



Original Article

# Papillary carcinoma thyroid - A 11 year epidemiological study with histopathological correlation in a tertiary care centre in South Malabar Region in Kerala, India

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## Keywords:

Papillary carcinoma thyroid.

## ABSTRACT

**Background:** Thyroid cancer is the commonest endocrine malignancy. Based on recent data, thyroid cancer is the fifth most common cancer in women. To our knowledge the present study is the first of its kind, correlating epidemiological and histomorphological data so as to assess the major cause hypothesis for thyroid cancers, focusing more on papillary carcinoma and its variants, comparing it with each other and with other thyroid carcinomas and also correlating with gender, life style and religion.

**Materials and Methods:** This study was conducted in the Department of Pathology, MES Medical College, Perinthalmanna, Kerala, India, from January 2004 to June 2015. Two thousand and fifty thyroidectomy cases were studied.

**RESULTS:** Out of the total 2050 cases, thyroid cancers constituted 295 (14.39%); of which 10.1% (208 cases) were papillary carcinoma thyroid (PCT) and its variants; 165 cases were seen in females (79.33%) and the incidence in males were only 20.68% (43 cases). The commonest variant encountered was classical papillary carcinoma (113 cases, 54.32%).

**CONCLUSION:** Our study of papillary thyroid carcinomas in South Malabar region, Kerala, India shows that there is a high incidence of thyroid carcinomas in our locality and this could be attributed to various factors like high intake of iodine along the coastal region, excessive salt iodization, increased consumption of processed food and fish, influence of female sex hormones, increased incidence of autoimmune thyroiditis and exposure to radiation. Our study also showed an increased incidence of PCT in females and among men and women of Islamic faith.

## INTRODUCTION

Thyroid gland is one of the most responsive and largest

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endocrine organs in the body and contains the maximum store of hormones. This gland plays an important role in the metabolic process through secretion of its hormones and responds to many stimuli. It is in a constant state of adaptation. During puberty, pregnancy or and any physiologic stress, thyroid gland increases in size and becomes more active.<sup>1</sup>

Thyroid diseases are very common in the general population,

**Table 1: Total thyroid carcinomas**

Religion	Hindu		Christian		Muslim		Male	Female
Gender	Male	Female	Male	Female	Male	Female		
Total	13	41	2	9	42	188	57	238
Grand Total	54 /295(18.3%)		11/295(3.73%)		230/295 (77.97%)		295 (100%)	
Percentage	24.7%	75.92%	18.18%	81.81%	18.26%	81.73%	19.32%	80.67%

especially in women and elderly and is a common cause of endocrine referrals.<sup>2</sup>

Thyroid malignancy is the commonest endocrine malignancy which accounts for about 90% of head and neck cancers. Incidence of thyroid neoplasms has increased about three fold in the past three decades and some of the causes for this increasing incidence include diagnostic or iatrogenic radiation exposure, change in body-mass index, dietary iodine content, menstrual cycle, pregnancy, fertility drugs, diet, environment and life style. Based on recent data, thyroid cancer is the fifth most common cancer in women.<sup>3</sup>

Most common type of thyroid malignancy is papillary carcinoma which constitutes about 70% - 80% of all thyroid cancers. It occurs most frequently in women and presents in the 20-55 years age group.<sup>4,5</sup> Papillary carcinoma thyroid (PCT) are discovered on routine examination as asymptomatic thyroid nodule that presents as a neck mass.<sup>6</sup>

In a survey conducted by the National Cancer Registry Program, thyroid cancers featured among the top five; Thiruvananthapuram, the capital of Kerala state, India had the highest relative frequency of cases enrolled in the hospital registry. 1.99% of cases were seen in males and 5.71% in females.<sup>6</sup> The reason for this high frequency of thyroid cancers or the reason for this high prevalence of endemic goiter despite extensive salt iodization are still not fully understood. Thyroid cancer incidence by gender, age and racial/ethnic groups is striking with rates being particularly high in women in younger age group.<sup>7,8</sup>

The present undertaking is a 11 year study in which we have attempted to highlight the various morphological patterns in papillary thyroid cancers and tried to assess its incidence with respect to gender, age and religious groups pertaining to South Malabar region in Kerala, India.

The aims of the study are as follows:

- 1: To assess the load of thyroid malignancies in South Malabar region, Kerala.
- 2: To specifically focus on the load of papillary thyroid carcinomas among these thyroid malignancies in this region.
- 3: To assess the correlation, if any, between age, gender, religion and dietary habits of the study population with

papillary thyroid carcinoma.

