from the tumour were not included in the study.

METHOD OF DATA COLLECTION

The clinical features such as age and sex of the patient and type of surgery done were noted. The details of gross characteristics of the tumor such as the number and size of nodules, circumscription, cut section and secondary changes like cystic degeneration, hemorrhage and necrosis were noted.

The tissues were fixed in 10% formalin for 24 hours. After formalin fixation, multiple bits were taken from representative areas. They were processed for

histopathological examination and paraffin blocks were made. The blocks were cut at 4 to 5 microns thickness and stained with hematoxylin and eosin.

The microscopic features including the type of tumour, grade, histological patterns, cellular features, capsular invasion, lymphatic and vascular invasion, secondary changes, multicentricity and status of uninvolved thyroid were studied.

The tumours were classified according to the WHO histological classification of thyroid tumours and the incidence of different histological types are noted.

Among these, 47 cases of papillary thyroid carcinoma and its variants and 55 cases of thyroid lesions which mimic it histologically (such as follicular adenoma, follicular carcinoma, Hurthle cell neoplasms, papillary hyperplasia and Hashimoto's thyroiditis) are randomly selected and paraffin embedded tissue blocks from the representative sections are collected. 4 microns thick sections were cut and then transferred on to gelatin and chrome alum coated slides and subjected to antigen retrival using the Microwave technique with Citrate buffer solution. Immunostaining for Cytokeratin 19 and thyroglobulin were done on these samples using the BioGenex Super Sensitive^{TM} Polymer-HRP IHC Detection System. The step by step procedure of immunohistochemistry is given in Annexure V.

ANTIGEN	VENDOR	SPECIES	DILUTION	POSITIVE CONTROL
Cytokeratin 19	BioGenex	Mouse	Ready to use	Colonic carcinoma
Thyroglobulin	BioGenex	Mouse	Ready to use	Follicular adenoma

The immunostained slides were analysed for the presence of reaction, and the percentage of cells stained and the intensity of the reaction and the results were recorded. An estimation of positivity in more than 10 percent of tumour cells is considered as a positive reaction for Cytokeratin 19.

The usefulness or role of immunohistochemistry in differentiating Papillary thyroid carcinoma and its variants from its histological mimickers is then evaluated and the results are compared with those reported in the literature.

The statistical analysis was performed using statistical package for social science software version 19 and WinPepi software version 11.15. The correlation of immunoreactivity between papillary carcinoma and its mimickers was analysed using the Pearson chi square test.

OBSERVATION AND RESULTS

During the study period from January 2009 to April 2011, out of 21535 specimens received in the Institute of Pathology, Madras Medical College for histopathological examination, 1080 were thyroid specimens. Among these, there were 307 thyroid neoplasms (28.4%). The incidence of thyroid neoplasms among the total specimens received was 1.43%. 307 thyroid neoplasms formed the subject for the present study.

TABLE 3: DISTRIBUTION OF THYROID LESIONS

THYROID LESIONS	NO OF CASES	PERCENTAGE
Nonneoplastic lesions	773	71.57
Neoplastic lesions	307	28.43
TOTAL	**1080**	100

Of the neoplastic lesions, benign and malignant tumours were 112 (36.48%) and 195 (63.52%) respectively.

TABLE 4: DISTRIBUTION OF THYROID NEOPLASMS

THYROID NEOPLASMS	NO OF CASES	PERCENTAGE
Benign neoplasms	112	36.48
Malignant neoplasms	195	63.52
TOTAL	**307**	100

CHART 1

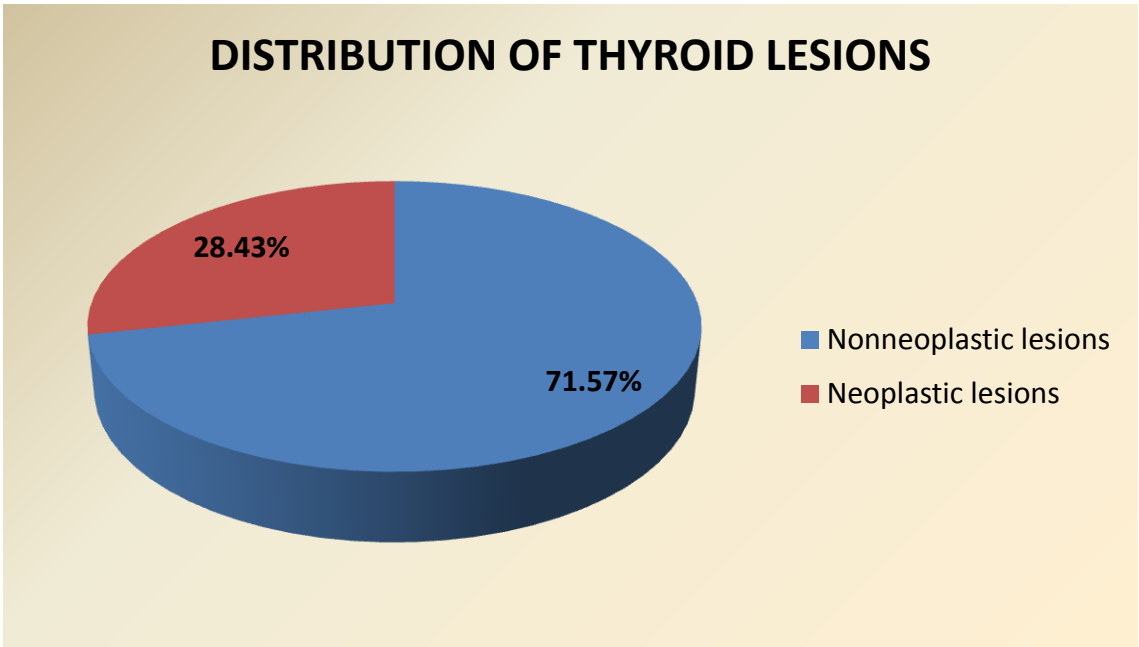
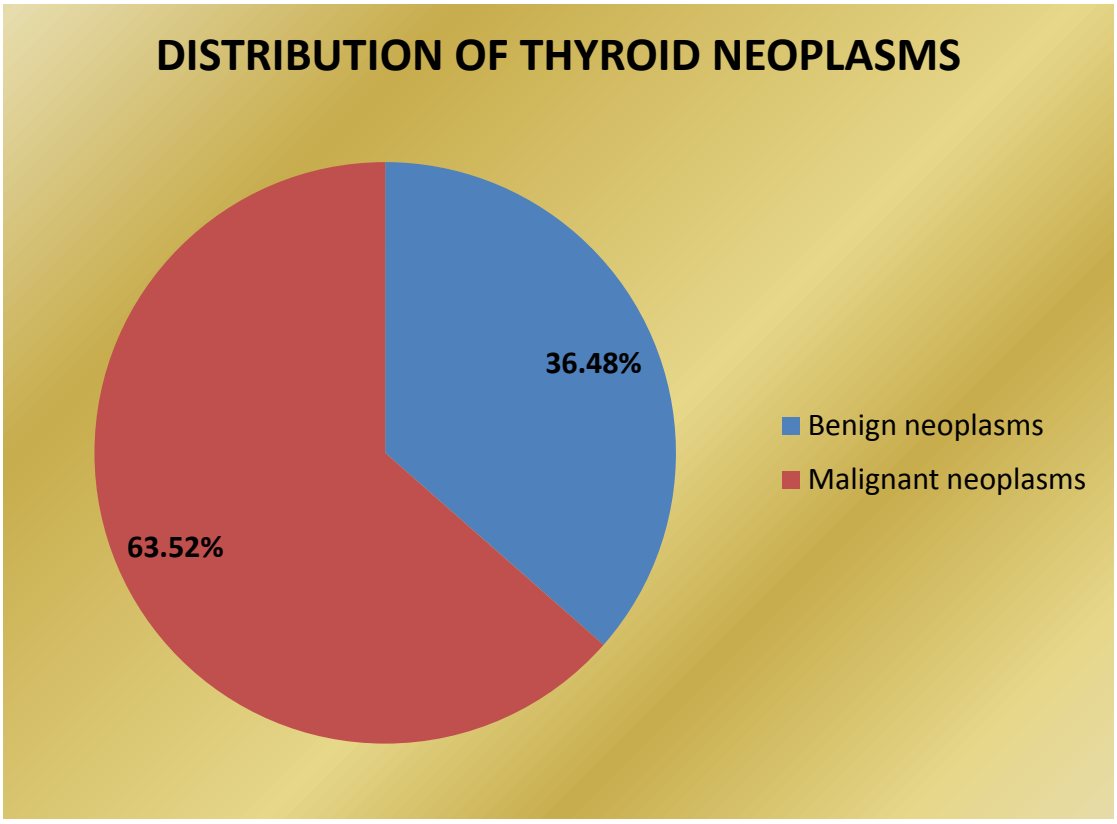


CHART 2



BENIGN NEOPLASMS

Of the 112 benign neoplasms, there were 107 cases of Follicular adenoma and 5 cases of Hyalinising trabecular adenoma.

TABLE 5: DISTRIBUTION OF BENIGN THYROID NEOPLASMS

BENIGN NEOPLASM	NO OF CASES	PERCENTAGE
Follicular adenoma	107	95.54
Hyalinising trabecular adenoma	5	4.46
TOTAL	**112**	**100**

Maximum incidence was observed during the 3rd and 4th decades of life accounting for 68 cases with a mean age of 36.47 years.

TABLE 6: AGE DISTRIBUTION IN BENIGN NEOPLASMS

BENIGN NEOPLASM	AGE IN YEARS								TOTAL
	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90	
Follicular adenoma	8	35	32	14	14	3	0	1	**107**
Hyalinising trabecular adenoma	1		1	3					**5**
TOTAL	**9**	**35**	**33**	**17**	**14**	**3**	**0**	**1**	**112**

CHART 3

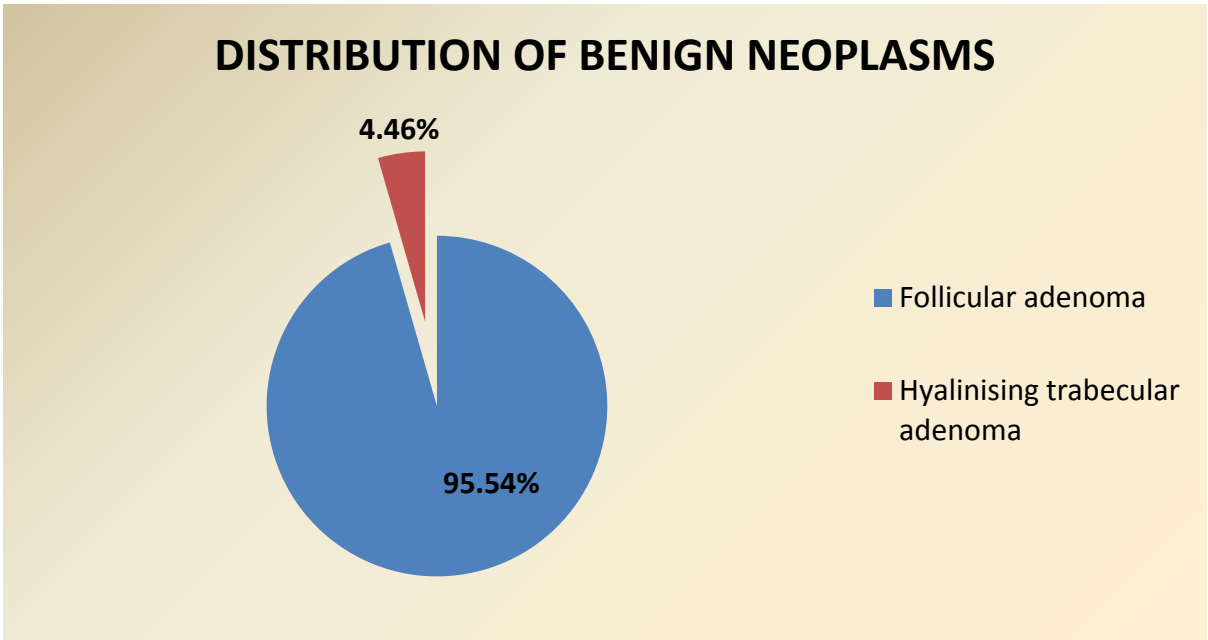
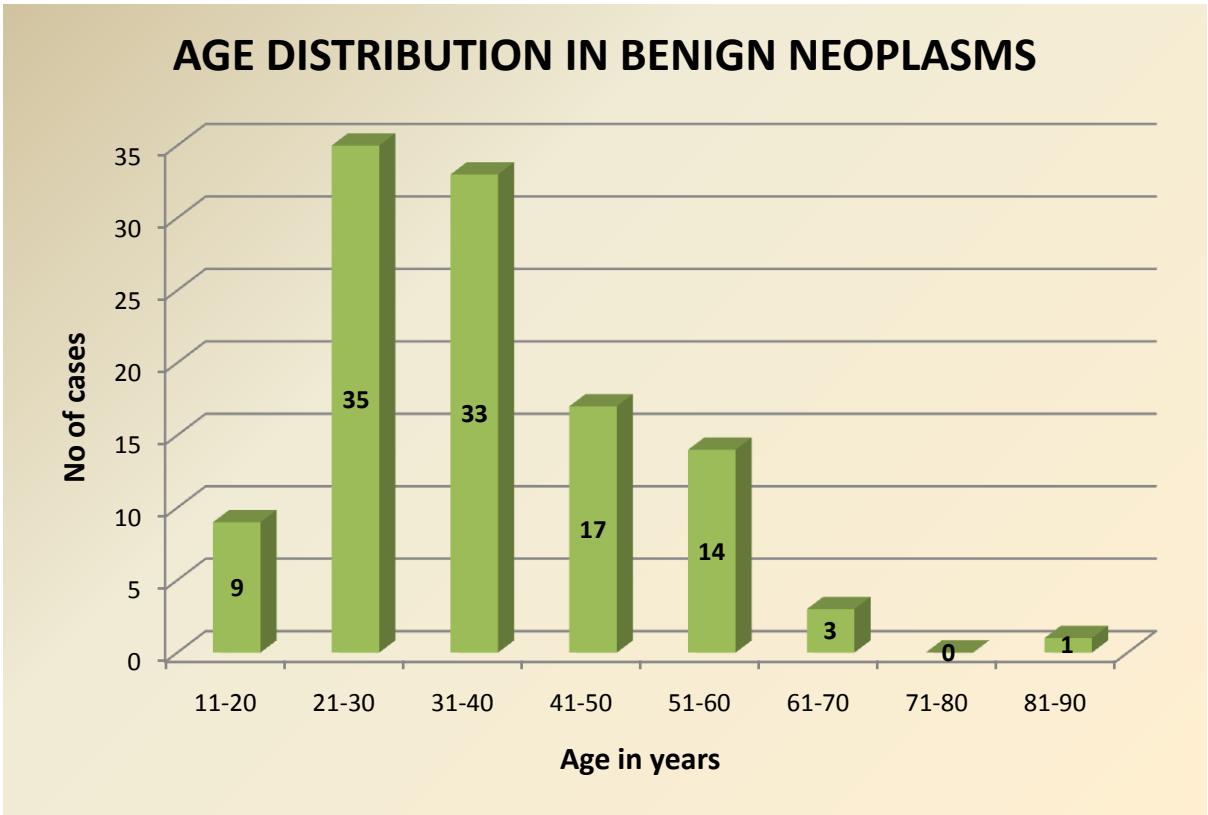


CHART 4



Maximum incidence was seen in females with male:female ratio of 1:7.

TABLE 7: SEX DISTRIBUTION IN BENIGN NEOPLASMS

BENIGN NEOPLASM	NO OF CASES		TOTAL
	MALES	FEMALES	
Follicular adenoma	14	93	**107**
Hyalinising trabecular adenoma	-	5	**5**
TOTAL	**14**	**98**	**112**

The size of the nodules ranged from 0.1 cm to 7 cm with a mean of 2.88 cm with majority of cases less than 4 cm.

TABLE 8: SIZE OF NODULES IN BENIGN NEOPLASMS

BENIGN NEOPLASM	≥ 2 cm	2 to 4 cm	> 4 cm	TOTAL
Follicular adenoma	38	55	14	**107**
Hyalinising trabecular adenoma	2	3	0	**5**
TOTAL	**40**	**58**	**14**	**112**

CHART 5

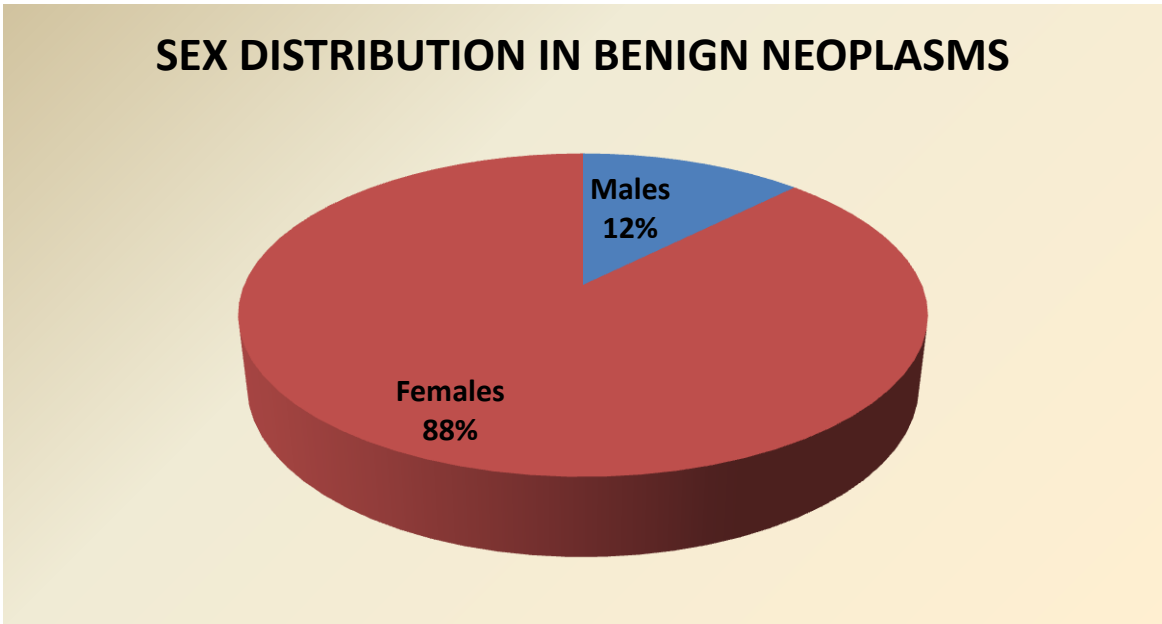
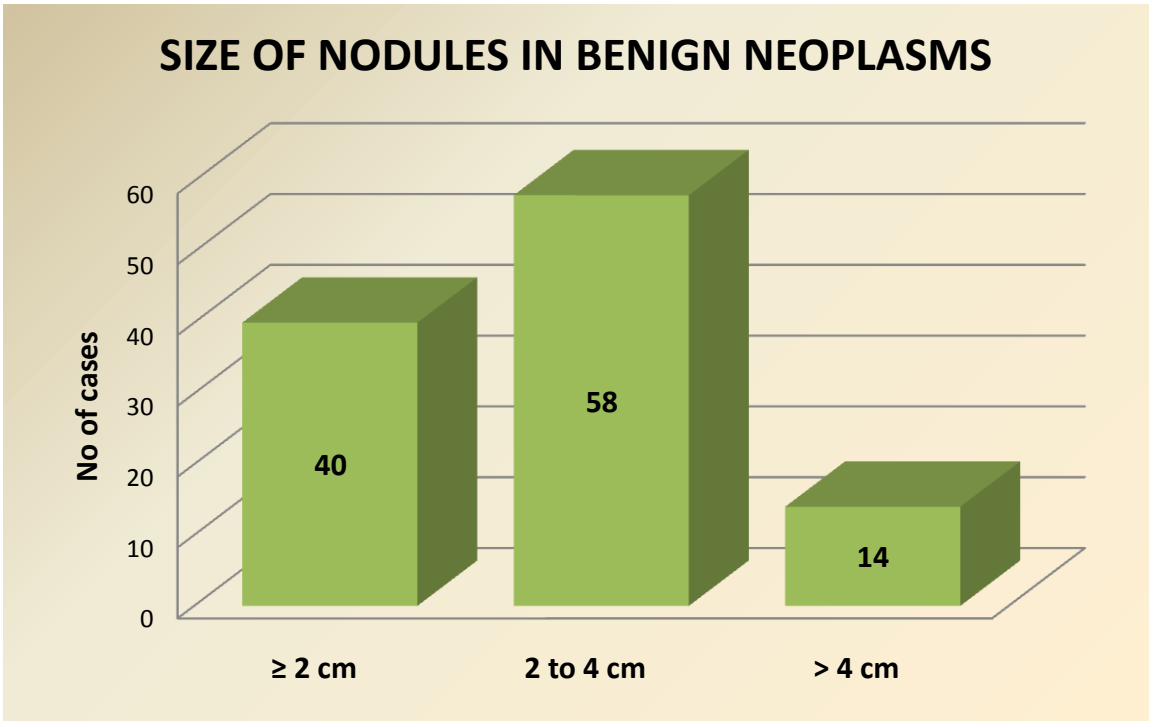


CHART 6



Among follicular adenoma, microfollicular variant was the most common.

TABLE 9: DISTRIBUTION OF SUBTYPES OF FOLLICULAR ADENOMA

FOLLICULAR ADENOMA	NO OF CASES	PERCENTAGE
Microfollicular	43	40.19
Micro & Macrofollicular	29	27.10
Micro & Normofollicular	6	5.61
Normofollicular	5	4.67
Normo & Macrofollicular	11	10.28
Macrofollicular	5	4.67
Embryonal	2	1.87
Hurthle cell variant	6	5.61
TOTAL	**107**	**100.00**

MALIGNANT MEOPLASMS

Of the 195 malignant neoplasms, there were 176 Papillary carcinoma, 4 follicular carcinoma, 2 anaplastic carcinoma, 5 each of medullary carcinoma and Poorly differentiated carcinoma and 1 each of Hurthle cell carcinoma, Squamous cell carcinoma and mixed papillary and medullary carcinoma. Papillary carcinoma formed the largest group forming 57.33% of all thyroid neoplasms followed by follicular adenoma (33.55%). Among malignant thyroid lesions, papillary carcinoma constituted 90.26%.

CHART 7

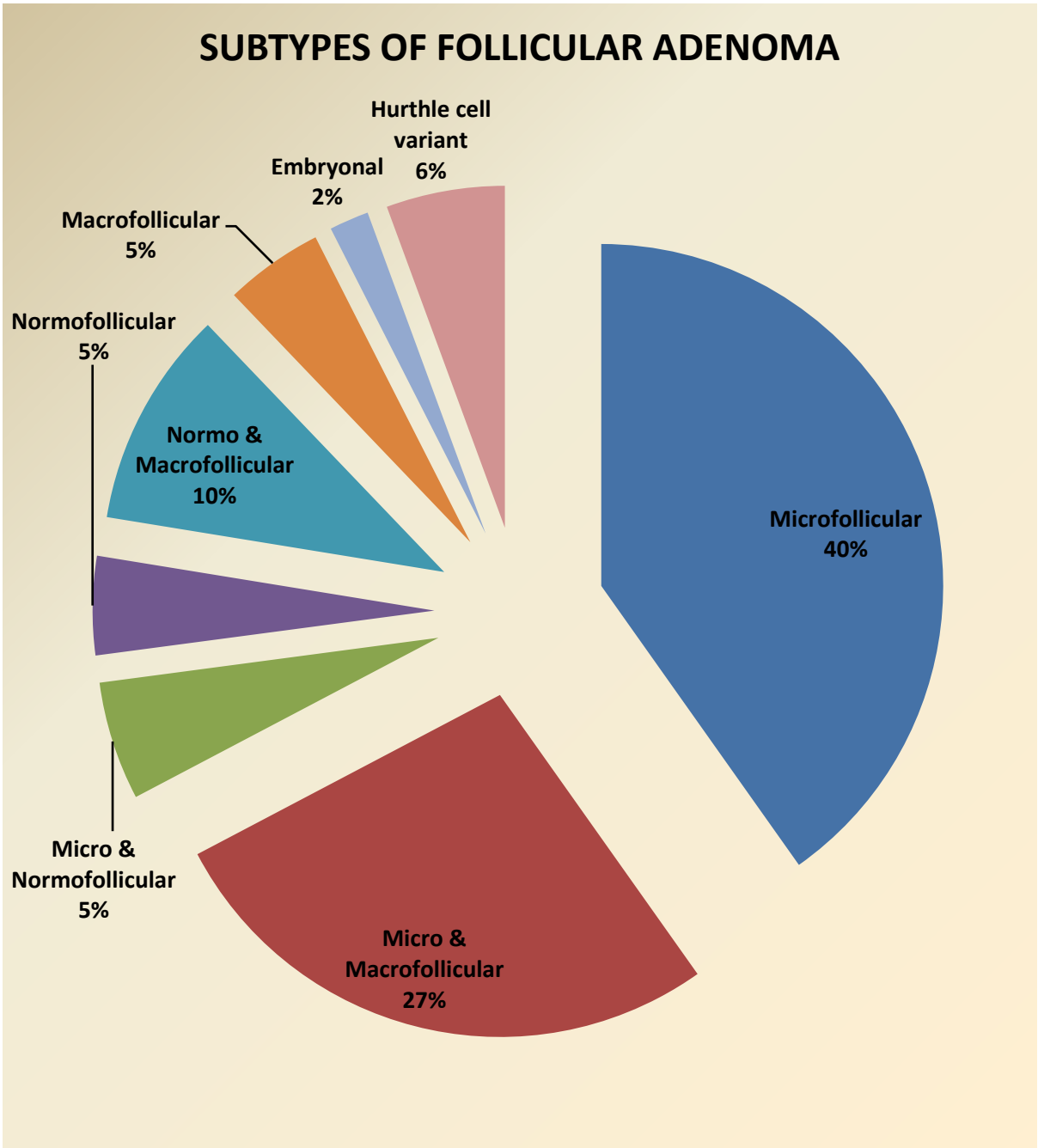

SUBTYPES OF FOLLICULAR ADENOMA
Hurthle cell variant 6%
Embryonal 2%
Macrofollicular 5%
Normofollicular 5%
Normo & Macrofollicular 10%
Microfollicular 40%
Micro & Normofollicular 5%
Micro & Macrofollicular 27%

TABLE 10: DISTRIBUTION OF MALIGNANT THYROID LESIONS

MALIGNANT NEOPLASM	NO OF CASES	PERCENTAGE
Papillary carcinoma	176	90.26
Follicular carcinoma	4	2.05
Hurthle cell carcinoma	1	0.51
Medullary Carcinoma	5	2.56
Anaplastic carcinoma	2	1.03
Insular carcinoma	5	2.56
Squamous cell carcinoma	1	0.51
Mixed PTC + MTC	1	0.51
TOTAL	**195**	**100**

Age distribution

Thyroid malignancies were found to occur in all age groups from second to the eighth decade. The youngest patient was 13 years and the oldest patient was 82 years of age with a mean of 38.18 years and a male:female ratio of 1:5.09. They were observed to be common during the 3rd to 5th decades of life accounting for 141 cases (72.31%).

