



Original Research Article

Familiar tumor with multiple faces- A 5 yr study of papillary thyroid carcinoma

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ABSTRACT

Papillary thyroid carcinoma (PTC) is the most common malignant tumour of thyroid. Papillary thyroid carcinoma, follicular, columnar, microcarcinoma, diffuse sclerosing. Several variants have been described considering size, architecture, cellular properties, additional tumour components, stromal features and combination of the above mentioned characteristics. Our aim is to study the histopathological variants of PTC. Age group of the patients ranged from 20-50yrs with female predominance. Of the total 44 cases of PTC, classical variant of PTC was the most common accounting for 48% (21) cases followed by 34% (15) of follicular variant. It is important to know all the possible morphological demonstrations of PTC to recognize this common tumour of the thyroid. Although some variants are just morphological challenges for the pathologists, some others may behave worse than conventional PTC and need a more aggressive clinical management.

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1. Introduction

Papillary thyroid carcinoma (PTC) is the most common histological type of thyroid cancer and accounts for 80-90% of primary thyroid malignancies.^{1,2} The incidence rate in women is about 3-4 times the men.³⁻⁵ It usually follows an indolent clinical course with overall 5-year relative survival being 97.5%.^{6,7} Many subtypes of PTC have been described, of which classical PTC is the most common (80%).^{5,8}

New WHO classification of thyroid gland tumors describes 14 variants of PTC. The new variants like cribriform morular and hobnail variants show aggressive behaviour and carries poor prognosis. Specific variants of PTC are well recognized: well differentiated (classical & follicular), intermediate differentiated (tall cell, columnar cell, diffuse sclerosing, oncocyctic, and insular), and poorly differentiated.⁹ Based on the biological behavior, these histological variants are usually divided into “aggressive” and “non-aggressive” categories.^{5,10}

In the present study, we reviewed the histological features of PTC diagnosed in our institution over a period of five years. The aim of our study is to document prevalence and clinicopathological characteristics of different histological variants of PTC.

2. Material and Methods

Five year study was conducted from June 2013 to May 2018 in the Department of pathology, J J M medical college, Davangere. The material for study comprised of 942 thyroidectomy specimens which were received in different forms. The specimen details were recorded. After fixation, representative areas were selected for embedding. In case of encapsulated lesions, adequate representation from tumour-capsule-thyroid interface was given. Sections of 3-5 microns thick were cut, stained with Haematoxylin and eosin (H&E) and studied.

3. Results

This study was conducted for a period of 5 years (3 years of retrospective study and 2 years of prospective

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study) from June, 2013 to May, 2018. A total of 942 thyroidectomy specimens were received of which 11% cases were neoplastic lesions of the thyroid. Of the neoplastic lesions, the most common malignant neoplasm was PTC and its variants accounting for 41% (44 cases) of all neoplastic lesions. (Graph 1)

Peak age range for occurrence of PTC was 21-30 years with M: F ratio was 1:4.5. The number of female cases were more in age group of 21-30 years followed by 41-50 years. (Graph 2)

Of the 44 cases of PTC, classical variant of PTC (CPTC) was the most common accounting for 48% (21) cases followed by 34% (15) of follicular variant (FVPTC), 12% (five) papillary microcarcinoma (PMC) and 2% (one) case each of tall cell variant PTC (TVPTC), columnar cell variant PTC (CCPTC) and diffuse sclerosing variant PTC (DSPTC). (Graph 3)

Grossly, the tumour size ranged from 1cm to 9cm. Three-fourths of PTC specimens showed solid areas on cut section with the remaining showing solid-cystic areas. Papillary excrescence were grossly seen in 32% cases and multicentricity in 21% cases. Haemorrhage was the most common secondary change observed in 18% cases followed by calcification and necrosis in 5% cases each. Mucoid material and fibrosis were observed in a single case.

Of the total 44 cases of PTC, 66% cases showed predominantly papillary growth pattern and 34% cases showed follicular growth pattern microscopically.

A set of nuclear features form the major criteria for the diagnosis of PTC. Thyroid neoplasms having a combination of nuclear features, even in the absence of papillae, were regarded as PTCs. Combination of nuclear feature such as ground glass, overlapping, nuclear grooves & crowding was observed in 64% cases. Table 1

Of the total 44 cases of PTC, 48% showed psammoma bodies. Dystrophic calcification was the most commonly observed secondary change seen in 21% cases followed by fibrosis in 11% cases and haemorrhage in 9% cases. Table 2 Lymphoplasmacytic thyroiditis was observed in 14% cases and adenomatous goitre in 11% cases.

