

## Morphological Variants of Papillary Carcinoma of Thyroid

\*Alam MA,<sup>1</sup> Islam KN,<sup>2</sup> Ali SM,<sup>3</sup> Rahman AN,<sup>4</sup> Kamal M<sup>5</sup>

An observational study was carried out at the Department of Pathology, BSMMU to see the different morphological variants of papillary carcinoma of thyroid with their detailed morphology and to see the correlation of variants with particular age and sex. The study was carried out during the period of January 2004 to December 2004. A total 103 cases of papillary carcinoma of thyroid were collected. Out of those 57(55.53%) cases were diagnosed as classic type or conventional type, 40(38.83%) cases as follicular variant, 3(2.91%) cases as trabecular variants, 2(1.94%) cases as oxyphilic variant and 1(0.97%) cases as tall cell variant. Psammoma body was observed in 42(40.77%) cases. Maximum numbers of subjects were in 2<sup>nd</sup> and 3<sup>rd</sup> decade and in 4<sup>th</sup> decade in case of classic type but in case of follicular variant maximum numbers of subjects were in 3<sup>rd</sup> and 4<sup>th</sup> decade and a fair number of follicular variant also observed in 5<sup>th</sup> decade. It appears that incidence of follicular variant becomes higher by a decade compared to classic type. About 90% cases of study subjects were female. Tall cell and columnar variant that shows worse prognosis was less evident in this study.

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**Key words:** Papillary carcinoma, Morphology, Thyroid

### Introduction

**P**apillary carcinoma of thyroid is a common thyroid malignancy and most common endocrine neoplasia in those countries where iodine is sufficient or excess in their diet.<sup>1,2</sup> Female are affected more commonly than male.<sup>3</sup> Mean age of initial diagnosis of papillary carcinoma is 40 years. In case of children 90% of thyroid malignancy is papillary carcinoma.<sup>4</sup> Papillary carcinoma of thyroid has a more favorable prognosis than other thyroid malignancy. Regional lymph node metastases are extremely common at initial presentation of papillary carcinoma of thyroid. This feature however doesn't adversely affect long time survival. Lymph node metastasis in papillary

carcinoma has minimal clinical significance for staging.<sup>1</sup>

There are various subtypes or variants of papillary carcinoma of thyroid. Some of those have a more aggressive clinical course and less favorable prognosis.<sup>5</sup> Many prognostic factors that influence survival of papillary carcinoma of thyroid such as AGES (age, grade, extension, invasion, size), Prognostic index (PI), the AMES system (age, metastasis, extension, size) etc.<sup>1</sup>

Many morphological variants of papillary carcinoma of thyroid other than classic type have been described in different series such as follicular, solid/trabecular, oxyphilic, diffuse sclerosing, tall cell, columnar variants etc.<sup>6</sup>

1. \*Dr. Md. Ashraf Alam, Associate Professor of Pathology, Rangpur Medical College.
2. Professor KM Nazrul Islam, Ex Chairman & Professor of Pathology, IPGMR (Presently BSMMU).
3. Professor Syed Mukarram Ali, Professor of Pathology, BCPS, Dhaka
4. Professor AJE Nahar Rahman, Ex Chairman, Department of Pathology, BSMMU.
5. Professor Mohammad Kamal, Chairman, Department of Pathology, BSMMU

\* For correspondence

The more aggressive subtypes of papillary carcinoma of thyroid include the tall cell and columnar variants. Tall cell variant is extremely aggressive and tends to recur in neck and more serious prognosis than usual type. Oxyphilic variant also have favorable prognoses than usual conventional or classical type.<sup>7</sup>

Prognosis of solid variant is controversial. Some studies show outcome are similar to usual type and other studies show more aggressive behavior. The prognosis of follicular variant is apparently same as that of classic variant; this variant has more chance to metastasize outside of neck and vascular invasion.<sup>2</sup>

Another important diagnostic feature of papillary carcinoma of thyroid is presence of psammoma body. Psammoma body strongly suggests papillary carcinoma of thyroid because occurrence in other thyroid carcinoma is exceptional and extremely uncommon<sup>8</sup>.

