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Histological Spectrum of Papillary Carcinoma of Thyroid – A Two Years Study

Gomathi Srinivasan[1], M. Vennila[2]

[1]Associate Professor Pathology, Government Medical College, Omandurar Estate, Chennai – 600 002

[2]Assistant Professor Pathology, Government Vellore Medical College, Vellore

Abstract: ***Introduction: Papillary carcinoma of thyroid is the most common malignant tumor constituting about 80% of all malignancies of Thyroid. It has an indolent course with an excellent prognosis. Histological variants with aggressive behavior have been reported. Further non-neoplastic and neoplastic lesions associated with papillary carcinoma have also been reported.Objectives: To analyze the various histological types and associated lesions in cases of papillary carcinoma of thyroid. Materials and Methods: Retrospective analysis of 108 cases of papillary carcinoma of thyroid over a period of two years from August 2006 to July 2008 has been done. Results: Conventional type of papillary carcinoma is the predominant histological pattern constituting about 75%. Other variants are follicular (14%), encapsulated (4%), tall cell (2%), occult (2%), diffuse sclerosing, cribriform &morular and macrofollicular (1% each).Associated lesions include nodular colloid goiter (14%), chronic lymphocytic thyroiditis (11%), follicular adenoma (2%). Normal morphology is seen in 73% of cases. Discussion: The commonest histological type is conventional papillary carcinoma which correlates with this study. The variants presenting in descending order of frequency are follicular variant, encapsulated variant (8 – 13%), microcarcinoma (5-10%), tall cell (10%), diffuse sclerosing (3%) according to literature. This study correlates with findings in the literature.***

Keywords: Thyroid, Papillary Carcinoma, Histological Variants, Prognosis, Incidence

1. Introduction

Papillary carcinoma of thyroid is the most common malignant tumor constituting about 80% of all malignancies. It has an indolent course with an excellent prognosis with a ten year survival rate in excess of 95%.Between 5 and 20% of patients have local or regional recurrences and 10-15% have distant metastases. Histological variants with aggressive behavior have been reported. Further non-neoplastic and neoplastic lesions associated with papillary carcinoma have also been reported.

2. Literature Survey

The variants presenting in descending order of frequency are follicular variant, encapsulated variant (8 – 13%), microcarcinoma (5-10%), tall cell (10%), diffuse sclerosing (3%) according to literature(Juan Rosai et al. Rosai and Ackermann's surgical pathology ninth edition p 532-542)

According to William C.Faquin,(Arch.Pathol. Lab med-vol.132 Apr.2008 page 627-629). Papillary thyroid carcinoma is the most common primary cancer of the thyroid gland, representing up to 80% of thyroid carcinomas, and it is characterized by an overall excellent clinical prognosis, with less than 6.5% mortality. Several variants of papillary thyroid carcinoma are recognized, but most have a clinical behavior that is similar to that of conventional papillary carcinoma. A few variants are particularly important because they can pose a diagnostic pitfall or because they are often associated with an aggressive clinical behavior. The follicular variant of papillary thyroid carcinoma is the most common variant (after the classic form of papillary carcinoma), representing 10% to 15% of papillary carcinomas. This variant is one of the most challenging for the pathologist evaluating a solitary encapsulated thyroid nodule with a follicular architecture and some form of atypia. The problem is when to diagnose the lesion as a follicular adenoma versus the follicular variant of papillary thyroid carcinoma. There seems to be a trend to overdiagnose the encapsulated follicular variant of papillary thyroid carcinoma. Among other reasons, this is due to the fact that minimum criteria to distinguish a follicular adenoma from an encapsulated variant of papillary thyroid carcinoma are not well defined. In addition, alternate terms, such as atypical neoplasm or tumor of uncertain malignant potential are confusing and have the potential to be overused.Because the prognosis associated with encapsulated follicular variant of papillary carcinoma is excellent, whereas the potential morbidity associated with overdiagnosing this tumor can be significant, a conservative approach is deemed warranted. Chan presents a useful set of guidelines for distinguishing the follicular variant of papillary carcinoma from follicular adenomas that includes the presence of at least 3 of 4 major histologic features (ovoid nuclei, nuclear crowding, pale chromatin or extensive nuclear grooves, psammoma bodies) and at least 4 minor features (abortive papillae, elongated irregular follicles, dark-staining colloid, nuclear pseudo inclusions, and multinucleated histiocytes within follicle lumens) when less than 4 major features are present. The cribriform-morular variant of papillary carcinoma is rare and interesting because of its unique histologic appearance and unusual clinical association. It is characterized by a cribriform growth pattern comprising empty spaces and occasional solid areas with squamous morules. The nuclear features are variable but include overlapping nuclei with grooves and pseudoinclusions. This variant has a prognosis similar to conventional papillary carcinoma but can be confused with other entities due to its peculiar appearance. The differential diagnosis includes hyalinizing trabecular tumor, spindle cell tumor with thymus-like differentiation, and metastatic carcinoma. A clinically significant feature of the cribriform-

