

An Indian Tertiary Care Hospital Scenario of Papillary Carcinoma of Thyroid

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ABSTRACT

Introduction: Thyroid carcinoma is the most common endocrine malignancy and its Papillary Histotype {Papillary Carcinoma of Thyroid (PTC)} is the most common type of Thyroid cancer. The clinicopathological features of PTC vary with geographical location.

Aim: To describe the clinicopathological profile of PTC in a Tertiary Care Hospital located in Chennai, Tamil Nadu, India.

Materials and Methods: Data on age, sex, centrality of the tumour, presence of calcifications, infiltration, metastasis, associated non malignant conditions and frequency of histological subtypes of all cases of PTC diagnosed in Department of Pathology, Madras Medical College Chennai, Tamil Nadu, India

between January 2007 and December 2011 were obtained from clinicopathological documents and analysed statistically.

Results: Statistically significant correlations were found between age and sex, age and metastasis, sex and centrality, sex and metastasis, size of lesion and sex, size of lesion and age, size and presence of calcifications and presence of calcifications and metastasis.

Conclusion: Scenario of PTC in our tertiary care setup which warrants attention is male preponderance of multicentric lesions. Further, a high association with colloid nodular goitre, while low incidence of tall cell variant is notable clinico pathological scenarios in this study.

Keywords: Calcifications, Centrality, Clinicopathological features, Metastasis, Tall cell variant

INTRODUCTION

Thyroid carcinoma is the most common endocrine cancer accounting for 92% of cancers of endocrine glands [1]. The papillary histotype of thyroid carcinoma is the most common type, accounting for 85% of all cases of thyroid carcinoma [2]. In the last three decades, the incidence of thyroid carcinoma has increased sharply, with the increasing trend restricted almost exclusively to the papillary histotype [3]. The epidemiology and clinicopathological features of this carcinoma vary greatly with geography and there is still a paucity of information regarding the clinicopathological features of PTC in this region. This has prompted us to obtain a clinicopathological profile of PTC from our Institute, which is a Tertiary Care Center. We aimed at analysing and correlating 377 cases of PTC diagnosed in our institution between January 2007 and December 2011 based on its clinicopathological features namely age, sex, centrality, calcifications, infiltration, metastasis, histological types and associated non malignant conditions. Many of these parameters carry an established prognostic significance, and for a few, the prognostic significance has not yet been established.

MATERIALS AND METHODS

This was a cross-sectional study conducted at our Tertiary Care Institute, Madras Medical College from 2007 to 2011 after getting ethical clearance from Ethical Committee. Data namely age, sex, infiltration, centrality and metastasis were collected from the Clinicopathological files and histopathology slides were reviewed for further information. Calcifications were identified by both histopathology and ultrasonography examinations.

To categorise patients into groups based on lesion size and age of patients, we reviewed the 17 staging systems available for PTC [4]. Among them, the most agreed upon prognostically relevant

categorisations of lesion size were <1 cm, 1-4 cm and >4cm at their maximum dimensions. This is based on Memorial Sloan Kettering's GAMES staging, University of Munster staging, National Thyroid Cancer Treatment Cooperative Study (NTCTCS) staging, Virgen de la Arrixaca University staging and American Joint Committee on Cancer's (AJCC) TNM staging [4]. We categorised patients as those under 45 years and those greater than 45 years of age as they were the most widely used categorisations being applied in the Noguchi Thyroid Clinic staging, GAMES staging, NTCTCS staging, AJCC staging and Ankara Oncology Training and Research Hospital staging [4].

STATISTICAL ANALYSIS

The data were computed using Microsoft Excel. Inferential analysis was conducted using Statistical Package for Social Sciences (SPSS) software version 16 with the proportional data of this study tested using Pearson's Chi Square test. The level of statistical significance was set as $p < 0.05$.