Of the 6 cases of PTC with lymph node involvement, cervical group of lymph nodes were involved in 19% cases of classical PTC and 7% cases of follicular variant PTC. Paratracheal lymph node was involved in one case of columnar cell PTC. Four cases were female and two were male with M: F ratio of 1:2. Table 3 Grossly, the involved lymph nodes in all six cases were grey white and solid on cut section.

3.1. Classical variant

CPTC constituted 48% (21) cases and was the most common variant of PTC in the present study. Peak age range for occurrence of CPTC was 21-30 years. Of the 21 cases of CPCT, 67% cases were females and 33% were males with

Table 1: Combination of nuclear features

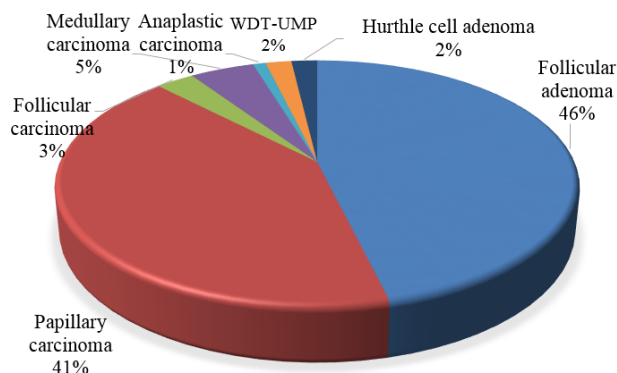
Nuclear features	No of cases
Ground glass+ inclusion+ overlapping+ grooves +enlargement+ crowding	6
Ground glass + overlapping+ grooves + crowding	28
Ground glass+ inclusion+ overlapping	8
Ground glass+ inclusion+ grooves + crowding	7
Ground glass+ grooves + crowding	26

Table 2: Secondary changes seen in PTC

Features	n=44 (%)
Dystrophic calcification	9 (21%)
Fibrosis	5 (11%)
Hemorrhage	4 (9%)
Sclerosis	2 (5%)
Squamous metaplasia	2 (5%)
Ossification	2 (5%)
Cystic	2 (5%)
Edematous	1 (2%)
Necrosis	1 (2%)
Cholesterol clefts	1 (2%)

Table 3: Lymph node involvement in PTC

Variant	Total no. cases	n=44 (%)
CPTC	21	4 (19%)
FVPTC	15	1 (7%)
Columnar PTC	1	1 (100%)



Graph 1: Percentage of thyroid neoplasms

Table 4: Age and sex distribution of variants of PTC (Put the full form of the variants in the text)

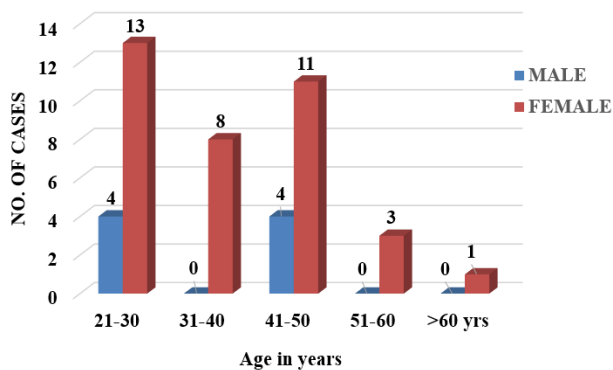
Variants	21-30	31-40	41-50	51-60	61-70	Total
	M:F	M:F	M:F	M:F	M:F	M:F
CPTC	12 4:8	1 0:1	7 3:4	0 -	1 0:1	21 1:2
FVPTC	3 0:3	5 0:5	6 1:5	1 0:1	0 -	15 1:14
PMC	1 0:1	2 0:2	1 0:1	1 0:1	0 -	5 0:5
TCPTC	-	-	1 0:1	-	-	1 0:1
DSPTC	1 0:1	-	-	-	-	1 0:1
CCPTC	-	-	-	1 0:1	-	1 0:1