morular variant is its occasional association with familial adenomatous polyposis. Therefore, whenever this variant of papillary carcinoma is diagnosed, the clinician should be alerted to test for familial adenomatous polyposis. Three unusual variants of papillary carcinoma that are often associated with an aggressive clinical behavior include the diffuse sclerosing, tall cell, and columnar cell variants. The diffuse sclerosing variant of papillary carcinoma, originally described by Vickery, is unusual in its histologic appearance and in its occurrence in children and young adults.1 This variant is associated with nearly invariable lymph node metastasis and frequent distant metastasis. Despite its aggressive clinical behavior, the prognosis of patients with the diffuse sclerosing variant of papillary carcinoma in some studies is similar to that of conventional papillary carcinoma, possibly due to the young age of the patients. Histologically, it is characterized by a diffuse growth pattern, including extrathyroidal extension, sclerotic stroma, abundant psammoma bodies, extensive lymphatic permeation by tumor, a lymphoplasmacytic infiltrate, and frequent squamous metaplasia .Except in areas exhibiting squamoid changes, the nuclei of the diffuse sclerosing variant exhibit conventional features of papillary carcinoma. The key differential diagnosis is with severe sclerosing chronic lymphocytic thyroiditis; however, the numerous scattered psammoma bodies will act as a beacon for identifying the scattered small intralymphatic islands of tumor that might otherwise be obscured. The tall cell variant of papillary carcinoma, first described by Hazard in 1968, has been associated in several studies with a clinically aggressive behavior, although itis not considered an independent prognostic predictor. It is more common in older male patients, tends to be large (5 cm), and often shows extrathyroidal extension. Histologically, the tall cell variant of papillary carcinoma is composed of cells at least three times as tall as they are wide that are arranged around fibrovascular cores, creating a prominent papillary architecture. The cells have abundant pink cytoplasm with basally located nuclei and, unlike conventional papillary carcinoma, mitotic activity and necrosis are often present. Because tall cells can be seen at least focally in many conventional papillary carcinomas, the tumor should be dominated by tall cells to qualify as the tall cell variant. The columnar cell variant of papillary carcinoma, first described by Evans in 1986, has also been termed columnar cell carcinoma, owing to the fact that it lacks the characteristic nuclear features of conventional papillary carcinoma. Like the tall cell variant of papillary carcinoma, it is rare and tends to be associated with advanced patient age, large size and extrathyroidal extension at presentation—features predictive of a clinically aggressive behavior. Histologically, the columnar cell variant is unique in the thyroid gland, being characterized by very elongate cells with hyperchromatic, stratified nuclei and sometimes clear cytoplasmic vacuoles. Focal areas of conventional papillary carcinoma can occasionally be seen, and solid areas with squamous morules, mitotic activity, and necrosis are also often present. The main differential diagnosis, especially in core biopsies or FNA samples, is with metastatic adenocarcinoma, particularly colon cancer.

Histologic Variants of Papillary Thyroid Carcinoma
Variants
• Follicular • Macrofollicular • Diffuse sclerosing • Warthin-like • Solid • Trabecular • Clear cell • Oncocytic • Tall cell • Columnar cell • Cribriform-morular

3. Problem Definition

To analyze the various histological types and associated lesions in cases of papillary carcinoma of thyroid.

4. Methodology / Approach

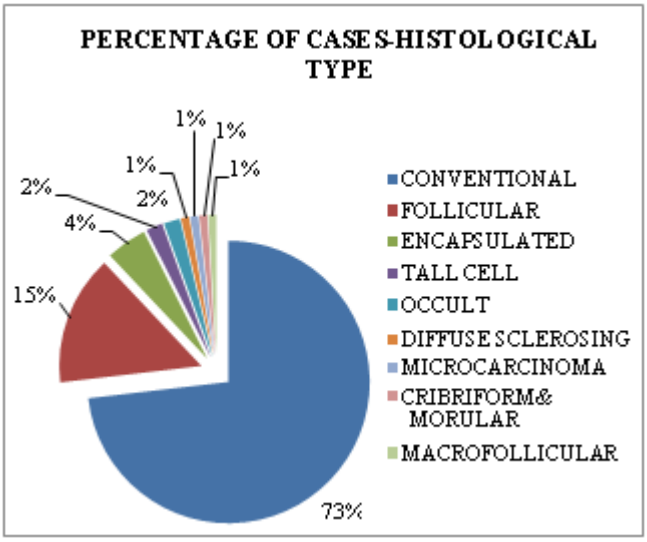
4.1 Materials and Methods

Retrospective analysis of 108 cases of papillary carcinoma of thyroid over a period of two years from August 2006 to July 2008 received in the Institute of Pathology, Madras Medical College.