They are present in papillary carcinoma of thyroid in only 50% cases.<sup>4</sup> Some author claimed presence of psammoma bodies in papillary carcinoma of thyroid as an indicator of good prognosis.<sup>9</sup> Psammoma bodies are usually found in singly or in clusters surrounded by small nests of tumour cell throughout the thyroid gland.<sup>8</sup>

Histopathological report of papillary carcinoma of thyroid should indicate whether the tumour is usual type or an unusual variant, which may have an adverse prognosis. In our country there is no report study about morphological variants of papillary carcinoma of thyroid.

### Methods

This study was carried out at the Department of Pathology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka during

the period of January 2004 to December 2004. A total 103 thyroid sample of papillary carcinoma, which fulfilled the inclusion criteria were selected for this study. For this purpose 103 cases of papillary carcinoma of thyroid was collected from BSMMU Hospital (n=41), Dhaka medical college hospital (n=3) and two private laboratories of the Dhaka city (n=59). Detailed gross examinations have been performed in 20 cases where specimens were collected in the department of pathology, BSMMU.

Clinical data were collected from hospitals record and histopathological requisition forms. In other 83 cases only paraffin blocks of papillary carcinoma of thyroid were collected from private laboratories and clinical data and gross description were collected from records. Cases of thyroid carcinoma, which were diagnosed as papillary carcinoma on histopathological examination, were selected for this study. Thyroid tumours other than papillary carcinoma of thyroid were excluded from study. Only metastatic foci of papillary carcinoma in lymph node without removal of any primary tumour also excluded from the study.

During gross examination of the specimens, particular emphasis given on nodule, visible granular area, and foci of microcarcinoma, any invasion into surrounding perithyroidal tissue, encapsulated or diffuse, cystic area and calcification were noted. Blocks were also taken from adjacent thyroid tissue and grossly suspected parathyroid tissue and resected lymph node(s).

Histological examination was done by light microscope and different morphological variants were identified with special emphasis on a) capsule: present/absent, invasion by tumour b) arrangement of cells: branching papillae/follicular/trabecular or

solid/cribriform) nuclear features: grooves/orphan annine/inclusion/mitosis c) psammoma bodies: present/absent d) non-psammomatous calcification, e) fibrosis: focal or diffuse f) any capsular, vascular or perithyroidal soft tissue invasion and d) necrosis.

All necessary and relevant data regarding samples were recorded methodically and meticulously as per as possible in data sheet. All relevant data were analyzed by standard statistical method using Chi-square test.

### Results

The main objectives of this study were to demonstrate the morphological variants of papillary carcinoma of thyroid in our population. Second objective of this study was to explore any relation of particular variant with age and sex. The third objective was to see any other important histological features of the variants.

For this purpose 103 cases of papillary carcinoma of thyroid was collected from BSMMU Hospital (n=41), Dhaka medical college hospital (n=3) and two private laboratories of the Dhaka city (n=59) during the period of January 2004 to December 2004. Detailed gross examinations have been performed in 20 cases where specimens were collected in the Department of Pathology, BSMMU.

The overall age and sex distribution of cases with papillary carcinoma of thyroid was done for papillary carcinoma of thyroid as a whole and also for each variant. The age range from 12-70 years with mean age 34.05 years (SD±13.88). The mean age of male patients was 40 years (SD±16.70), mean age of female patient was 32.69 years (SD#12.89). The majority of the patients 77(74.75%) were between 11 to 40 years of age. Out of these 103 cases 19 (18.4%) were male and 84 (81.6%) were female; with a male to female ratio is 1:4.4.

Chi square test was done to see any significant difference of number of papillary carcinoma of thyroid between sexes. Numbers of female cases were very highly significant ( $p < .001$ ).

Fifty seven cases were classic type, out of this 14 cases were in second decade, 18 cases were in third decade, 13 cases were in fourth decade, 7 cases were in fifth decade, 3 cases were in sixth decade and 2 cases were in seventh decade. In case of follicular variant out of 40 cases, 5 cases were in second decade, 10 cases were in third decade, 13 cases were in fourth decade, 7 cases were in fifth decade, 2 cases were in six decade and 3 cases were in seventh decade. In cases of oxyphilic both cases were in third decade, in case of trabecular variant both cases were in third decade and 1 case were fourth decades. Tall cell variant case was in seventh decade