CHART 8

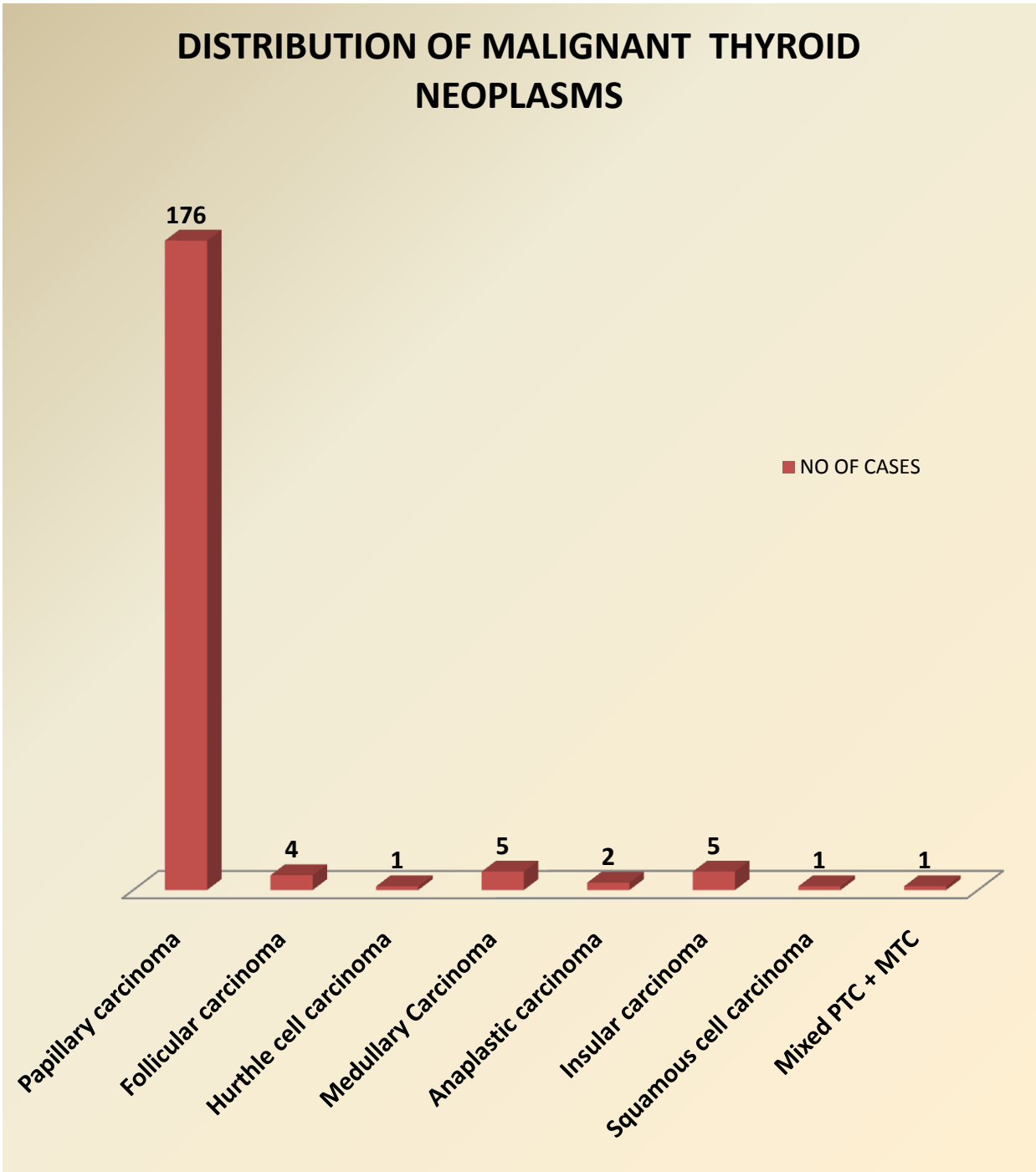

DISTRIBUTION OF MALIGNANT THYROID NEOPLASMS
176
4
1
5
2
5
1
1
NO OF CASES
Papillary carcinoma
Follicular carcinoma
Hurthle cell carcinoma
Medullary Carcinoma
Anaplastic carcinoma
Insular carcinoma
Squamous cell carcinoma
Mixed PTC + MTC

TABLE 11: AGE DISTRIBUTION OF MALIGNANT THYROID NEOPLASMS

MALIGNANT NEOPLASM	AGE IN YEARS							TOTAL
	11-20	21-30	31-40	41-50	51-60	61-70	71-80	
Papillary carcinoma	15	40	59	31	20	6	5	**176**
Follicular carcinoma		1	1		1	1		**4**
Hurthle cell carcinoma			1					**1**
Medullary carcinoma		1	1		3			**5**
Anaplastic carcinoma			1	1				**2**
Insular carcinoma		3			1	1		**5**
Squamous cell carcinoma					1			**1**
Mixed PTC + MTC				1				**1**
TOTAL	**15**	**45**	**63**	**33**	**26**	**8**	**5**	**195**

TABLE 12: SEX DISTRIBUTION OF MALIGNANT THYROID NEOPLASMS

MALIGNANT NEOPLASM	NO OF CASES		TOTAL
	MALES	FEMALES	
Papillary carcinoma	29	147	**176**
Follicular carcinoma		4	**4**
Hurthle cell carcinoma		1	**1**
Medullary Carcinoma	2	3	**5**
Anaplastic carcinoma		2	**2**
Insular carcinoma	1	4	**5**
Squamous cell carcinoma		1	**1**
Mixed PTC + MTC		1	**1**
TOTAL	**32**	**163**	**195**

CHART 9

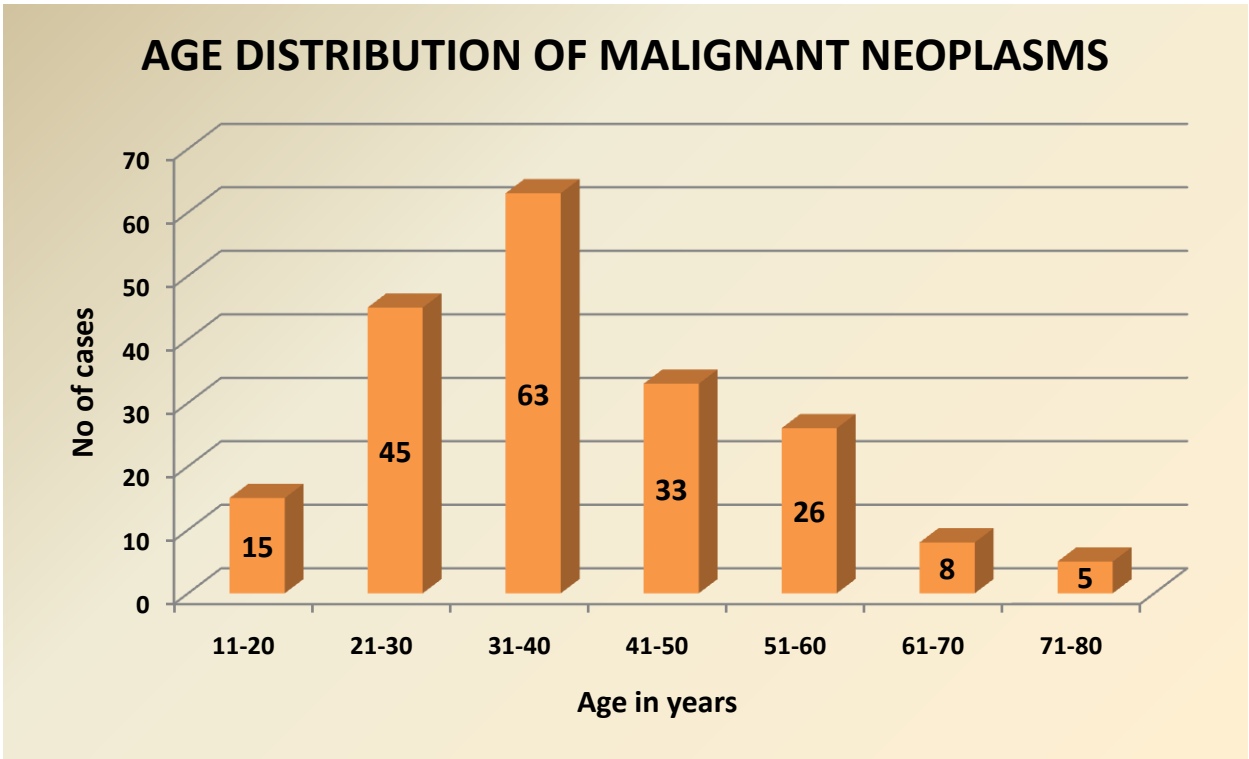
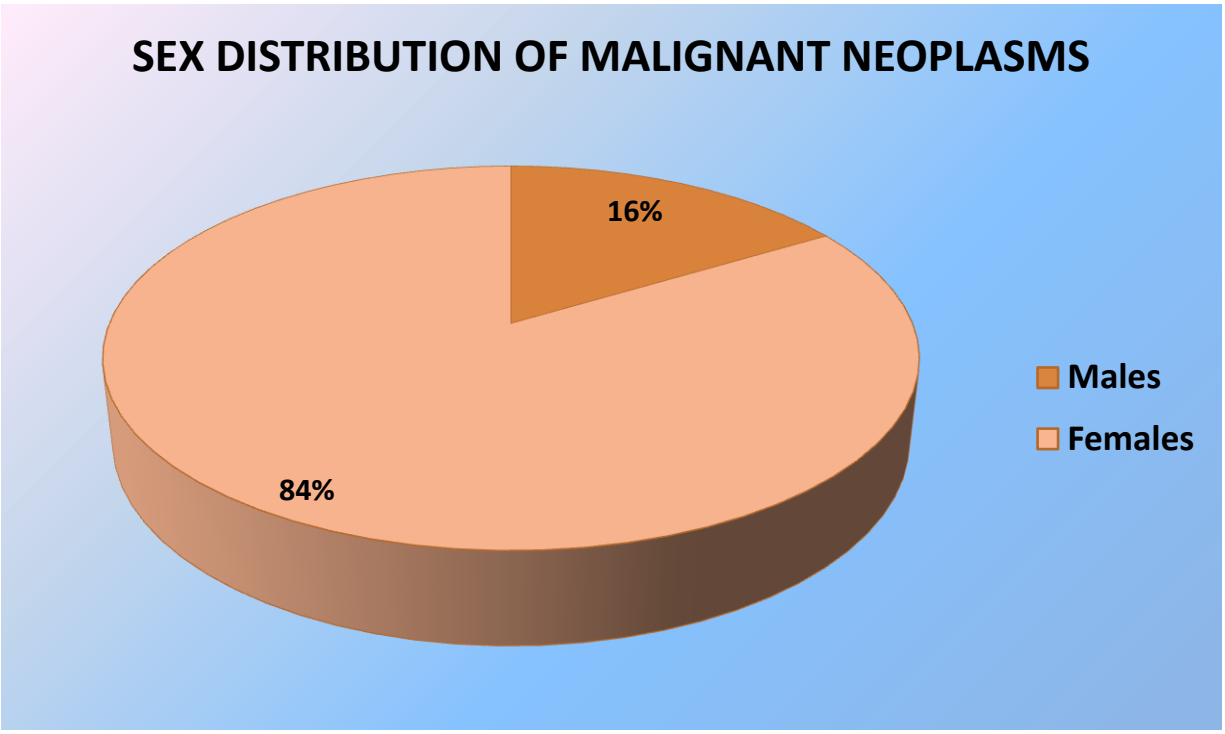


CHART 10



The size of the nodules ranged from 0.1 cm to 11 cm with a mean of 2.94 cm.

TABLE 13: SIZE OF NODULES IN MALIGNANT NEOPLASMS

MALIGNANT NEOPLASM	≥ 2 cm	2 to 4 cm	> 4 cm	TOTAL
Papillary carcinoma	80	72	24	**176**
Follicular carcinoma	0	2	2	**4**
Hurthle cell carcinoma	0	0	1	**1**
Medullary carcinoma	1	1	3	**5**
Anaplastic carcinoma	0	1	1	**2**
Insular carcinoma	2	1	2	**5**
Mixed PTC + MTC	1	0	0	**1**
Squamous cell carcinoma	0	1	0	**1**
TOTAL	**84**	**78**	**33**	**195**

PAPILLARY CARCINOMA

There were 176 cases of papillary carcinoma which constituted 57.33% of all thyroid neoplasms and 90.26% of all thyroid malignancies. Of these 58.52% were of the conventional type followed by the follicular variant (24.43%).

TABLE 14: SUBTYPES OF PAPILLARY CARCINOMA

SUBTYPE OF PTC	NO OF CASES	PERCENTAGE
Conventional	103	58.52
Microcarcinoma	10	5.68
Follicular	43	24.43
Encapsulated follicular	6	3.41

SUBTYPE OF PTC	NO OF CASES	PERCENTAGE
Diffuse follicular	3	1.70
Solid	3	1.70
Oncocytic	3	1.70
Trabecular	2	1.14
Nod Fas Stroma	1	0.57
Dedifferentiated	2	1.14
TOTAL	**176**	**100**

More than 50% of patients were in the age range of 21 to 40 years (56.82%) with a peak incidence during 3rd to 5th decades of life (130 cases) and male:female ratio of 1:5.07.

TABLE 15: AGE DISTRIBUTION OF PAPILLARY CARCINOMA

SUBTYPE OF PTC	AGE IN YEARS							TOTAL
	11-20	21-30	31-40	41-50	51-60	61-70	71-80	
Conventional	10	23	34	20	12	2	2	**103**
Microcarcinoma		2	3	2	3			**10**
Follicular	4	8	17	6	4	2	2	**43**
Encapsulated follicular		4	1	1				**6**
Diffuse follicular			2			1		**3**
Solid	1		1		1			**3**
Oncocytic		2		1				**3**
Trabecular			1	1				**2**
Nod Fas Stroma		1						**1**
Dedifferentiated						1	1	**2**
TOTAL	**15**	**40**	**59**	**31**	**20**	**6**	**5**	**176**

CHART 11

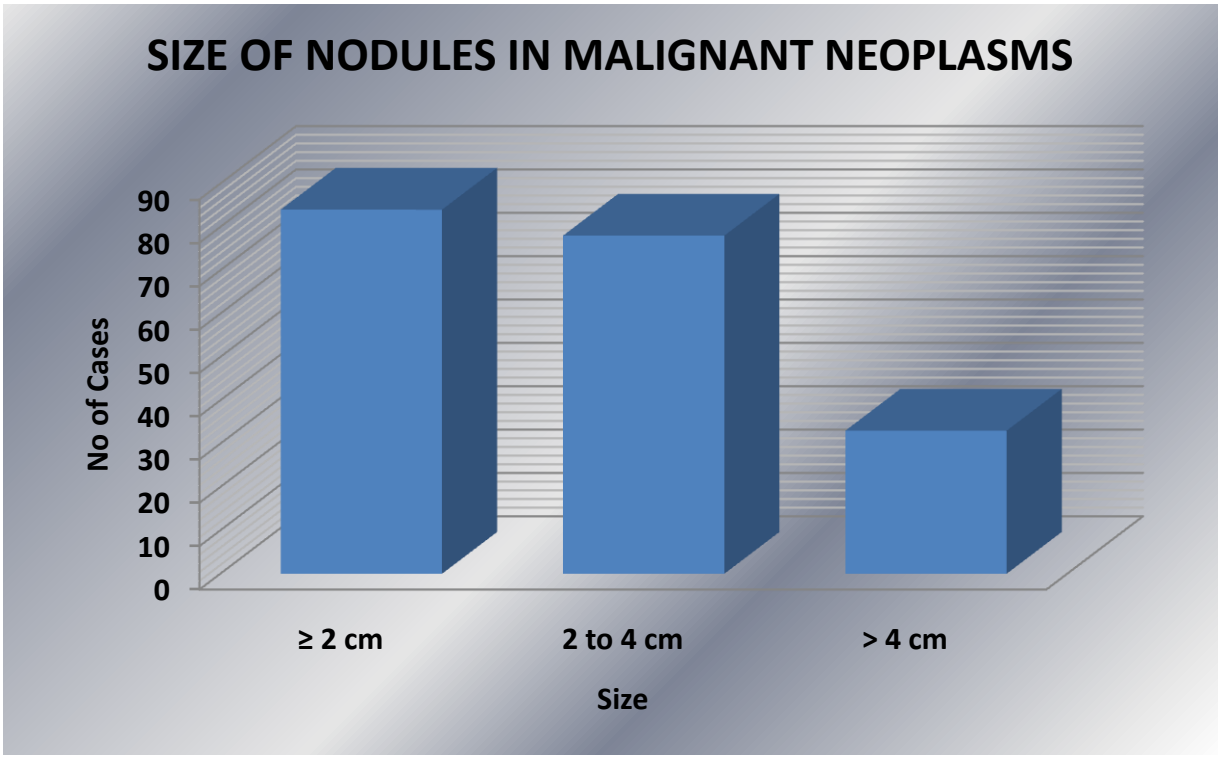


CHART 12

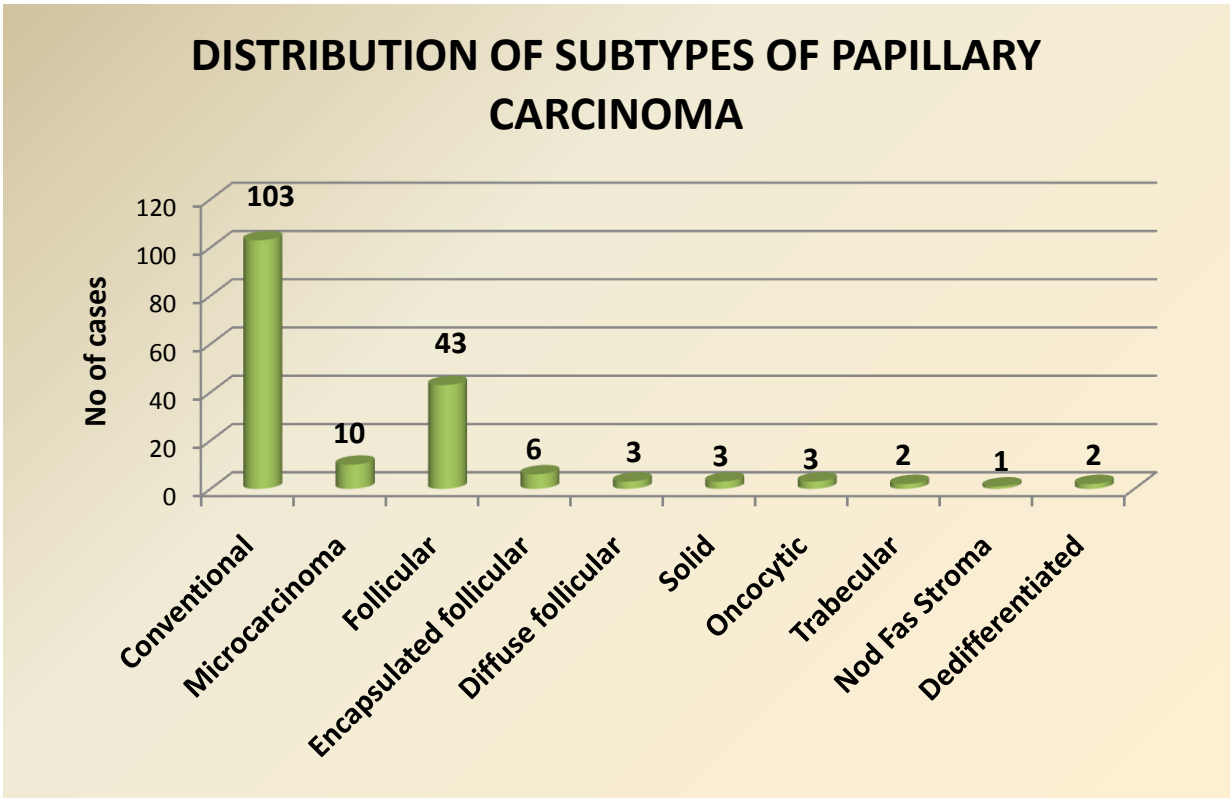


CHART 13

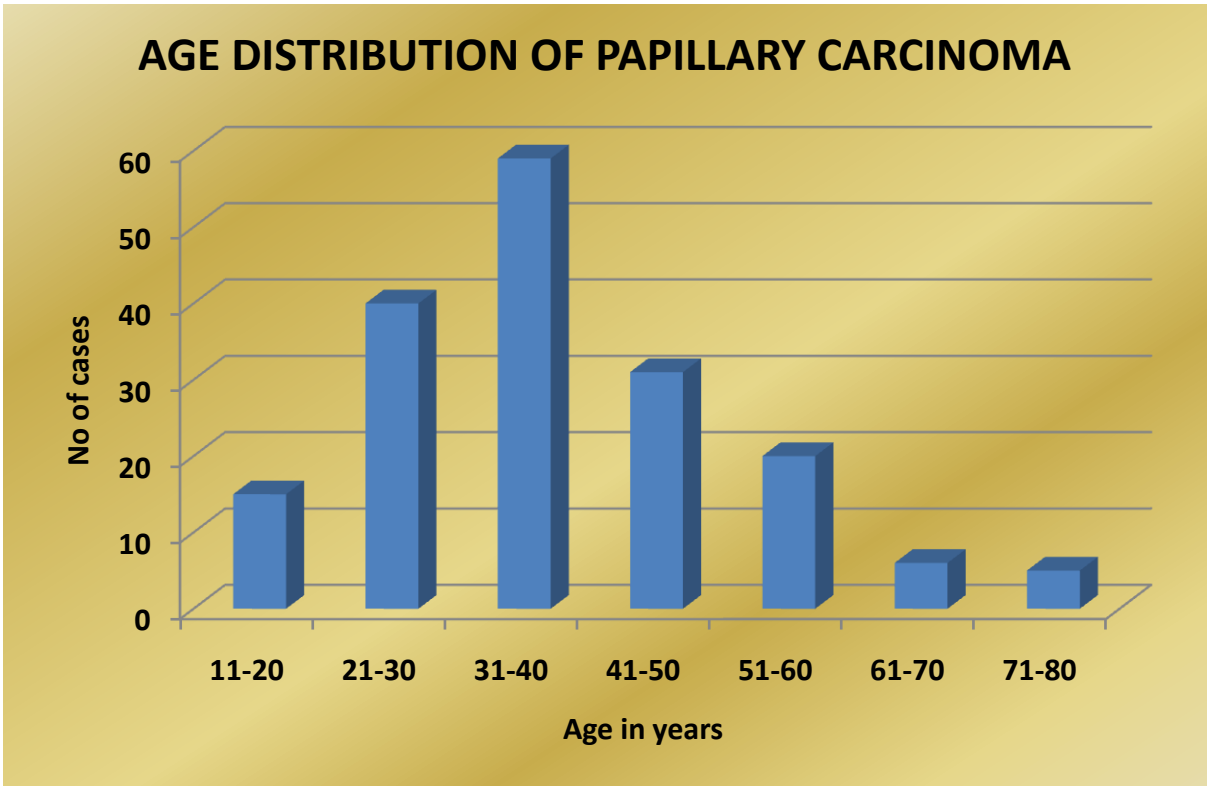


CHART 14

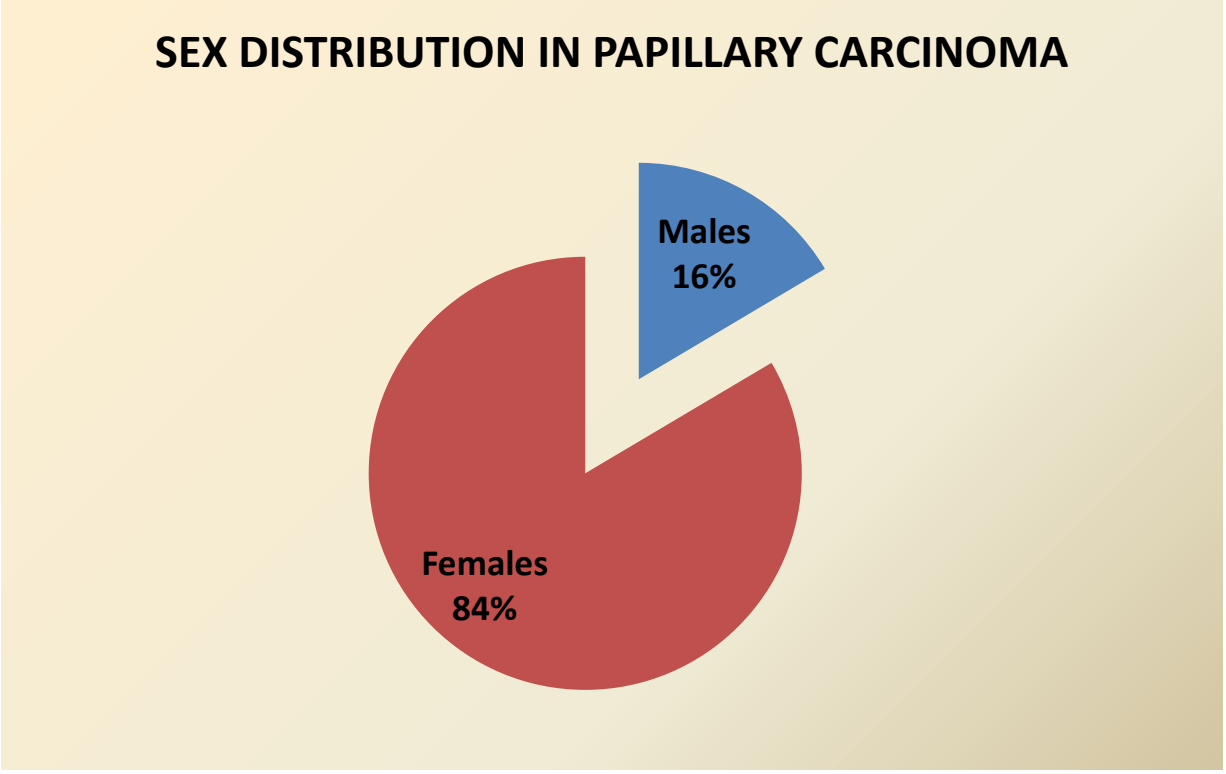


TABLE 16: SEX DISTRIBUTION OF PAPILLARY CARCINOMA

SUBTYPE OF PTC	NO OF CASES		TOTAL
	MALES	FEMALES	
Conventional	15	88	**103**
Microcarcinoma	1	9	**10**
Follicular	7	36	**43**
Encapsulated follicular	2	4	**6**
Diffuse follicular		3	**3**
Solid	1	2	**3**
Oncocytic	1	2	**3**
Trabecular		2	**2**
Nod Fas Stroma		1	**1**
Dedifferentiated	2		**2**
TOTAL	**29**	**147**	**176**

TABLE 17: MACROSCOPIC FEATURES OF PAPILLARY CARCINOMA

GROSS FEATURES	NO OF CASES	PERCENTAGE
Unicentric	90	52.33
Multicentric	80	46.51
Entire thyroid involvement	2	1.16
Solid nodule	153	87.93
Cystic nodule	20	11.49
Solid & cystic	1	0.57
Capsulated nodules	121	69.54

In the present study, unicentric cases were 80 (46.51%), multicentric cases were 90 (52.33%) and entire thyroid involvement in 2 cases (1.16%), 153 cases (87.93%) appeared solid on gross examination, 20 cases (11.49%) were cystic and 1 (0.57%) was solid and cystic.

Nodules varied in size from 0.1 cm to 10 cm with a mean of 2.78 cm

Microscopically arborizing papillary processes with fibrovascular core was seen in the classic type. Ground glass nuclei were seen in 97.7% cases and psammoma bodies in 23.86% cases. Nuclear grooving was present in 98.9% cases, nuclear pseudoinclusions were seen in 24.5% cases. Capsule was present in 69.54% of cases, capsular invasion in 47.11% of capsulated PTC cases, lymphatic invasion in 29.89% and vascular invasion in 29.89% and necrosis in 11.36%.

TABLE 18: MICROSCOPIC FEATURES OF PAPILLARY CARCINOMA

MICROSCOPIC FEATURES	NO OF CASES	PERCENTAGE
Arborizing papillary processes	123	69.89
Ground glass nuclei	172	97.73
Nuclear grooving	174	98.86
Nuclear pseudoinclusions	43	24.5
Psammoma bodies	42	23.86
Capsular invasion	57	47.11
Lymphatic invasion	52	29.89
Vascular invasion	52	29.89
Necrosis	20	11.36

CHART 15

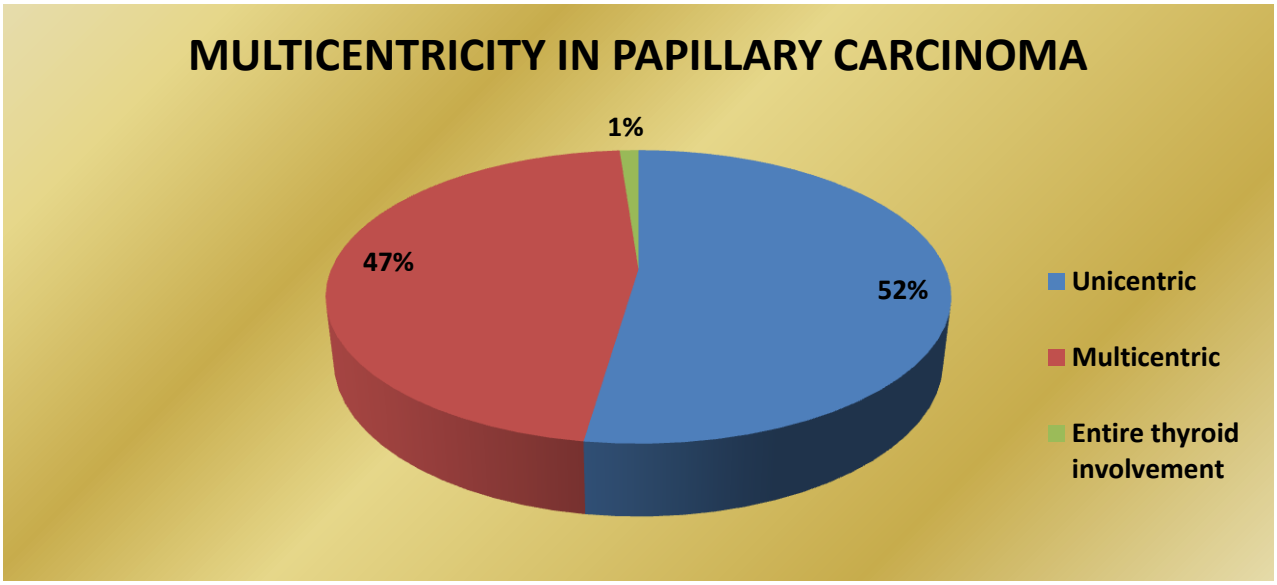
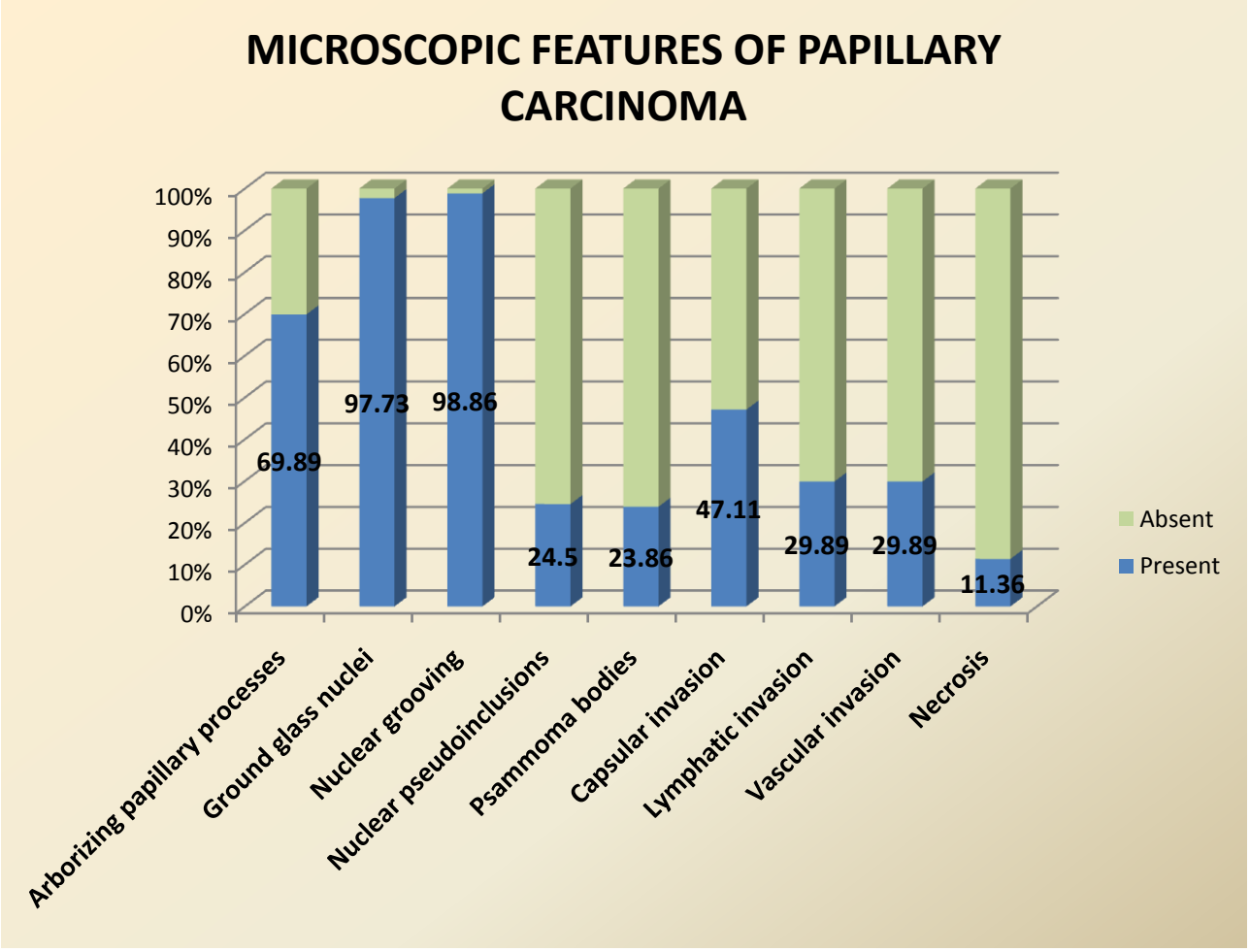


CHART 16



The most common associated lesion was Colloid goitre (38.07%) followed by Hashimoto's thyroiditis (13.64%) and lymphocytic thyroiditis (9.09%).