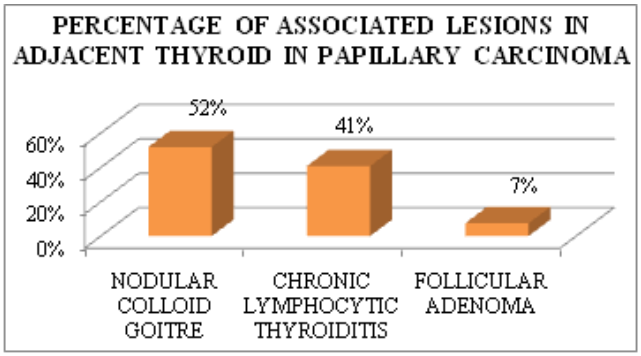
4.2 Results

Conventional type of papillary carcinoma is the predominant histological pattern constituting about 75%. Other variants are follicular (14%), encapsulated (4%), tall cell (2%), occult (2%), diffuse sclerosing, cribriform &morular and macrofollicular (1% each). Associated lesions include nodular colloid goiter (14%), chronic lymphocytic thyroiditis (11%), follicular adenoma (2%). Normal morphology is seen in 73% of cases.

Results		
Histological Type	*No. of Cases*	*Percentage of Cases*
Conventional	79	73%
Follicular	16	15%
Encapsulated	5	4%
Tall Cell	2	2%
Occult	2	2%
Diffuse Sclerosing	1	1%
Microcarcinoma	1	1%
Cribriform&Morular	1	1%
Macrofollicular	1	1%

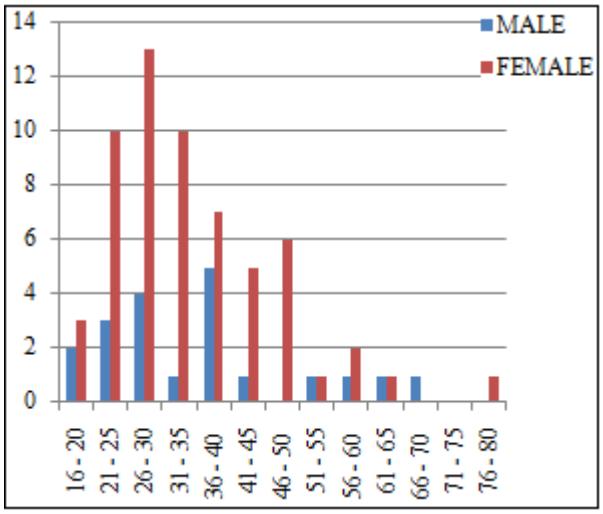


Results .. Contd		
Associated Lesions In Papillary Carcinoma In Adjacent Thyroid	*No. of Cases*	*Percentage of Cases*
Nodular Colloid Goitre	14	52%
Chronic Lymphocytic Thyroiditis	11	41%
Follicular Adenoma	2	7%



Conventional Papillary Carcinoma - Incidence in Male & Female		
Age Distribution	*Male*	*Female*
16 - 20	2	3
21 - 25	3	10
26 - 30	4	13
31 - 35	1	10
36 - 40	5	7
41 - 45	1	5
46 - 50	0	6
51 - 55	1	1
56 - 60	1	2
61 - 65	1	1
66 - 70	1	0
71 - 75	0	0
76 - 80	0	1
TOTAL	**20**	**59**

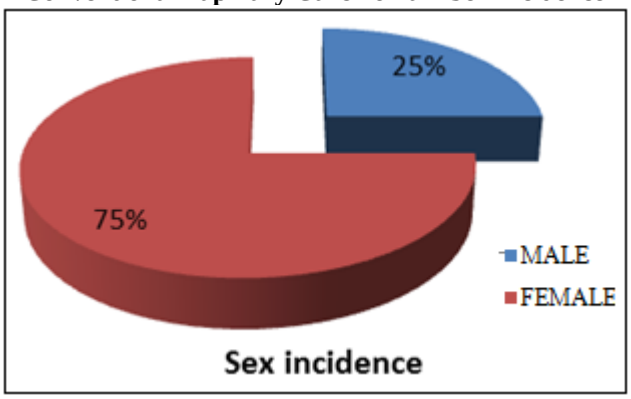
Conventional Papillary Carcinoma- Incidence in Male and Female