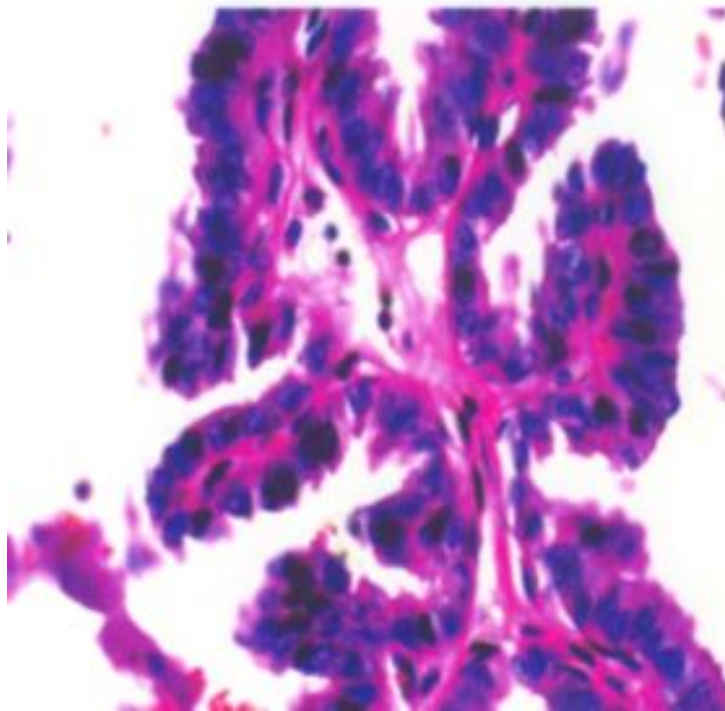


Figure 1. Photomicrograph showing a typical papilla (study case no 77 H & E stain x 400)

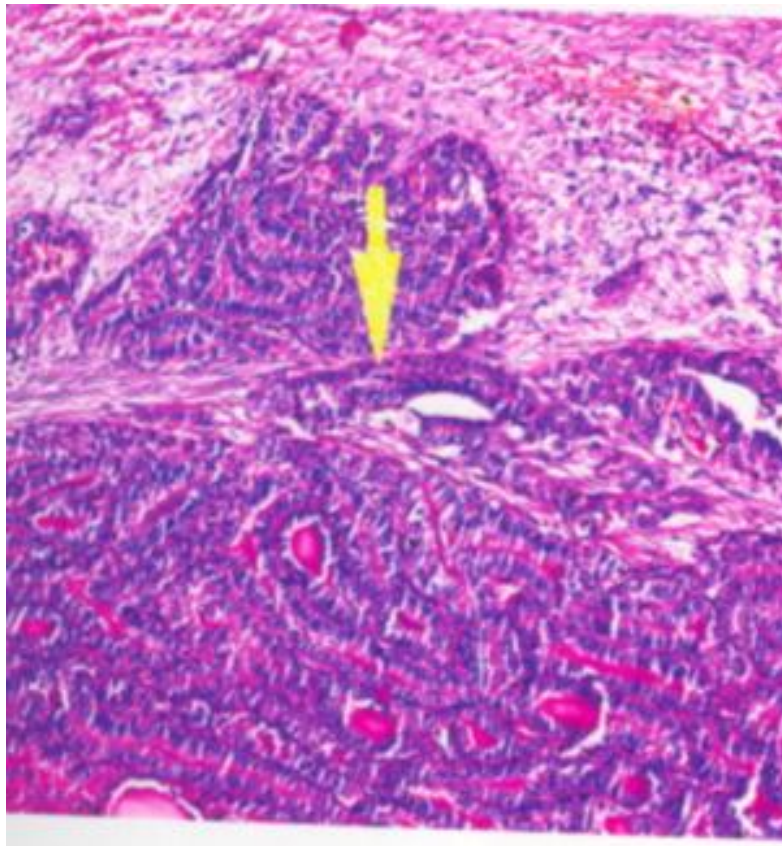


Figure 2. Photomicrograph showing tall cell variant (study case no 47 H & E stain x 400)