Table 5: Peak age and sex distribution of PTC

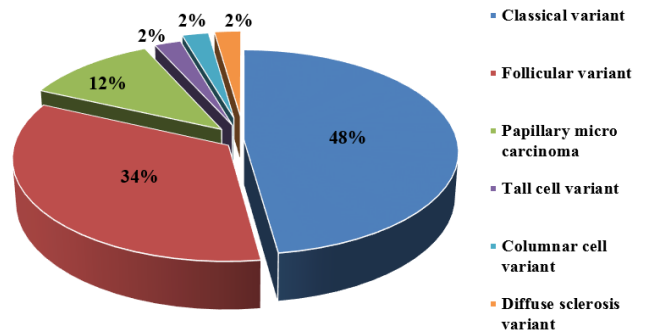
Authors	Peak age	M:F ratio
Lam et al 2005 16	—	1:3
Ariyibi et al 2013 15	21-30	1:3
Girardi et al 2013 18	—	1:4.5
Albasri et al 2014 14	21-30	1:3
Ahmad et al 2015 13	21-30	1:6
Shi et al 2015 17	—	1:3
Present study	21-30	1:4.5

Table 6: Incidence of variants of PTC

Authors	CPTC	FV-PTC	PCM	TC-PTC	DS-PTC	CC-PTC
Lam et al 2005 16	46%	18%	28%	4%	2%	1%
Adeniran et al 2006 22	55%	31%	4%	6%	2%	—
Ito et al 2008 29	86%	7%	—	4%	1%	1%
Kazaure et al 2012 39	98%	—	—	1%	1%	—
Girardi et al 2013 18	32%	16%	42%	1%	1%	1%
Albasri et al 2014 14	51%	31%	15%	3%	—	—
Shi et al 2015 17	75%	18%	—	4%	—	—
Xu et al 2015 20	26%	58%	12%	2%	—	1%
Fridman et al 2015 44	40%	29%	—	8%	8%	—
Present study	48%	34%	12%	2%	2%	2%



Graph 2: Age and sex wise distribution of PTC



Graph 3: Variants of PTC

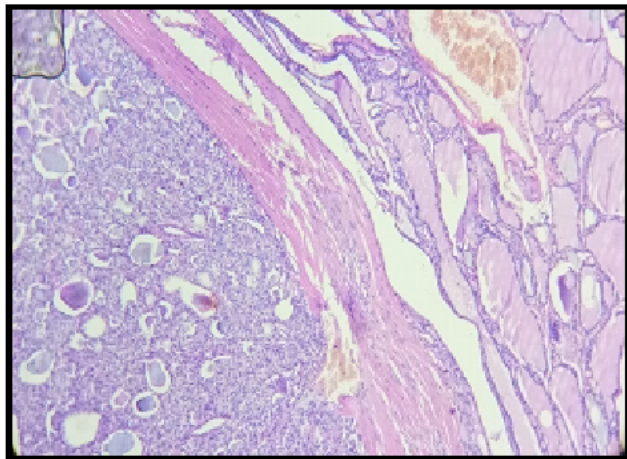


Fig. 1: Photomicrograph of follicular variant PTC showing follicles showing classical PCT nuclear features (x400 H&E stain)

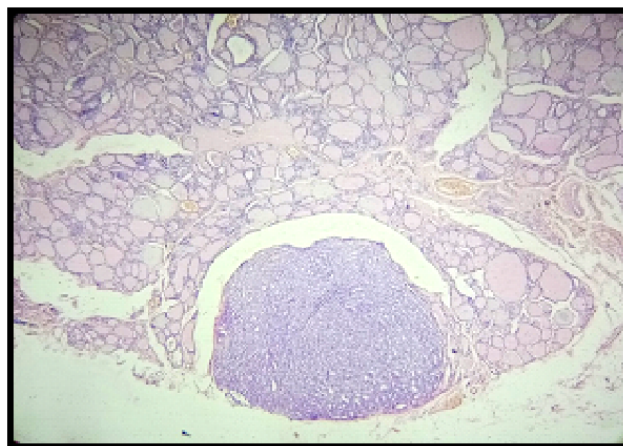


Fig. 3: Photomicrograph of papillary microcarcinoma showing tumor bordered by variable sized follicles filled with colloid (MNG changes) 40x, H&E stain)