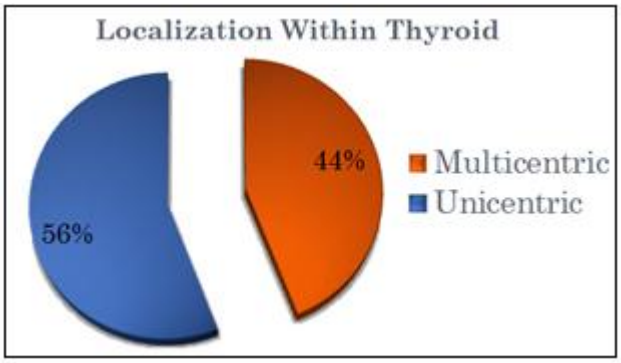
The incidence in females was found in the age group between 17 and 80 years. In males, it was found to be between 22 and 67 years.

Conventional Papillary Carcinoma (73%) is predominant histological pattern of papillary carcinoma seen in study group. This type of carcinoma is found more in females as compared to males

Conventional Papillary Carcinoma – Sex Incidence



Conventional Papillary Carcinoma - Unicentric or Multicentric



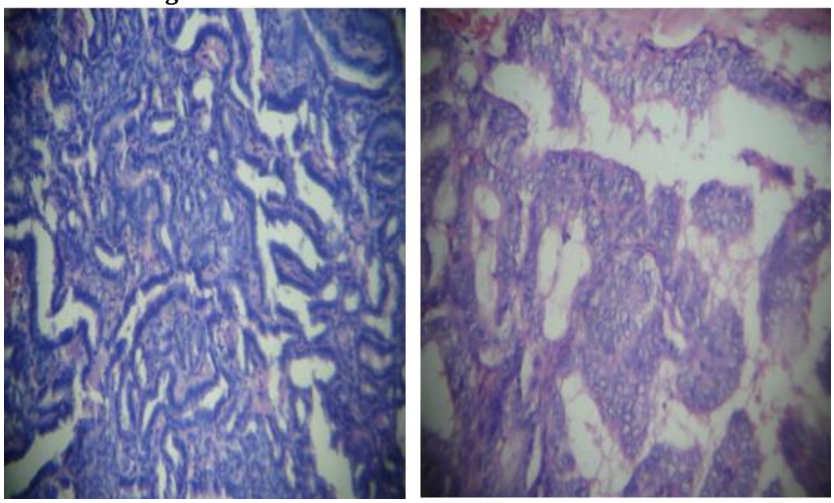
Invasiveness in conventional palillary carcinoma

Lymph Node Deposit was seen in 25% of cases and Lymphatic/Blood Vessel Invasion in 30% andIntrathoracic extension of Thyroid Tumor was seen in 1% .

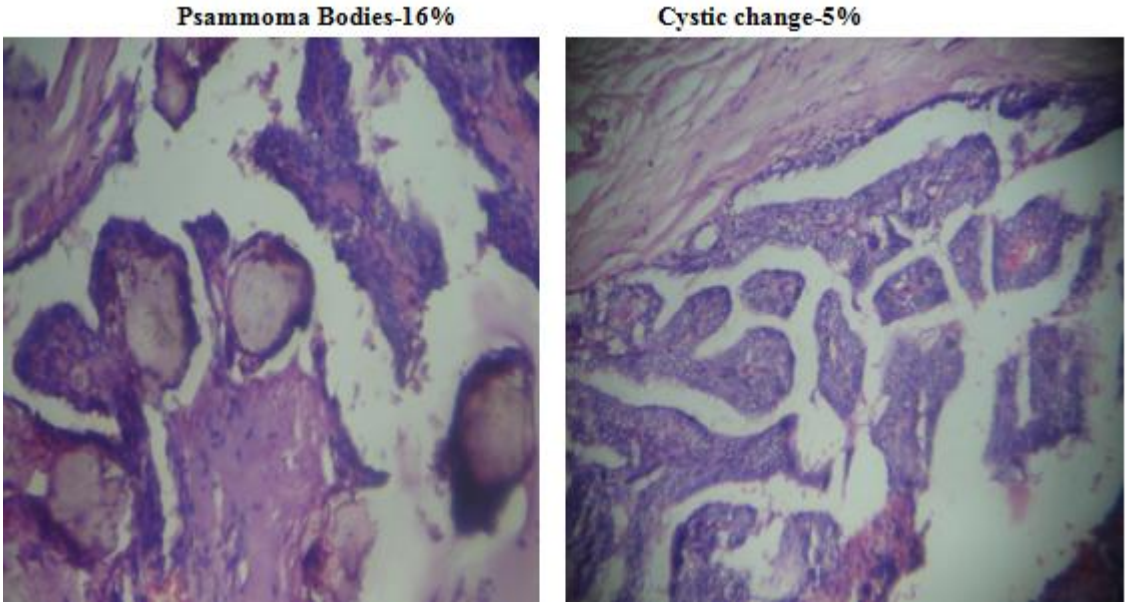
Associated findings of Conventional Papillary Carcinoma Thyroidseen in the tumor