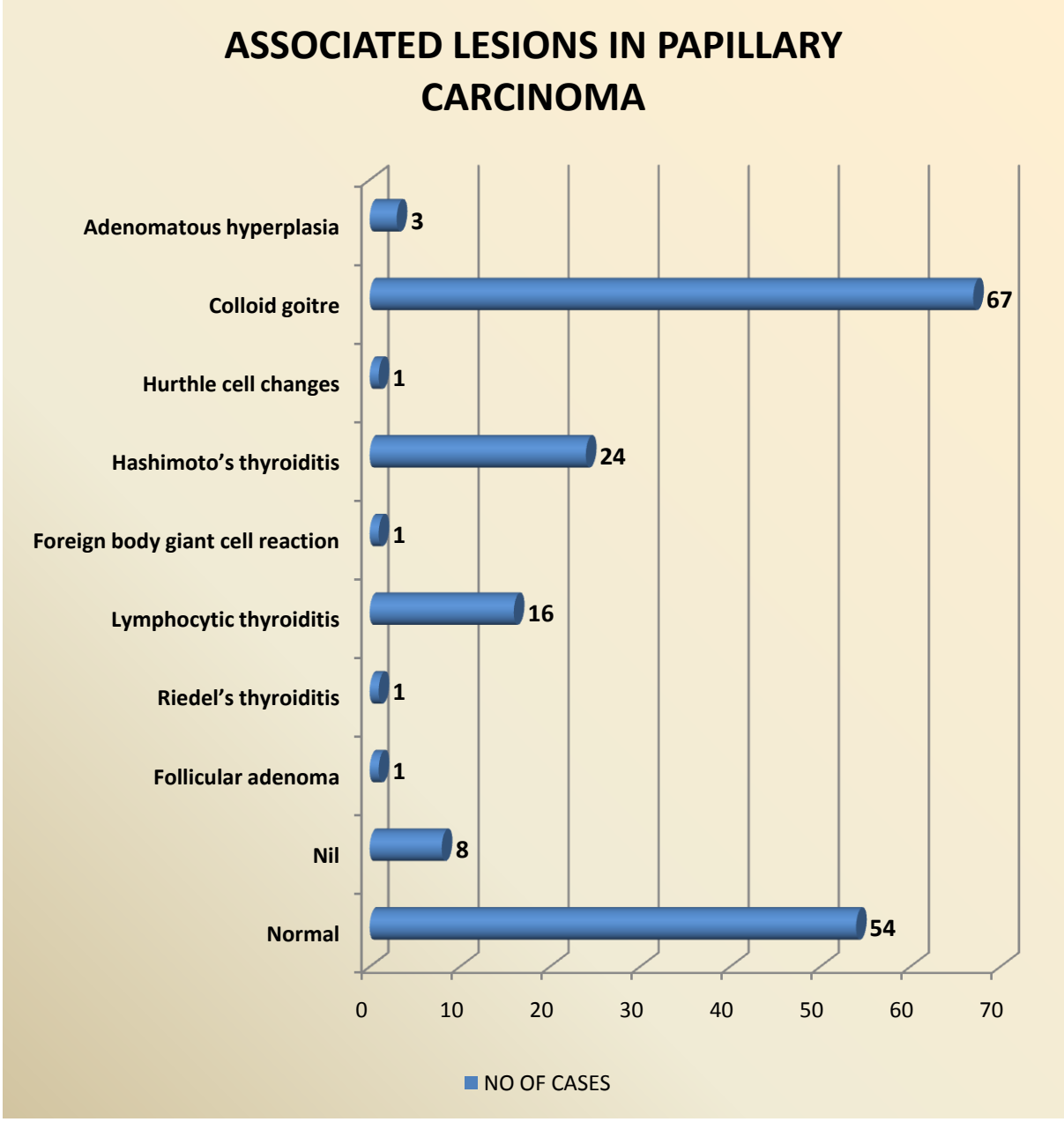
TABLE 19: ASSOCIATED LESIONS IN PAPILLARY CARCINOMA

	ASSOCIATED LESION	NO OF CASES	PERCENTAGE
1.	Adenomatous hyperplasia	3	1.70
2.	Colloid goitre	67	38.07
3.	Focal Hurthle cell changes	1	0.57
4.	Hashimoto's thyroiditis	24	13.64
5.	Inflammatory cell infiltration with foreign body giant cell reaction	1	0.57
6.	Lymphocytic thyroiditis	16	9.09
7.	Riedel's thyroiditis	1	0.57
8.	Follicular adenoma	1	0.57
9.	Nil	8	4.55
10.	Normal	54	30.68
TOTAL		**176**	**100**

FOLLICULAR CARCINOMA

There were 4 cases of follicular carcinoma accounting for 2.05% of malignant thyroid lesions. It occurred from 3rd to 7th decades of life and all were female patients. Grossly, 2 cases showed entire thyroid involvement while the other 2 cases were unicentric. The mean size was 5.25 cm. Microscopically, all 4 cases showed capsular invasion while 2 cases showed lymphovascular invasion. All 4 cases showed necrosis.

CHART 17


ASSOCIATED LESIONS IN PAPILLARY CARCINOMA
Adenomatous hyperplasia
3
Colloid goitre
67
Hurthle cell changes
1
Hashimoto's thyroiditis
24
Foreign body giant cell reaction
1
Lymphocytic thyroiditis
16
Riedel's thyroiditis
1
Follicular adenoma
1
Nil
8
Normal
54
0
10
20
30
40
50
60
70
NO OF CASES

POORLY DIFFERENTIATED CARCINOMA

There were 5 cases of insular type of poorly differentiated carcinoma constituting 2.56% of thyroid malignancies. The mean age was 41 years with male:female ratio of 1:4. Grossly, the nodules varied from 1 cm to 8 cm size with a mean of 3.8 cm. One case was associated with papillary carcinoma.

ANAPLASTIC CARCINOMA

There were 2 cases of anaplastic carcinoma, both females with mean age of 43 years and mean size of 7.25 cm.

MEDULLARY CARCINOMA

There were 5 cases of medullary carcinoma (2.56% of thyroid malignancies), with a mean age of 45.4 years and male:female ratio of 1:1.5. All cases showed Congo red positivity and one case had associated C cell hyperplasia.

SQUAMOUS CELL CARCINOMA

There was one case of primary squamous cell carcinoma in a 55 year old female. Microscopy showed sheets of malignant squamous cells along with bizarre tumour giant cells, necrosis, calcification and hyalinisation. The malignant cells were positive for cytokeratin and negative for thryoglobulin. 3 out of 5 ceervical lymph nodes showed metastatic deposits.

IMMUNOHISTOCHEMISTRY

Immunohistochemistry for CK19 and Thyroglobulin was done for a total of 102 cases, of which 47 were papillary carcinomas and 55 were the lesions histologically mimicking it. The PTC included 20 conventional, 17 follicular, 4 encapsulated follicular, 2 diffuse follicular, 2 solid and 2 oncocytic variants. The histological mimickers included 22 FA, 4 HTA, 1 FTC, 2 insular carcinoma, 12 papillary hyperplasia and 14 Hashimoto's thyroiditis.

Thyroglobulin showed diffuse positivity in all the 102 cases.

Among PTC, all cases of conventional type showed diffuse strong positivity, whereas among the follicular variant, 70.59% showed strong positivity which was diffuse in 2 cases and focal in 10 cases, PTC EFV showed 75% positivity and the other variants showed 50% positivity.

TABLE 20: CYTOKERATIN 19 IMMUNOSTAINING IN PAPILLARY CARCINOMA

PAPILLARY CARCINOMA	POSITIVE	NEGATIVE	% POSITIVE	% NEGATIVE
PTC Conventional	20	0	100	0
PTC Follicular	12	5	70.59	29.41
PTC Encapsulated follicular	3	1	75	25
PTC Diffuse follicular	1	1	50	50
PTC Solid	1	1	50	50
PTC Oncocytic	1	1	50	50
TOTAL	**38**	**9**	**80.85**	**19.15**

Among the histological mimickers of PTC, 95.45% of follicular adenoma showed negativity while 1 case showed a focal weak positivity. 2 cases of insular carcinoma showed positivity.

TABLE 21: CYTOKERATIN 19 IMMUNOSTAINING IN PAPILLARY CARCINOMA MIMICS

PTC MIMICKERS	POSITIVE	NEGATIVE	% POSITIVE	% NEGATIVE
Follicular adenoma	1	21	4.55	95.45
Hyalinising trabecular adenoma	1	3	25	75
Follicular carcinoma	0	1	0	100
Insular carcinoma	2	0	100	0
Papillary hyperplasia	1	11	8.33	91.67
Hashimoto's thyroiditis	2	12	14.29	85.71
TOTAL	**7**	**48**	**12.73**	**87.27**

Cytokeratin 19 was positive in 80.85% of cases of papillary carcinoma, whereas it is positive only in 12.73% of cases of PTC mimickers and this difference is statistically significant with $P<0.001$.

TABLE 22: COMPARISON OF CK19 IMMUNOSTAINING IN PAPILLARY CARCINOMA AND ITS HISTOLOGIC MIMICS

	PTC	PTC MIMICS	TOTAL	PEARSON'S CHI SQUARE TEST
POSITIVE	38	7	45	$\chi 2=47.706$ P = 0.000 [5.0E-12] (Statistically significant)
NEGATIVE	9	48	57	
TOTAL	47	55	102	

For a diagnosis of Papillary carcinoma, CK19 had a sensitivity of 80.85% and specificity of 87.27%. The predictive value of positivity was 84.44% and the predictive value of negativity was 84.21% while the false positivity rate was 12.73% and false negativity rate was 19.15%. The diagnostic accuracy was 84.31%.

TABLE 23: CK19 IN THE DIAGNOSIS OF PAPILLARY CARCINOMA

PARAMETER	PERCENTAGE
Sensitivity	80.85 %
Specificity	87.27 %
Predictive value of positivity	84.44 %
Predictive value of negativity	84.21 %
False positivity rate	12.73 %
False negativity rate	19.15 %
Diagnostic Accuracy	84.31 %

CHART 18

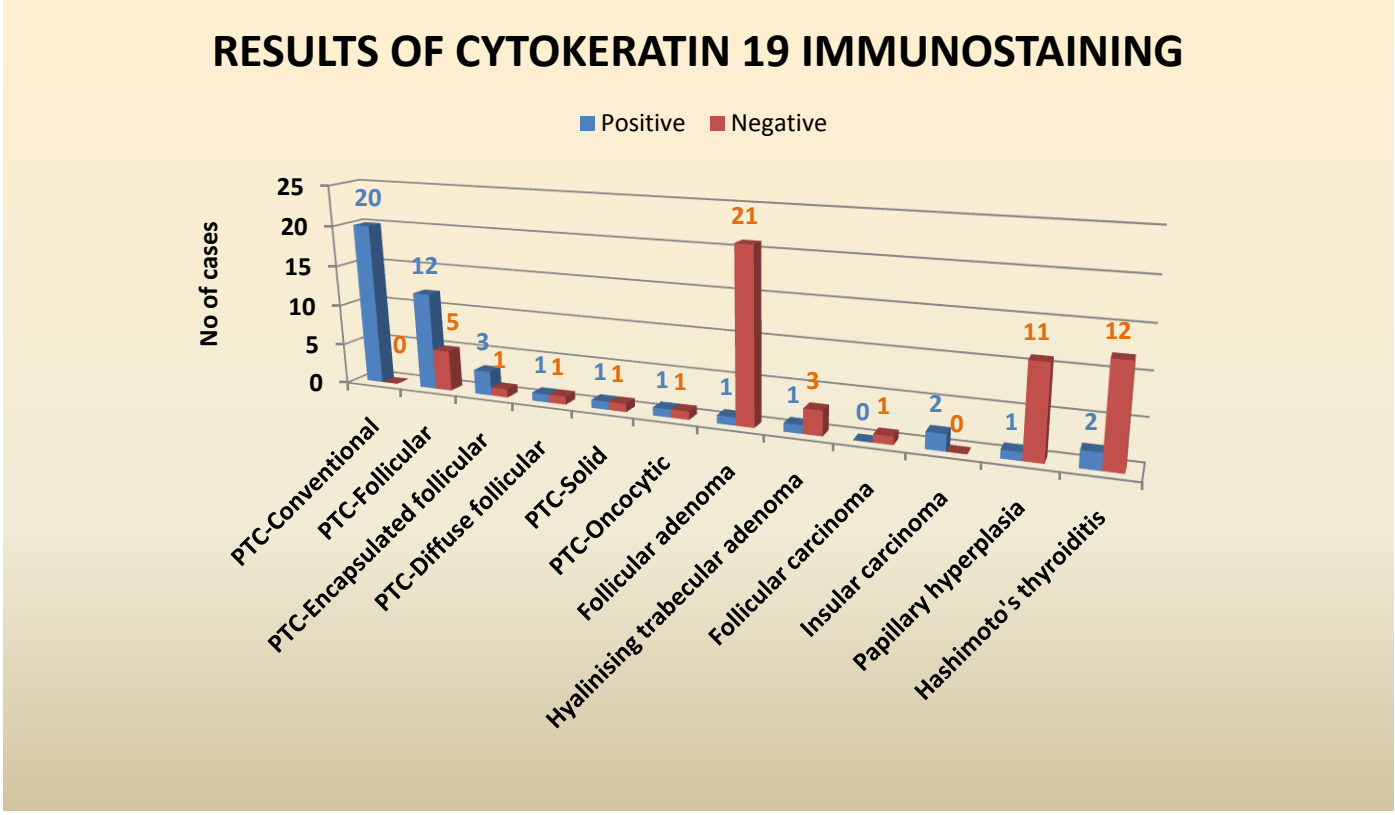
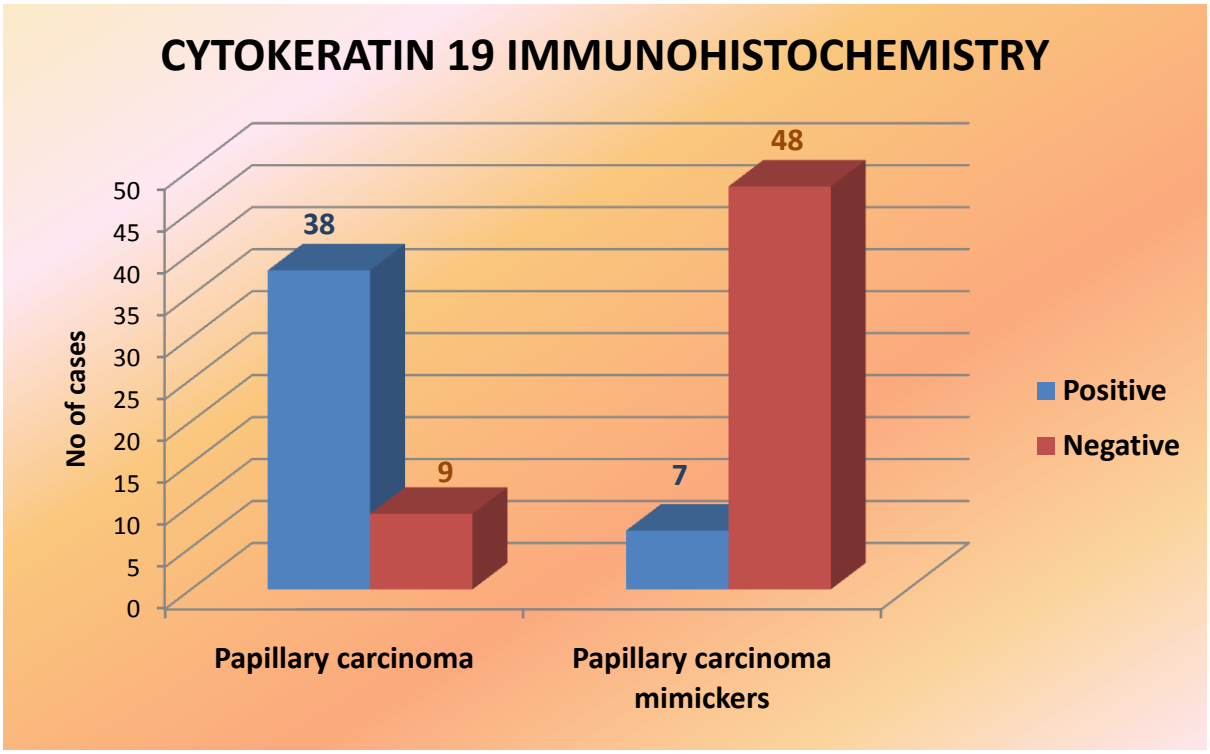


CHART 19



DISCUSSION

Out of a total of 1080 thyroid specimens received, 773 were Nonneoplastic and 307 were neoplastic constituting 71.57% and 28.43% respectively. A study by Sankaran V[75] reviewed 127 cases and found the percentage of nonneoplastic and neoplastic lesions as 85.8% and 14.2% respectively.

Out of the neoplasms, benign and malignant tumours were 112 (36.48%) and 195 (63.52%) respectively.

BENIGN NEOPLASMS

Of the total 112 benign neoplasms, follicular adenoma was the most common lesion (107 cases) followed by hyalinising trabecular adenoma (5 cases).

Maximum incidence was seen during the 3rd and 4th decades of life with female preponderance with a mean age of 36.47 years. Accetta et al[76] found that benign thyroid lesions had a highest incidence during the fifth and sixth decades of life with a mean age of 51.8 years.

The nodules varied in size from 0.1 cm to 7 cm with a mean of 2.88 cm and the majority (87.5%) were less than 4 cm in maximum diameter.

Among follicular adenoma, microfollicular variant was more common accounting for 40.19% of FAs and embryonal type was the least common (1.87%). Hurthle cell adenoma constituted 6 cases (5.61%).

MALIGNANT TUMOURS

Carcinoma of the thyroid gland is a relatively rare disease accounting for 1 % of all malignant neoplasms.[3]

In a study by Yeole BB et al, thyroid cancer constituted 1.3% of total cancers.[77] In our study, the incidence of thyroid malignancies among the total specimens received was 0.95%. Malignant tumours comprised 195 cases of a total of 307 neoplasms studied accounting for 63.52% of all thyroid neoplasms.

Thyroid malignancies occur more commonly in females than in males. Ananthakrishnan et al[78], Budhraja et al,[79] Kishore et al[80] and Freitag et al[81] in their study found a higher incidence of thyroid carcinoma in females compared to males. The present study also showed a highly increased incidence in females with a male to female ratio of 1:5.09.

TABLE 24: COMPARATIVE SEX RATIO OF MALIGNANT THYROID LESIONS

STUDY	MALE: FEMALE RATIO
Ananthakrishnan et al[78]	1:3
Budhraja et al[79]	1:2.2
Kishore et al[80]	1:2.38
Freitag et al[81]	1:5.46
Present study	**1:5.09**

Freitag et al[81] also found that although the relation of 1 male to 5 females with thyroid carcinoma shows a clear dependence on sex, the histological type distribution is

identical in both male and female. Therefore, several different factors seem to influence the development of thyroid carcinoma. One of these factors depends on sex and supports an increased development of carcinoma in female patients. Another factor doesn't depend on sex and causes different histological types.

Thyroid malignancy can occur at any age. Papillary carcinomas occur at a relatively younger age group whereas follicular carcinomas occur at an older age group. Kishore et al[80] and Selzer G et al[82] observed a higher frequency of thyroid malignancies on the third to fifth decades of life. The present study showed a peak incidence of thyroid malignancies in the third to fifth decades of life accounting for 141 cases (72.31%).

TABLE 25: COMPARISON OF AGE INCIDENCE OF THYROID CARCINOMA

STUDY	KISHORE ET AL[80]	SELZER G ET AL[82]	PRESENT STUDY
1st decade	-	3	**-**
2nd decade	6	20	**15**
3rd decade	24	68	**45**
4th decade	31	84	**63**
5th decade	11	40	**33**
6th decade	10	19	**26**
7th decade	7	14	**8**
8th decade	1	6	**5**

Histologically the most common type of thyroid carcinoma was papillary carcinoma. Different studies show varying incidence of histological types. Ananthakrishnan et al,[78] Selzer G et al,[82] Kishore et al,[80] and Budhraja et al[79] also found a high incidence of papillary carcinoma in their study accounting for 46.8%, 52.8%, 47.5%, and 51.2% of all malignant thyroid neplasms respectively. In the present study also papillary carcinoma was the most common type accounting for 90.26% of all malignant thyroid neoplasms followed by medullary carcinoma and insular carcinoma.

TABLE 26: PERCENTAGE INCIDENCE OF THYROID CARCINOMA IN DIFFERENT STUDIES

STUDY	**ANANTHA KRISHNAN ET AL[78]**	**KISHORE ET AL[80]**	**SELZER G ET AL[82]**	**BUDHRAJA ET AL[79]**	**FREITAG ET AL[81]**	**PRESENT STUDY**
Papillary carcinoma	54.6	54.23	52.8	51.2	70.3	**90.26**
Follicular carcinoma	32.5	22.9	30.7	23	18.47	**2.05**
Hurthle cell Ca	-	-	-	-	-	**0.51**
Medullary Carcinoma	5.2	14.7	3.5	2.6	6.24	**2.56**
Poorly differentiated & Anaplastic Ca	3.9	3.27	10.2	20.5	4.99	**3.60**
Lymphoma	1.2	-	1.6	-	-	**-**
Squamous cell Ca	-	-	-	-	-	**0.51**
Mixed PTC + MTC	-	-	-	-	-	**0.51**
Others	2.6	4.9	1.2	2.7	-	**-**

PAPILLARY CARCINOMA

Papillary carcinoma is the most common type of thyroid malignancy and is one of the few neoplasms where the prognosis is good with early diagnosis and proper management. Its incidence appears to have increased in the recent past which may be partially related to a change in the diagnostic criteria, particularly, the recognition of follicular variant.

Papillary carcinoma accounted for 90.26% of all malignant neoplasms in the present study. In a study by Lam AK et al,[83] papillary carcinoma accounted for 72.8% of all primary thyroid cancers.

There seems to be no age exemption for papillary carcinoma. It occurs in a relatively younger age group than follicular carcinoma. Kishore et al[80] in their study found an increased incidence of papillary carcinoma in the third and fourth decade of life. In the present study also a peak incidence of papillary carcinoma was noted in the third to fifth decades (130 out of 176 cases) which coincide with the other two studies.

TABLE 27: AGE INCIDENCE OF PAPILLARY CARCINOMA

STUDY	1ST DECADE	2ND DECADE	3RD DECADE	4TH DECADE	5TH DECADE	6TH DECADE	7TH DECADE	8TH DECADE
Srikhande et al[84]	1	7	28	23	21	25	15	3
Carcangiu et al[31]	1	20	42	62	54	32	25	5
Kishore et al[80]	-	1	7	12	1	4	4	4
Present study	**-**	**15**	**40**	**59**	**31**	**20**	**6**	**5**

Srikhande et al[84] and Carcangiu et al[31] noted a higher incidence of papillary carcinoma in females, with a male to female ratio of 1:1.9 and 1:2.6 respectively.

In the present study, papillary carcinomas were seen to have a higher incidence in females than in males, the male to female ratio being 1:5.07 which is much higher than the other studies.

TABLE 28: COMPARATIVE STUDY OF SEX INCIDENCE OF PAPILLARY CARCINOMA

STUDY	MALE: FEMALE RATIO
Srikhande et al[84]	1:1.9
Carcangiu et al[31]	1:2.6
Lam AK et al[83]	1:3.26
Present study	**1:5.07**

Microscopically ten variants of papillary carcinoma were identified including the conventional type in the present study. The most common type was conventional (58.52 %) followed by follicular variant (24.43%) and the least common was a case of PTC with nodular fasciitis like stroma.

TABLE 29: COMPARISON OF SUBTYPES OF PAPILLARY CARCINOMA

SUBTYPE OF PAPILLARY CARCINOMA	PERCENTAGE OF CASES		
	LAM AK ET AL[83] (N=652)	MUZAFFAR M ET AL[85] (N=82)	PRESENT STUDY (N=176)
Conventional	46.01	70.7	58.52
Microcarcinoma	27.76	-	5.68
Follicular	17.64	15.9	24.43
Encapsulated follicular	-	-	3.41
Diffuse follicular	0.77	-	1.7
Solid	0.77	-	1.7
Oncocytic	0.15	2.4	1.7
Trabecular	-	-	1.14
Nod Fas Stroma	0.31	-	0.57
Dedifferentiated	0.46	-	1.14
Tall cell	3.99	3.7	-
Diffuse sclerosing	1.84	-	-
Columnar cell	0.31	7.3	-

In the present study, unicentric cases were 80 (46.51%), multicentric cases were 90 (52.33%) and entire thyroid involvement in 2 cases (1.16%), the mean size was 2.78cm, 153 cases (87.93%) appeared solid on gross examination, 20 cases (11.49%) were cystic and 1 (0.57%) was solid and cystic.

Microscopically arborizing papillary processes with fibrovascular core was seen in the classic type. Ground glass nuclei were seen in 97.7% cases and psammoma bodies in 23.86% cases. In the study by Srikande et al, 69.9% cases showed ground glass nuclei and 46.3% cases showed psammoma bodies. In a study by Chan JKC et al[19] ground glass nuclei were seen in 84.3% of cases. Klink and Winship[92] found psammoma bodies in 43% of cases of papillary carcinomas and only once in a review of 2153 benign thyroid lesions and thus they represent a very important clue to diagnosis.

In the present study nuclear grooving was present in 98.9% cases, which is in concurrence with the study by Chan JKC.[19] The present study showed nuclear pseudoinclusons in 24.5% cases in contrast to the study by Chan JKC[19] where 46% cases showed nuclear pseudoinclusions.

In the present study, capsule was present in 69.54% of cases, capsular invasion in 47.11% of capsulated PTC cases, lymphatic invasion in 29.89% and vascular invasion in 29.89% and necrosis in 11.36%.

The most common associated lesion was Colloid goitre (38.07%) followed by Hashimoto's thyroiditis (13.64%) and lymphocytic thyroiditis (9.09%). In a study by Selzer G et al,[82] lymphocytic thyroiditis was found in association with 21 tumours (8.2%).

FOLLICULAR CARCINOMA

Follicular carcinoma accounts for 20% of all thyroid tumors. Budhraja et al, Kishore et al,[80] Ananthakrishnan et al[78] and Chan JKC et al[19] observed that follicular carcinoma ranked next to papillary carcinoma in occurrence accounting for 23%, 22.9%, 32.5% and 7.8% of cases respectively. In the present study, follicular carcinoma accounted for 2.05% of all thyroid malignancies.

Follicular carcinomas occur in a relatively older age group compared to papillary carcinomas. Budhraja et al[79] observed that follicular carcinoma occurred in an older age group. Kishore et al[80] observed follicular carcinoma occurring from second to fifth decade. In the present study, follicular carcinomas were observed to occur from 3rd to 7th decades and all the 4 patients were females.

TABLE 30: SEX INCIDENCE OF FOLLICULAR CARCINOMA IN DIFFERENT STUDIES

STUDY	MALE: FEMALE RATIO
Selzer G et al[82]	1:3.6
Kishore et al[80]	1:6
Budhraja et al[79]	All 9 cases females
Present study	**All 4 cases females**

Schmidth RJ et al[86] observed both capsular and vascular invasion in all the 19 cases which they reported. Pilotti et al[87] found 29 cases of widely invasive follicular carcinoma in a study of 720 cases of non medullary carcinomas. In the present study,

microscopically all 4 cases showed capsular invasion while 2 cases showed lymphovascular invasion.

POORLY DIFFERENTIATED CARCINOMA

Pilotti et al[87] in their study of 720 cases of nonmedullary thyroid carcinomas found 4% cases of insular carcinoma. Volante et al[88] observed 6.3% cases of poorly differentiated carcinoma. In the present study, there were 5 cases of insular type of poorly differentiated carcinoma constituting 2.56% of thyroid malignancies, which is less when compared to the other two studies.

TABLE 31: COMPARISON OF INCIDENCE OF POORLY DIFFERENTIATED CARCINOMA

STUDY	PERCENTAGE INCIDENCE
Pilotti et al[87]	4 %
Volante et al[88]	6.3 %
Present study	**2.56 %**

Pilotti et al[87] and Volante et al[88] found the mean age of patients affected to be 53 years and 57 years respectively. In the present study, the mean age was 41 years.

ANAPLASTIC CARCINOMA

Anaplastic carcinoma accounts for 5-10% of all primary malignant thyroid neoplasms. They occur in an older age group and are highly aggressive neoplasms. Kishore et al[80] and Ananthakrishnan et al[78] found 3.27% and 3.9% of cases of anaplastic carcinoma respectively. In the present study there were 2 cases of anaplastic carcinoma accounting for 1.03% of thyroid malignancies. Budhraja et al[79] and Kishore

et al[80] observed a high incidence of anaplastic carcinoma in females. In the present study, both cases were females with mean age of 43 years. Microscopically, highly pleomorphic cells with increased mitotic figures were observed in the present study.

MEDULLARY CARCINOMA

Selzer G et al,[82] Budhraja et al[79] and Kishore et al[80] observed the incidence of medullary carcinoma to be 3.5%, 2.6% and 14.7% respectively. In the present study, medullary carcinoma constituted 2.56% of all malignant thyroid neoplasms which compares well with the study by Budhraja et al.

Kishore et al noticed a male:female ratio of 1:2 with all patients between the age group of 20 to 49 years. Budhraja et al observed a single case of medullary carcinoma in a 50 year male. In the present study, there were 5 cases with a male:female ratio of 1:1.5 with a mean age of 45.4 years.

Chong GC et al[89] in their study of 139 cases of medullary carcinoma found 29 cases of familial medullary carcinomas, these patients found to have a younger age at presentation. In the present study, no familial medullary carcinoma was observed.

The present study had 5 cases of medullary carcinoma which on microscopy showed solid proliferation of cells with highly vascularised stroma and hyalinized collagen. All cases showed amyloid deposition which was confirmed by Congo red staining. One case was found to have associated C-cell hyperplasia.

IMMUNOHISTOCHEMISTRY

Thyroglobulin showed diffuse positivity in all the 102 cases, confirming them to be derived from thyroid follicular epithelium .

PTC have been shown to express strong and diffuse immunoreactivity for CK19 in 80 to 100% of cases.[72] Unfortunately CK19 is also expressed focally in normal thyroid epithelium, Hashimoto's thryoiditis and some benign tumours but the majority of the immunoreactivity occurred in areas of degeneration indicating the reactive nature of CK19 positivity. Nevertheless, diffuse positivity may have diagnostic value. In a study by Carol C Cheung et al,[1] diffuse CK19 immunoreactivity is demonstrated in 66% of papillary carcinomas and few cases of insular carcinomas and Hurthle cell carcinomas.