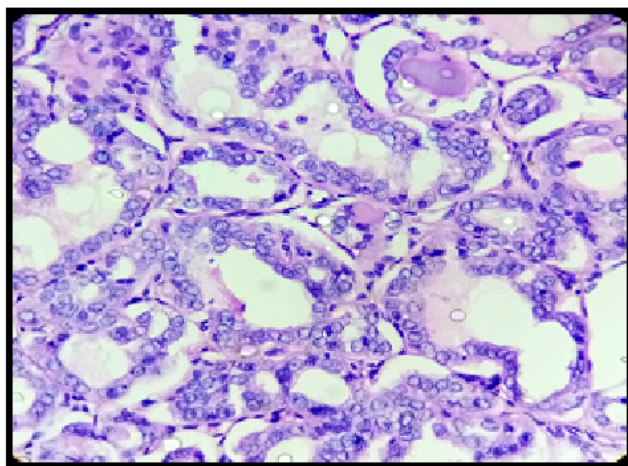


Fig. 2: Photomicrograph of follicular variant PTC showing neoplastic cells are arranged in follicles bordered by normal thyroid tissue (x100 H&E stain)

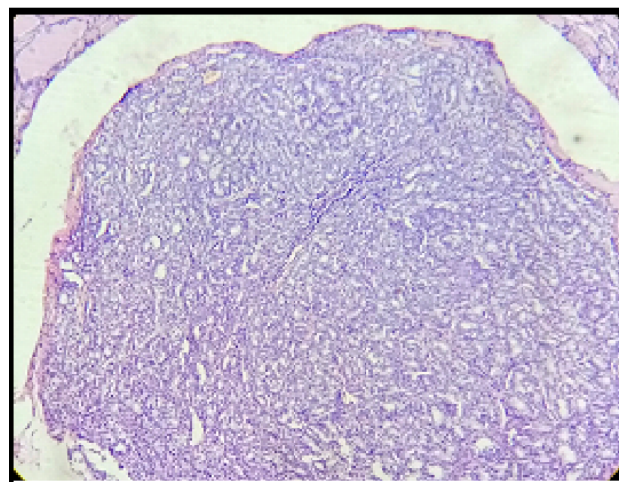


Fig. 4: Photomicrograph of papillary microcarcinoma showing tumor is well circumscribed showing follicular pattern (x100 H & E stain)

M: F ratio of 1:2. Table 4 The tumour size ranged from 1.5 cm to 9 cm. papillary excrescences were grossly seen in 43% cases and multicentricity in 24% cases. Cystic change was the most common secondary change observed in 29% cases followed by haemorrhage in 24% and calcification in 10% cases.

Microscopically, all cases of CPTC showed predominantly papillary growth pattern with cuboidal cells with 14% cases showed focal follicular pattern and 10% cases showed tumour cells in nests. The nuclei showed various combination of many typical nuclear features described for PTC and finding of mitosis was seen in a 5% cases.

The stroma of the papillae was slender with fibrovascular stalks in most cases, though 19% cases showed lymphoplasmacytic infiltration, and a single case each with presence of hemosiderin laden macrophages and giant cells within

stroma of papillae and between the papillae in different areas.

Of the total 21 cases of CPTC, 67% cases showed psammoma bodies. Dystrophic calcification was the most commonly observed secondary change seen in 33% cases followed by fibrosis and haemorrhage in 10% cases each.

3.2. Follicular variant

FVPTC constituted 34% (15) cases and was the 2nd common variant of PTC in the present study. Peak age range for occurrence of FVPTC was 41-50 years with male to female ratio of 1:14. (Table 4) Of the total 15 cases of FVPTC, 54% cases were completely encapsulated, 33% with an absence of capsule and 13% cases with partial