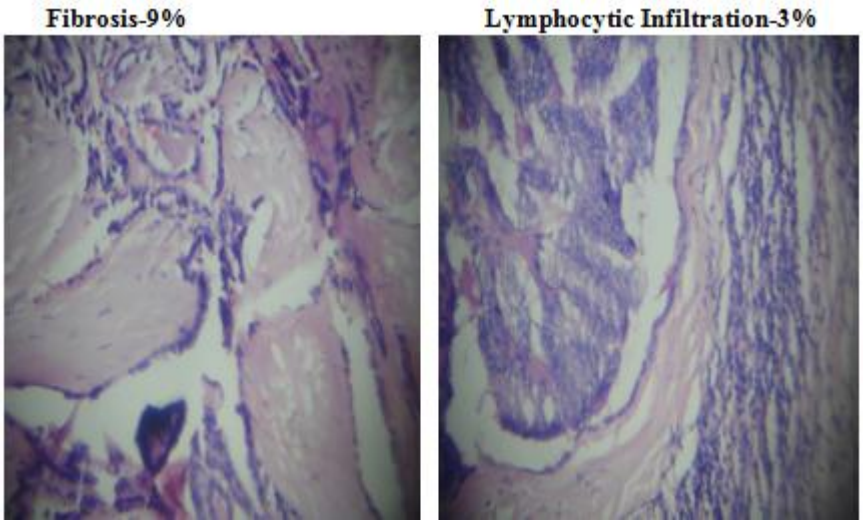
- Psammoma Bodies-16%
- Fibrosis-9%
- Cystic Change-5%
- Hyalinisation-3%
- Giant Cell Reaction-3%
- Lymphocytic Infiltration-3%

Conventional Papillary Carcinoma-figure



Conventional Papillary Carcinoma-Associated findings -Figure



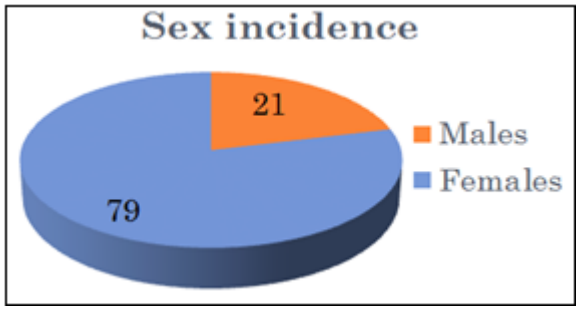


Follicular Variant of Papillary Carcinoma

Follicular variant of papillary carcinoma is the second most common type seen in the study group constituting 14%. This type was also common in the females found in 79%. The incidence in males was 21%.

The age group found to be affected in the study group was between 21 and 55 years in females and between 32 and 45 years in males. Calcification and Multicentricity was seen in 7% of cases respectively.

Invasiveness-lymph node deposit was seen in 7% of cases.



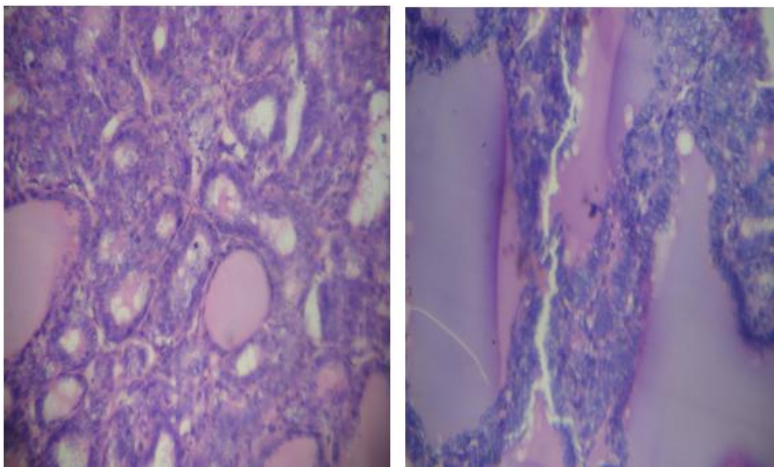


Figure - Follicular Variant

Encapsulated Variant

Incidence of this type found to be 4% in study group.Equal incidence was found in Males&Females in the study group.Lymph node invasion was seen in 25% of cases.Associated follicular adenoma was seen in adjacent thyroid in one case.