In the present study, CK19 was positive in 80.85% of cases of papillary carcinoma, whereas it is positive only in 12.73% of cases of PTC mimics. Among PTC, all cases of conventional type showed diffuse strong positivity, whereas among the follicular variant, 70.59% showed strong positivity, PTC EFV showed 75% positivity and the other variants showed 50% positivity.

Statistically significant correlation between Cytokeratin 19 and diagnosis of papillary carcinoma was observed in the present study similar to the various studies as given in Table 32.

TABLE 32: COMPARISON OF CK19 IMMUNOREACTIVITY IN PAPILLARY CARCINOMA AND ITS MIMICS IN VARIOUS STUDIES

STUDY	CK19	PTC	PTC MIMICS	PEARSON'S CHI SQUARE TEST
Carol C Cheung et al[1]	Positive	91	18	$\chi 2=47.619$ P = 0.000 [5.2E-12] (Statistically significant)
	Negative	47	74	
Manju L Prasad et al[91]	Positive	48	9	$\chi 2=42.610$ P = 0.000 [6.7E-11] (Statistically significant)
	Negative	19	53	
Dina el Demellawy et al[71]	Positive	61	17	$\chi 2=47.791$ P = 0.000 [4.7E-12] (Statistically significant)
	Negative	11	48	
Guyetant et al[90]	Positive	59	6	$\chi 2=89.128$ P = 0.000 [3.7E-21] (Statistically significant)
	Negative	0	46	
Michel R Nasr et al[73]	Positive	51	39	$\chi 2=19.326$ P = 0.000 [1.1E-5] (Statistically significant)
	Negative	0	18	
Mustafa Kosem et al[2]	Positive	60	22	$\chi 2=47.280$ P = 0.000 [6.2E-12] (Statistically significant)
	Negative	0	30	
Present study	**Positive**	**38**	**7**	**$\chi 2=47.706$ P = 0.000 [5.0E-12] (Statistically significant)**
	Negative	**9**	**48**	

TABLE 33: COMPARISON OF CK19 IMMUNOREACTIVITY IN PAPILLARY CARCINOMA IN VARIOUS STUDIES

Study	Sensi-tivity	Speci-ficity	Predictive value of positivity	Predictive value of negativity	False +ve rate	False –ve rate	Diagnostic accuracy
Carol C Cheung et al[1]	65.94	80.43	83.49	61.16	19.57	34.06	71.74
Manju L Prasad et al[91]	71.64	85.48	84.21	73.61	14.52	28.36	78.29
Dina El Demellawy et al[71]	84.72	73.85	78.21	81.36	26.15	15.28	79.56
Guyetant et al[90]	100	88.46	90.77	100	11.54	0	94.59
Michel R Nasr et al[73]	100	31.58	56.67	100	68.42	0	63.89
Mustafa Kosem et al[2]	100	57.69	73.17	100	42.31	0	80.36
Present study	**80.85**	**87.27**	**84.44**	**84.21**	**12.73**	**19.15**	**84.31**

Thus, there is a statistically significant association between CK19 positivity and papillary carcinoma with a diagnostic accuracy of 84.31%. Yet, there occurred a few false negative and false positive cases. However to get a diagnostic accuracy of 100%, additional panels like HBME-1, Galectin-3 and CITED-1 could be useful in the differentiation of papillary thyroid carcinoma from its histologic mimics as suggested by Carol C Cheung et al,[1] Sandra Fischer et al[72] and Michel R Nasr et al.[73]

SUMMARY AND CONCLUSION

A total of 307 thyroid specimens received during the study period from January 2009 to April 2011 were studied histomorphologically and were classified according to the WHO histological classification.

The incidence of thyroid neoplasms was 1.43% of all the specimens received in this institution and found to be more common among females (with male:female ratio of 1:7 in benign lesions and 1:5.09 in malignant lesions).

Among thyroid neoplasms, malignant lesions (63.52%) were more common compared to benign lesions (36.48%) with papillary carcinoma (57.33% of all neoplasms) as the most common neoplasm followed by follicular adenoma (33.55%).

Among papillary carcinoma, conventional type was most common (58.52%) followed by follicular variant (24.43%). Multicentric PTC accounted for 46.51%. Ground glass nuclei were seen in 97.7%, psammoma bodies in 23.86%, Nuclear grooving in 98.9% cases and nuclear pseudoinclusons in 24.5% cases.

Capsule was present in 69.54% of cases, capsular invasion in 47.11% of capsulated PTC cases, lymphatic invasion in 29.89% and vascular invasion in 29.89% and necrosis in 11.36%.

The most common associated lesion in papillary carcinoma was Colloid goitre (38.07%) followed by Hashimoto’s thyroiditis (13.64%) and lymphocytic thyroiditis (9.09%).

Immunohistochemical analysis of Cytokeratin 19 and thyroglobulin was done in 102 cases selected randomly from cases of Papillary carcinoma and its histological mimickers (FA, HTA, FTC, Insular carcinoma, Papillary hyperplasia and Hashimoto's thyroiditis). Thyroglobulin showed diffuse positivity in all the cases confirming them to be of follicular origin.

CK19 was positive in 80.85% cases of papillary carcinoma whereas it is positive in 12.73% of lesions histologically mimicking papillary carcinoma and this difference was found to be statistically significant with $P<0.001$ which was in accordance with the other studies reported in the literature. CK19 was 80.85% sensitive and 87.27% specific for papillary carcinoma with a positive predictive value of 84.44% and a diagnostic accuracy of 84.31%. The false positivity rate was 12.73% and the false negativity rate was 19.15%. The results were similar to the studies reported in the literature.

Though there is a statistically significant association between CK19 immunoreactivity and the diagnosis of papillary thyroid carcinoma, there are often few false positive cases, especially in insular carcinoma and few cases of Hashimoto's thyroiditis and false negative cases, especially in the follicular and solid variants of papillary carcinoma.

Thus, Cytokeratin 19 when used alone, the diagnostic accuracy could be 84% and to get 100% accuracy, additional panels may be suggested such as HBME-1, Galectin-3 and CITED-1 as reported in the literature. This, when combined with molecular markers for RET/PTC and BRAF gene mutations, will be highly useful for a definitive diagnosis of papillary carcinoma, especially in difficult cases.

BIBLIOGRAPHY

1. Carol C Cheung, Shereen Ezzat, Jeremy L Freeman, Irving B Rosen, Sylvia L Asa. Immunohistochemical diagnosis of papillary thyroid carcinoma. Mod Pathol 2001; 14 (4): 338-342.
2. Mustafa Kösem, Sabriye Polat, Mustafa Öztürk, Çetin Kotan, Hanefi Özbek and Ekrem Algün. Differential diagnosis of papillary thyroid carcinoma: Immunohistochemical study of 112 cases. Eastern Journal of Medicine 2005; 10: 15-19.
3. DeLellis RA, Williams ED et al. Tumors of thyroid and parathyroid. In: DeLellis RA, Lloyd RV, Heitz PU, Eng C (eds) Pathology and genetics: tumors of endocrine organs. IARC, Lyon, 2004; pp 49–123.
4. Virginia A, Livolsi R. Surgical Pathology of Thyroid, In; Major problems in Pathology Vol 22. Philadelphia : WB Saunders Co ; 1990 ; p. 150 – 159.
5. Evans HL. Follicular Neoplasms of the thyroid. A study of 44 cases followed for a minimum of 10 years, with emphasis on differential diagnosis. Cancer 1984; 54 : 535 – 540.
6. Koren R, Yaniv E, Kristt D et al. Capsular collagen staining of follicular thyroid neoplasms by picrosirius red: role in differential diagnosis. Acta Histochem 2001; 103 (2): 151–157.
7. Eldar S, Sabo E. Cohen A, Misselevich I, Abrahanson J, Cohen O, et al. The value of histomorphometric Nuclear Parameters in the diagnosis of well differentiated follicular carcinoma and follicular adenomas of the thyroid gland. Histopathology

1999 ; 34 : 453 – 461.

8. Carney JA, Ryan J, Goellner JR Hyalinizing trabecular adenoma of the thyroid gland. Am J Surg Pathol 1987; 11 (8): 583–591.
9. Evenson A, Mowschenson P, Wang H et al. Hyalinizing trabecular adenoma: An uncommon thyroid tumor frequently misdiagnosed as papillary or medullary thyroid carcinoma. Am J Surg 2007; 193 (6): 707–712.
10. Cheung CC, Boerner SL, MacMillan CM, Ramyar L, Asa SL. Hyalinizing trabecular tumor of the thyroid: A variant of papillary carcinoma proved by molecular genetics. Am J Surg Pathol 2000; 24 (12): 1622–1626.
11. Fonseca E, Nesland JM, Sobrinho-Simoes M. Expression of stratified epithelial-type cytokeratins in hyalinizing trabecular adenomas supports their relationship with papillary carcinomas of the thyroid. Histopathology 1997; 31 (4): 330–335.
12. Hirokawa M, Carney JA, Ohtsuki Y. Hyalinizing trabecular adenoma and papillary carcinoma of the thyroid gland express different cytokeratin patterns. Am J Surg Pathol 2000; 24(6): 877–881.
13. Galgano MT, Mills SE, Stelow EB. Hyalinizing trabecular adenoma of the thyroid revisited: a histologic and immunohistochemical study of thyroid lesions with prominent trabecular architecture and sclerosis. Am J Surg Pathol 2006; 30 (10): 1269–1273.
14. Gowrishankar S, Pai SA, Carney JA. Hyalinizing trabecular carcinoma of the thyroid gland. Histopathology 2008; 52 (4): 529–531.
15. Mazzateri EL , Young RL. Papillary thyroid carcinoma: A 10 year Follow up report of the impact of therapy in 576 patients. Am J Med 1981; 70: 511-518.

16. Mazzateri EL. An overview of the management of papillary and follicular thyroid carcinoma. Thyroid 1999; 9: 421-427.
17. Chan JKC. Tumors of the thyroid and parathyroid glands, In: Fletcher CDM, editor. Diagnostic Histopatholigy of tumors Vol 2. Edinburg: Churchill Livingstone 2007; p. 997 – 1063.
18. Hawk WA, Hazard JB. The many appearances of papillary carcinoma of the thyroid. Cleve Clin Q 1976; 43 (4): 207–215.
19. Chan JKC, Saw D. The grooved nucleus - A useful diagnostic criterion of papillary carcinoma of the thyroid. Am J Surg Pathol 1986; 10: 672-679.
20. Scopu CD, Mechirnou M, Saradopoulou C et al. The significance of the grooved nucleus in thyroid lesions. Mod Pathol 1993; 6: 691-694.
21. Oyama T et al. A histopathological, immunohistochemical and ultrastructural study of intranuclear cytoplasmic inclusions in thyroid papillary carcinoma. Virchows Arch Pathol Anat Histopathol 1989; 414: 91-104.
22. Carcangiu M L, Sibloy RK, Rosai J. Clear Cell change in primary thyroid tumors. Am J Surg Pathol 1985; 9: 705-722.
23. Dickersin GR, Vickery A L, Jr., Smith SB. Papillary carcinoma of thyroid oxyphil cell type, "Clear cell variant" - A light and electron microscopic study. Am J Surg Pathol 1980; 4: 501-509.
24. Yamashita H, Noguchi S, Murakami N et al. DNA Ploidy and stromal bone formation as prognostic indications of thyroid papillary carcinoma in aged patients - A retrospective study. Acta Pathol Japan 1993; 43: 22-27.
25. Chan JK, Tse CC: Mucin production in metastatic papillary carcinoma of the

thyroid. Hum Pathol 1988; 19:195-200.

26. Hubert JP Jr, Kiernan PD, Beahrs OH, McConahey WM, Woolner LB. Occult papillary carcinoma of the thyroid. Arch Surg 1980; 115 (4): 394–398.
27. Fink A, Tomlinson G, Freeman JL, Rosen IB, Asa SL. Occult micropapillary carcinoma associated with benign follicular thyroid disease and unrelated thyroid neoplasms. Mod Pathol 1996; 9 (8): 816–820.
28. Roti E, Rossi R, Trasforini G et al. Clinical and histological characteristics of papillary thyroid microcarcinoma: results of a retrospective study in 243 patients. J Clin Endocrinol Metab 2006; 91 (6): 2171–2178.
29. Elio R, Degli Uberti E, Braverman L, Bondanelli M. Thyroid papillary microcarcinoma - A descriptive and meta-analysis study. Eur J Endocrinol 2008; 159 (6): 659–673.
30. Lugli A, Terracciano L M, Obelholzer M et al. Macrofollicular variant of Papillary carcinoma of thyroid: A histologic, cytologic and immunohistochemical study of 3 cases and review of literature. Arch Pathol Lab Med 2004; 128: 54-58.
31. Carcangiu ML, Zampi G, Pupi A, Castagnoli A, Rosai J. Papillary carcinoma of the thyroid. A clinico Pathological study of 241 cases. Cancer 1985; 55: 805-28.
32. Rosai J, Carcangiu ML. Pitfalls in the diagnosis of thyroid neoplasms. Pathol Res Pract 1987; 182: 169-79.
33. Montone KT, Baloch ZW, LiVolsi VA. The thyroid Hurthle (oncocytic) cell and its associated pathologic conditions: a surgical pathology and cytopathology review. Arch Pathol Lab Med 2008; 132 (8):1241–1250.
34. Civantos F, Albores-Saavedra J, Nadji M et al. Clear cell variant of papillary

thyroid carcinoma. Am J Surg Pathol 1984; 8: 187-192.

35. Uchino S, Noguchi S, Yamashita H et al Mutational analysis of the APC gene in cribriform-morula variant of papillary thyroid carcinoma. World J Surg 2006; 30 (5):775–779.

36. Fenton PA, Clarke SE, Owen W, Hibbert J, Hodgson SV. Cribriform variant papillary thyroid cancer: a characteristic of familial adenomatous polyposis. Thyroid 2001; 11 (2): 193–197.

37. Cameselle-Teijeiro J, Chan JK. Cribriform-morular variant of papillary carcinoma: a distinctive variant representing the sporadic counterpart of familial adenomatous polyposis-associated thyroid carcinoma. Mod Pathol 1999; 12 (4): 400–411.

38. Apel RL, Asa SL, LiVolsi VA. Papillary thyroid carcinoma with lymphocytic stroma. “Warthin-like tumor” of the thyroid. Am J Surg Pathol 1995; 19 (7): 810–814.

39. Baloch ZW, LiVolsi VA. Warthin-like papillary carcinoma of the thyroid. Arch Pathol Lab Med 2000; 124 (8): 1192–1195.

40. Mizukami Y, Kurumaya H, Kitagawa T et al. Papillary carcinoma of the thyroid gland with fibromatosis-like stroma: A case report and review of the literature. Mod Pathol 1995; 8 (4): 366–370.

41. Basu S, Nair N, Shet T, Borges AM. Papillary thyroid carcinoma with exuberant nodular fasciitis-like stroma: treatment outcome and prognosis. J Laryngol Otol 2006; 120 (4): 338–342.

42. Akslen L A, Machle B O. Papillary thyroid carcinoma with lipomatous stroma. Am J Surg Pathol 1997; 21: 1256–1257.

43. Vergilio J, Baloch Z W, Livolsi VA. Spindle cell metaplasia of the thyroid arising in association with papillary carcinoma and follicular adenoma. Am J Clin Pathol 2002; 117: 199-204.

44. Ivanova R, Soares P, Castro P, Sobrinho-Simoes M. Diffuse (or multinodular) follicular variant of papillary thyroid carcinoma: a clinicopathologic and immunohistochemical analysis of ten cases of an aggressive form of differentiated thyroid carcinoma. Virchows Arch 2002; 440 (4): 418–424.

45. Thompson LD, Wieneke JA, Heffess CS. Diffuse sclerosing variant of papillary thyroid carcinoma: a clinicopathologic and immunophenotypic analysis of 22 cases. Endocr Pathol 2005; 16 (4): 331–348.

46. Hazard JB, Crile G Jr, Dinsmore RS, Hawk WA, Kenyon R. Neoplasms of the thyroid: classification, morphology, and treatment. AMA Arch Pathol 1955; 59 (4): 502–513.

47. Liu J, Singh B, Tallini G et al. Follicular variant of papillary thyroid carcinoma: a clinicopathologic study of a problematic entity. Cancer 2006; 107 (6): 1255–1264.

48. Williams ED. Guest Editorial: Two proposals regarding the terminology of thyroid tumors. Int J Surg Pathol 2000; 8 (3): 181–183.

49. Renshaw AA, Gould EW. Why there is the tendency to “overdiagnose” the follicular variant of papillary thyroid carcinoma. Am J Clin Pathol 2002; 117 (1): 19–21.

50. Baloch ZW, Livolsi V. Pathology of thyroid gland. In: Livolsi V, Asa SL (eds) Endocrine pathology 2002. Churchill Livingstone, Philadelphia, pp 61–88.

51. Baloch ZW, LiVolsi VA. Encapsulated follicular variant of papillary thyroid

carcinoma with bone metastases. Mod Pathol 2000; 13 (8): 861–865.

52. F. Grünwald; Biersack, H. J.; Grunwald, F. Thyroid cancer. Berlin: Springer 2005.
53. New York Thyroid Center. Thyroid Cancer. Prognosis and Staging (http://www.cumc.columbia.edu/dept/thyroid/staging.html)
54. Baloch ZW, Virginia AL. Follicular patterned lesions of the thyroid: The bane of the pathologist. Am J Surg Pathol 2002; 117: 143-50.
55. Georgi LW, Aunch GM, Kiebzke E. The differentiation of atypical adenomas and encapsulated follicular carcinomas in the thyroid. Virchow Arch 1980; 385: 125-41.
56. Thompson LD, Wieneke JA, Paal E, Frommelt RA, Adair CF, Heffess CS. A clinicopathologic study of minimally invasive follicular carcinoma of the thyroid gland with review of literature. Cancer 2001; 91 (3): 505–524.
57. Goldstein NS, Czako P, Neill JS. Metastatic minimally invasive (encapsulated) follicular and Hurthle cell thyroid carcinoma: A study of 34 patients. Mod Pathol 2000; 13 (2): 123–130.
58. Alexander Stojadinovic, Ronald A Ghossein, Alex Hoos, Marshal J Urist, Ronald H Spiro, Jatin P Shah, Murray F Brennan, Ashok R Shaha, Bhuvanesh Singh. Hurthle Cell Carcinoma: A critical histopathologic appraisal. Am J Clin Oncol 2001; 10 (19): 2616-2625.
59. Karmen Stankov, Giovanni Romeo. Oxyphilic carcinoma of the thyroid gland. Arch Oncol 2003; 11 (2): 81-89.
60. Stojadinovic A, Hoos A, Ghossein RA, Urist MJ, Leung DH, Spiro RH et al. Hurthle cell carcinoma: A 60-year experience. Ann Surg Oncol 2002; 9 (2): 197-203.

61. Cheung CC, Ezzat S, Ramyar L, Freeman JL, Asa SL. Molecular basis of hurthle cell papillary thyroid carcinoma. J Clin Endocrinol Metab 2000; 85 (2): 878–882.

62. Sobrinho Simoes M, Sambade C, Fonseca E, Soares P. Poorly differentiated carcinomas of the thyroid gland: A review of the clinicopathologic features of a series of 28 cases of a heterogenous clinically aggressive group of thyroid tumours. Int J Surg Pathol 2002; 10: 123-131.

63. Hiltzik D, Carlson DL, Tuttle RM et al. Poorly differentiated thyroid carcinomas defined on the basis of mitosis and necrosis: A clinicopathologic study of 58 patients. Cancer 2006; 106 (6): 1286–1295.

64. Volante M, Collini P, Nikiforov YE et al. Poorly differentiated thyroid carcinoma: the Turin proposal for the use of uniform diagnostic criteria and an algorithmic diagnostic approach. Am J Surg Pathol 2007; 31 (8): 1256–1264.

65. Nonaka D, Tang Y, Chiriboga L, Rivera M, Ghossein R. Diagnostic utility of thyroid transcription factors Pax8 and TTF-2 (FoxE1) in thyroid epithelial neoplasms. Mod Pathol 2008; 21 (2): 192–200.

66. Hazard JB, Hawk WA, Crile G Jr. Medullary (solid) carcinoma of the thyroid: A clinicopathologic entity. J Clin Endocrinol Metab 1959; 19 (1): 152–161.

67. Williams ED et al. Histogenesis of medullary carcinoma of the thyroid. J Clin Pathol 1966; 19 (2): 114–118.

68. Ozkara SK, Gurbuz Y, Muezzinoglu B et al. Encapsulated cystic papillary variant of medullary carcinoma of thyroid gland. Endocr Pathol 2002; 13 (2): 167–171.

69. Hales M, Rosenau W, Okerlund MD, Galante M. Carcinoma of the thyroid with a mixed medullary and follicular pattern. Morphologic, immunohistochemical and

clinical laboratories studies. Cancer 1982; 50: 1352 – 1359.

70. Su L, Beals T, Bernacki EG, Giordano TJ. Spindle epithelial tumor with thymus-like differentiation: a case report with cytologic, histologic, immunohistologic, and ultrastructural findings. Mod Pathol 1997; 10 (5): 510–514.
71. Dina El Demellawy, Ahmed Nasr and Salem Alowami. Application of CD56, P63 and CK19 immunohistochemistry in the diagnosis of papillary carcinoma of thyroid. Diagnostic Pathology 2008, 3:5:10.1186:3-5.
72. Sandra Fischer, Sylvia L Asa. Application of immunohistochemistry to thyroid neoplasms. Arch Pathol Lab Med 2007; 132 (3): 359-372.
73. Michel R Nasr, Sanjay Mukhopadhyay, Shengle Zhang and Anna-Luise A Katzenstein. Immunohistochemical markers in diagnosis of papillary thyroid carcinoma: utility of HBME1 combined with CK19 immunostaining. Modern Pathology 2006; 19: 1631–1637.
74. Raphael SJ, McKeown-Eyssen G, Asa SL. High molecular weight cytokeratin and Cytokeratin 19 in the diagnosis of thyroid tumours. Mod Pathol. 1994; 7 (3): 295-300.
75. Sankaran V. Swellings of the thyroid. J Indian Med Assoc. 1960; 16 (34): 485-488.
76. Accetta P, Araújo MS, Accetta R, Campos KB. Total thyroidectomy for benign thyroid diseases. Rev Col Bras Cir. 2011; 38 (4): 223-226.
77. Yeole BB. Descriptive epidemiology of thyroid cancer in Greater Bombay. Ind J Cancer 1998; 35:57-64.
78. Ananthakrishnan N, Rao KM, Narasimhan R et al. the single thyroid nodule - A south Indian profile of 503 patients with special reference to the incidence of

malignancy. Ind J Surg 1993; 55 (10); 487-492.

79. Budhraja SN, Perianayagam WJ, Chandra K. Carcinoma of the thyroid gland - A study of 41 cases. Indian J Cancer. 1972; 9 (1): 56-65.
80. Kishore N, Srivasthava A, Sharma LK, Chumber S et al. Thyroid neoplasms - A profile. Ind J Surg 1996; 56: 143-148.
81. Freitag T, Baier A, Dewitz D. Age and sex distribution of primary thyroid cancer in relation to histological type. Zentralbl Chir. 1999; 124 (4): 331-335.
82. Selzer G, Kahn LB, Albertyn L. Primary malignant tumors of the thyroid gland: A clinicopathologic study of 254 cases. Cancer. 1977; 40 (4): 1501-1510.
83. Lam AK, Lo CY, Lam KS. Papillary carcinoma of thyroid: A 30 years clinicopathological review of the histological variants. Endocr Pathol. 2005; 16 (4): 323-330.
84. Shrikhande SS, Phadke AA. Papillary carcinoma of the thyroid gland. A clinicopathological study of 123 cases. Ind J. Cancer 1982; 19: 87-92.
85. Muzaffar M, Nigar E, Mushtaq S, Mamoon N. The morphological variants of papillary carcinoma of the thyroid: A clinico pathological study - AFIP experience. J Pak Med Assoc. 1998; 48 (5): 133-137.
86. Schmidt RJ, Wang CA. Encapsulated follicular carcinoma of the thyroid - Diagnosis, treatment and results. Surgery 1986; 100: 1068-1077.
87. Pilotti S, Collini P, Mariani L, Placucci M, Bongarzone I, Vigneri P, Cipriani S, Falcetta F, Miceli R, Pierotti MA, Rilke F. Insular carcinoma: a distinct de novo entity among follicular carcinomas of the thyroid gland. Am J Surg Pathol 1997; 21 (12): 1466-1473.

88. Volante M, Landolfi S, Chiusa L, Palestini N, Motta M, Codegone A, Torchio B, Papotti MG. Poorly differentiated carcinomas of the thyroid with trabecular, insular, and solid patterns: A clinicopathologic study of 183 patients. Cancer. 2004; 100 (5): 950-957.

89. Chong GC, Beahrs OH, Sizemore GW, Woolner LH. Medullary carcinoma of the thyroid. Cancer 1975; 35: 695-704.

90. Guyetant S, Michalak S, Valo I, Saint-Andre JP. Diagnosis of the follicular variant of papillary thyroid carcinoma - Significance of immunohistochemistry. Ann Pathol 2003; 23 (1): 69-70.

91. Manju L Prasad, Natalia S Pellegata, Ying Huang, Haikady N Nagaraja, Albert de la Chapelle and Richard T Kloos. Galectin-3, fibronectin-1, CITED-1, HBME1 and cytokeratin-19 immunohistochemistry is useful for the differential diagnosis of thyroid tumors. Mod Pathol 2005; 18: 48–57.

92. Klink GH, Winship T. Psammoma bodies and thyroid cancer. Cancer 1959; 12: 656-661.

ANNEXURE I

PROFORMA

HPE No.

Case no. _____

Name : _____ **Date** : ___-___-_____

Age : _____ years **IP. No** : _____

Sex : ☐ Male ☐ Female **Unit** : _____

SPECIMEN SENT : ☐ Total thyroidectomy ☐ Right hemithyroidectomy

☐ Neartotal thyroidectomy ☐ Left hemithyroidectomy

☐ Subtotal thyroidectomy

GROSS FEATURES :

One lobe : Size

Nodules ☐ Single ☐ Multiple

Size of Nodule(s)

Other features

Other lobe : Size

Nodules ☐ Single ☐ Multiple

Size of Nodule(s)

Other features

MICROSCOPIC FEATURES :

Type of Tumour :

Variant :

Grade : ☐ Low grade ☐ High grade

Encapsulation : ☐ Present ☐ Absent

Capsular invasion : ☐ Present ☐ Absent

Lymphatic invasion : ☐ Present ☐ Absent

Vascular invasion : ☐ Present ☐ Absent

Multicentricity : ☐ Unicentric ☐ Multicentric

☐ Necrosis ☐ Papillary processes ☐ Psammoma bodies

☐ Ground glass nuclei ☐ Nuclear grooving

Other features :

Uninvolved Thyroid : ☐ Normal ☐ Hashimoto's thyroiditis

☐ Colloid goitre ☐ Lymphocytic thyroiditis

☐ C cell hyperplasia ☐ Others

Node status :

SPECIAL STAINS :

IMMUNOHISTOCHEMISTRY :

Cytokeratin 19

Thyroglobulin

ANNEXURE II

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 III

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 IV

PROGNOSTIC FACTORS IN PAPILLARY CARCINOMA

1. AGES: Age, Grade, Extent of disease & Size

2. AMES:

PARAMETER	LOW RISK	HIGH RISK
Age Males	< 40 years	> 40 years
Females	< 50 years	> 50 years
Distant **M**etastases	No	Yes
Extent of primary disease	Intrathyroidal	Extrathyroidal
Size	< 5 cm	> 5 cm

3. MACIS:

FACTORS		SCORE
Distant **M**etastasis	Yes	3
	No	0
Age (when tumour was identified)	Less than 39 years	3.1
	Over 40 years	0.08 x Age
Completeness of Surgical Resection	Incomplete	1
	Complete	0
Invasion into surrounding areas of neck	Yes	1
	No	0
Size of tumour		0.3 x Size in cm

Sum of MACIS score	< 6	6 to 6.99	7 to 7.99	> 8
20 year survival	99 %	89 %	56 %	24 %

4. DAEMS: DNA content, Age, Extent of disease, Metastasis & Size of tumour

ANNEXURE V

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.

ANNEXURE VI

INSTITUTIONAL ETHICAL COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No: 04425305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To

Dr. R. Vimal Chander
PG in MD Pathology
Institute of Pathology
Madras Medical College, Chennai -3

Dear Dr. R. Vimal Chander

The Institutional Ethical Committee of Madras Medical College reviewed and discussed your application for approval of the proposal entitled " Histomorphological study of Thyroid neoplasms with special reference to Papillary Thyroid Carcinoma and its neoplastic histological mimickers" No 92082010.

The following members of Ethical committee were present in the meeting held on 24.08.2010 conducted at Madras Medical College, Chennai -3.