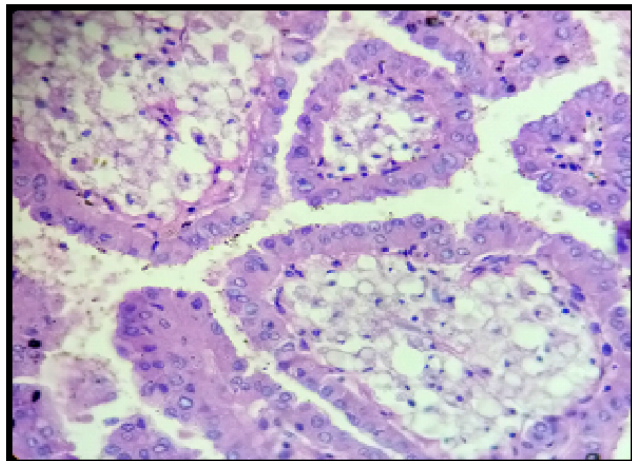


Fig. 5: Photomicrograph of tall cell variant PTC showing papillae lined by tall cells whose height is at least three times their width, stromal showing foamy macrophages and lymphocytic infiltration (x100 H & E)

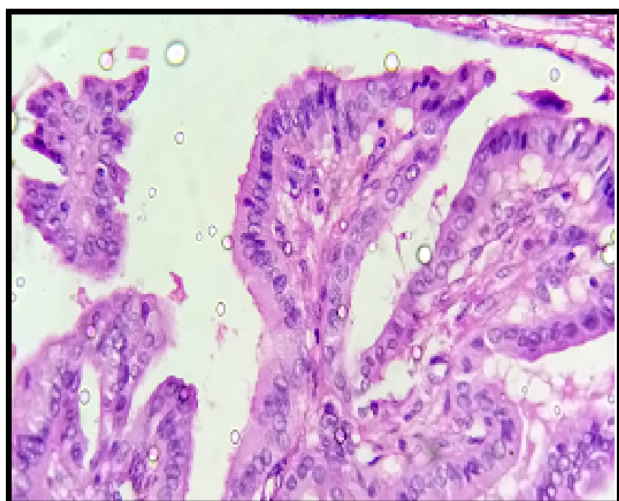


Fig. 6: Photomicrograph of columnar cell variant showing papillae lined by pseudostratified tall columnar cells reminiscent of those of early secretory endometrium (x400 H & E)

encapsulation with breach in the capsule. Multicentricity was grossly seen in 20% cases followed by cystic change and haemorrhage in 13% case each. The nuclei showed various combination of typical nuclear features described for PTC and 13% case showed occasional mitosis. Of the total 15 cases of FVPTC, 27% cases showed psammoma bodies. Dystrophic calcification, fibrosis, haemorrhage and ossification was observed in one case each.

3.3. Papillary microcarcinoma

PMC constituted 12% cases of PTC in the present study. Of the total five cases, 40% cases were seen in age group of

31-40 years and all five cases were females. Table 4 Of the total five cases, 60% cases were unencapsulated and 40% showed encapsulation. Multinodularity was grossly seen in 60% cases. Cystic change was most common secondary change observed in 60% cases and 20% showed papillary excrescence. The nuclei showed various combination of many typical nuclear features described for PTC in all the five cases. Hemosiderin laden macrophages were seen in 40% of the cases.

3.4. Diffuse sclerosing variant

A single case (2%) of DSPTC was diagnosed in a 28 year old female. The tumour size was 6 cm and showed invasion into the surrounding thyroid parenchyma. On microscopic examination, dense sclerosis and fibrosis with a few scattered foci of papillae having typical nuclear features were seen. Squamous metaplasia with lymphoplasmacytic infiltrate was seen with occasional mitotic figures (2-4/10HPF).

3.5. Tall cell variant

A single case (2%) of TCPTC was diagnosed in a 47 year old female. The tumour was well encapsulated measured 4.5x3.5 cm with papillary excrescences. Microscopic examination showed papillary structures lined by tall columnar cells with height three times the width, basally placed nuclei and abundant amount of eosinophilic cytoplasm. Surrounding stroma showed foamy macrophages and tumour giant cells with focal areas of necrosis.

3.6. Columnar cell variant

A single case (2%) of CCPTC was diagnosed in a 55 year old female who presented with neck swelling. The tumour was well encapsulated measured 5 cm with papillary excrescences. Microscopic examination showed papillary growth pattern lined by pseudostratified tall columnar cells having hyperchromatic elongated nuclei and typical PTC nuclear features. One lymph node sent along with tumour showed metastatic deposits.