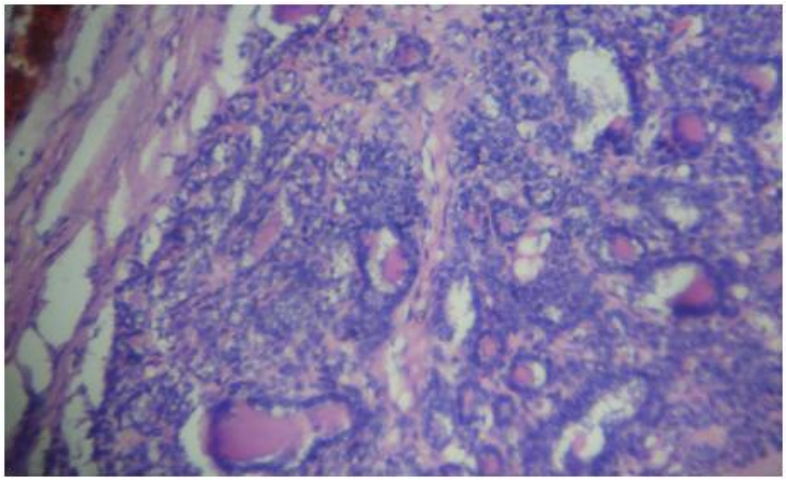


Figure - Encapsulated Variant

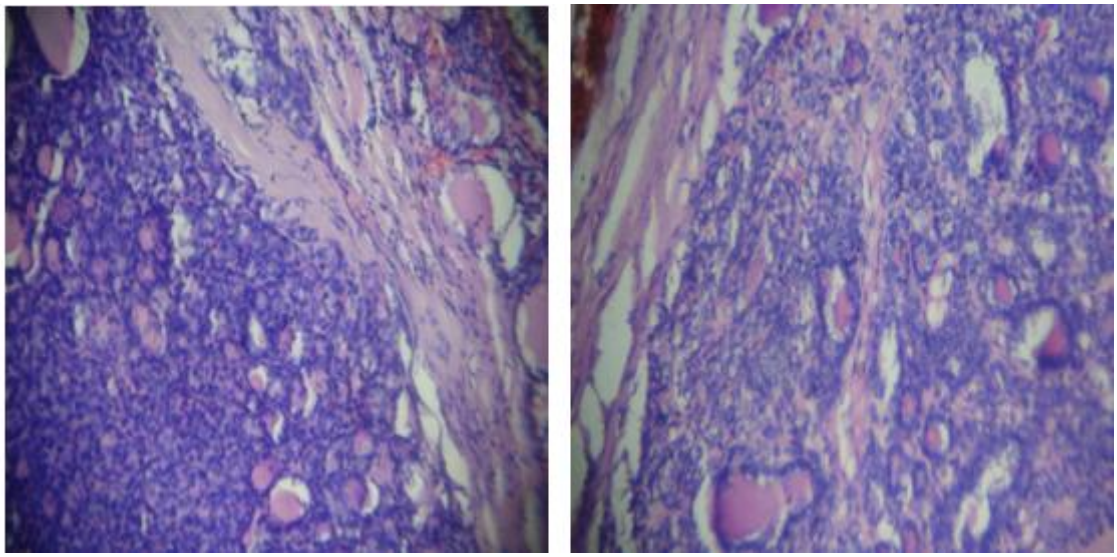


Figure - Associated Lesion - Follicular Adenoma With Encapsulated Variant

Tall Cell Variant

Incidence was found to be 2% in the study group. This type was seen in older age group 50-55 yrs in the study group.

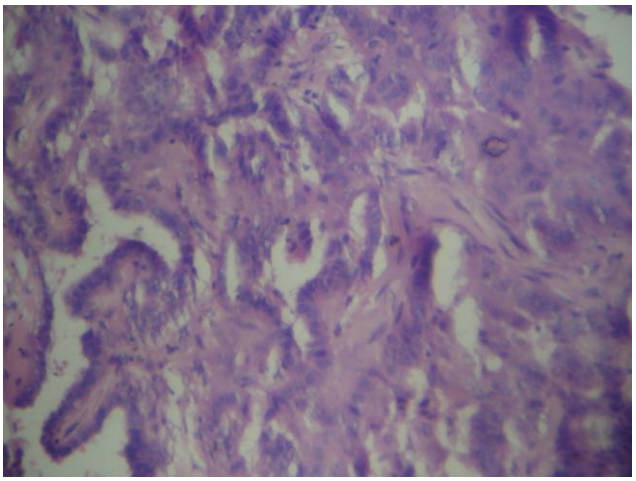


Figure: Tall Cell Variant

Papillary Microcarcinoma

Incidence was found to be 2% in the study group. In the first case the nodule was<0.5cm- with 2/3 lymph nodes – showing deposit. **In the second case**the Nodule was< 0.5cm with 2/8 lymph node showing deposit