1. Prof. S.K. Rajan, MD	-- Chairperson
2. Prof. J. Mohanasundaram, MD,Ph.D,DNB Dean, Madras Medical College, Chennai -3	-- Deputy Chairman
3. Prof. A. Sundaram, MD Vice Principal , MMC, Chennai -3	-- Member Secretary
4. Prof R. Nandhini, MD Director, Institute of Pharmacology, MMC, Ch-3	-- Member
5. Prof. C. Rajendiran , MD	-- Member
Director, Institute of Internal Medicine, MMC, Ch-3	-- Member
6. Prof. Md. Ali, MD, DM	-- Member
Professor & Head ,,Dept. of MGE, MMC, Ch-3	-- Member
7 Prof. Shantha Ravishankar, MD Professor of Neuro Pathology, MMC, Ch-3	-- Member
8. Tmt. Arnold Soulina	-- Social Scientist

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

Sd /. Chairman & Other Members

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

Member Secretary, Ethics Committee

MASTER CHART

S.No.	HPE NO.	AGE	SEX	DIAGNOSIS		NODULE			CAPS	CI	LI	VI	NEC	PAP	CL NUC	GRV	PSAM	REST OF THYROID	LNS	CK19	TG
				TYPE	VARIANT	NO	SIZE	APP													
1	63/09	60	F	PTC	FOL	M	2	SOL	P	+	-	-	+	A	P	P	P	NORMAL	NIL	Negative	+++
2	170/09	35	F	PTC	SOL	M	2	CYS & SOL	P	-	-	-	-	P	P	P	A	HASH	NIL	Negative	++
3	503/09	18	F	FA	MIC & MAC	U	3.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
4	551/09	42	F	PTC	CON	M	2.5	CYS	P	+	-	-	-	P	P	P	A	COLL GOIT LYM AGG	NIL		
5	554/09	35	F	PTC	FOL	U	3	SOL	P	+	+	+	-	A	P	P	A	NORMAL	NIL		
6	611/09	25	F	PTC	CON	U	2	SOL	P	-	-	-	-	P	P	P	A	COLL GOIT	NIL		
7	734/09	40	M	PTC	FOL	U	4	SOL	P	+	-	-	-	A	P	P	A	HASH	NIL		
8	853/09	30	F	PTC	CON		2	SOL	A		-	-	-	P	P	P	A	NORMAL	NIL		
9	1103/09	52	F	PTC	CON	M	6.5	SOL	P	+	-	-	-	P	P	P	P	NORMAL	NIL		
10	1195/09	27	M	FA	MIC	M	2	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL	Negative	+++
11	1305/09	32	M	PTC	CON	U	5	CYS	P	+	-	-	-	P	P	P	P	NORMAL	NIL		
12	1318/09	55	F	PTC	CON	M	4	SOL	P	-	-	-	-	P	P	P	A	COLL GOIT	NIL		
13	1536/09	40	F	PTC	CON	M	3.5	SOL	A		+	+	+	P	P	P	A	COLL GOIT	NIL		
14	1688/09	26	M	INSCA		M	8	SOL	P	+	+	+	+	A	A	A	A	COLL GOIT	NIL		
15	1783/09	44	F	PTC	CON	U	4	CYS	P	-	-	-	-	P	P	P	P	COLL GOIT	NIL		
16	1851/09	25	F	FA	MIC	U	2	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL	Negative	+++
17	1854/09	21	F	PTC	CON	U	3.5	SOL	P	+	-	-	-	P	P	P	A	COLL GOIT	NIL		
18	1957/09	39	F	PTC	CON	M	4	SOL	P	+	-	-	-	P	P	P	P	COLL GOIT	NIL		
19	1960/09	45	F	PTC	CON	M	3	SOL	P	-	-	-	-	P	P	P	A	COLL GOIT	NIL		
20	2025/09	35	F	FA	MIC & MAC	U	4	SOL	P	-	-	-	-	A	A	A	A	HASH	NIL		
21	2101/09	38	M	FA	MIC	U	2	SOL	P	-	-	-	-	A	A	A	A	LYM THYR	NIL	Negative	+++
22	2156/09	32	F	FA	MIC	U	2.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
23	2502/09	38	F	FA	HUR	U	4	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL	Negative	+++
24	2698/09	34	F	FA	MIC & MAC	U	5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
25	2797/09	40	F	FA	MIC	U	2	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		

S.No.	HPE NO.	AGE	SEX	DIAGNOSIS		NODULE			CAPS	CI	LI	VI	NEC	PAP	CL NUC	GRV	PSAM	REST OF THYROID	LNS	CK19	TG
				TYPE	VARIANT	NO	SIZE	APP													
26	2881/09	29	F	FA	MIC & MAC	U	3	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL	Negative	+++
27	2883/09	29	F	FA	MIC	U	2.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
28	2936/09	24	F	FA	MIC	U	2	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
29	3182/09	40	F	PTC	CON	U	2.5	CYS	P	-	-	-	-	P	P	P	A	COLL GOIT	NIL		
30	3202/09	65	M	PTC	DEDIF	M	5	SOL	P	+	+	+	+	P	P	P	A	NIL	NIL		
31	3412/09	26	F	FA	MIC & MAC	U	0.1	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
32	3737/09	35	F	FA	MIC	M	3.5	CYS	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
33	3822/09	20	F	PTC	CON	U	4	SOL	A		-	-	-	P	P	P	P	NORMAL	1/1		
34	4223/09	15	F	PTC	SOL	U	3	SOL	P	+	-	+	-	P	P	P	A	NORMAL	NIL		
35	4435/09	28	F	PTC	CON	U	2.5	SOL	P	-	+	+	-	P	P	P	A	NORMAL	1/1		
36	4470/09	45	M	PTC	CON	U	1.5	SOL	P	+	-	-	-	P	P	P	P	NORMAL	NIL		
37	4528/09	31	F	FA	MIC	U	4.5	SOL	P	-	-	-	-	A	A	A	A	HASH	NIL	Negative	+++
38	4669/09	22	F	PTC	CON	U	1.5	SOL	P	-	-	-	-	P	P	P	A	HASH	NIL		
39	4705/09	32	F	FA	MIC	U	3	SOL	P	-	-	-	-	A	A	A	A	LYM THYR	NIL		
40	4788/09	40	F	PTC	FOL	M	2	SOL	P	-	-	-	-	A	P	P	A	COLL GOIT	NIL		
41	4790/09	26	F	FA	MIC & MAC	U	3	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
42	4799/09	57	F	PTC	CON	M	2	SOL	P	-	-	-	-	P	P	P	A	HASH	NIL		
43	4967/09	22	M	FA	MIC	U	4	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
44	5007/09	38	F	PTC	CON	M	1.5	SOL	P	-	-	-	-	P	P	P	A	COLL GOIT	NIL		
45	5026/09	40	F	PTC	CON	M	2	SOL	P	-	-	-	-	P	P	P	A	NORMAL	NIL		
46	5038/09	46	F	FA	MIC & MAC	U	5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
47	5046/09	40	F	PTC	CON	U	1.5	SOL	P	-	-	-	-	P	P	P	A	NORMAL	NIL		
48	5250/09	57	M	PTC	CON	M	3	SOL	P	-	-	+	-	P	P	P	A	COLL GOIT	2/19		
49	5367/09	25	F	PTC	CON	M	3	SOL	P	-	-	-	-	P	P	P	A	NORMAL	NIL		
50	5453/09	45	F	PTC	CON	U	1.5	CYS	P	-	-	-	-	P	P	P	A	COLL GOIT	NIL		
51	5520/09	65	M	PTC	CON								-	P	P	P	A	NORMAL	1/5		
52	5529/09	26	M	PTC	FOL	U	5	SOL	P	-	-	-	-	A	P	P	A	COLL GOIT	NIL		
53	5574/09	65	F	FA	MIC & MAC	U	3	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		

S.No.	HPE NO.	AGE	SEX	DIAGNOSIS		NODULE			CAPS	CI	LI	VI	NEC	PAP	CL NUC	GRV	PSAM	REST OF THYROID	LNS	CK19	TG
				TYPE	VARIANT	NO	SIZE	APP													
54	5623/09	45	F	FA	MIC	U	2	CYS	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
55	5652/09	32	F	PTC	CON	U	1.5	SOL	A		-	-	-	P	P	P	P	NORMAL	NIL		
56	5710/09	34	F	PTC	CON	M	1.75	SOL	P	-	-	-	-	P	P	P	A	HASH	NIL		
57	5892/09	13	F	HTA		U	2.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
58	5894/09	25	F	PTC	FOL	U	2.5	CYS	P	+	-	-	-	A	P	P	A	LYM THYR	NIL		
59	6007/09	26	F	FA	MIC	U	3	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
60	6020/09	37	F	PTC	CON	U	4.5	SOL	A		-	-	-	P	P	P	A	COLL GOIT	NIL		
61	6021/09	33	F	PTC	MICRCA	M	0.5	SOL	A		-	-	-	P	P	P	A	COLL GOIT	NIL		
62	6077/09	42	F	HTA		U	2.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL	Negative	+++
63	6122/09	32	F	FA	MIC & MAC	U	3	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
64	6203/09	77	M	PTC	CON	U	2	SOL	A		-	-	-	P	P	P	A	COLL GOIT	NIL		
65	6223/09	17	F	PTC	FOL	U	1	SOL	A		+	+	-	A	P	A	A	NORMAL	10/18		
66	6256/09	45	F	FA	MIC & MAC	M	5	SOL	P	-	-	-	-	A	A	A	A	HASH	NIL		
67	6257/09	27	F	FA	MIC	U	3	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
68	6296/09	35	F	PTC	CON	M	2.5	SOL	A		-	-	-	P	P	P	A	COLL GOIT	2/2		
69	6455/09	60	M	FA	MIC & MAC	M	2	CYS	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
70	6540/09	82	F	FA	MIC	M	2	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
71	6837/09	25	M	PTC	CON	U	4	SOL	P	-	-	-	-	P	P	P	A	NORMAL	NIL		
72	6946/09	29	F	PTC	CON	U	1.5	SOL	P	-	-	-	-	P	P	P	A	LYM THYR	NIL		
73	7030/09	21	F	FA	MIC & MAC	U	1.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL	Negative	+++
74	7108/09	48	F	PTC + MTC			2	SOL	P	+	+	+	-	P	P	P	P	COLL GOIT	11/11		
75	7119/09	78	F	PTC	CON	U	3.5	CYS	A		-	-	-	P	P	P	A	COLL GOIT	NIL		
76	7190/09	20	F	FA	MIC & MAC	U	2	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL	Negative	+++
77	7210/09	23	F	FA	MIC	U	4.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL	Negative	+++
78	7283/09	30	F	FA	MIC & MAC	U	3	SOL	P	-	-	-	-	A	A	A	A	HASH	NIL		
79	7298/09	41	F	PTC	FOL	U	3	SOL	A		-	-	-	A	P	P	A	COLL GOIT	NIL		
80	7304/09	34	F	PTC	CON	M	2	SOL	P	-	-	-	-	P	P	P	A	NORMAL	NIL		
81	7307/09	55	M	MTC			5	SOL	A		-	-	+	A	A	A	A	COLL GOIT	2/2		

S.No.	HPE NO.	AGE	SEX	DIAGNOSIS		NODULE			CAPS	CI	LI	VI	NEC	PAP	CL NUC	GRV	PSAM	REST OF THYROID	LNS	CK19	TG
				TYPE	VARIANT	NO	SIZE	APP													
82	7342/09	50	M	FA	MIC	U	6	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
83	7493/09	57	F	MTC	SPC		5	SOL	A		-	+	+	A	A	A	A	NORMAL	NIL		
84	7496/09	60	F	PTC	MICRCA	U	0.1	SOL	A		+	-	-	P	P	P	A	COLL GOIT	1/7		
85	7503/09	20	F	PTC	CON	U	3	SOL	P	-	-	-	-	P	P	P	P	HASH	NIL		
86	7590/09	30	F	FA	MAC	U	4	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL	Negative	+++
87	7671/09	26	F	FA	MIC & MAC	U	3	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
88	7678/09	24	M	PTC	EFV	U	2.5	SOL	P	-	-	-	-	A	P	P	A	NORMAL	NIL		
89	7719/09	32	F	PTC	FOL	U	2	SOL	P	-	-	-	-	A	P	P	A	LYM THYR	NIL		
90	7741/09	35	M	PTC	CON	U	5	SOL	P	+	+	-	-	P	P	P	P	NORMAL	4/4		
91	7746/09	35	F	PTC	CON	U	2	SOL	P	-	-	-	-	P	P	P	A	LYM THYR	NIL		
92	7766/09	65	F	FA	MIC	U	4	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
93	7773/09	46	F	HTA		U	3	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL	Negative	++
94	7856/09	32	M	MTC			5	SOL	P	-	-	-	-	A	A	A	A	LYM THYR	9/9		
95	7868/09	65	M	PTC	CON	M	1.5	SOL	P	-	+	+	-	P	P	P	A	NORMAL	7/7		
96	7871/09	38	F	PTC	FOL	U	5	SOL	A		+	+	+	A	P	P	A	LYM THYR	2/5		
97	7876/09	58	F	FA	MIC	U	5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
98	7958/09	65	F	FTC		ET	2.5	SOL	P	+	+	+	+	A	A	A	A	NORMAL	NIL		
99	7971/09	42	M	FA	MIC & MAC	U	1.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
100	8043/09	33	M	PTC	FOL	U	5	SOL	P	-	-	-	-	A	P	P	A	NORMAL	NIL	Foc +++	+++
101	8044/09	19	F	PTC	FOL	U	2	SOL	P	-	-	-	-	P	P	P	A	NORMAL	NIL	Foc ++	+++
102	8149/09	30	F	FA	MIC	M	3	SOL	P	-	-	-	-	A	A	A	A	HASH	NIL		
103	8253/09	23	F	FA	MIC & MAC	U	3	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
104	8263/09	15	F	PTC	CON	U	2	SOL	A		-	-	-	P	P	P	P	HASH	13/22		
105	8391/09	30	F	FA	MIC	U	2	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
106	8446/09	30	M	FA	MIC	U	2.5	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
107	8553/09	32	F	PTC	CON	M	2.5	SOL	P	-	-	-	-	P	P	P	P	COLL GOIT	NIL		
108	8575/09	29	F	FA	MIC & MAC	U	4	SOL	P	-	-	-	-	A	A	A	A	LYM THYR	0/2		
109	8623/09	48	F	PTC	CON		2						-	P	P	P	A	NORMAL	NIL		

S.No.	HPE NO.	AGE	SEX	DIAGNOSIS		NODULE			CAPS	CI	LI	VI	NEC	PAP	CL NUC	GRV	PSAM	REST OF THYROID	LNS	CK19	TG
				TYPE	VARIANT	NO	SIZE	APP													
110	8649/09	39	F	PTC	CON	U	3	SOL	A		-	-	-	P	P	P	A	NORMAL	NIL		
111	8733/09	38	F	PTC	FOL	U	3.5	SOL	P	-	-	-	-	A	P	P	A	COLL GOIT	NIL	Foc ++	+++
112	59/10	29	F	PTC	CON	U	2	CYS	P	+	+	+	-	P	P	P	P	COLL GOIT	NIL		
113	68/10	20	F	PTC	ONC	U	1	SOL	P	+	+	+	-	A	P	P	A	COLL GOIT	0/1	Negative	+++
114	160/10	57	F	PTC	FOL	U	2.5	SOL	P	+	-	-	-	A	P	P	P	COLL GOIT	NIL		
115	164/10	33	F	PTC	CON	M	3	SOL	P	-	+	+	-	P	P	P	A	HASH	NIL	Dif +++	+++
116	167/10	30	F	PTC	CON	U	2.5	SOL	P	+	+	+	-	P	P	P	A	NORMAL	NIL	Dif +++	++
117	168/10	28	F	PTC	EFV	M	5	SOL	P	-	-	-	-	A	P	P	A	NORMAL	NIL	Negative	+++
118	181/10	34	F	PTC	FOL	U	3	SOL	A		-	-	-	P	A	P	A	NORMAL	NIL		
119	234/10	54	F	FA	NOR	M	0.5	SOL	P	-	-	-	-	A	A	A	A	HASH	NIL		
120	248/10	45	F	PTC	FOL	U	3	SOL	A		-	-	-	A	P	P	A	HASH	0/1	Negative	+++
121	261/10	38	F	PTC	CON	M	2	SOL	P	+	+	+	-	P	P	P	A	COLL GOIT	NIL	Dif ++	+++
122	370/10	30	F	PTC	FOL	U	6	CYS	P	+	-	-	-	A	P	P	A	COLL GOIT TOX CHN	NIL	Foc ++	+++
123	512/10	23	F	PTC	FOL	M	2.5	SOL	P	+	+	+	+	A	P	P	A	NORMAL	NIL		
124	568/10	32	F	FA	NOR & MAC	U	3	SOL	P	-	-	-	-	A	A	A	A	LYM THYR	NIL		
125	580/10	47	F	FA	NOR & MAC	M	4	CYS	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
126	598/10	30	F	PTC	CON	U	3	SOL	P	-	+	+	-	P	P	P	P	LYM THYR	4/4		
127	692/10	19	F	PTC	CON	M	1.5	SOL	P	+	+	+	+	P	P	P	A	NORMAL	20/20		
128	760/10	19	F	PTC	CON	M	2	SOL	P	-	-	-	-	P	P	P	A	COLL GOIT ADEN HYP	NIL		
129	822/10	34	F	PTC	TRAB	U	3	SOL	A		-	-	-	P	P	P	A	LYM THYR	NIL		
130	852/10	30	F	FA	NOR	U	3	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
131	869/10	19	F	PTC	CON	M	3	SOL	P	+	-	-	+	P	P	P	A	COLL GOIT	6/10		
132	884/10	32	M	PTC	FOL	M	3	SOL	P	+	-	-	-	A	P	P	A	COLL GOIT	NIL		
133	956/10	33	F	FA	MIC & NOR	U	3	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
134	961/10	50	F	ANTC		ET	11	SOL	A		-	-	+	A	A	A	A	NIL	NIL		
135	970/10	30	F	FA	NOR & MAC	M	3	CYS	P	-	-	-	-	A	A	A	A	LYM THYR	NIL		
136	1015/10	40	F	HURCA		U	5	SOL	A		+	+	+	A	A	A	A	COLL GOIT	NIL		

S.No.	HPE NO.	AGE	SEX	DIAGNOSIS		NODULE			CAPS	CI	LI	VI	NEC	PAP	CL NUC	GRV	PSAM	REST OF THYROID	LNS	CK19	TG
				TYPE	VARIANT	NO	SIZE	APP													
137	1043/10	42	F	PTC	CON	M	1.5	SOL	A		-	-	-	P	P	P	A	NORMAL	NIL		
138	1073/10	40	F	PTC	FOL	M	3	SOL	P	-	-	-	-	A	P	P	A	NORMAL	0/2		
139	1079/10	30	F	PTC	FOL	U	4	SOL	P	+	-	+	-	A	P	P	A	NIL	NIL		
140	1108/10	57	F	FA	NOR & MAC	U	3	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
141	1178/10	40	F	FA	MIC	U	2	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
142	1193/10	30	F	PTC	CON	M	2	SOL	A		-	+	-	P	P	P	A	COLL GOIT	NIL	Dif ++	+++
143	1422/10	25	F	FA	NOR	U	3.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
144	1436/10	35	F	PTC	CON	M	2	CYS	P	-	-	+	-	P	P	P	P	COLL GOIT PAP HYP	NIL	Foc +++	+++
145	1442/10	30	F	MTC	SMC		0.7	SOL	A		+	-	-	A	A	A	A	C CELL HYP	5/11		
146	1501/10	45	F	PTC	TRAB	U	2	SOL	P	+	-	-	-	P	P	P	A	COLL GOIT	NIL		
147	1615/10	34	F	PTC	CON	M	3.5	SOL	A		+	+	-	P	P	P	A	LYM THYR	NIL		
148	1677/10	38	F	FA	MIC	M	3	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
149	1756/10	14	F	PTC	CON	U	2.5	SOL	P	-	-	-	-	P	P	P	A	NORMAL	NIL	Dif +++	++
150	1810/10	32	F	PTC	FOL	M	3	SOL	P	+	-	-	-	A	P	P	A	COLL GOIT	NIL		
151	2025/10	47	M	PTC	CON	U	2	SOL	P	+	+	+	-	P	P	P	A	NORMAL	NIL	Dif ++	++
152	2028/10	50	F	PTC	EFV	ET	7	SOL	P	-	-	-	-	A	A	P	A	NORMAL	NIL		
153	2242/10	23	M	PTC	EFV	U	4	SOL	P	+	+	+	+	A	P	A	A	NORMAL	NIL	Dif +++	++
154	2262/10	53	F	PTC	CON	U	3	SOL	P	-	-	-	-	P	P	P	P	HASH	NIL		
155	2296/10	39	F	PTC	CON	M	1.5	SOL	P	+	-	-	-	P	P	P	A	HASH	NIL	Dif +++	+++
156	2368/10	40	F	PTC	FOL	M	3.5	SOL	P	-	-	-	-	A	P	P	A	COLL GOIT	NIL		
157	2409/10	32	F	FA	MIC & NOR	U	2	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL	Negative	+++
158	2414/10	24	F	FA	MIC	U	1	SOL	P	-	-	-	-	A	A	A	A	LYM THYR	NIL	Foc +	+++
159	2581/10	26	F	PTC	CON	M	2	SOL	A		+	+	-	P	P	P	A	HASH	6/9	Dif +++	+++
160	2689/10	65	M	PTC	FOL	M	5	CYS	P	-	-	+	-	A	P	P	A	NORMAL	NIL		
161	2692/10	55	F	FTC		ET	10	SOL	P	+	+	+	+	A	A	A	A	NIL	NIL	Negative	+++
162	2694/10	35	F	PTC	CON	U	3	SOL	A		+	+	+	P	P	P	A	LYM THYR	NIL		
163	2716/10	45	F	FA	MAC	U	7	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
164	2733/10	42	F	PTC	CON	M	2	SOL	A		+	-	-	P	P	P	P	NORMAL	NIL	Dif +++	++

S.No.	HPE NO.	AGE	SEX	DIAGNOSIS		NODULE			CAPS	CI	LI	VI	NEC	PAP	CL NUC	GRV	PSAM	REST OF THYROID	LNS	CK19	TG
				TYPE	VARIANT	NO	SIZE	APP													
165	2748/10	55	F	PTC	CON	U	6	SOL	A		-	+	-	P	P	P	A	HASH	0/3		
166	2751/10	38	F	PTC	DFV	U	2	SOL	P	+	-	-	-	A	P	P	A	NIL	NIL	Negative	++
167	2809/10	60	M	PTC	SOL	U	6	SOL	P	+	+	+	-	A	A	P	A	LYM THYR	NIL	Dif +++	+++
168	2877/10	32	F	PTC	DFV	U	6	SOL	A		-	-	+	A	P	P	A	HASH	NIL		
169	2941/10	33	F	FA	MAC	U	2.5	CYS	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
170	3042/10	29	F	PTC	CON	U	5	SOL	P	+	+	+	-	P	P	P	P	NORMAL	1/3	Dif +++	+++
171	3056/10	26	F	FA	MIC & MAC	U	2	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
172	3076/10	38	F	PTC	CON	M	2	SOL	P	+	-	-	-	P	P	P	A	COLL GOIT ADEN HYP	NIL		
173	3136/10	25	F	FA	MAC	U	2.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
174	3282/10	55	F	FA	NOR & MAC	M	4	SOL	P	-	-	-	-	A	A	A	A	HASHT	NIL		
175	3286/10	45	F	HTA		U	1.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL	Negative	+++
176	3308/10	31	F	FA	MIC	U	3.5	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
177	3324/10	29	F	FA	NOR	U	1.5	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
178	3410/10	32	F	FA	MIC & NOR	U	1	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT ADEN HYP	NIL		
179	3495/10	40	F	FA	NOR & MAC	M	3	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT ADEN HYP	NIL		
180	3504/10	30	F	INSCA		U	3	SOL	A		+	+	+	A	A	A	A	NIL	NIL		
181	3515/10	35	F	PTC	EFV	M	4	SOL	P	+	-	-	-	A	P	P	P	ADEN HYP	NIL	Dif ++	+++
182	3520/10	42	F	FA	HUR	U	2	SOL	P	-	-	-	-	A	A	A	A	HASH	NIL		
183	3561/10	40	F	FA	MIC	U	3	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
184	3563/10	30	F	PTC	CON	M	1.5	SOL	A		-	-	-	P	P	P	A	NORMAL	NIL		
185	3640/10	45	F	PTC	CON	M	3	SOL	P	+	-	-	-	P	P	P	P	HASH	1/1	Dif +++	+++
186	3687/10	61	M	FA	NOR & MAC	U	4.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
187	3716/10	20	M	FA	MIC	M	1	CYS	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
188	3765/10	48	M	FA	EMB	U	3	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL	Negative	++
189	3794/10	28	F	FA	NOR	U	4	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
190	3807/10	55	F	FA	MIC & MAC	U	3	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		

S.No.	HPE NO.	AGE	SEX	DIAGNOSIS		NODULE			CAPS	CI	LI	VI	NEC	PAP	CL NUC	GRV	PSAM	REST OF THYROID	LNS	CK19	TG
				TYPE	VARIANT	NO	SIZE	APP													
191	3846/10	40	F	FA	MIC & NOR	U	4	CYS	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
192	3848/10	18	F	FA	MIC	U	2.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
193	3898/10	24	F	PTC	NF	M	4	SOL	A		-	-	-	P	P	P	P	NORMAL	NIL		
194	3951/10	49	F	PTC	MICRCA	M	0.5	SOL	P	-	-	-	-	P	P	P	P	INF FBGC	NIL		
195	3954/10	35	F	PTC	CON	U	3.5	CYS	A		+	+	+	P	P	P	A	NIL	NIL		
196	3991/10	60	F	FA	MIC & NOR	U	1.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
197	4082/10	40	F	PTC	CON	M	5	SOL	P	+	-	-	-	P	P	P	A	COLL GOIT PAP HYP	NIL		
198	4097/10	60	F	FA	HUR	U	7	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
199	4154/10	50	F	PTC	CON	U	4.5	SOL	A		+	+	-	P	P	P	A	NIL	NIL		
200	4167/10	23	F	FA	NOR & MAC	U	1.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
201	4192/10	45	F	PTC	FOL	M	2.5	SOL	A		+	+	-	A	P	P	A	HASH	2/2	Foc +++	+++
202	4510/10	57	M	PTC	CON	M	1.5	SOL	P	+	+	+	+	P	P	P	A	COLL GOIT	12/12	Dif +++	+++
203	4700/10	39	F	PTC	CON	U	2.5	SOL	A		+	+	-	P	P	P	P	NORMAL	NIL	Dif +++	++
204	4744/10	31	F	PTC	FOL	U	4.5	SOL	P	+	-	-	-	A	P	P	A	NORMAL	NIL	Dif +++	+++
205	4758/10	23	M	PTC	MICRCA	U	1	CYS	P	-	-	-	-	P	P	P	A	COLL GOIT	NIL		
206	4765/10	37	F	FA	MIC & MAC	U	1	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL	Negative	++
207	4907/10	26	F	PTC	CON	U	2	SOL	A		-	-	-	P	P	P	A	LYM THYR	NIL		
208	5069/10	36	F	FA	MIC & MAC	U	3	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL	Negative	+++
209	5070/10	18	F	FA	MIC	U	4	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL	Negative	++
210	5072/10	27	F	FA	MIC	U	0.5	SOL	P	-	-	-	-	A	A	A	A	LYM THYR	NIL	Negative	+++
211	5193/10	29	F	PTC	ONC	U	3	SOL	A		+	+	-	A	P	P	P	NORMAL	1/1	Dif +++	++
212	5211/10	43	F	PTC	CON	M	3.5	SOL	P	-	-	-	-	P	P	P	A	HASH	NIL	Dif +++	+++
213	5255/10	37	F	PTC	CON	M	3	SOL	P	-	-	-	-	P	P	P	P	COLL GOIT	NIL	Dif +++	+++
214	5262/10	32	F	PTC	FOL	M	1.5	SOL	P	+	+	+	-	A	P	P	A	NORMAL	NIL	Foc ++	+++
215	5466/10	20	F	PTC	FOL	U	1.5	SOL	P	-	-	-	-	A	P	P	A	NORMAL	NIL	Dif +++	++
216	5581/10	54	F	INSCA		M	6	SOL	P	+	+	+	+	A	A	A	A	NORMAL	0/10		
217	5839/10	50	M	PTC	ONC & CRIB	M	3	SOL	A		+	+	+	A	P	P	P	LYM THYR	15/15		
218	5868/10	29	F	PTC	CON	M	1.5	CYS	P	-	-	-	-	P	P	P	P	NORMAL	NIL	Dif +++	+++

S.No.	HPE NO.	AGE	SEX	DIAGNOSIS		NODULE			CAPS	CI	LI	VI	NEC	PAP	CL NUC	GRV	PSAM	REST OF THYROID	LNS	CK19	TG
				TYPE	VARIANT	NO	SIZE	APP													
219	5884/10	30	F	PTC	FOL	U	4	SOL	P	-	-	-	-	A	P	P	A	LYM THYR	NIL	Negative	+++
220	6080/10	80	M	PTC	DEDIF	U	5	SOL	P	+	+	-	+	A	P	P	A	NIL	NIL		
221	6282/10	36	F	FTC	WD	U	3.5	CYS	P	+	-	-	+	A	A	A	A	NORMAL	NIL		
222	6442/10	15	F	PTC	CON	U	1.5	SOL	P	-	+	+	-	P	P	P	P	COLL GOIT	5/5	Dif +++	+++
223	6489/10	25	F	PTC	FOL	M	1	SOL	P	+	-	-	-	A	P	P	A	LYM THYR	NIL		
224	6515/10	55	F	SQCC			2.5	SOL	A		+	+	+	A	A	A	A	NIL	3/5		
225	6646/10	14	M	FA	MIC	U	4.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
226	6730/10	47	F	FA	MIC	U	2.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL	Negative	+++
227	6753/10	45	F	PTC	CON	M	4	SOL	P	-	-	-	-	P	P	P	P	NORMAL	NIL	Dif +++	+++
228	6846/10	23	F	FA	MIC	U	3.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
229	6977/10	26	F	FTC	WD	U	5	SOL	P	+	-	-	+	A	A	A	A	NIL	NIL		
230	7184/10	26	F	PTC	CON	U	3	SOL	P	+	+	+	-	P	P	P	P	NORMAL	NIL	Dif +++	+++
231	7201/10	75	F	PTC	FOL	M	3	SOL	A		-	-	-	P	P	P	A	NORMAL	NIL	Foc ++	+++
232	7333/10	55	F	FA	MIC & MAC	M	2	CYS	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL	Negative	+++
233	7345/10	34	M	FA	MIC	U	2	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
234	7356/10	65	F	INSCA		U	1	SOL	A		-	-	+	A	A	A	A	COLL GOIT	NIL	Foc +	++
235	7618/10	45	F	PTC	MICRCA	U	1	CYS	A		-	-	-	P	P	P	A	COLL GOIT	NIL		
236	7710/10	59	M	PTC	CON	M	3.5	SOL	P	-	-	-	-	P	P	P	P	HURTHLE CHANGES	7/7		
237	7872/10	50	F	PTC	CON	U	2.5	SOL	P	+	-	-	-	P	P	P	A	COLL GOIT	NIL		
238	8175/10	27	F	FA	MIC	M	2	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
239	8256/10	55	F	FA	HUR	U	2	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL	Negative	+++
240	8261/10	53	F	MTC	ONC		4	SOL	A		-	-	-	A	A	A	A	ADEN HYP	NIL		
241	8308/10	60	F	PTC	CON	M	2	SOL	A		-	-	-	P	P	P	A	NORMAL	1/1		
242	8557/10	40	M	PTC	CON	M	2.5	SOL	A		-	-	-	P	P	P	A	NORMAL	3/3		
243	8611/10	25	F	PTC	CON	M	2	CYS	A		-	-	-	P	P	P	P	ADEN HYP	NIL		
244	8766/10	55	F	FA	MAC	U	4	CYS	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
245	8930/10	38	F	PTC	FOL	U	2	SOL	P	-	-	-	-	A	A	P	P	HASH	0/1		
246	8939/10	71	M	PTC	FOL	U	3	SOL	P	-	-	-	-	A	P	P	A	ADEN HYP	NIL	Negative	+++