4. Discussion

Thyroid cancer has been much in the news lately because of reports of large increases in incidence. The clinical spectrum of thyroid malignancies is varied and associated with variations in biological characteristics.^{11,12} The increased incidence can be attributed to advances in sonography, resulting in detection of small PTCs in asymptomatic healthy populations.^{12,13}

The fourth edition of the World Health Organization (WHO) classification of endocrine tumours, published in 2017 contain significant revisions. The revisions arose as a result in a better understanding of pathogenesis, clinical

behaviour, along with inclusion of cytogenetics of the thyroid lesions.

The other explanation is a real increase in the incidence of thyroid cancer, driven by changes to risk-factor exposure. Evidence in support of this view includes the increase in large thyroid cancers as well as smaller cancers. In addition, some authors have suggested that if over-detection alone is responsible for the rise, this should have resulted in a greater improvement in survival than has been observed in some studies.¹³

The present study may contribute in gathering some baseline data of PTC in our institution and the load of thyroidectomies in the tertiary care teaching hospital. PTC was the most common malignant neoplasm, accounting for 41% of thyroid neoplasms in the present study. PTC is acknowledged to be the most common histological type of primary malignant thyroid tumour worldwide and is seen in iodine sufficient areas.

In the present study, maximum number of cases were in the age group of 21-30 years. Similar observation were made in the study conducted by Ahmad et al, Albasri et al & Ariyibi et al and.^{13–15}

The fact that most of the PTCs occur in patient less than 50 years of age, as seen in the present study (44 cases, 90.90%) and by other authors, may explain the better prognosis seen in the PTC. There were 4 cases in older age group, of which one case was associated with lymph node metastases. The M: F ratio for PTC was 1:4.5 with female predominance, almost similar to the observation made by Ahmad et al, Albasri et al, Ariyibi et al, Lam et al, Shi et al & Girardi et al.^{13–18} (Table 5) This female predominance probably due to the willingness of female patients to undergo surgery for cosmetic reasons.

The histological classification of thyroid carcinomas has evolved considerably in recent decades, leading to a plethora of variants of PTCs, which have been included in the recent WHO classification. In the current study, apart from the common variants namely classical and follicular, other four variants were observed.

In the current study, 25% cases showed cystic change, as it had been reported by Carcangiu et al¹⁹ that tumours with marked cystic changes had a significantly greater chance of disease-free survival.

Extent of tumour was divided into intrathyroidal and extrathyroidal extension. The tumour with intrathyroidal extension had infiltrating margins accounted for 34% of PTC cases in the present study. Extrathyroidal extension into the surrounding tissue was seen in 7% cases. Xu et al observed extrathyroidal extension in 2.53% cases, Shi et al observed in 31% and Roh et al in 54.3%.^{17,20,21}

Girardi et al showed papillary pattern (33.65%) was the predominant pattern followed by follicular pattern in 4.83% cases.¹⁸ The finding is concordant with our study wherein papillary pattern was seen most frequently followed by

follicular pattern. The typical nuclear features of PTC were seen in a combination of varying proportion, rather than in isolation. Ground glass appearance was uniformly present in all cases in the present study. Nuclear overlapping, grooves, enlargement and crowding were seen in most cases in the present study. The findings are in agreement with similar studies on the topic conducted by Lam et al, Aderinan et al and Radu et al.^{16,22,23} Similar to the study conducted by Aderinan et al²² intranuclear inclusion was not uniformly present in all the cases in the present study.

Psammoma bodies were found in 48% cases of PTC and similar to findings in studies conducted by Carcangiu et al, Lam et al, Aderinan et al, Jennifer et al & Girardi et al.^{16,18,19,22,24} The finding of psammoma bodies in the capsule, around blood vessels and surrounding thyroid parenchyma probably represents dissemination of tumour cells and subsequent degeneration leaving behind psammoma bodies as evidence of their presence.