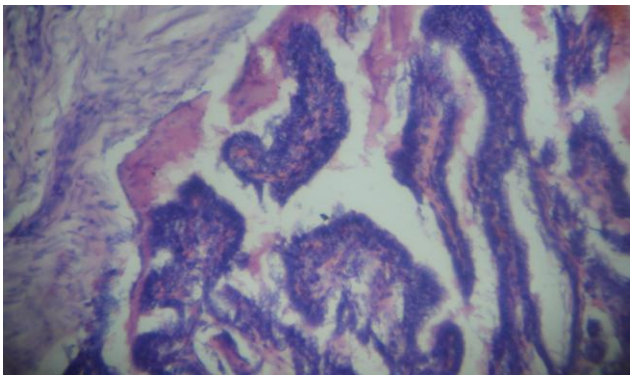


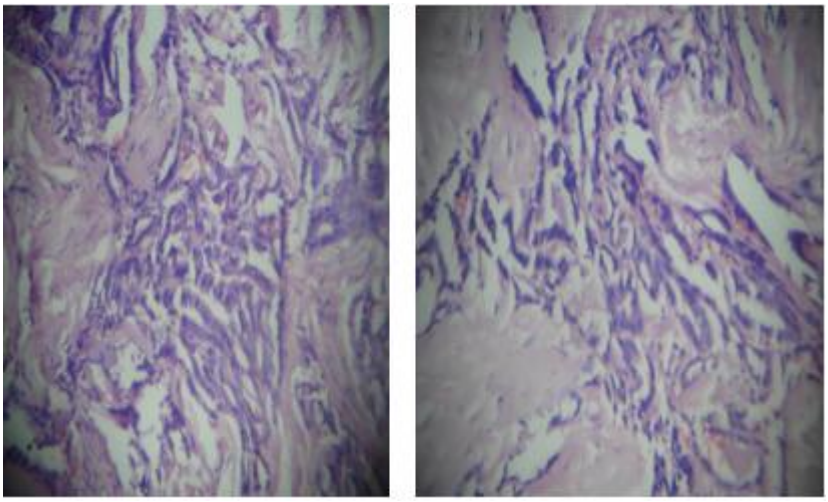
Figure: Papillary Microcarcinoma

Occult Papillary Carcinoma

Incidence was found to be 1% in the study group. 1/3-Lymph Node showeddeposit. No Tumor in thyroid was detected

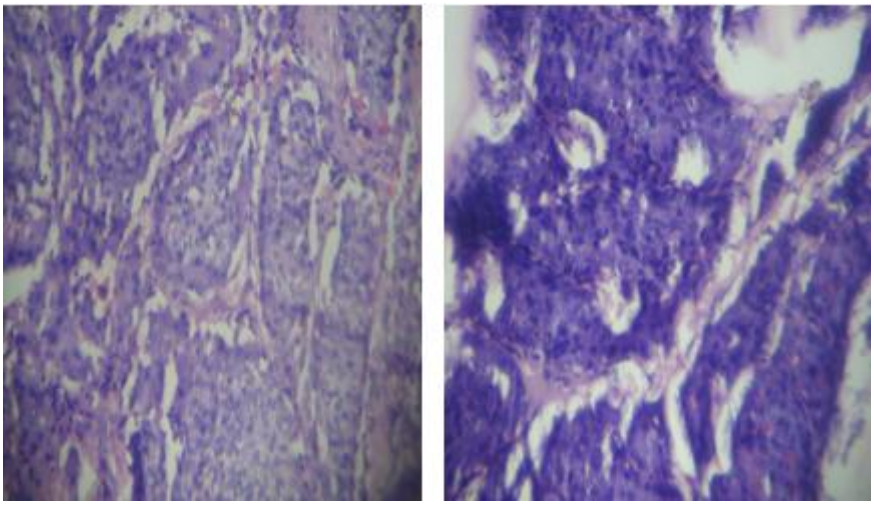
Diffuse Sclerosing Type

Incidence was found to be 1% in the study group. Lymphatic invasion was seen



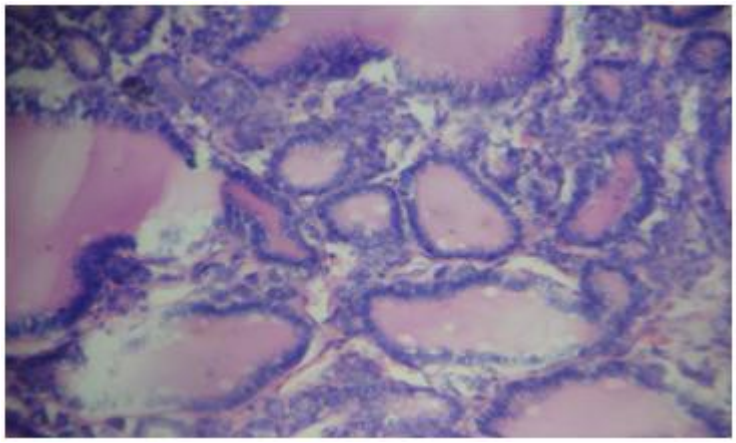
Cribriform – Morular Variant

Incidence was found to be 1% in the study group. No Association with FAP was found in this case.