S.No.	HPE NO.	AGE	SEX	DIAGNOSIS		NODULE			CAPS	CI	LI	VI	NEC	PAP	CL NUC	GRV	PSAM	REST OF THYROID	LNS	CK19	TG
				TYPE	VARIANT	NO	SIZE	APP													
247	9014/10	30	F	INSCA		M	1	SOL	A		-	-	-	A	A	A	A	HASH	NIL	Foc ++	++
248	9035/10	52	F	FA	HUR	U	6	CYS	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL	Negative	++
249	9190/10	41	F	PTC	CON	M	1.5	CYS	P	-	-	-	-	P	P	P	A	COLL GOIT	NIL		
250	9194/10	55	F	PTC	CON	U	2	SOL	P	-	-	-	-	P	P	P	A	HASH	NIL		
251	9243/10	62	F	PTC	FOL		5	SOL	P	+	+	+	+	A	P	P	A	NIL	NIL	Negative	+++
252	9370/10	55	F	PTC	CON	M	4	CYS	P	-	-	-	-	P	P	P	A	COLL GOIT	NIL		
253	9406/10	34	F	FA	MIC & MAC	M	3	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
254	82/11	38	F	PTC	MICRCA	M	0.5	SOL	A		-	-	-	P	P	P	A	COLL GOIT	NIL		
255	192/11	48	F	PTC	CON	M	1.5	CYS	P	-	+	+	-	P	P	P	P	COLL GOIT	NIL		
256	235/11	36	F	ANTC		U	3.5	SOL	P	+	-	-	+	A	A	A	A	COLL GOIT	NIL		
257	279/11	55	F	FA	MIC	U	3	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
258	433/11	40	F	PTC	CON	M	2.5	SOL	P	-	-	-	-	P	P	P	A	COLL GOIT	NIL		
259	515/11	45	F	PTC	CON	M	2.5	SOL	A		-	-	-	P	P	P	A	HASH	NIL		
260	589/11	57	F	PTC	MICRCA	U	1	SOL	P	+	-	-	-	P	P	P	A	COLL GOIT ADEN HYP	NIL		
261	590/11	32	F	HTA		M	1.5	SOL	P	-	-	-	-	A	A	A	A	ONC ADEN HYP	NIL	Foc +	+++
262	600/11	62	F	PTC	DFV	ET	4	SOL	A		+	+	+	A	P	P	A	NIL	1/1	Foc ++	++
263	663/11	45	F	PTC	CON	U	10	SOL	P	+	+	-	+	P	P	P	P	NORMAL	10/12		
264	776/11	29	F	PTC	EFV	U	3	SOL	P	+	+	+	-	P	P	P	A	COLL GOIT LYM AGG	NIL	Dif +++	++
265	892/11	32	F	PTC	FOL	M	3	SOL	P	+	+	+	-	A	P	P	A	COLL GOIT	NIL	Foc +++	+++
266	917/11	43	F	FA	NOR & MAC	M	1	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
267	998/11	57	F	PTC	FOL	U	6.5	SOL	P	+	+	+	-	A	P	P	A	RIEDELS	NIL	Foc +++	++
268	1140/11	34	F	FA	MIC	U	1.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
269	1165/11	38	F	PTC	MICRCA	U	0.5	SOL	A		-	-	-	P	P	P	P	FA	NIL		
270	1234/11	47	M	PTC	CON	M	1.5	SOL	A		+	-	-	P	P	P	P	COLL GOIT	4/7		
271	1300/11	39	F	PTC	CON	M	1.5	SOL	P	+	+	+	+	P	P	P	P	COLL GOIT TOX CHN	NIL		
272	1310/11	26	F	PTC	CON	U	1.5	SOL	P	+	-	-	-	P	P	P	A	NORMAL	NIL		

S.No.	HPE NO.	AGE	SEX	DIAGNOSIS		NODULE			CAPS	CI	LI	VI	NEC	PAP	CL NUC	GRV	PSAM	REST OF THYROID	LNS	CK19	TG
				TYPE	VARIANT	NO	SIZE	APP													
273	1314/11	24	F	PTC	CON	M	1.5	SOL	A		+	+	-	P	P	P	A	NORMAL	NIL		
274	1368/11	50	F	PTC	FOL	U	3.5	SOL	P	+	+	+	-	A	P	P	A	COLL GOIT ADEN HYP	NIL	Foc +	++
275	1521/11	58	M	PTC	CON	U	5	SOL	P	+	+	+	+	P	P	P	A	LYM THYR	NIL		
276	1527/11	28	F	PTC	FOL	U	1	SOL	A		-	-	-	A	P	P	A	COLL GOIT	NIL		
277	1578/11	57	F	PTC	MICRCA	M	0.5	SOL	P	-	-	-	-	P	P	P	A	HASH	NIL		
278	1736/11	37	M	FA	MIC	U	2	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
279	1741/11	55	F	FA	MIC & MAC	M	2	CYS	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
280	1778/11	39	M	FA	MIC & MAC	U	4.5	CYS	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
281	1800/11	19	F	FA	NOR & MAC	U	3	CYS	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
282	1802/11	25	F	FA	EMB & HUR	M	2	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL	Negative	++
283	1808/11	40	F	FA	MIC & NOR	U	2	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
284	1948/11	22	F	PTC	CON	U	1.5	SOL	P	-	-	-	-	P	P	P	P	COLL GOIT	NIL		
285	1949/11	37	F	PTC	CON	U	2	SOL	A		-	-	-	P	P	P	A	COLL GOIT TOX CHN	NIL		
286	1992/11	33	F	FA	MIC & MAC	M	2.5	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
287	2004/11	46	M	PTC	FOL	M	1	SOL	P	+	-	-	-	A	P	P	A	COLL GOIT	NIL		
288	2128/11	45	F	FA	MIC & MAC	U	4	SOL	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
289	2138/11	40	F	FA	HUR	U	2	CYS	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
290	2245/11	22	F	FA	MIC & MAC	U	3.5	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
291	2281/11	39	F	FA	MIC	U	3	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
292	2410/11	48	F	PTC	FOL	M	4	CYS	P	+	+	+	-	A	P	P	A	HASH	NIL		
293	2467/11	22	F	PTC	FOL	U	2	SOL	P	+	-	-	-	A	P	P	A	LYM THYR	NIL		
294	2589/11	29	F	PTC	CON	M	1.5	SOL	P	-	-	-	-	P	P	P	A	COLL GOIT	NIL		
295	2620/11	24	F	FA	NOR & MAC	U	4.5	SOL	P	-	-	-	-	A	A	A	A	ONC ADEN HYP	NIL		
296	2696/11	35	F	PTC	CON	M	2	SOL	A		-	-	-	P	P	P	A	COLL GOIT	NIL		
297	2736/11	48	M	PTC	CON	U	2	SOL	P	+	+	+	-	P	P	P	A	HASH	NIL		
298	2737/11	27	F	PTC	MICRCA	U	0.5	SOL	A		-	-	-	P	P	P	P	COLL GOIT	NIL		
299	2767/11	47	F	FA	MIC	M	0.5	CYS	P	-	-	-	-	A	A	A	A	NORMAL	NIL		

S.No.	HPE NO.	AGE	SEX	DIAGNOSIS		NODULE			CAPS	CI	LI	VI	NEC	PAP	CL NUC	GRV	PSAM	REST OF THYROID	LNS	CK19	TG
				TYPE	VARIANT	NO	SIZE	APP													
300	2773/11	48	F	FA	MIC	U	3	SOL	P	-	-	-	-	A	A	A	A	NORMAL	NIL		
301	2778/11	20	F	PTC	CON	M	2	SOL	A		+	-	-	P	P	P	P	COLL GOIT	NIL		
302	2851/11	34	F	PTC	CON	M	4	SOL	P	-	-	-	-	P	P	P	A	COLL GOIT	NIL		
303	2857/11	19	F	FA	MIC	U	3	CYS	P	-	-	-	-	A	A	A	A	COLL GOIT	NIL		
304	3033/11	38	F	PTC	FOL	U	3	SOL	P	-	-	-	-	A	P	P	A	COLL GOIT	NIL		
305	3105/11	55	F	PTC	FOL & SOL	M	2	SOL	A		-	+	+	A	P	P	A	COLL GOIT	NIL		
306	3131/11	19	F	PTC	CON	U	1.5	SOL	P	-	-	-	-	P	P	P	A	HASH	NIL		
307	3138/11	40	F	PTC	CON	M	1.5	SOL	A		+	-	-	P	P	P	A	COLL GOIT	5/28		
308	890/09	34	F	HASH									-	A	A	A	A	NIL	NIL	Negative	+++
309	979/09	30	F	PAPHYP									-	P	A	A	A	NIL	NIL	Negative	+++
310	1281/09	22	F	HASH									-	A	A	A	A	NIL	NIL	Negative	+++
311	1325/09	27	F	HASH									-	A	A	A	A	NIL	NIL	Negative	+++
312	1537/09	25	F	PAPHYP									-	P	A	A	A	NIL	NIL	Negative	+++
313	1833/09	49	F	HASH									-	A	A	A	A	NIL	NIL	Negative	+++
314	1852/09	33	F	HASH									-	A	A	A	A	NIL	NIL	Negative	+++
315	2174/09	45	F	PAPHYP									-	P	A	A	A	NIL	NIL	Negative	+++
316	2307/09	24	M	PAPHYP									-	P	A	A	A	NIL	NIL	Negative	+++
317	2622/09	45	F	PAPHYP									-	P	A	A	A	NIL	NIL	Negative	+++
318	3015/09	42	F	HASH									-	A	A	A	A	NIL	NIL	Negative	+++
319	6379/09	45	F	HASH									-	A	A	A	A	NIL	NIL	Negative	+++
320	6721/09	35	F	HASH									-	A	A	A	A	NIL	NIL	Negative	+++
321	872/10	45	F	HASH									-	A	A	A	A	NIL	NIL	Negative	+++
322	1625/10	35	F	HASH									-	A	A	A	A	NIL	NIL	Negative	+++
323	2186/10	40	F	PAPHYP									-	P	A	A	A	NIL	NIL	Foc +	+++
324	2325/10	50	F	PAPHYP									-	P	A	A	A	NIL	NIL	Negative	+++
325	2879/10	38	F	PAPHYP									-	P	A	A	A	NIL	NIL	Negative	+++
326	3055/10	40	F	PAPHYP									-	P	A	A	A	NIL	NIL	Negative	+++
327	3138/10	30	F	HASH									-	A	A	A	A	NIL	NIL	Foc ++	+++

S.No.	HPE NO.	AGE	SEX	DIAGNOSIS		NODULE			CAPS	CI	LI	VI	NEC	PAP	CL NUC	GRV	PSAM	REST OF THYROID	LNS	CK19	TG
				TYPE	VARIANT	NO	SIZE	APP													
328	3468/10	28	F	PAPHYP									-	P	A	A	A	NIL	NIL	Negative	+++
329	3699/10	57	M	PAPHYP									-	P	A	A	A	NIL	NIL	Negative	+++
330	3705/10	34	F	PAPHYP									-	P	A	A	A	NIL	NIL	Negative	+++
331	6652/10	55	F	HASH									-	A	A	A	A	NIL	NIL	Negative	+++
332	7249/10	45	F	HASH									-	A	A	A	A	NIL	NIL	Foc ++	+++
333	9349/10	27	F	HASH									-	A	A	A	A	NIL	NIL	Negative	+++

KEY TO MASTER CHART

+	-	Weak positivity
++	-	Moderate positivity
+++	-	Strong positivity
A	-	Absent
ADEN HYP	-	Adenomatous hyperplasia
ANTC	-	Anaplastic thyroid carcinoma
APP	-	Gross appearance
C HYP	-	C cell hyperplasia
CAPS	-	Capsule
CI	-	Capsular invasion
CK19	-	Cytokeratin 19
CL NUC	-	Ground glass nuclei (Nuclear clearing)
COLL GOIT	-	Colloid goitre
COLL GOIT ADEN HYP	-	Colloid goitre with focal adenomatous hyperplasia
COLL GOIT LYM AGG	-	Colloid goitre with focal lymphoid aggregates
COLL GOIT PAP HYP	-	Colloid goitre with focal papillary hyperplasia
COLL GOIT TOX CHN	-	Colloid goitre with focal toxic changes
CON	-	Conventional
CRIB	-	Cribriform variant
CYS	-	Cystic
DEDIF	-	Dedifferentiated variant
DFV	-	Diffuse follicular variant
Dif	-	Diffuse positivity
EFV	-	Encapsulated follicular variant
EMB	-	Embryonal variant
ET	-	Entire thyroid involvement
FA	-	Follicular adenoma
FA	-	Follicular adenoma
Foc	-	Focal positivity
FOL	-	Follicular variant

FTC	-	Follicular thyroid carcinoma
GRV	-	Nuclear grooving
HASH	-	Hashimotos thyroiditis
HASHT	-	Hashitoxicosis
HTA	-	Hyalinising trabecular adenoma
HUR	-	Hurthle cell variant
HURCA	-	Hurthle cell carcinoma
HURTHLE CHANGES	-	Hurthle cell changes
INF FBGC	-	Dense inflammatory infiltrate & foreign body giant cell reaction
INSCA	-	Insular carcinoma
LI	-	Lymphatic invasion
LNS	-	Lymph node status
LYM THYR	-	Lymphocytic thyroiditis
M	-	Multicentric
MAC	-	Macrofollicular variant
MIC	-	Microfollicular variant
MICRCA	-	Microcarcinoma
MTC	-	Medullary thyroid carcinoma
NEC	-	Necrosis
NF	-	Nodular fasciitis like stroma
NOR	-	Normofollicular variant
NORMAL	-	Normal
ONC	-	Oncocytic variant
ONC ADEN HYP	-	Oncocytic adenomatous hyperplasia
P	-	Present
PAP	-	Papillary processes
PAPHYP	-	Papillary hyperplasia
Pos	-	Positive
PSAM	-	Psammoma bodies
PTC	-	Papillary thyroid carcinoma
PTC+MTC	-	Mixed papillary and medullary thyroid carcinoma
RIEDELS	-	Riedels thyroiditis
SMC	-	Small cell variant
SOL	-	Solid
SPC	-	Spindle cell variant
SQCC	-	Squamous cell carcinoma
TG	-	Thyroglobulin
TRAB	-	Trabecular variant
U	-	Unicentric
VI	-	Vascular invasion
WD	-	Well differentiated

BENIGN THYROID NEOPLASMS

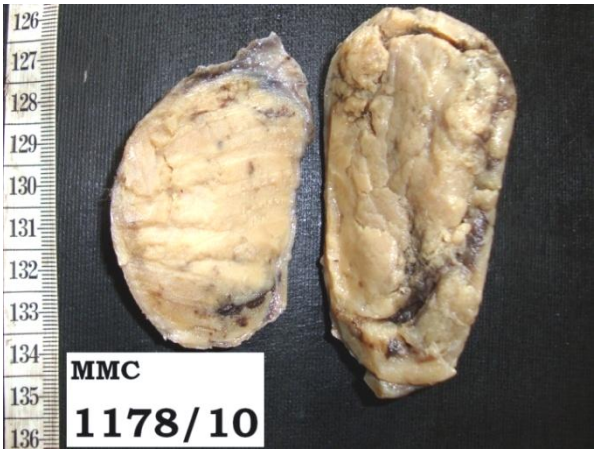


Figure 1: Follicular adenoma gross appearance

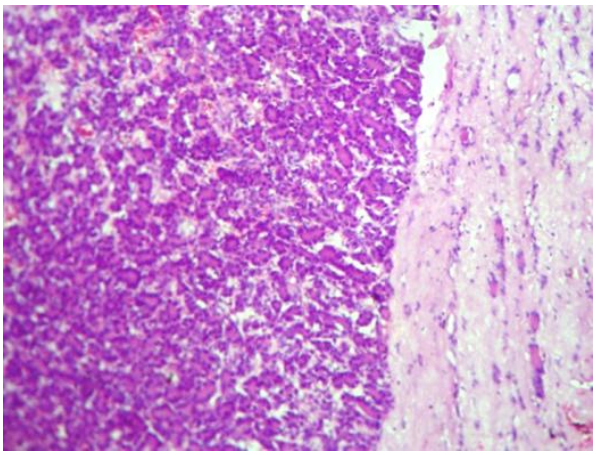


Figure 2: Microfollicular type of follicular adenoma (H&E x100)

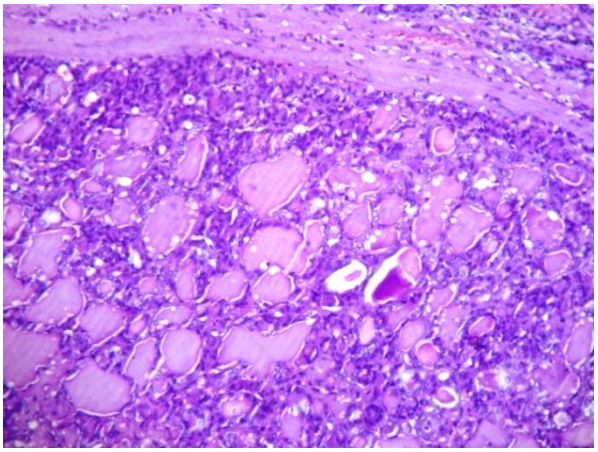


Figure 3: Micro and normofollicular type of follicular adenoma (H&E x100)

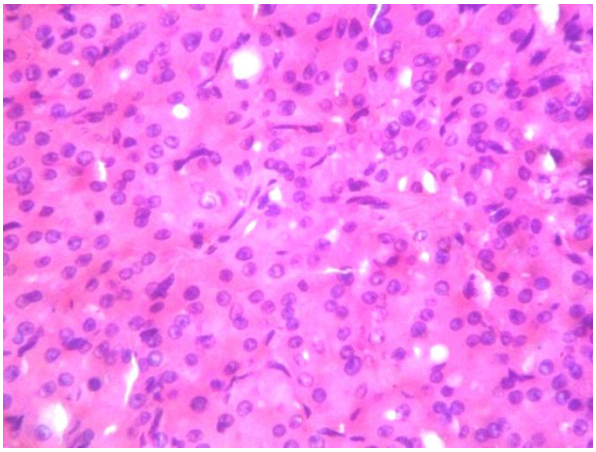


Figure 4: Hurthle cell type of follicular adenoma (H&E x400)

Figure 5: Hyalinising trabecular adenoma presenting as a capsulated well defined homogenous gray tan solid nodule with coexisting colloid nodule

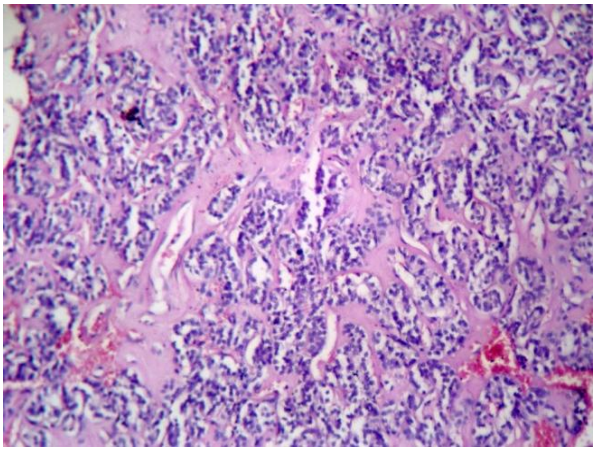


Figure 6: Hyalinising trabecular adenoma (H&E x100)

PAPILLARY THYROID CARCINOMA

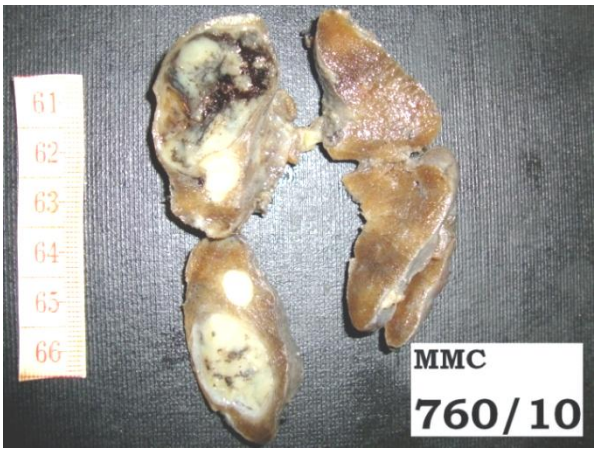


Figure 7: Macroscopic appearance of papillary carcinoma

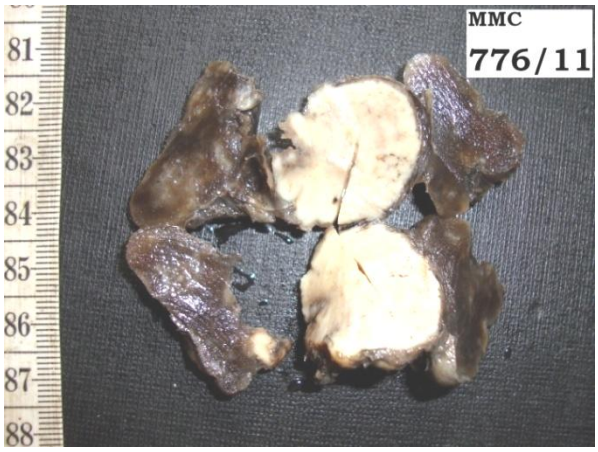


Figure 8: Papillary carcinoma presenting as isthmic nodule

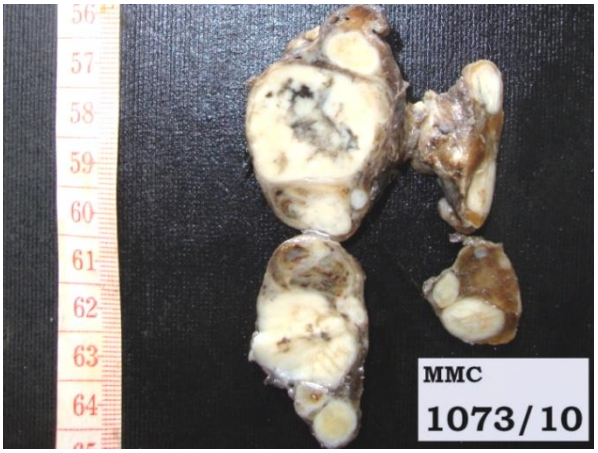


Figure 9: Multicentric papillary carcinoma with areas of necrosis

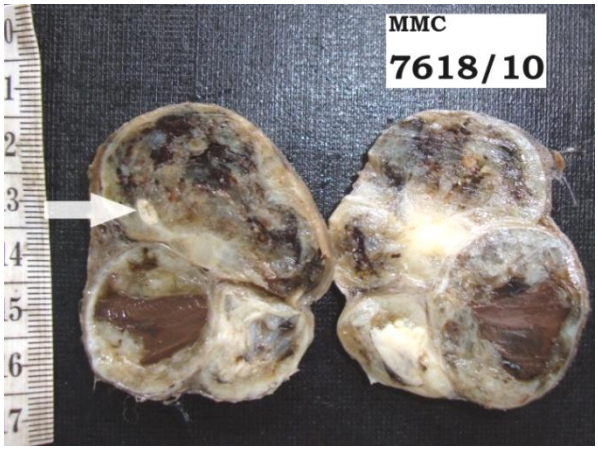


Figure 10: Papillary microcarcinoma presenting as a tiny solid area (arrow) within a nodular colloid goiter

Figure 11: Papillary carcinoma - Solid variant

Figure 12: Lymph node metastasis of papillary thyroid carcinoma presenting as a multicystic mass with a solid portion showing projection of papillary processes into the cystic space

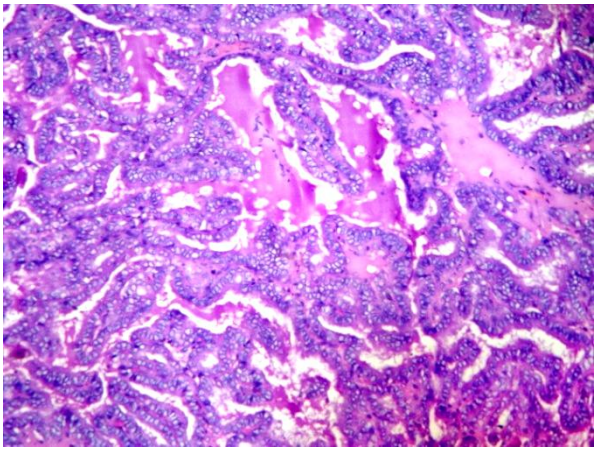


Figure 13: Conventional type of papillary carcinoma with arborising papillary processes (H&E x100)

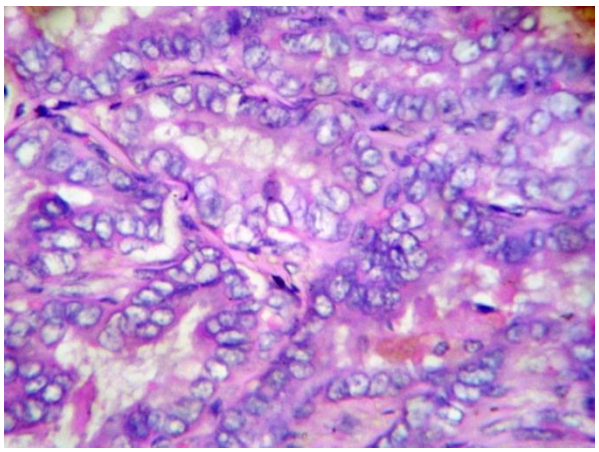


Figure 14: Papillary carcinoma with characteristic nuclear features (H&E x400)

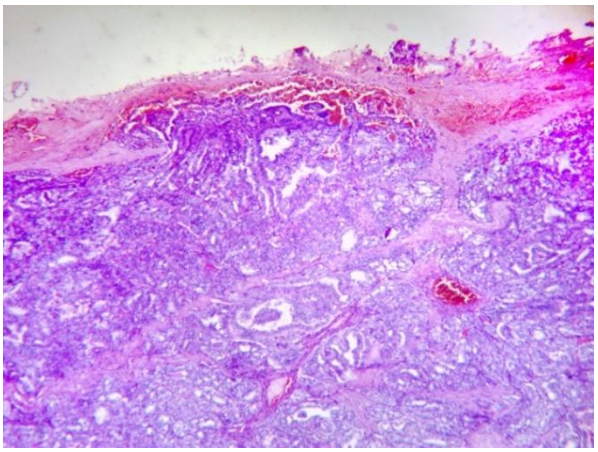


Figure 15: Papillary carcinoma showing capsular invasion (H&E x40)

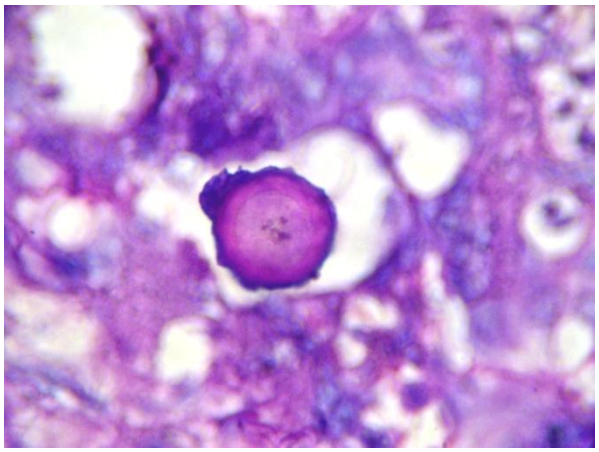


Figure 16: Papillary carcinoma showing psammoma bodies

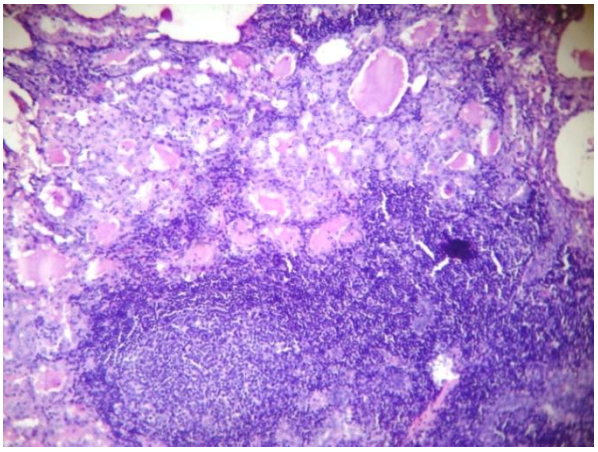


Figure 17: Papillary carcinoma associated with Hashimoto's thyroiditis (H&E x100)

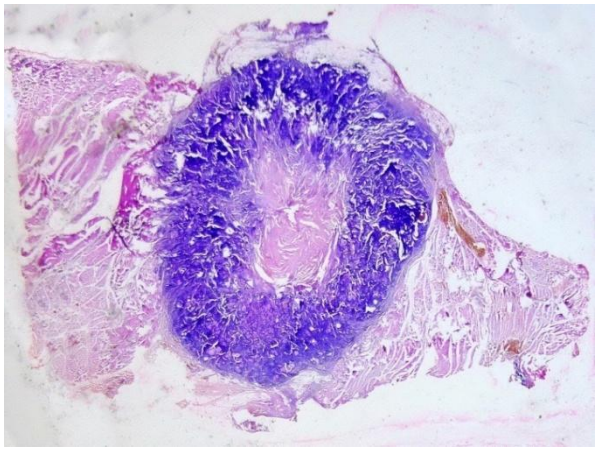


Figure 18: Whole mount view of papillary carcinoma metastasis within sternocleidomastoid muscle

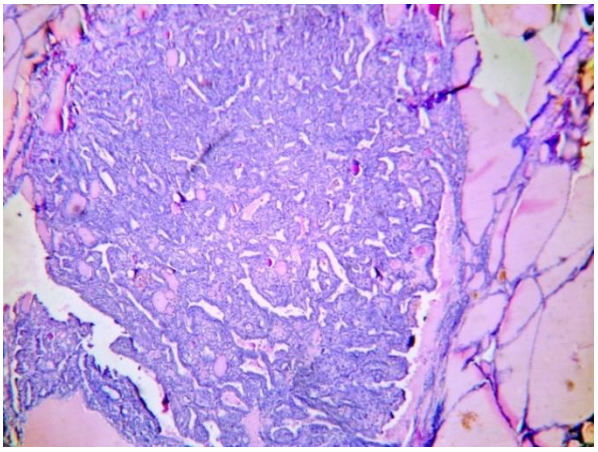


Figure 19: Papillary microcarcinoma surrounded by normal thyroid parenchyma (H&E x40)