RESULTS

Age and Sex wise Distribution

Among the 377 cases, 278 cases (73.7%) occurred in ages 45 and less, 99 cases (26.3%) occurred in ages above 45. Three hundred and seven (81.4%) cases were females and 70 cases were (18.6%) males. The mean age of diagnosis in females was 37.26 {95% confidence interval (35.82, 38.71)} and the mean age of diagnosis in males was 45.74 {95% confidence interval (41.95, 49.54)}. A total of 32 cases (8.5%) had lesions less than 1 cm in size, a great majority of cases – 289 (76.66%) had lesions between 1-4 cm in size and 56 cases (14.85%) had lesions greater than 4 cm in size.

Centricity and Metastasis wise Distribution

The lesions were multicentric in 158 (41.9%) of cases and unicentric in 215 (57%) of cases. In four cases, the centricity was not noted in records. Lesions contained calcifications in 90 (23.9%) cases. A total of 72 cases (19.1%) showed evidence of metastasis to lymph nodes and elsewhere. There were four cases of metastasis to fibrofatty tissue, two into the strap muscles and one into the skin. One hundred and two (27.1%) cases showed capsular invasion. A total of 115 (30.5%) showed blood vessel invasion. Ninety six (25.46%) cases showed lymphatic invasion.

[Table/Fig-1] shows the frequency of the various histological variants that were found. The conventional variant was the most common followed by follicular and micro papillary carcinoma variants. [Table/Fig-2] shows the frequency of non neoplastic conditions that were found in association with PTC in our patients. Colloid nodular goitre was by far the most common associated non malignant condition followed by autoimmune thyroiditis. Seventy two cases (19.1%) had metastasis.

Correlation by Statistical Analysis

There was a correlation between the age of patients and the sex of the patient ($p < 0.001$). There were a greater percentage of male cases above the age 45 whereas most female cases occurred at ages less than 45 [Table/Fig-3]. We found correlation between age of patient and metastasis ($p = 0.035$). Percentage of metastasis was higher in patients greater than 45 years of age [Table/Fig-4]. There were associations between sex and centricity ($p = 0.041$) and sex and metastasis ($p = 0.025$). Male cases had more multicentric lesions and female cases had more unicentric lesions [Table/Fig-5].

More female cases were associated with metastasis than males [Table/Fig-6]. We found correlation between lesion size and sex of the patient ($p = 0.015$) and between lesion size and age of the patients ($p = 0.014$). There were greater number of larger lesions in females [Table/Fig-7] and in patients less than 45 years of age [Table/Fig-8]. There was a correlation between size of the lesions and presence of calcifications in the lesions ($p = 0.017$). The presence of calcifications increased with increase in size of the lesions [Table/Fig-9]. There was a correlation between presence of calcifications and metastasis ($p = 0.016$), with increased frequency of presence of calcifications in tumours showing metastasis [Table/Fig-10]. Micro papillary carcinoma variants were not associated with blood and lymphatic invasion, though two cases (18.1%) were associated with capsular invasion.

Histological type	Frequency (%)
Conventional	259 (68.7%)
Follicular	67 (17.8%)
Micropapillary Carcinoma	11 (2.9%)
Clear Cell	1 (0.3%)
Cribriform	1 (0.3%)
Dedifferentiated Carcinoma	2 (0.5%)
Diffuse Sclerosing	2 (0.5%)
Encapsulated Follicular	16 (4.2%)
Macrofollicular	3 (0.8%)
Nodular Fascitis Like	1 (0.3%)
Oncocytic	4 (1.1%)
Poorly Differentiated	1 (0.3%)
Solid	4 (1.1%)
Tall Cell	1 (0.3%)
Trabecular	4 (1.1%)

[Table/Fig-1]: Frequencies of histological types of PTC.

Associated Non-neoplastic conditions	Frequency (%)
Colloid Nodular Goitre	106 (28.1%)
Autoimmune Thyroiditis	48 (12.7%)
Follicular Adenoma	4 (1.1%)
Lymphocytic Thyroiditis	24 (6.4%)
Colloid Cyst	1 (0.3%)
Foreign Body Granuloma	1 (0.3%)
Hyalinising Trabecular Adenoma	2 (0.5%)
Microfollicular Adenoma	1 (0.3%)
Papillary Hyperplasia	2 (0.5%)
Reidels Thyroiditis	1 (0.3%)

[Table/Fig-2]: Incidence of non malignant lesions associated with PTC.