## MATERIALS AND METHODS

This retrospective and prospective study was done in the Department of Pathology, MES Medical College, Perinthalmanna, which is a tertiary referral hospital in South Malabar region in Kerala, India, from January 2004 to June 2015. Prior to the study, permission was obtained from Institutional Ethical Committee. Consent form was signed from the concerned individual in prospective study. Two thousand and fifty thyroidectomy cases were studied. The age, gender, ethnicity and dietary habits of all the cases were taken into consideration. All the lesions were classified according to the latest WHO classification of Tumors of Endocrine organs, 2004<sup>9</sup>. In the retrospective cases, the preserved slides were restained with Haematoxylin and Eosin (H&E) stains, reviewed and reclassified. Repeat deeper sections were taken from the respective blocks wherever necessary. In the prospective cases, requisite number of bits was taken from appropriate areas during grossing; sections were stained with routine H&E and studied.

## RESULTS

The total number of thyroid cases studied in the last 11 years were 2050, out of which malignancy was seen in 295 cases (14.39%); among this, 10.1% was Papillary carcinoma thyroid (208 cases).

In our 11 year study we obtained a total of 2050 cases; 295 cases (14.4%) were thyroid malignancies and the incidence of malignancies in females (11.6%) were much higher when compared to males (2.8%) (Table 1).

Out of the total thyroid malignancies (295 cases), 208 cases (10.15%) were papillary carcinoma and its variants. So we can infer from this that PCT is the most commonest malignancy to affect the thyroid gland.

Out of the total 208 cases of PCT; 165 were seen in females (79.33%); the incidence in males were only 20.68% (43 cases), with male to female ratio being 1:4.

Out of 208 cases of PCT, 113 cases (54.32%) were classical papillary carcinoma, follicular variant of papillary

**Table 2: Comparison of Religion and Gender Distribution Of Papillary Carcinoma Variants (n=208)**

<b>Classical Papillary Carcinoma (fig.1)</b>								
<b>Religion</b>	<b>Hindu</b>		<b>Christian</b>		<b>Muslim</b>		<b>Total</b>	<b>Total</b>
<b>Gender</b>	Male	Female	Male	Female	Male	Female		
Total	5	11	1	4	24	68	30	83
Grand Total	16		5		92			113
Percentage	31.25%	68.75%	20%	80%	26.08%	73.91%	26.54%	73.45%
<b>Papillary Microcarcinoma(fig.2)</b>								
<b>Religion</b>	<b>Hindu</b>		<b>Christian</b>		<b>Muslim</b>		<b>Total</b>	<b>Total</b>
<b>Gender</b>	Male	Female	Male	Female	Male	Female		
Total	2	10	0	1	2	23	4	34
Grand Total	12		1		25			38
Percentage	16.66%	83.33%	0	100%	8%	92%	10.52%	89.48%
<b>Follicular Variant of Papillary Carcinoma (fig.3)</b>								
<b>Religion</b>	<b>Hindu</b>		<b>Christian</b>		<b>Muslim</b>		<b>Total</b>	<b>Total</b>
<b>Gender</b>	Male	Female	Male	Female	Male	Female		
Total	1	4	0	1	5	27	6	32
Grand Total	5		1		32			38
Percentage	20%	88%	0	100%	15.62%	84.37%	15.78%	84.21%
<b>Hurthle Cell Variant of Papillary Carcinoma(fig.4)</b>								
<b>Religion</b>	<b>Hindu</b>		<b>Christian</b>		<b>Muslim</b>		<b>Male</b>	<b>Female</b>
<b>Gender</b>	Male	Female	Male	Female	Male	Female		
Total	1	3	0	0	0	5	1	8
Grand Total	4		0		5			9
Percentage	44.44%	0%	0	0%	0%	55.56%	11%	89%
<b>Tall Cell Variant of Papillary Carcinoma (fig.5)</b>								
<b>Religion</b>	<b>Hindu</b>		<b>Christian</b>		<b>Muslim</b>		<b>Total</b>	<b>Total</b>
<b>Gender</b>	Male	Female	Male	Female	Male	Female		
Total	0	0	0	0	0	1	0	1
Grand Total	0		0		1			1
Percentage	0%	0%	0	0%	0%	100%	0%	100%
<b>Hyalinizing trabecular variant of Papillary Carcinoma</b>								
<b>Religion</b>	<b>Hindu</b>		<b>Christian</b>		<b>Muslim</b>		<b>Total</b>	<b>Total</b>
<b>Gender</b>	Male	Female	Male	Female	Male	Female		
Total	0	0	0	0	0	1	0	1
Grand Total	0		0		1			1
Percentage	0%	0%	0	0%	0%	100%	0%	100%
<b>Encapsulated follicular variant of Papillary Carcinoma (Lindsay Tumour; fig. 6)</b>								
<b>Religion</b>	<b>Hindu</b>		<b>Christian</b>		<b>Muslim</b>		<b>Total</b>	<b>Total</b>
<b>Gender</b>	Male	Female	Male	Female	Male	Female		
Total	1	1	0	0	1	5	2	6
Grand Total	2		0		6			8
Percentage	50%	50%	0	0%	16.6%	83.3%	25%	75%