It is important to note that non – tumour-associated psammoma bodies were found in conjunction with microscopic, incidental thyroid carcinomas. This was observed in 44.44% cases in the Jennifer et al study, implying sampling of the entire surgical specimen is crucial.²⁴

Psammomatoid bodies are those foci of calcification which lack characteristic lamellation of psammoma bodies. Such bodies were seen in 21% cases in present study. Similar observation were made by Lam et al, Aderinan et al & Radu et al.^{16,22,23}

Ossification in the stroma of thyroid was seen in 5% cases in the present study, similar observation was made in study by Lam et al.¹⁶ Pillai et al mentioned presence of calcification / ossification in the stroma of thyroid carcinomas could be a feature of aggressive thyroid carcinomas.²⁵ Lam et al reported the presence of osseous metaplasia in a patient with DSVPTC, who eventually died of the disease.¹⁶

Foci of squamous metaplasia were seen in 5% cases in the present study. Carcangiu et al observed similar finding in 18.67% of cases and also mentioned squamous metaplasia is more often seen in tumours with a predominantly papillary pattern of growth than in those that featured many follicles, and seemed to bear some topographic relationship with the solid areas.¹⁹

Fibrosis was seen in 11% cases in present study, similar to Carcangiu et al, Aderinan et al & Radu et al study.^{19,22,23} Sclerosis was seen in 5% of cases in present study similar to Carcangiu et al study.¹⁹ Infiltration of the surrounding thyroid parenchyma by lymphocytes, sometimes accompanied by other mononuclear inflammatory cells, was seen in 13.63% cases in the present study. Similar observation was made by Carcangiu et al, Aderinan et al, Girardi et al, Pillai et al & Collini et al.^{18,19,22,25,26}

In the present study, 14% cases showed metastatic deposits of PTC in lymph node. Cervical lymph nodes were the most commonly involved group. Studies have shown that, despite some histological differences observed between CPTC and FVPTC, both neoplasms have favorable prognosis and similar cancer-specific survival at 10 and 15 years.

In the present study, high rate of lymph node metastases observed in CPTC, similar to the study conducted by Lam et al.¹⁶ Lang et al observed fewer metastatic lymph nodes and lower extraglandular overflow rate among the FVPTC cases when compared to the usual forms of PTC. Aderinan et al concluded that high rate of LN metastases was associated with BRAF mutation.²² In study conducted by Kazuare et al and Shi et al, high incidence of lymph node metastases was due to their inclusion of aggressive variants of PTC namely DSVPTC and TCVPTC. Both associated with high lymph node metastases and extrathyroidal extension.^{17,27} The LN metastases have been associated with high rates of locoregional recurrence and poor survival observed by Roh et al.²¹

4.1. Classical variant

CPTC was the most commonly observed variant similar to the observation made by above studies. (**Graph 3**) In the present study, CPTC was observed in more number of female patients. Similar observation was made by many authors. In our study, 67% cases showed presence of psammoma bodies, 33% cases showed calcified bodies, 5% cases with ossification and 19% cases associated with LN metastases. Similar observations were made in study by Lam et al.¹⁶

4.2. Follicular variant

In the present study, PVPTC was observed in more number of female patients. Similar observation was made by Lam et al, Ito et al, Girardi et al & Shi et al study.^{16-18,28} In our study, 7% cases showed presence of calcification and bone formation. Similar observation was made by Lam et al.¹⁶ Bone formation seen less oftenly in follicular variant of PTC when compared with conventional type.

Follicular variant rarely shows lymph node metastases with only a single case showing the same in the current study. Lang et al observed fewer metastatic lymph nodes and lower extraglandular overflow rate among the follicular variant cases when compared to the usual forms of PC.²⁹ Ozdemir et al showed greater tumour diameter, although lower prevalence of capsular invasion and extraglandular extravasation among FVPTC when compared to the CPCT.³⁰

4.3. Papillary microcarcinomas

PMC which are ≤ 1.5 cm in diameter, were seen in 12% of all PTC cases in the present study. All these cases were resected either as multinodular goitre or as solitary nodules. All the five cases in our study were diagnosed incidentally, almost similar observation was made by Roti et al & Neuhold et al.^{31,32} There was a high incidence of PMC in Lombardi et al study due to high incidence of goiter in the study area and patients were usually referred to their center from areas in which goiter was endemic.³³ Neuhold et al observed that number of PMCs with multiple foci and the number of separate tiny tumours within a gland increased significantly with the number of paraffin blocks. They finally concluded that detection rate of PMC was significantly determined by the accuracy of the histological workup of thyroid specimens.³² In the present study, maximum number of cases (2) were in the age group of 31-40 years. Similar observation were made in the study conducted by Lombardi et al, Neuhold et al & Zhou et al.³²⁻³⁴ In the present study, all five cases of papillary microcarcinoma were females, almost similar to observation of female predominance made by many authors.