Age (Years)	Females	Males	Total	Pearson chi-square value	p-value
<45	241 (86.7%)	37 (13.3%)	278	19.359	0.001
>45	66 (66.7%)	33 (33.3%)	99		
Total	307 (81.4%)	70 (18.6%)	377 (100%)		

[Table/Fig-3]: Correlation between age and sex.

Age (years)	Presence of metastasis	Absence of metastasis	Total (No. of cases)	Pearson chi-square value	p-value
<45	46 (16.5%)	232 (83.5%)	278	4.460	0.035
>45	26 (26.3%)	73 (73.7%)	99		
Total	72 (19.1%)	305 (80.9%)	377 (100%)		

[Table/Fig-4]: Correlation between age and metastasis.

Sex	Multicentric	Unicentric	Total no. of cases	Pearson chi-square value	p-value
Female	122 (39.75%)	183 (59.6%)	305 (99.3%)	6.402	0.041
Male	36 (51.4%)	32 (45.7%)	68 (67.1%)		
Total	158 (41.9%)	215 (57%)	373 (98.9%)		

[Table/Fig-5]: Correlation between sex and centricity.

Sex	Presence of metastasis	Absence of metastasis	Total (No. of cases)	Pearson chi-square value	p-value
Female	255 (83.1%)	52 (16.9%)	307 (100%)	4.993	0.025
Male	50 (71.4%)	20 (28.6%)	70 (100%)		
Total	305 (80.9%)	72 (19.1%)	377		

[Table/Fig-6]: Correlation between sex and metastasis.

Size	Females	Males	Total	Pearson chi-square value	p-value
<1 cm	28 (87.5%)	4 (12.5%)	32	8.338	0.015
1-4 cm	241 (83.4%)	48 (16.6%)	289		
>4 cm	38 (67.9%)	18 (32.1%)	56		
Total	307	70	377		

[Table/Fig-7]: Correlation between size of the lesion and sex of the patient.

Size of the lesion	Age (<45 years)	Age (>45 years)	Total	Pearson chi-square value	p-value
<1 cm	22 (68.8%)	10 (31.3%)	32 (100%)	8.504	0.014
1-4 cm	223 (77.2%)	66 (22.8%)	289 (100%)		
>4 cm	33 (58.9%)	23 (41.1%)	56 (100%)		
Total	278 (73.7%)	99 (26.3%)	377 (100%)		

[Table/Fig-8]: Correlation between size of the lesion and age of the patient.

Size of the lesion	Presence of calcification	Absence of calcification	Total	Pearson chi-square value	p-value
<1 cm	3 (9.4%)	29 (90.6%)	32 (100%)	8.097	0.017
1-4 cm	67 (23.2%)	222 (76.8%)	289 (100%)		
>4 cm	20 (35.7%)	36 (64.3%)	56 (100%)		
Total	90 (23.9%)	287 (76.1%)	377 (100%)		

[Table/Fig-9]: Correlation between size of lesion and calcification.

Calcification	Presence of metastasis	Absence of metastasis	Total	Pearson chi-square value	p-value
Present	65 (72.2%)	25 (27.8%)	90 (100%)	5.764	0.016
Absent	240 (83.6%)	47 (16.4%)	287 (100%)		
Total	305 (80.9%)	72 (19.1%)	377		

[Table/Fig-10]: Correlation between calcification and metastasis.

DISCUSSION

Thyroid gland malignancies are the most common neoplasms of endocrine glands in India. Carcinomas constitute 5-10% of all thyroid nodules [5]. Malignancies measuring 1 cm or smaller showed 49% increases from the year 1988 to 2002. Mortality from thyroid cancer was stable between 1973 and 2002. This increasing incidence with stable mortality reflects increased detection of subclinical disease and not an increase in the true occurrence of thyroid cancer [6]. A 60% of thyroid malignancies in Bangalore and Chennai were Papillary carcinomas, whereas in other registries this was around 40% [7].