**Table 3: Comparison of Gender distribution of total thyroid carcinomas**

Authors	Prades et al10	Lumachi et al11	Chehrei et al12	Present study
Male	18%	22.4%	16.4%	19.32%
Female	82.18%	77.6%	83.6%	80.68%

**Table 4: Comparison of age range and mean age of total thyroid carcinomas**

	Huber et al	Lumachi et al	Cherit et al	Present study
Age range	19-84yrs	18-76yrs	21-76yrs	10-85yrs
Mean age	44yrs	43yrs	43.8yrs	34.5yrs

carcinoma - 38cases ( 18.27%),papillary microcarcinoma -38 cases(18.27%),Hurthle cell variant- 9 cases (4.33%), Lindsay tumour was -8 cases (3.8%), tall cell and hyalinizing trabecular variant constituted one case each (0.48%).

Classical PCT was the commonest variant encountered. Muslims were seen to be more affected among the religious groups (162 cases, 77.88%). Muslim men were commonly affected when compared to men of other religious groups [Muslims- (32 cases) 15.38%, Hindus-( 10 cases ) 4.80%, Christians-(1 case,0.48%)(table2)]. In general, Muslim females and Muslim males were more affected in all variants of papillary carcinoma thyroid in all religious groups whereas Christians (12.01%) were the least affected group (Table 2).

## DISCUSSION

In this study we are correlating epidemiological and histomorphological data so as to assess the major cause hypothesis for thyroid cancers, focusing more on papillary carcinoma and its variants, comparing it with each other and with other thyroid carcinomas and also correlating with gender, life style and religion. Most of the previous studies however have combined only any two of the three aspects.

Of the total 295 thyroid malignancies in our study, 57 patients were males and 238 were females. Our study showed female preponderance which was comparable to the other studies in literature 13 (Table 3).

It is a well-known fact that thyroid cancer occurs 3 times more in virtually all geographic regions in females than males. The reasons however are not clear. Several studies have shown evidence that female sex hormones play a role in the etiology of thyroid cancers. Pregnancy and hormonal treatment have also been associated with thyroid cancers among women. The hormone-related factors probably act as promoters of tumor growth.<sup>14-16</sup> In our study too, the female predominance was grossly evident in the incidence of total thyroid cancers as well as in the incidence of PCT category.

The incidence of PCT among females was 80.28% (167 cases) and among males was only 20.7% (43 cases). This

was in concordance with all the studies in literature; that is papillary carcinoma thyroid is more common among females.

Different literature has stated that there is a highest incidence of papillary carcinoma in women which has been attributed to sex hormones causing carcinogenesis. Literature has shown that early menarche, young parous women with recent pregnancy, all have an increased risk of PCT<sup>16</sup>. This could be a reason of increased incidence of papillary carcinomas in females our region, as almost all of the women were young and multiparous.

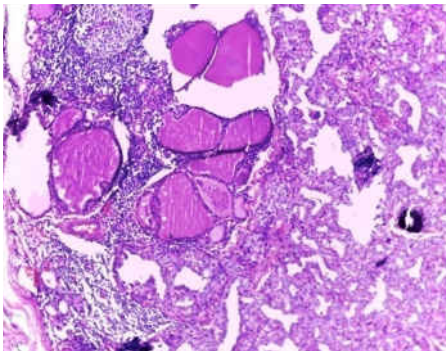
Age range of our study was 10-85yrs with mean age of 34. 5 yrs, which is low compared to the other studies in literature. This highlighted the high incidence of thyroid malignancies in younger age group in our study (Table 4).