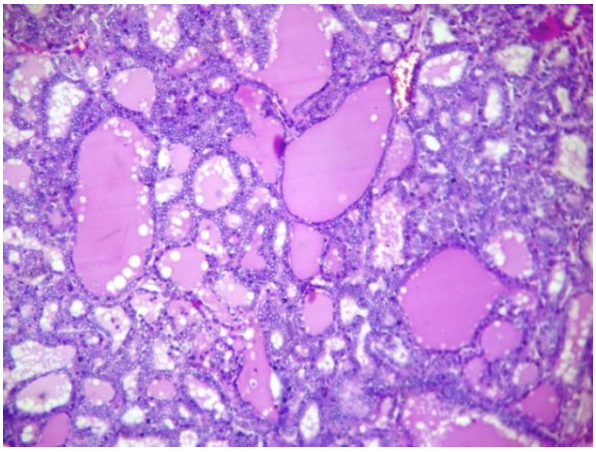


Figure 20: Follicular variant of papillary carcinoma showing predominantly follicular pattern (H&E x100)

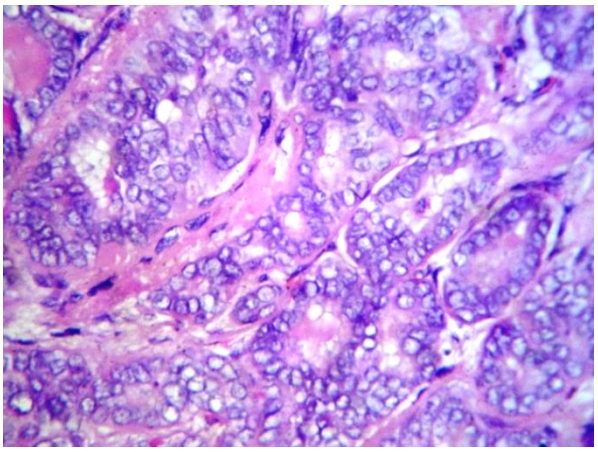


Figure 21: Follicular variant of papillary carcinoma with characteristic nuclear features (H&E x400)

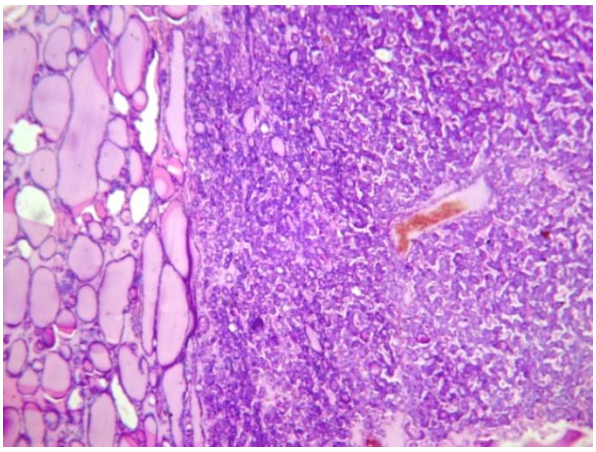


Figure 22: Unencapsulated follicular variant of papillary carcinoma (H&E x100)

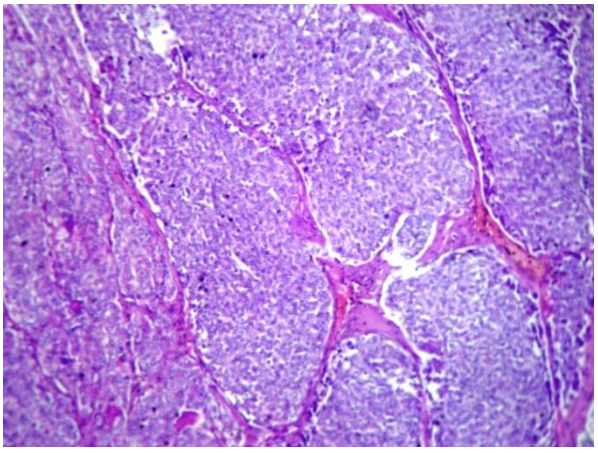


Figure 23: Solid variant of papillary carcinoma - islands of tumour cells traversed by delicate fibrovascular septae (H&E x100)

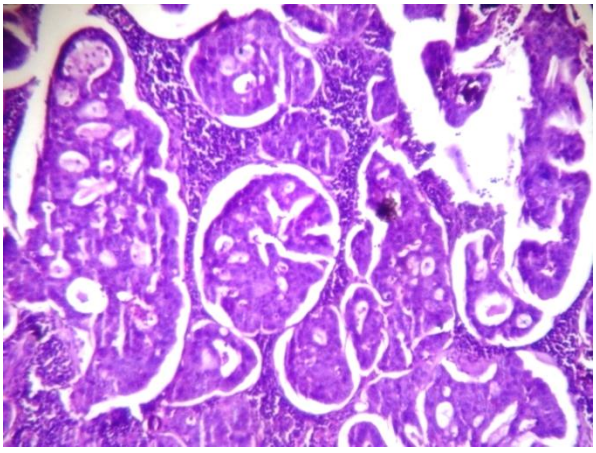


Figure 24: Focal cribriform pattern in solid variant of papillary carcinoma (H&E x100)

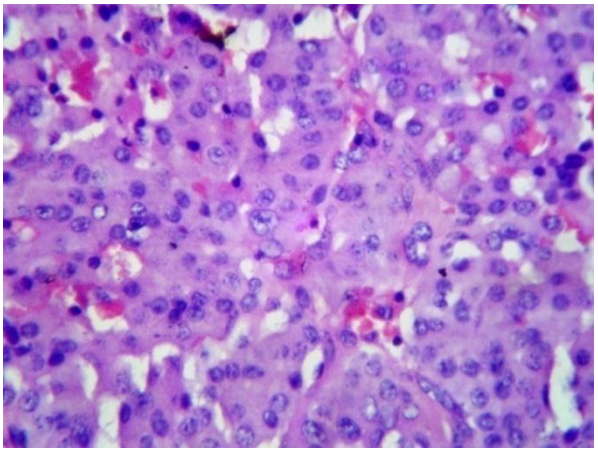


Figure 25: Oncocytic variant of papillary carcinoma (H&E x400)

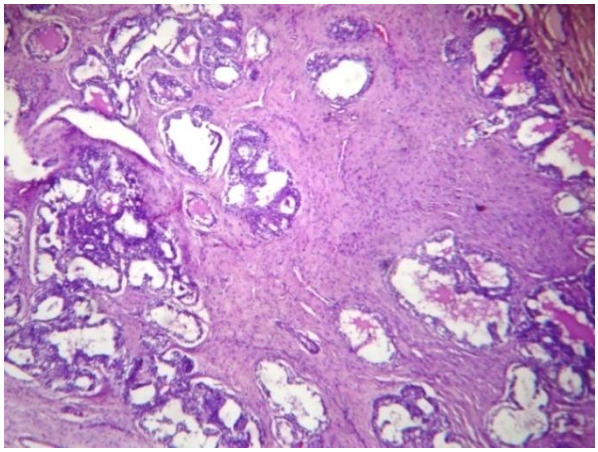


Figure 26: Papillary carcinoma with exuberant nodular fasciitis like stroma (H&E x40)

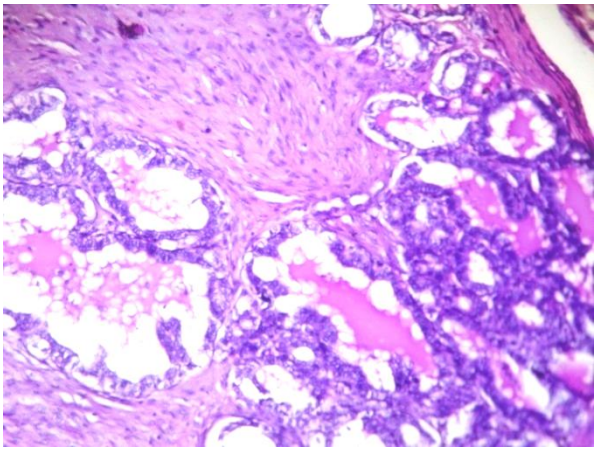


Figure 27: Papillary carcinoma with exuberant nodular fasciitis like stroma (H&E x100)

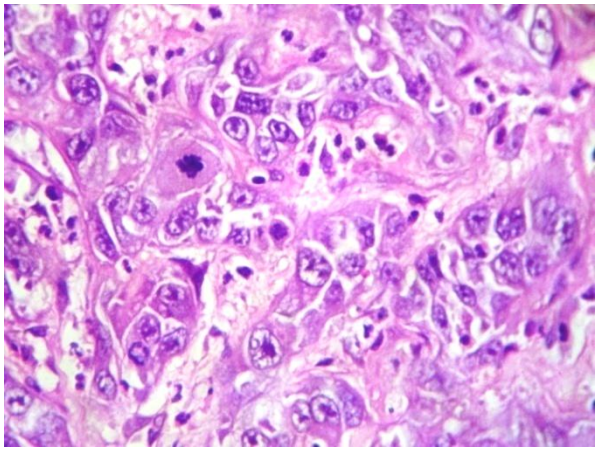


Figure 28: Papillary carcinoma dedifferentiated type with bizarre pleomorphic giant tumour cells with prominent nucleoli and increased mitotic figures some of them showing abnormal mitoses (H&E x400)

FOLLICULAR THYROID CARCINOMA

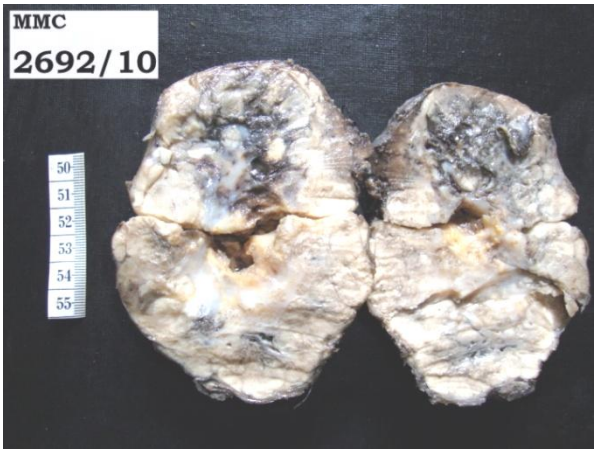


Figure 29: Follicular carcinoma replacing entire thyroid with areas of necrosis and hemorrhage

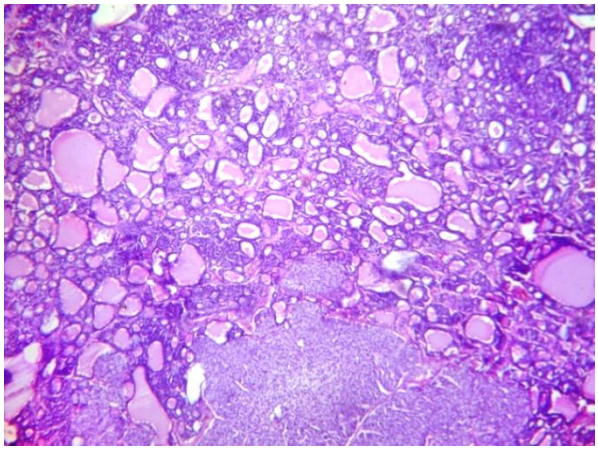


Figure 30: Follicular carcinoma showing invasion into adjacent normal thyroid parenchyma (H&E x40)

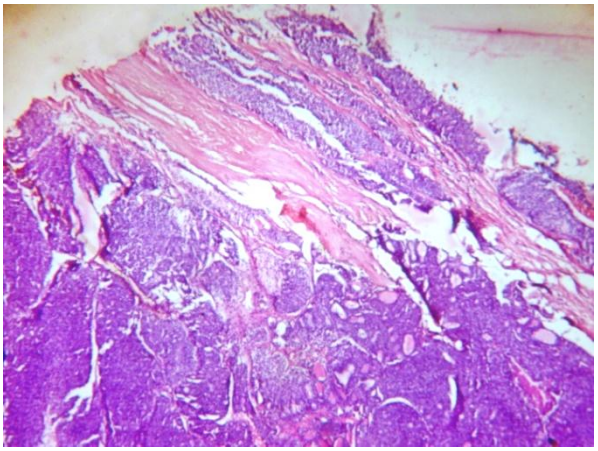


Figure 31: Follicular carcinoma showing capsular invasion (H&E x40)

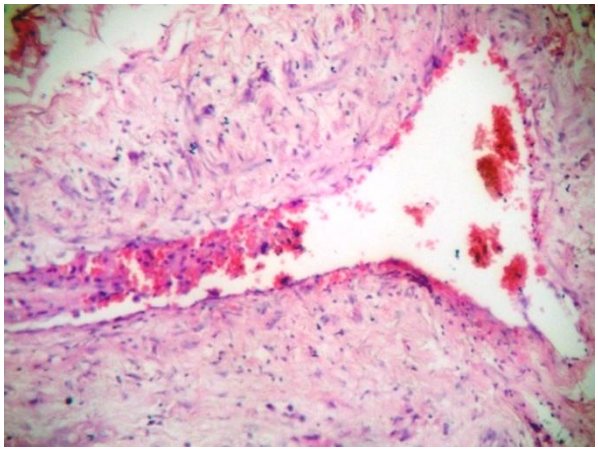


Figure 32: Follicular carcinoma showing capsular invasion (H&E x100)

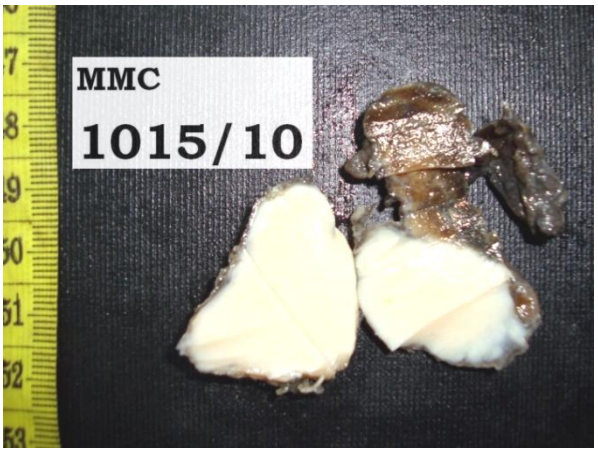


Figure 33: Hurthle cell carcinoma grossly appearing as homogenous gray white infiltrative mass

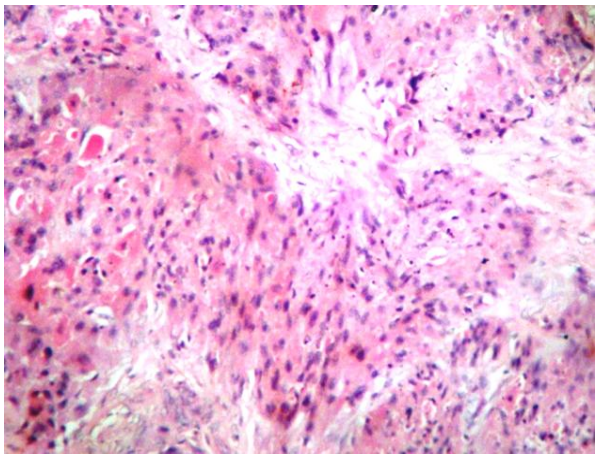


Figure 34: Hurthle cell carcinoma microscopy (H&E x100)

MEDULLARY THYROID CARCINOMA

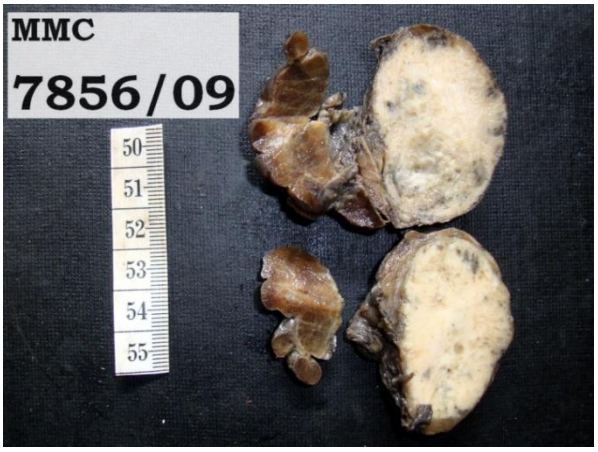


Figure 35: Gross appearance of medullary carcinoma involving one lobe of thyroid

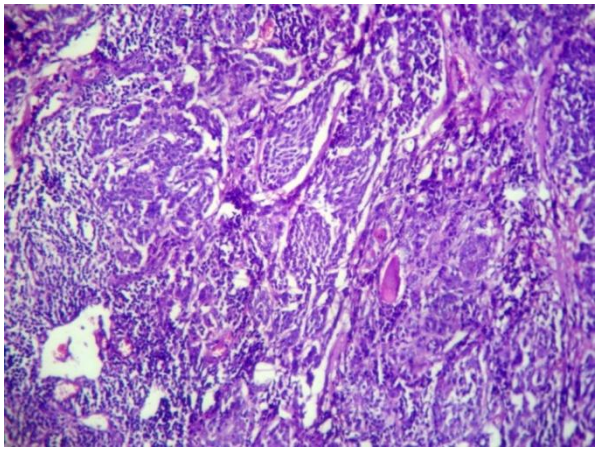


Figure 36: Medullary carcinoma showing sheets and nests of polygonal to spindle shaped tumour cells with round to oval nuclei (H&E x100)

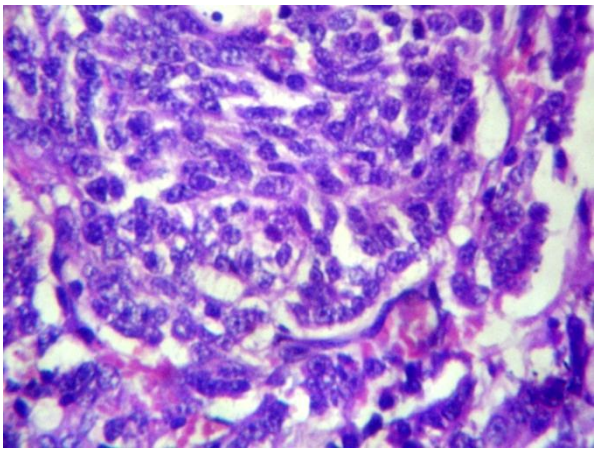


Figure 37: Tumour cells showing stippled chromatin (H&E x400)

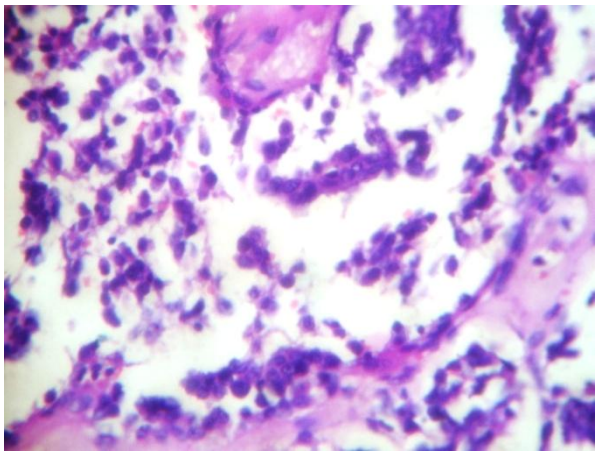


Figure 38: Loosely cohesive tumour cells (H&E x400)

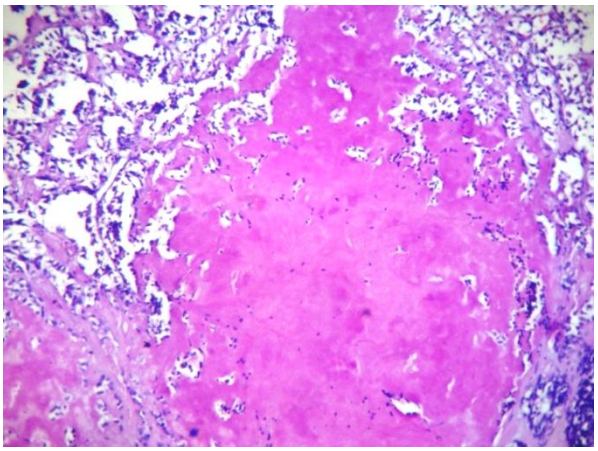


Figure 39: Tumour cells with amyloid (H&E x100)

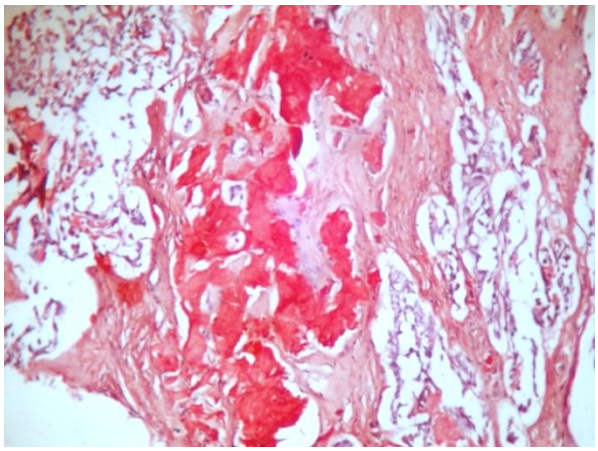


Figure 40: Amyloid showing Congo Red positivity (x100)

IMMUNOHISTOCHEMISTRY

CYSTIC PAPILLARY CARCINOMA

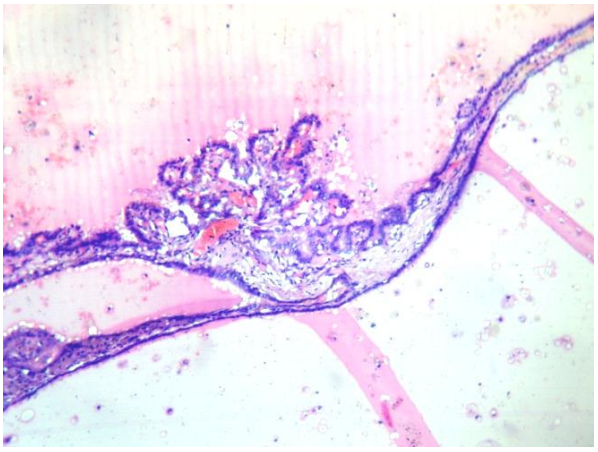


Figure 41: Cystic papillary carcinoma conventional type. (H&E x100)

PAPILLARY HYPERPLASIA

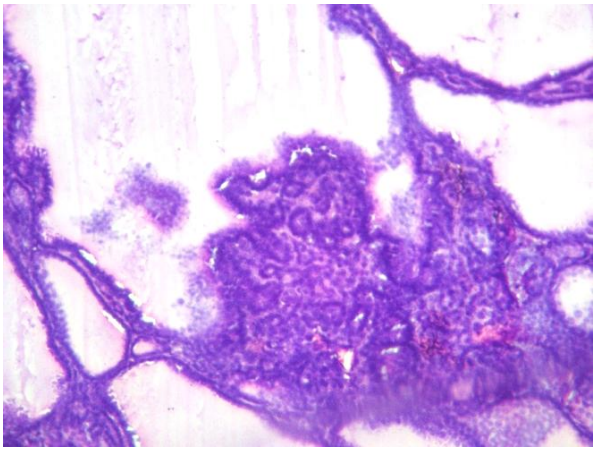


Figure 42: Papillary hyperplasia in a colloid goitre. (H&E x100)

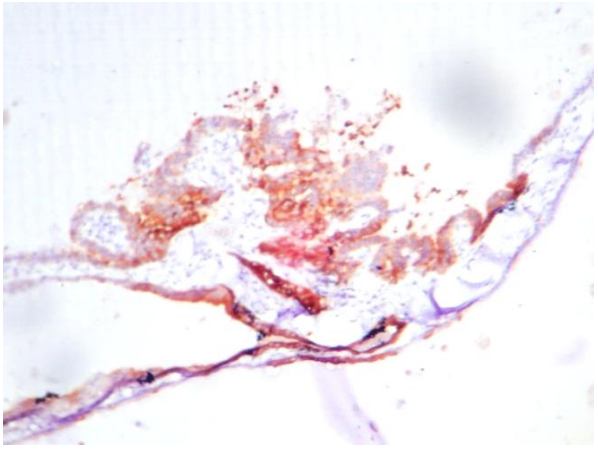


Figure 43: CK19 diffuse strong positivity in cystic papillary carcinoma. (x100)

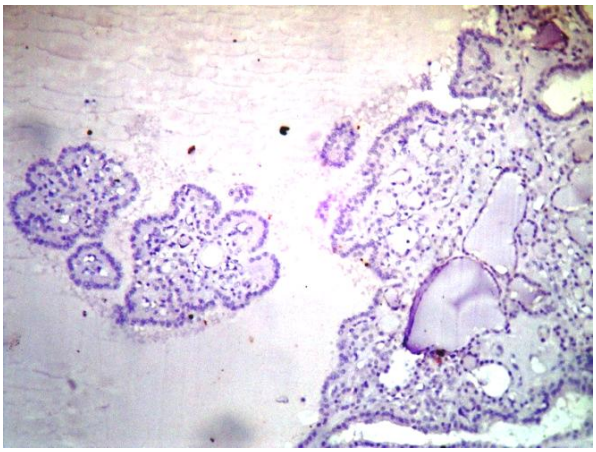


Figure 44: CK19 negativity in Papillary hyperplasia. (x100)

PTC CONVENTIONAL

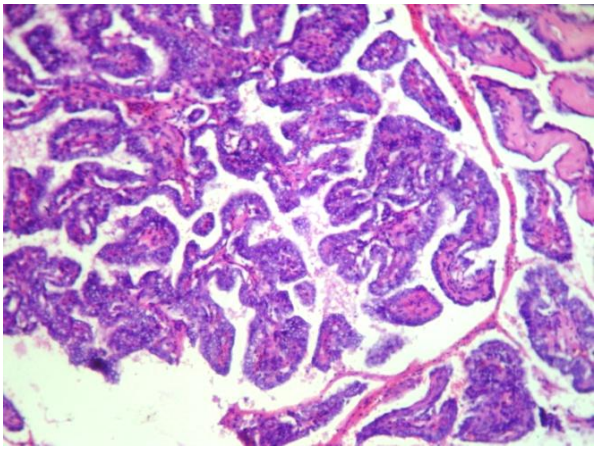


Figure 45: Papillary carcinoma conventional type showing arborising papillary processes. (H&E x100)

HYALINISING TRABECULAR ADENOMA

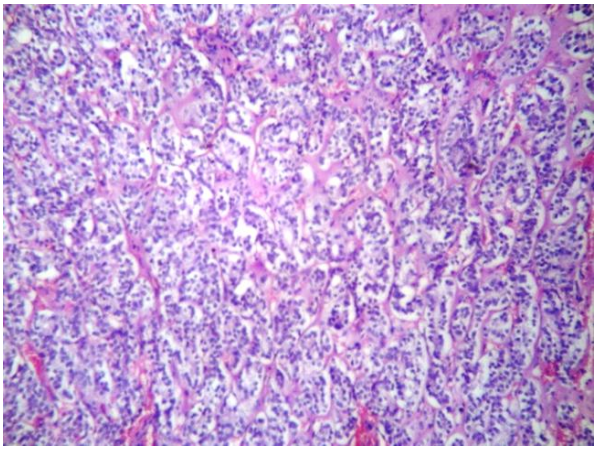


Figure 46: Hyalinising trabecular adenoma. (H&E x100)

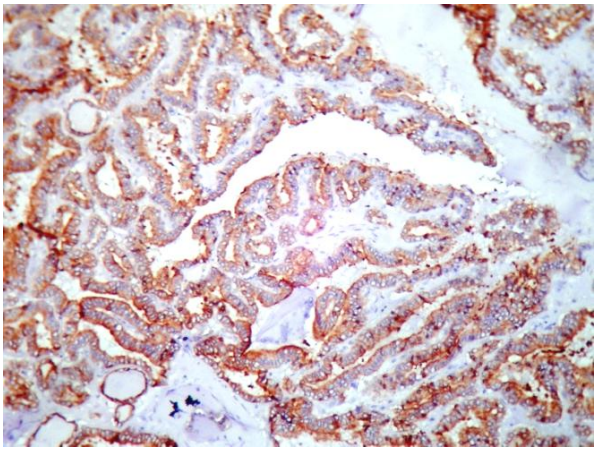


Figure 47: CK19 diffuse strong immunoreactivity in conventional type of papillary carcinoma. (x100)

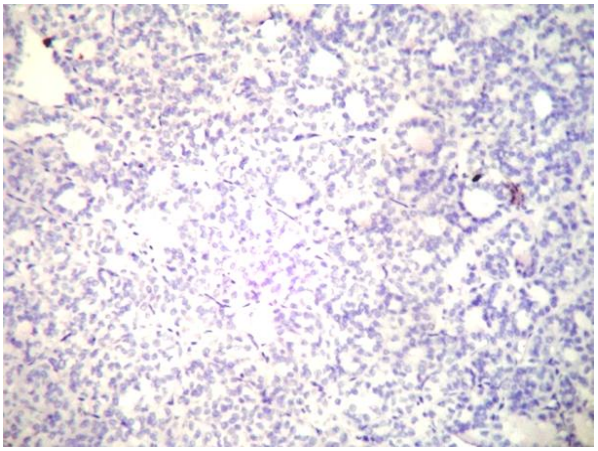


Figure 48: CK19 negativity in Hyalinising trabecular adenoma. (x100)

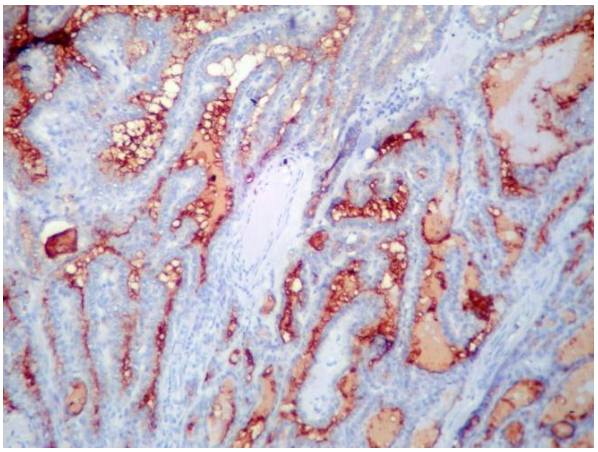


Figure 49: Thyroglobulin positivity in conventional type of papillary carcinoma (x100)

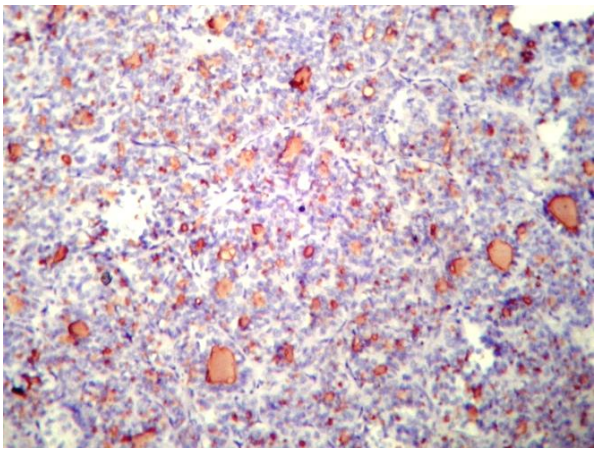


Figure 50: Thyroglobulin positivity in hyalinising trabecular adenoma (x100)