Thyroid microcarcinoma with papillary pattern prevalence was 99% in meta-analysis study conducted by Roti et al.³¹ This finding was consistent with our study.

The rate of lymph node metastases was only 2.7% in Neuhold et al study and it was mentioned that patients with papillary micro carcinoma had a lower prevalence of lymph node metastases than conventional PTC. The outcome of patients with papillary micro carcinoma is generally favorable even in the presence of lymph node metastases and local invasion.³² Extrathyroid tumour extension, multifocality, and significant tumour fibrosis have been associated with aggressive behavior of TPMCs in Niemeier et al study.³⁵

4.4. Diffuse sclerosing variant

Diffuse sclerosing variant was seen in one (2%) case in the present study. The reported incidence of DSVPTC in the literature varies from 0.74% to 5.3% and correlates with the present study. In Malandrino et al study the incidence was 0.9%.³⁶

In the present study, DSVPTC was diagnosed in a 28-year-old female. In the studies conducted by Lam et al, Pillai et al, Chereau et al and Malandrino et al DSVPTC showed a mean age of 28 years with female predominance.^{16,25,36,37} Both findings were in agreement with the findings of our study. On microscopy, areas of dense sclerosis and fibrosis with a few scattered small foci of PTC having typical nuclear features, were seen. Prominent areas of squamous metaplasia with lymphoplasmacytic infiltrate and psammoma bodies were seen. Occasional mitotic figures (2-4/10HPF) were present.

Similar observations were made in the studies mentioned above.^{16,25,36,37}

4.5. Tall cell variant of PTC

Tall cell variant of PTC was diagnosed in one case (2%) in the present study, similar to the study conducted by Wang et al (1.33%).³⁸ In studies conducted by Kazuare et al, Axelson et al, Wang et al, Regalbuto et al, Morris et al and Ganly et al a female predominance was observed which is concordant with the current study.^{5,38–42}

The diagnostic criteria for this variant of PTC is presence of tall cells (>30%) with height thrice as much as the width, 4-5/10HPF and areas of necrosis. Ganly et al and Wang et al mentioned presence of mitotic figures and necrosis implies tumour transformation to poorly differentiated carcinoma or anaplastic carcinoma and aggressiveness.^{38,42} In that regard, Akslen and Livolsi found a higher frequency of tumour necrosis in TCVPTC compared to other subtypes of PTC. They also found that the histologic grade (defined as nuclear atypia, tumour necrosis, and vascular invasion) and tumour size, rather than PTC subtype, were independent prognostic factors.⁴³

In Ganly et al study 2.4% cases transformed into poorly differentiated or anaplastic carcinoma in their recurrence. This is an example of the higher aggressive biological behavior of TCV, and should prompt the pathologist to sample these tumours extensively for microscopic examination in search of an anaplastic or poorly differentiated component, especially in older patients. These tumours usually shows extrathyroidal extension and lymph node metastases.⁴² In the present study, these features were absent.

4.6. Columnar cell variant

CCVPTC accounted for 0.4% in Ito et al²⁸ study, which is similar to the incidence demonstrated in our study. In the present study CCVPTC was diagnosed in 55 years old female who presented with neck swelling and paratracheal lymph node enlargement. Tumour was completely encapsulated and measured 5 cm. Microscopic examination showed predominant papillary pattern, composed of pseudostratified tall columnar cells having hyperchromatic elongated nuclei with focal typical PTC nuclear features. Paratracheal lymph node showed metastatic deposits.

In the Lam et al¹⁶ study, two cases of columnar cell variant of PTC was diagnosed, both of them were females and presented with lymph node metastases. This was concordant with present study.

5. Conclusion

In conclusion this study has shown that thyroid diseases are common in this environment and affects all ages mainly middle age group. Thyroid neoplasms are predominantly

seen in females, and the most common type is PTC, which has the highest incidence in the third decade. It is not rare to find a PTC showing characteristics of more than one variant. The challenge that remains is distinguishing the common lesions that likely do not require aggressive radioactive iodine therapy from the minority of PTCs that will recur and metastasize. A small percentage of PTC variants recognized by their greater potential for aggression. There are associations between these PTC variants and several other histopathological factors already recognized for their prognostic value, which may, by themselves, influence the outcome of these cases.

6. Source of funding

None.

7. Conflict of interest

None.

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