Machens A et al., in his study on gender disparities between male and female patients with thyroid cancer found that increase in primary tumour diameters and lymph node metastasis were seen significantly more often in male patients [8]. Although, clear relation between gender and PTC (and other histological types of thyroid cancer) has been established, the exact reason behind these gender disparities in thyroid cancer remains to be solved and the effects of oestrogen on thyroid cancer cells is being actively explored [9].

Multicentricity is a marker of worse prognosis. A study by Carcangiu M et al., reported that patients with multicentric involvement exhibited higher incidence of nodal and pulmonary metastases [10]. We observed a correlation between centricity of the tumours and gender. PTC in male patients showed a significantly increased frequency of multicentricity, though a retrospective study by Kawaura M et al., in Canada on 165 patients concluded that there were no correlations between gender and multicentricity [11].

We found that the frequency of presence of calcifications increased with tumour size. Calcifications were also found in significantly increased frequency in tumours showing metastasis, thus showing that they are indicators of poor prognosis. A study in Canada by Khoo M et al., on 462 patients who underwent thyroidectomy showed an association between calcifications and malignancy. It concluded that when calcifications were present on a solitary thyroid nodule, the risk of malignancy was very high and suggested that surgery should be recommended regardless of fine needle aspiration cytology findings [12]. In one of the conclusions of a multicentric retrospective study in Korea by Moon W et al., detection of calcifications on ultrasonogram was a helpful criterion in discrimination of malignant from benign nodules [13].

In a study in China on 589 patients by Brian Hung-Hin Lang et al., 41.9% of patients showed lymph node metastasis and 1.7% showed distant metastasis. A study in Japan by Ito Y et al., on 759 patients with PTC reported metastases to central lymph nodes in 63% of patients and lateral node metastasis in 62% of patients. Our study showed metastasis to lymph nodes and elsewhere in 19.1% of patients only. The Tall Cell variant is an aggressive variant associated with poor prognosis. In our study, of the 377 cases only

one Tall Cell variant (0.3%) was diagnosed. Review of literature showed that the prevalence of tall cell variant varied widely between 3.8% and 18.4% [14-19]. These studies were reported from France, Sweden, Argentina, Spain and the United States. But no study reported prevalence as low as in the present study.

Females had higher rates of concurrent non neoplastic thyroid lesions reflecting the fact that many thyroid disorders are more common in females than males.

Colloid nodular goitre (27.6%) and Autoimmune Thyroiditis (12.7%) were the most common non neoplastic diseases that were detected concurrently. Their association with PTC is controversial, though several studies support their association [20-22]. A meta-analysis suggested that the survival of patients with PTC may be superior in coexistent autoimmune thyroiditis [23]. How colloid nodular goitre affects prognosis of PTC is not yet studied.

Numerous studies have shown that infiltration into the capsule, blood vessels or the lymphatic systems are associated with poorer prognosis. Mai KT et al., in his review of 134 cases of PTC observed that infiltrating tumour growth was an indicator of malignant behaviour [24]. Our study showed 46.4% of the patients with infiltration either into the capsule, lymphovascular systems or both at the time of diagnosis – factors that contribute to unfavourable prognosis.

LIMITATION

The diagnosis of micro papillary carcinoma variant is most of the time incidental diagnosis, so diagnosis of this type needs complete scrutinising of all non neoplastic lesions of thyroid also. Here we have taken already diagnosed micro papillary carcinoma of thyroid only.

CONCLUSION

The frequency of the aggressive Tall cell variant and the frequency of metastasis were lower when compared to studies on PTC in other parts of the world. In agreement with previous works on gender disparities in PTC, our study showed that frequency of PTC is very less in males when compared to females. Our study also showed PTC in males was more multicentric than unicentric and that presence of calcifications increased with tumour size and with presence of metastasis. To summarise, a PTC has association with colloid nodular goitre and autoimmune thyroiditis, larger, multicentric lesions in males, positive correlation between calcification to tumour size and tendency for metastasis and low incidence of Tall cell variant are the hitherto unobserved, highlights of our study.

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