PTC FOLLICULAR VARIANT

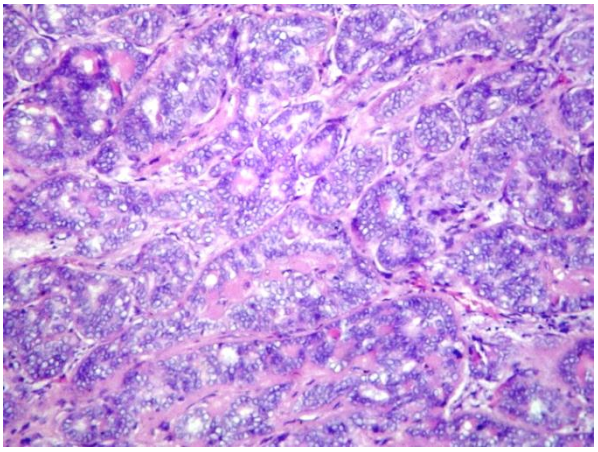


Figure 51: Follicular variant of papillary carcinoma (H&E x100)

FOLLICULAR ADENOMA

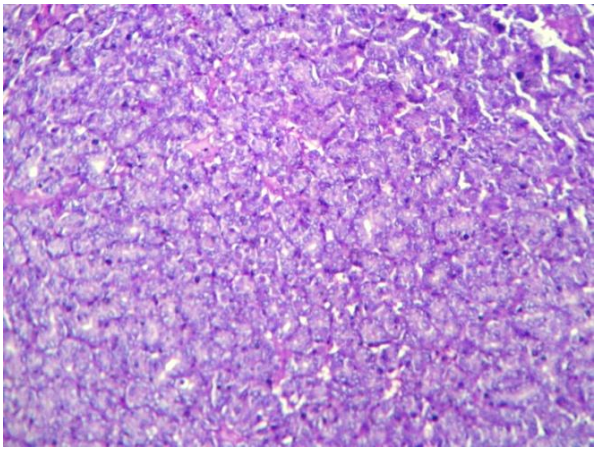


Figure 52: Follicular adenoma (H&E x100)

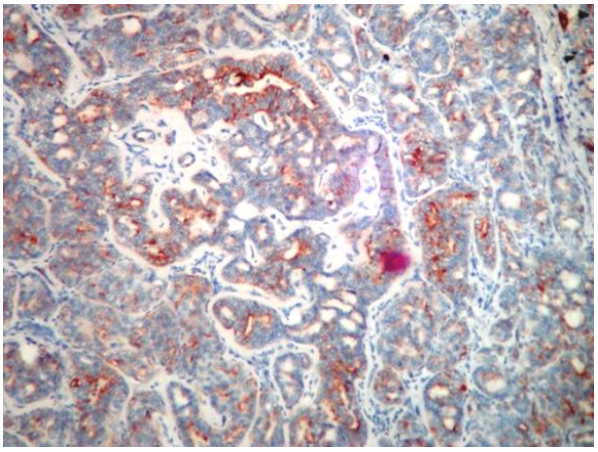


Figure 53: CK19 diffuse strong positivity in follicular variant of papillary carcinoma. (x100)

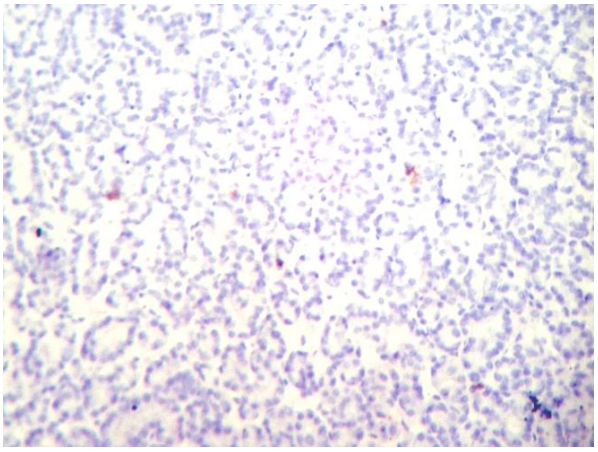


Figure 54: CK19 negativity in Follicular adenoma. (x100)

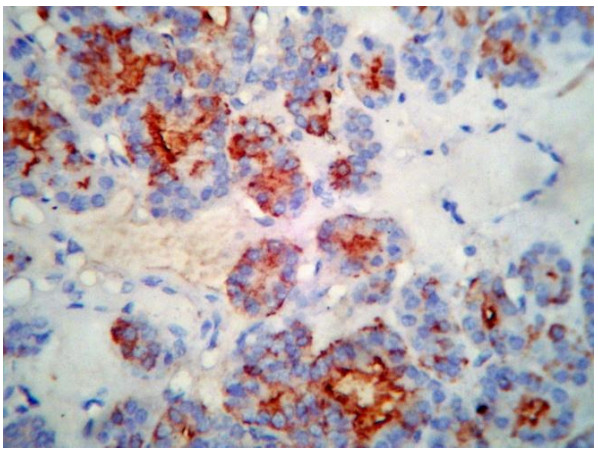


Figure 55: Thyroglobulin positivity in follicular variant of papillary carcinoma (x200)

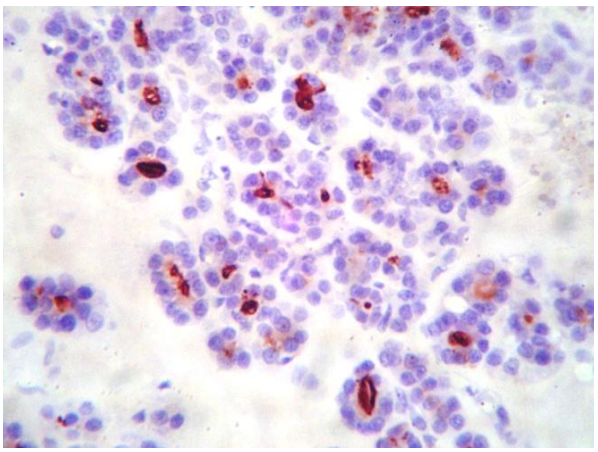


Figure 56: Thyroglobulin positivity in follicular adenoma (x200)

PTC FOLLICULAR VARIANT

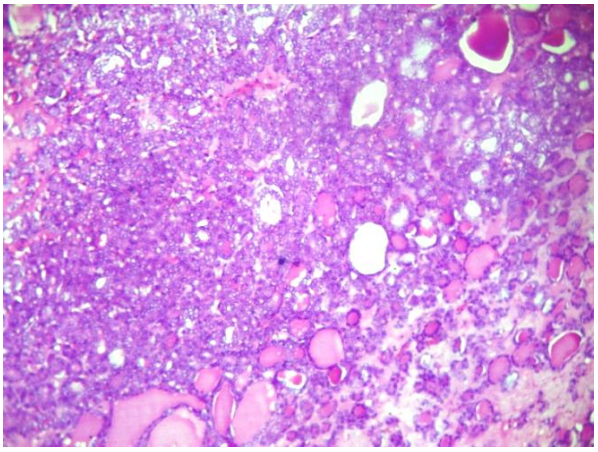


Figure 57: Follicular variant of papillary carcinoma. (H&E x100)

FOLLICULAR CARCINOMA

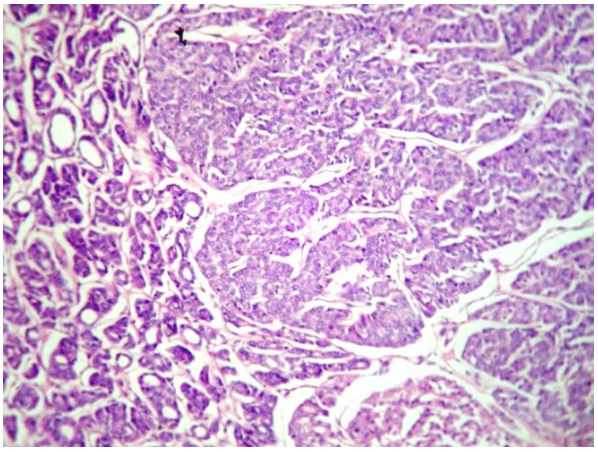


Figure 58: Follicular carcinoma. (H&E x100)

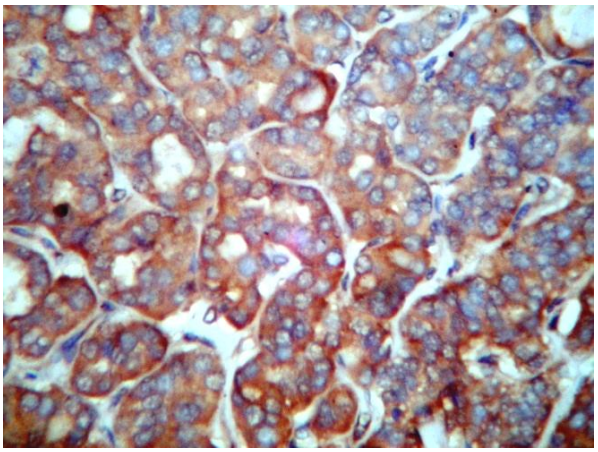


Figure 59: CK19 diffuse strong positivity in follicular variant of papillary carcinoma. (x100)

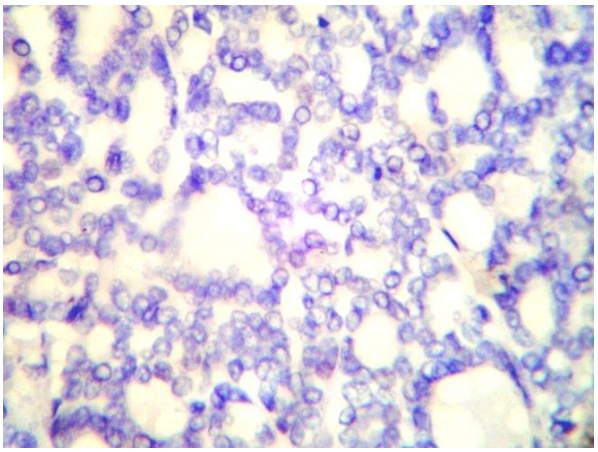


Figure 60: CK19 negativity in follicular carcinoma. (x200)

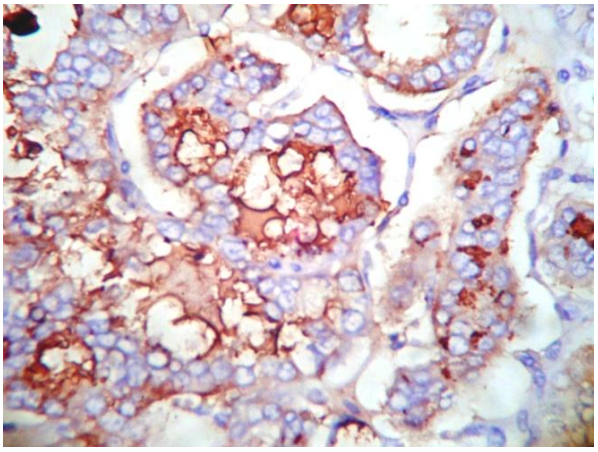


Figure 61: Thyroglobulin positivity in follicular variant of papillary carcinoma (x200)

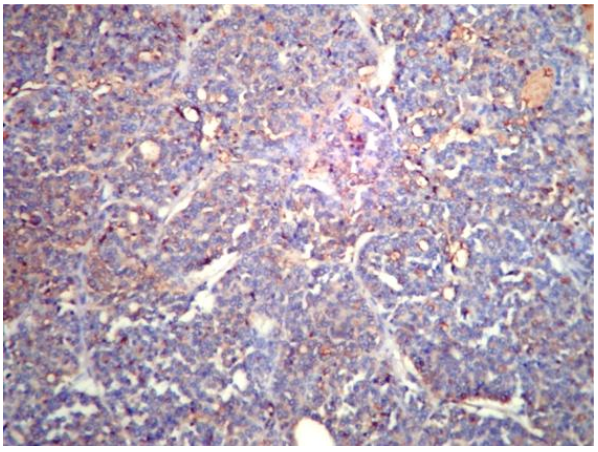


Figure 62: Thyroglobulin positivity in follicular carcinoma (x100)

PTC ONCOCYTIC VARIANT

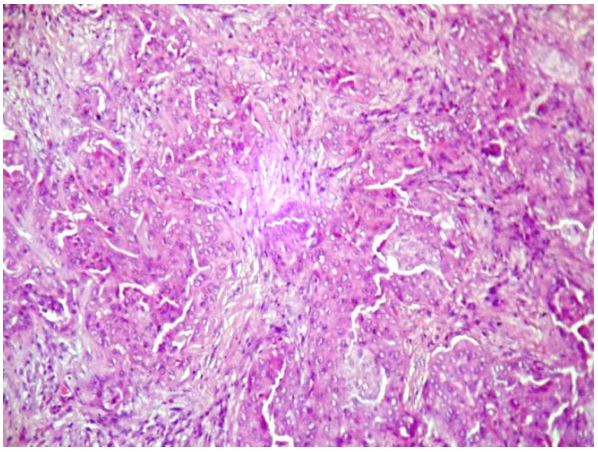


Figure 63: Oncocytic variant of papillary carcinoma. (H&E x100)

HURTHLE CELL ADENOMA

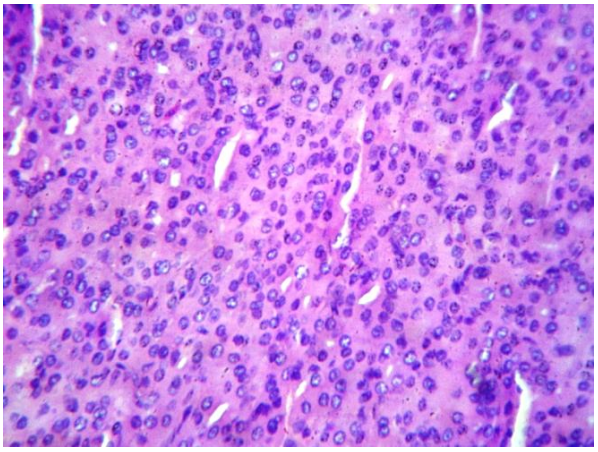


Figure 64: Hurthle cell adenoma. (H&E x100)

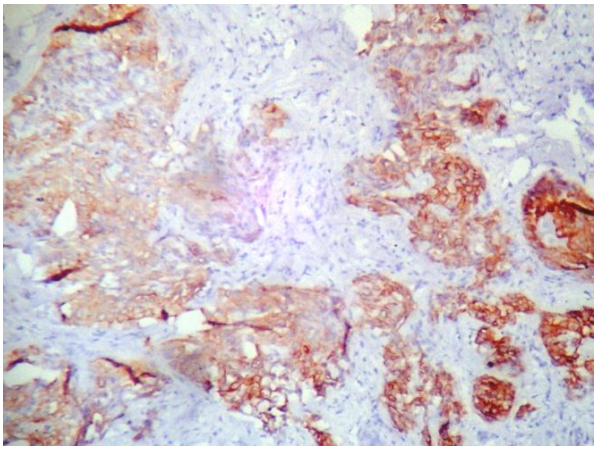


Figure 65: CK19 diffuse strong positivity in oncocytic variant of papillary carcinoma. (x100)

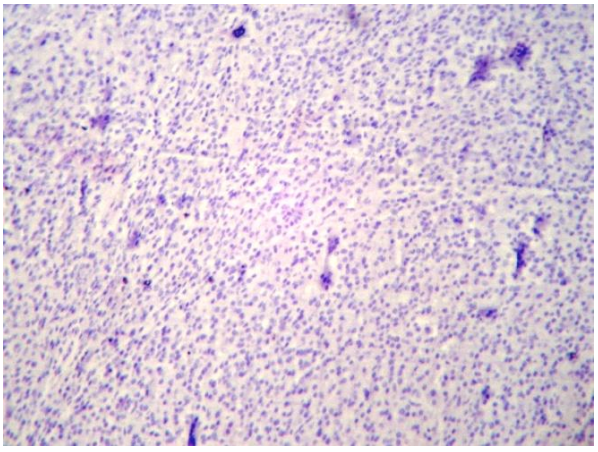


Figure 66: CK19 negativity in Hurthle cell adenoma. (x100)

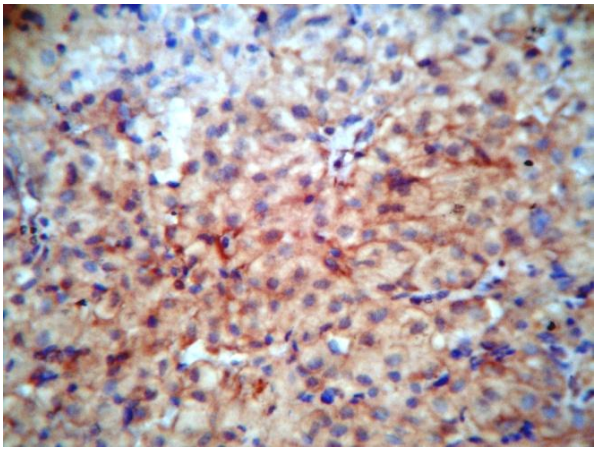


Figure 67: Thyroglobulin positivity in oncocytic variant of papillary carcinoma (x200)

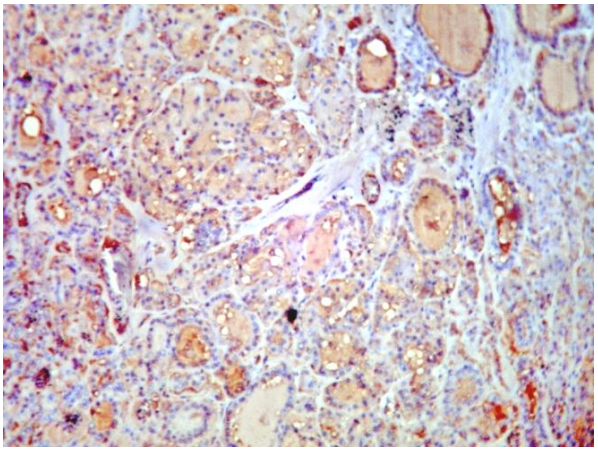


Figure 68: Thyroglobulin positivity in follicular adenoma (x100)

PTC SOLID VARIANT

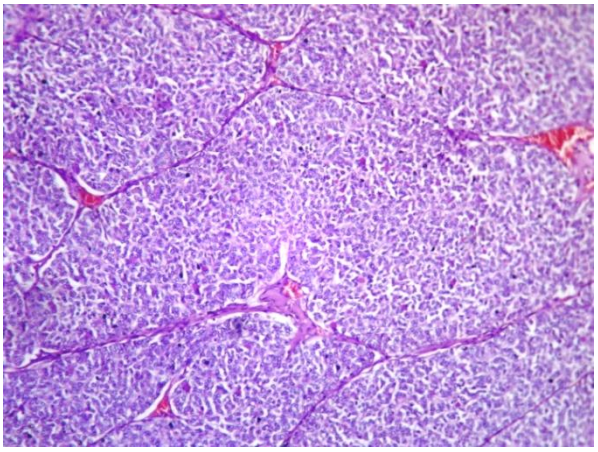


Figure 69: Solid variant of papillary carcinoma. (H&E x100)

INSULAR CARCINOMA

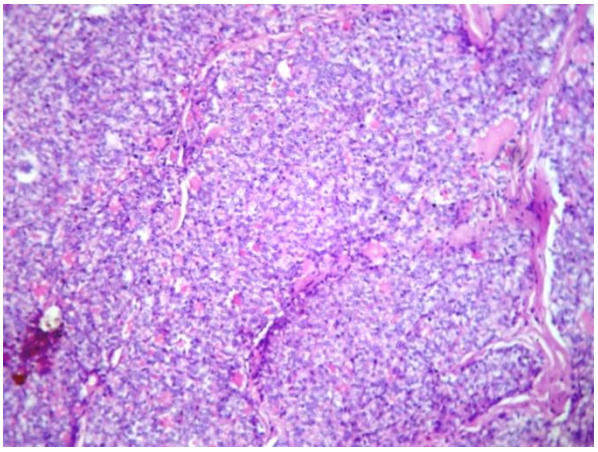


Figure 70: Insular carcinoma. (H&E x100)

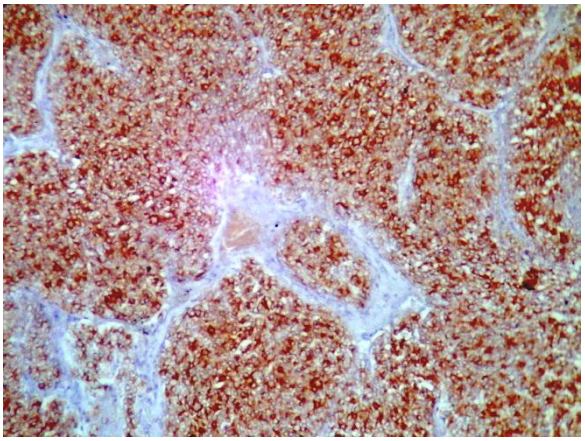


Figure 71: CK19 diffuse strong positivity in solid variant of papillary carcinoma. (x100)

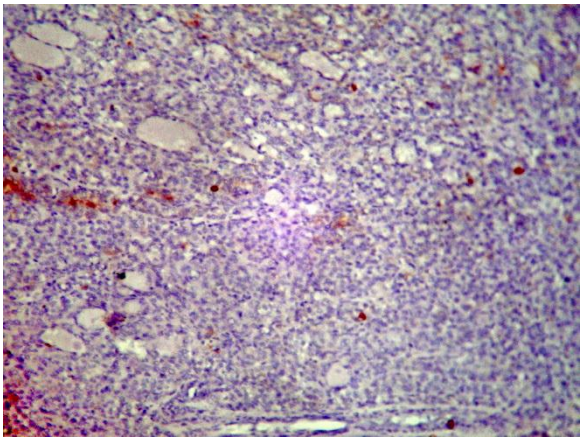


Figure 72: CK19 focal positivity in insular carcinoma. (x100)

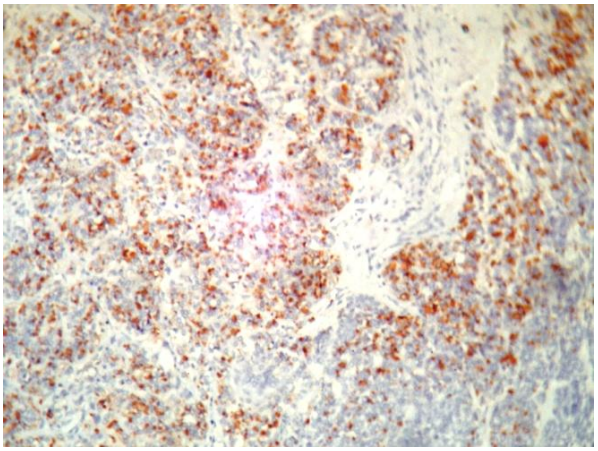


Figure 73: Thyroglobulin positivity in solid variant of papillary carcinoma (x200)

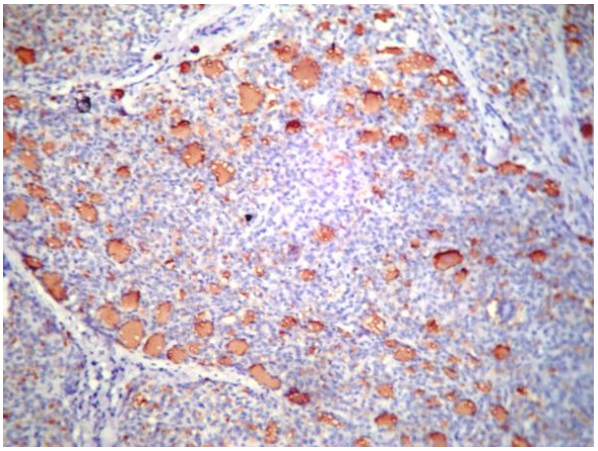


Figure 74: Thyroglobulin positivity in insular carcinoma (x100)

PTC WITH LYMPHOCYTIC INFILTRATION

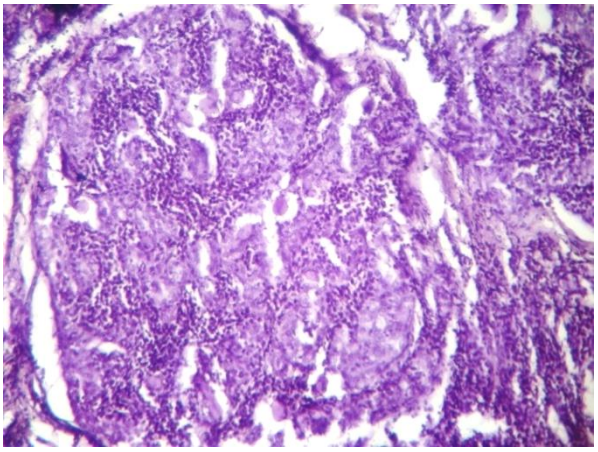


Figure 75: Papillary carcinoma with lymphocytic infiltration. (H&E x40)

HASHIMOTO'S THYROIDITIS

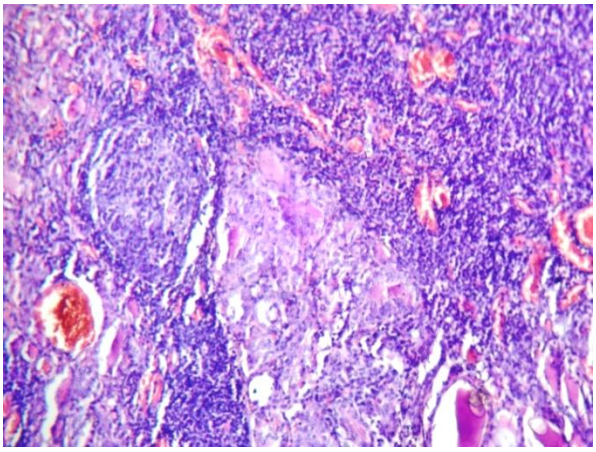


Figure 76: Hashimoto's thyroiditis. (H&E x100)

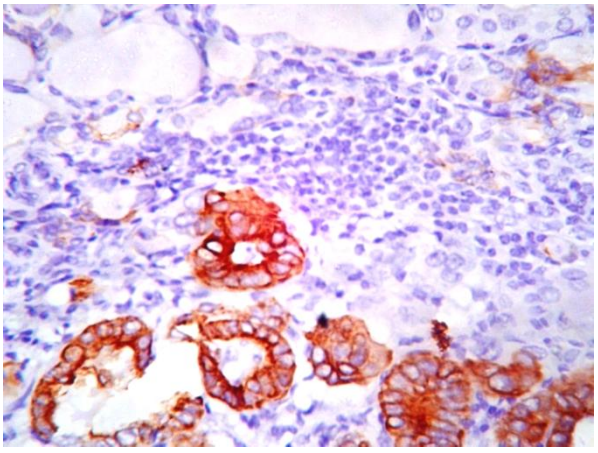


Figure 77: CK19 diffuse strong positivity in papillary carcinoma with lymphocytic infiltration. (x200)

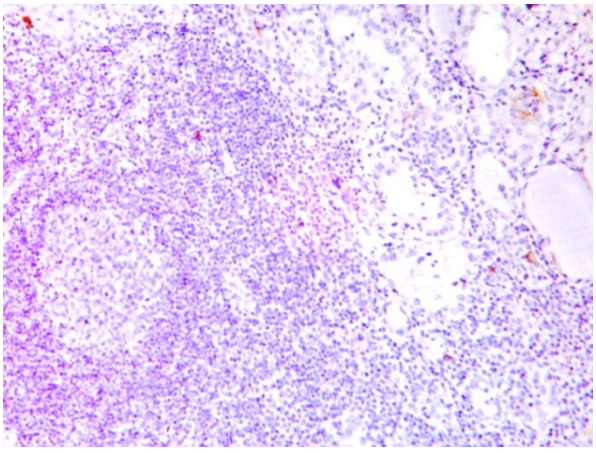


Figure 78: CK19 negativity in Hashimoto's thyroiditis. (x100)

Figure 79: Immunohistochemistry Reagents using Super Sensitive^{TM} Polymer HRP IHC Detection System.

ABSTRACT

HISTOMORPHOLOGICAL STUDY OF THYROID NEOPLASMS WITH SPECIAL REFERENCE TO PAPILLARY THYROID CARCINOMA AND ITS NEOPLASTIC HISTOLOGICAL MIMICKERS

BACKGROUND AND OBJECTIVES: More than 95% of thyroid neoplasms arise from follicular epithelial cells. Papillary carcinoma has an excellent long term prognosis. Yet, at times, its diagnostic nuclear features remain controversial and its distinction from its histological mimickers may sometimes be difficult. Immunohistochemistry might be of immense help in such situations. The present study aims to histologically classify all thyroid neoplasms and to study the histomorphological characteristics and to evaluate the expression of Cytokeratin 19 and thyroglobulin in cases of papillary thyroid carcinoma and its histological mimickers.

METHODS: 307 thyroid neoplasms received from January 2009 to April 2011 were studied histomorphologically and classified according to WHO classification. 47 cases of papillary thyroid carcinoma and its variants and 55 cases of its histological mimickers are randomly selected and cytokeratin 19 and thyroglobulin immunoreactivity were evaluated and its role in differentiating papillary carcinoma and its variants from its histological mimickers is then evaluated.

RESULTS: The incidence of thyroid neoplasms was 1.43% of which papillary carcinoma was the most common, among which, conventional type was most common followed by follicular variant. Multicentric lesions were seen in 46.51%, nuclear clearing in 97.7%, nuclear grooving in 98.9% and psammoma bodies in 23.86%. The most common associated lesion was Colloid goitre (38.07%) followed by Hashimoto's thyroiditis (13.64%).

Thyroglobulin showed diffuse positivity in all cases confirming them to be of follicular origin. CK19 was positive in 80.85% cases of papillary carcinoma and in 12.73% of its histological mimickers and this difference was found to be statistically significant with $P<0.001$. CK19 was 80.85% sensitive, 87.27% specific for papillary carcinoma with a diagnostic accuracy of 84.31%.

CONCLUSION: Though there is a statistically significant association between CK19 immunoreactivity and papillary carcinoma, there are often few false positive and false negative cases. Thus, Cytokeratin 19 when used alone, the diagnostic accuracy could be 84% and to get 100% accuracy, additional panels including HBME-1, Galectin-3 and CITED-1 will be highly useful for a definitive diagnosis of papillary carcinoma, especially in difficult cases.

KEY WORDS: Papillary thyroid carcinoma, Cytokeratin 19, Thyroid neoplasms, Immunohistochemistry