Thyroid cancer can occur at any age ,but the risk peaks earlier for women (3<sup>rd</sup> and 6<sup>th</sup> decades) than men ( 7<sup>th</sup> and 8<sup>th</sup> decades).<sup>17</sup> In our study the mean age affected was 37.2 yrs for females and 38. 9 yrs for males. So in our population of males, the incidence of thyroid cancer was much earlier.

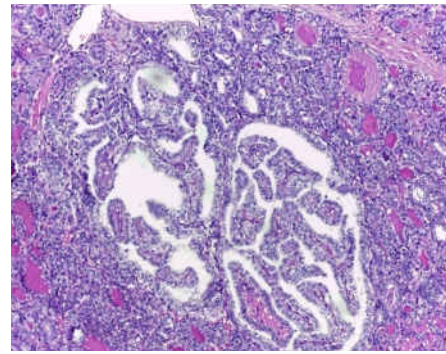
Iodine has an essential role in production and regulation of thyroid hormones. Both iodine deficiency and excess have been considered risk factors of thyroid cancer. Chronic hyper secretion of Thyroid stimulating hormone (TSH) leads to thyroid follicular cell hyperplasia and hypertrophy and this is thought to increase the risk of neoplastic transformation. Long term intake of excessive amounts of iodine can also affect the functioning of the thyroid gland and this can lead to elevated hormone levels.<sup>18-24</sup>

It has also been suggested that deficient iodine intake increase the risk of follicular type and excesses intakes increases the risk of papillary thyroid cancer (world cancer research fund, 1997). Fish, particularly salt water fish, salted dry fish and shell fish is the best natural source of iodine and also most diet like bread, dairy products and iodized table salt are the main source of this mineral. Several studies have pointed out that consumption of processed fish, products such as cheese, butter, cruciferous and pickled vegetables were also associated with excessive consumption of iodine. One author even commented that chicken consumption also

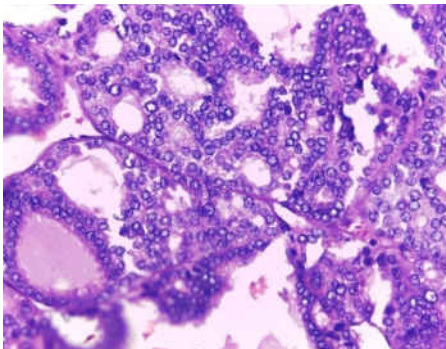




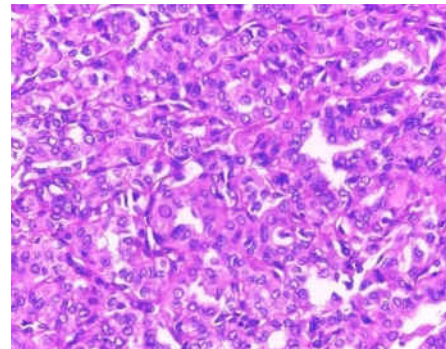
**Figure 1:** Hashimoto's thyroiditis with papillary carcinoma (HE Stain, X100).



**Figure 2:** Papillary microcarcinoma of thyroid (HE Stain, X100).



**Figure 3:** Follicular variant of papillary carcinoma (HE Stain, X400).



**Figure 4:** Hurthle cell variant of papillary carcinoma (HE Stain, X400).

could be the cause of thyroid carcinoma.<sup>18-24</sup>

South Malabar region in Kerala, India, is located along the Arabian coast; because of its coastal location, fish has always been an important component of the local diet. This could be one of the reasons for the increased incidence of PCT seen in our study.

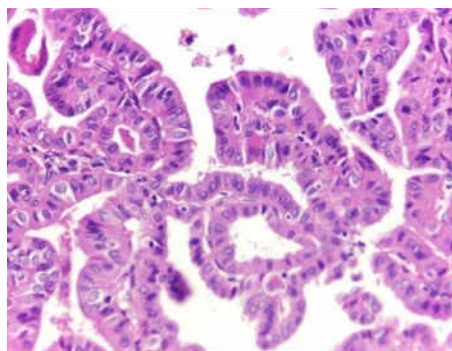
In addition to iodine itself, dietary factors that interfere with iodine organification and thyroid hormone synthesis, such as cruciferous vegetables could also increase thyroid cancer risk. Frequent contamination of nitrate in drinking water is seen in areas of agriculture and it is found that there are high levels of nitrates in some vegetables and processed food. A high average nitrate level in water supplies is associated with an increased risk of thyroid cancers.<sup>25-28</sup> Our area, being an agricultural one, there is a high chance of pesticides pollution and water pollution. Along with that we have an increased Middle East influence which leads to increased consumption of processed foods; all these factors might eventually be the cause of increased incidence of PCT in our region.