Macrofollicular Type

Incidence was found to be 1% in the study group. Capsular invasion waspresent in the case.Differential Diagnosis include-nodular goitre/macrofollicular adenoma



Associated Lesions in Adjacent Thyroid in Cases of Papillary Carcinoma Thyroid

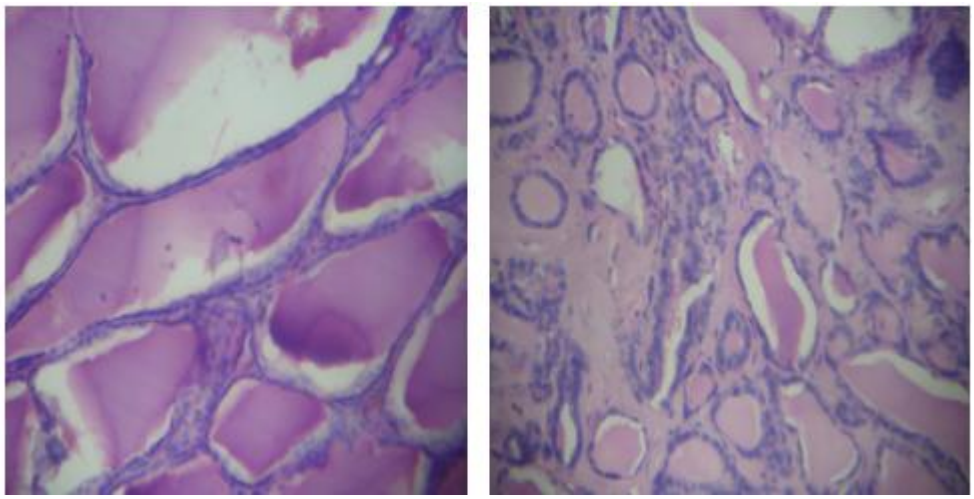


Figure: Nodular Colloid Goitre-14%

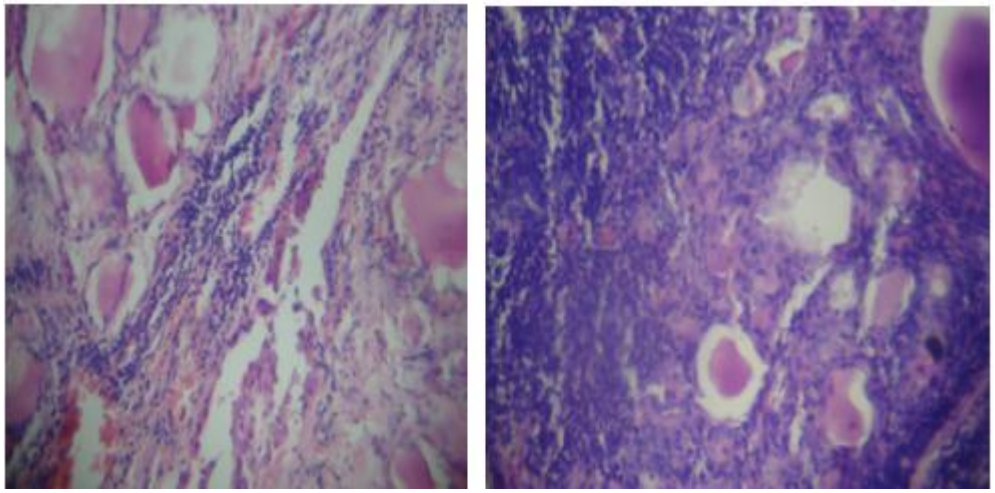


Figure: Chronic Lymphocytic Thyroiditis-11%

5. Conclusion

1) Incidence of Conventional Papillary Carcinoma andFollicular Variant-correlates with literature.
2) Incidence of Encapsulated, TallCell, OccultMicrocarcinoma, DiffuseSclerosing Type – Less compared to literature.
3) Increasing Age Incidence in Males is seen in the study group.
4) Multicentric Lesions-Significant in Number when compared to literature.
5) Uncommon Associated Lesion was found in the study group - Encapsulated Follicular Variant & Follicular Adenoma

6. Acknowledgement

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