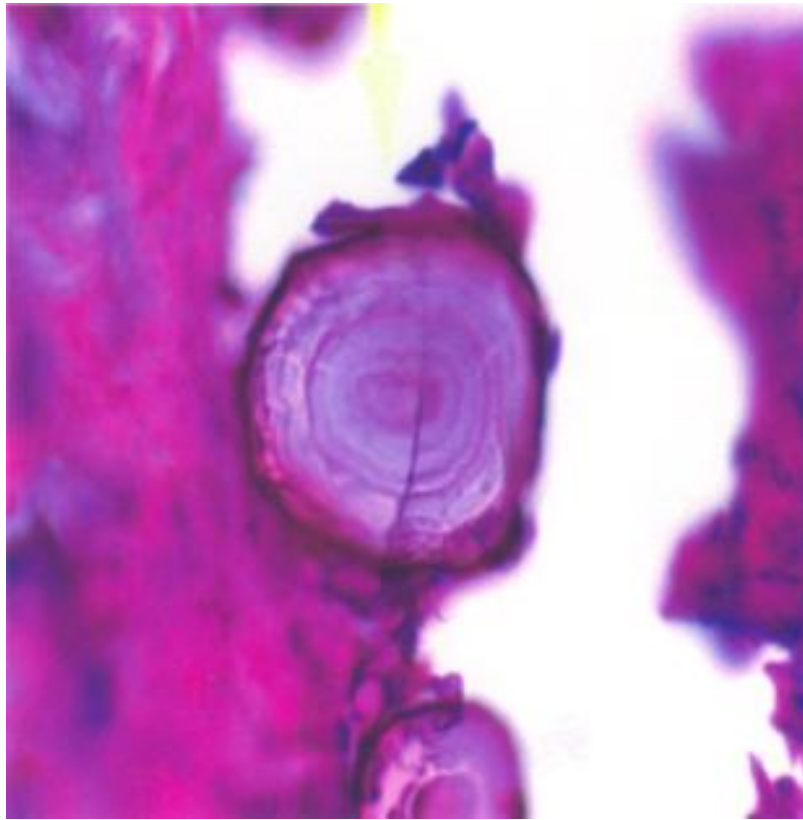


Figure 3. Photomicrograph showing a typical psammoma body (study case 43 H & E x400)

The age ranged for classic type is from 12-68 years with a mean age of 32.98 years. The mean age for male patient was a decade higher than females (41 years, compared to mean age of female patients of 30.84 years). The majority of the patients were in second, third and fourth decades, 14(24.56%), 18(31.57%) and 13 (22.80%) respectively. Out of these 57 cases, 11(19.29%) were male and 46(80.70%) female; with male to female ratio of 1:4.1 (Table 1).

Table I: Age distribution of patients with classic type papillary carcinoma of thyroid

Age Group(Years)	Male	Female	Total
10-20	1	13	14
21-30	2	16	18
31-40	4	9	13
41-50	2	5	7
51-60	1	2	3
61-70	1	1	2
Total			57

The age range for follicular variant of papillary carcinoma was from 12-70 years with a mean age of 34.25 years. The mean age of male patient was 41.75 years, and that of

female patient was 35.88 years. The majority of the patients were in the third and fourth decades, 10(25%) and 13(32.5%) respectively. Relative numbers of patients were also more in 5<sup>th</sup> decade compared to classic variant. It appears that follicular variant appears a decade later than classic type. Out of the 40 cases 4(10%) were male and 36 (90%) were female; with male to female ratio is 1.9 (Table II).

Table II: Age distribution of follicular variant of papillary carcinoma

Age Group(Years)	Male	Female	Total
11-20	0	5	5
21-30	0	10	10
31-40	3	10	13
41-50	0	7	7
51-60	1	1	2
61-70	0	3	3
Total			40

The age range of trabecular variant was from 26-40 years with a mean age 32.66 years, all were female patient. One patient was in second decade and 2 patients were in third decade.

Two oxyphilic variants were observed during the present study; both of them were females in their third decade, with a mean age of 36 years.

A single patient of tall cell variant was seen who was a male of seventh decade. (Table III)

Table III: Variants of papillary carcinoma in different age groups

Variants	Age groups in			Sex		Total
	Year			Male	Female	
	21-30	31-40	61-70			
Trabecular	2	1	0	0	3	3
Oxyphilic	2	0	0	0	2	2
Tall cell	0	0	1	1	0	1

Clinical information's and relevant investigations were found in 21 of 103 cases. Out of 21 cases, 7(33.33%) were clinically diagnosed as having solitary thyroid nodule of both lobes, and 5 (23.80%) were multiple nodules either of lobes. Solitary nodule in the isthmus was found in 5 (23.80%) cases, and diffuse enlargements of thyroid gland were found in 4 (19.04%) cases. Relevant investigations were available in 17 cases, out of these 12 (70.58%) cases were biochemically euthyroid, 3(2.91%) cases were hyperthyroid and 2 (2.91%) cases were hypothyroid. <sup>131</sup>I uptake test was available in 11 cases out of 21 cases. Low <sup>131</sup>I uptake was found in 6(5.82%) cases indicating cold nodule and high indicating hot nodule was found in 5 (4.85%) cases.