We found that the incidence of PCT was around 77.9% in Muslims, 18.6% in Hindus and 3.52% in Christians, however, saying that PCT is more common among the Islamic population is not relevant as the area under study was a Muslim predominant one.

In our study we found there was 23 cases (11%) of Hashimoto/lymphocytic thyroiditis along with PCT. All the cases were seen in females and all had high TSH levels. Attempts have been made to correlate autoimmune thyroiditis and TSH levels. Increasing TSH levels because of the autoimmune process, in turn produces proinflammatory cytokines and oxidative stress. This might trigger thyroid tumorigenesis. Literature has proved that PCT is frequent in patients with autoimmune thyroiditis and is directly related to serum TSH value.<sup>28-31</sup> Our study was comparable to other studies in literature.

Exposure to ionizing radiation is a well-documented risk factor for cancer. The thyroid may be irradiated more than other tissues because of its position in the body and its ability to concentrate iodine. The thyroid gland is very sensitive at a young age. Children exposed to radiation frequently develop PCT. A recent analysis indicated that thyroid cancer risk and children exposed to head and neck radiation is inversely correlated to the age, decreasing to a statistically insignificant level by age 15. Recent report indicates that dental and medical x rays may increase thyroid cancer risk also in adults. One third of all CT scans are performed in the head and neck, where the thyroid is exposed to radiation.<sup>28,32-35</sup>

Numerous histopathological variants have been described in literature and their different behaviors are characterized. Various studies have shown classical papillary carcinoma



**Figure 5:** Tall cell variant of papillary carcinoma (HE Stain, X400).

to be the most common variant, followed by papillary microcarcinoma and follicular variant of papillary carcinoma, in decreasing order.<sup>1,36</sup> In our study too, classical papillary carcinoma was the commonest followed by equal numbers of papillary microcarcinoma and follicular variant of papillary carcinoma. The tall cell and Hyalinizing trabecular variants was the least encountered types in our study.

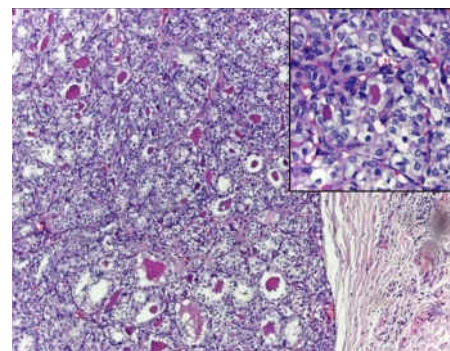
Papillary carcinoma thyroid is the most common malignancy among thyroid cancers. It has an excellent clinical behavior in spite of the presence of lymph node metastasis. Our study of papillary thyroid carcinomas in South Malabar region, Kerala, India shows that there is a high incidence of thyroid carcinomas and this could be attributed to various factors like high intake of iodine along coastal region, excessive salt iodization, increased consumption of processed food and fish, influence of female sex hormones, increased incidence of autoimmune thyroiditis and exposure to radiation. Our study also showed increased incidence of PCT in females and men and women of Islamic faith. Classical PCT was the commonest variant encountered in our study.

## CONCLUSION

Papillary carcinoma thyroid is the most common malignancy among thyroid cancers. It has an excellent clinical behavior in spite of the presence of lymph node metastasis. Our study of papillary thyroid carcinomas in South Malabar region, Kerala, India shows that there is a high incidence of thyroid carcinomas and this could be attributed to various factors like high intake of iodine along coastal region, excessive salt iodization, increased consumption of processed food and fish, influence of female sex hormones, increased incidence of autoimmune thyroiditis and exposure to radiation. Our study also showed increased incidence of PCT in females and men and women of Islamic faith. Classical PCT was the commonest variant encountered in our study.

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**Figure 6:** Lindsay tumour (HE Stain, X100). Inset showing high power view of Lindsay tumour.

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