Ultrasonographic finding was available in 11 cases. Out of this both solid and cystic areas were found in 3 (2.91%) cases, and only cystic area was found in 9 (75%) cases.

Histologically capsule was found in 42 (40.77%) cases. Out of them 22 (52.38%) cases were classic type, 19 (45.23%) were follicular variant and 1 (2.38%) case was tall cell variant.

Histologically capsule was found in 42(40.77%) cases. Out of them 22(52.38%) cases were classic type, 19(45.23%) were follicular variant and 1(2.38%) case was tall cell variant (fig-1 and 2).

Psammoma bodies (fig-3) and non-psammomatous calcification were found in 89(86.40%) of 103 cases. Out of them psammoma bodies were observed in 42 (40.77%) cases and non-psammomatous calcification was found in 47(45.23%) cases. Variant distribution of psammoma body in different morphological type of papillary carcinoma as follows: 34 (80.95%) cases of classic type, 6(14.28%) cases of follicular variant, 1(2.38%) cases of trabecular variant and 1(2.38%) of oxyphilic variant.

Lymphoid follicles were found in 21(20.38%) of 103 cases. Out of 21 cases, 14 cases were of classic type, 5 cases of follicular variant, 1 case of oxyphilic variant and 1 case was of tall cell variant.

Out of 103 cases only 1 (0.97%) case of classic type showed vascular invasion and 2 (1.94%) cases (1 classic type and 1 follicular variant) had capsular invasion. Out of 103 cases, 11 (10.67%) cases showed papillary carcinoma with lymph node metastasis. 9 of these cases were classic type and 2 were of follicular variant. Primary tumour and metastatic foci in lymph node were same morphological variant in 10 cases, where different variant observed only 1 case. Metastatic focus showed follicular variant where primary tumour was a classic type.

### Discussion

There are different morphological variants of papillary carcinoma of thyroid. Prognosis of most of the variants is similar to usual conventional or classic type, but prognosis of some variants is worse<sup>3</sup>.

In this study the age of the study subjects ranged from 12 years to 70 years with mean age of 34.44 years. Maximum number subjects in this study were in 2<sup>nd</sup> to 4<sup>th</sup> decades as compared with other studies,

where investigator described highest incidence of papillary carcinoma from 3<sup>rd</sup> to 5<sup>th</sup> decade<sup>2</sup>

Out of 103 cases 81.6% cases were female, and 18.4% cases were male, with male to female ratio of 1:1.44, indicating female predominance. The observation is similar to findings, (89.1% female cases out of 183)<sup>10</sup>. Mean age of male patients was 52.4 years and female patients was 44 years<sup>10</sup>, the study shows mean age of male patients was 40 years and mean age of female patients 32.69 years. Age incidence varies country to country as shown in another study<sup>6</sup>.

During gross examination capsule was found in 20% of the specimens. But according to Rosai (1996) grossly 10% cases are capsulated. This discrepancy may be due to small sample size in which gross examination done. In this study no encapsulated variant was observed. This may be due to small sample size of specimens in which gross examination done. May be due to capsular invasion by tumour due to late coming of patient for treatment.

Similarly no micro carcinoma was observed in this study. It may be due to inadequate serial sections of thyroid specimens. 10% of cases show cystic area<sup>4</sup>, but present findings is 35%. A valid comment on capsule or cystic changes can not be made depending on this small size of samples.

Grossly cut surface of papillary carcinoma show granular area, which is an important indicator of malignancy<sup>11</sup>. More than half of cases (55%) revealed granular area during the present series.

The number of classic type during the present study corresponds with the other findings<sup>6, 12</sup>. But follicular variant is much higher in present study (38.83%) than their study

(15.9%). More cases of oxyphilic variant were described by Khan and Eshy (1998) study (6%) than present study (2.91%). The tall cell variant case was seventh decade in the present study. Tall cell variant are common in elderly persons and this age consistent with other findings.<sup>4, 6, 12</sup>

The variation in variant distribution observed during the present study indicates a slightly different pattern in our country calls for a larger scale study. The present study also shows incidence of devastating tall cell variant in our country is much lower than the study done in other countries.

In classic type, mean age of patients was 32.98 years, maximum number of patients was in second, third and fourth decades. Female predominance was evident in classic type, which is also supported by others<sup>6</sup>

In follicular variant, mean age of the patient was 41.75 years and majority of patient were in third and fourth decades. Seven cases were also observed in 5<sup>th</sup> decade. It appears that incidence of follicular variant becomes higher by decade compared to classic type. Follicular variant also revealed marked female predominance (90%), a similar prevalence (85.71%) was also observed by others.<sup>6</sup>

Tall cell variant case was in seventh decade in the present study. Tall cell variant are common in elderly persons and this age consistent with findings of other<sup>4, 6, 12</sup> According to Rosai et al (1992) the paediatric group is more commonly affected by trabecular variant. In present study mean age of three cases was 32.66 years. This discrepancy in age distribution of trabecular variant cannot be explained with current knowledge and the small number of cases.

Some author<sup>9</sup> claimed, presence of psammoma bodies in papillary carcinoma

thyroid indicates a good prognosis. According to some author<sup>4</sup> psammoma bodies are seen approximately half of cases of papillary carcinoma of thyroid. During the present study psammoma bodies were found comparatively lower number of cases 42(40.77%). Among the variants of papillary carcinoma, classic type had the highest percentage of psammoma body (38.20%). Percentage of follicular (6.47%), oxyphilic (1.12%) and trabecular variant (1.12%) were low for psammoma body.

According to Rosai (1996) 10% of the papillary carcinoma thyroid is completely capsulated. So; histological examination should reveal about 10% or even less, because some can be lost during normal tissue processing. But in present study, histopathological examination shows much higher (40.77%) percentage of capsulated cases.

Evidence of old haemorrhage has not be specifically described in papillary carcinoma of thyroid. In present study, cases with mild to moderate amount of haemorrhage were found in 64(62.13%) cases. This finding cannot explain with current knowledge. This may be due to haemorrhagic tendency of papillary carcinoma, like that are usually found in giant cell tumour of bone and renal cell carcinoma.

According to Roasi et al (1992) approximately one third of papillary carcinoma of thyroid show lymphatic infiltration (that represents host reaction to tumour). During the present study a lower percentage (20%) of lymphoid follicles was observed. Among the variants only classic type showed higher (66.66%) percentage of cases having lymphoid follicles indicating response was lower than expected.



According to a study<sup>2</sup> 50% or more patients had nodal metastasis at initial diagnosis. But in present study a much lower (10.67%) number of metastasis were found.

This can be due to serious reasons, viz. due to inadequate removal of lymph node(s) during thyroidectomy, small number of sections etc.

Parathyroid insufficiency following thyroid operation is a complication, due to accidental removal of parathyroid gland. The incidence of this condition should be less than 0.5 %<sup>13</sup>. But this study showed parathyroid tissue association with thyroid tissue in 4(3.88%) cases. This is much higher than expected.

### Conclusion

Papillary carcinoma of thyroid is the most common thyroid malignancy, and endocrine neoplasia. 70-80% cases of thyroid malignancy are papillary carcinoma. A total 103 case of papillary carcinoma of thyroid were studied from January 2004 to December 2006, with the aim to identify morphological variants, their histological presentation, incidence in different age groups and prevalence of variants having worse prognosis. Cases were collected mostly from BSMMU, two private laboratories of Dhaka city and small number from Dhaka Medical College.

Five morphological variants were observed viz. classic (55.33%), follicular (38.83%), trabecular (1.94%), oxyphilic (2.91%) and tall cell (0.97%). Classic or conventional type is the commonest variant observed in this study and also studies done by others (Khan and Eshy, 1998, and Muzaffar et al, 1998). In case of classic type predominant patients were female and majority was in 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> decade. Prevalence of follicular variant is much higher in present observation than studies done by others and 90% of cases were female. In this study relative number of

patient of follicular variant was in 5<sup>th</sup> decade compared to classic type.

Prevalence of devastating types, such as tall cell and diffuse sclerosing variants is less evident in this study compared to studies done abroad. Psammoma body was observed in 40.77% of cases in this study. Highest percentage was observed in classic type than the other variants. One of the important observations was presence of mild to moderate amount of old haemorrhage in tumorous areas, a finding which has not been reported or explained by any.

Another important observation was presence of thyroid follicle, predominantly in classic type. These follicles may be due to immune response of host to tumour or it may be an indication of pre-existing thyroiditis.

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