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Original Research Article

Demographic profile of thyroid malignancies in a tertiary care centre in South India

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ABSTRACT

Background: Thyroid carcinomas were significantly on the rise all over the world, with 5.86 lakh new cases and 43,664 deaths reported in 2020. In this study, we focused on a detailed analysis pertaining to the incidence and demographic profile of all histological types of thyroid malignancies.

Materials and Methods: All cases of thyroid carcinomas reported in the department of Pathology at a tertiary care center in South India from January 2016-December 2020 were included in this study. The demographic profile and patient details were obtained from the medical records section. Pathology reports of the included cases were retrieved, and associated factors were analysed.

Results: Out of the 98 cases included in the study, 16 cases (16.3%) were below 30 years of age, 44 cases (44.9%) were 30-50 years of age and 38 cases (38.8%) were above 50 years of age. The mean age was 45.78. Female preponderance was noted, with 66 cases (67.3%) being females and 32 cases (32.65%) were males. The histopathology results revealed 90 cases (91.8%) to be papillary carcinoma, 1 case (1.02%) of medullary carcinoma, 1 case (1.02%) of Insular carcinoma, 5 cases (5.102%) of follicular carcinoma and 1 case (1.02%) of anaplastic carcinoma. Most of the cases were classified as T1 tumours (45.91%) under the TNM classification. 24 cases (24.49%) were graded as N1 (Metastasis to regional nodes). 3 cases (3.06%) exhibited distant metastasis. Majority of the cases (71.42%) were samples from a total thyroidectomy procedure.

Conclusion: In our demographic study, we have noted that thyroid carcinomas have a peak incidence in the fourth decade of life with a female preponderance. Majority of the cases were noted to be papillary carcinomas in histological type. Understanding the histopathology and TNM staging of thyroid carcinomas is crucial for the selection of appropriate treatment modalities, predicting patient prognosis and clinical outcomes.

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1. Introduction

The thyroid gland is a crucial endocrine gland in the body, secreting thyroxine, a hormone that plays a significant role in metabolic processes. Thyroid malignancies make up to 2.1% of all cancers, making them the most common type of endocrine cancer. The first thyroid cancer case was

reported in the year 1811. The disease was first described by William Stewart Halsted, an American surgeon, in the late nineteenth century. The Indian Council of Medical Research (ICMR) established the National Cancer Registry Program, and has collected the data of more than 3,00,000 cancer cases between 1984 and 1993. The data showed 5614 cases of thyroid cancer, which included 3617 females and 2007 males. Six centers were involved in the studies which included Mumbai, Delhi, Thiruvananthapuram, Dibrugarh,

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Chandigarh, and Chennai. Thiruvananthapuram had the highest relative incidence of cases of thyroid cancer 1.99% among males and 5.71% among females showing a female preponderance. This infers that incidence of thyroid cancers is higher in coastal areas than in inland areas. The high risk factors for thyroid malignancies include radiation exposure and chromosomal alterations while low risk factors include iodine in diet, increased BMI, environmental pollutants etc.

Since the increase in incidence have been observed for small and localized tumors having a significant increased rate of survival, the incidence trends are attributed to overdiagnosis, in view of widespread use of diagnostic radioimaging and more sensitive diagnostic modalities. Increased incidence of large and advanced thyroid malignancies, as well as thyroid cancer mortality, suggest that etiological factors play a significant role to rising incidence of the disease, albeit to a lesser extent than overdiagnosis.

Histologically, thyroid tissue consists of thyroid follicles, along with parafollicular C-cells. Thyroid follicular cells are associated with two major groups of cancers: differentiated (papillary and follicular) and undifferentiated (anaplastic) carcinomas. Parafollicular C-cells, which originate from the neural crest, lead to the development of medullary thyroid carcinomas. The most common subtype among thyroid cancers is papillary, accounting for 70-80% of all cases. It is important to note that the prevalence of thyroid malignancies varies significantly based on geographical location. Some European countries, such as Denmark and Netherlands, have low rates, while areas like Hawaii experience higher rates. Furthermore, the incidence of thyroid cancer exhibits unique variations related to age, sex, and ethnicity.

Immunohistochemical (IHC) markers of thyroid malignancies can be divided into two major subtypes: those related to the cell types and those related to the type of pathology. The most important markers in the first category are thyroglobulin and TTF-1 for follicular cells, and calcitonin, CEA, and chromogranin for parafollicular C cells. Markers in the second category are primarily directed at papillary carcinoma and includes galectin 3, S-100 protein, cytokeratin 19, high-molecular weight keratin (identifiable with antibody 34betaE12), HBME-1 and p27kip1.

Given these considerations, this study aims to investigate the epidemiological and morphological patterns of selected cases of thyroid neoplasms in a South Indian tertiary care centre across a 8 year period. It will focus on factors such as age, sex, histological subtype, TNM staging, the number of thyroidectomies performed and associated complications with an insight into the recent immunohistochemical updates of thyroid carcinomas.

2. Materials and Methods

All cases of thyroid carcinomas reported in the department of Pathology at a tertiary care center in South India from January 2016- December 2020 were included in this study. Few cases have been confirmed through the intraoperative frozen section which were clinically and radiologically skeptical. The demographic profile, patient details and other relevant information were obtained from the medical records section. Pathology reports of the included cases were retrieved and analyzed for histopathological subtype and TNM staging. Institutional ethical clearance CSP/21/AUG/97/407 was obtained prior to the start of the study.

A structured proforma was designed to record the clinical details, which included age, gender, presenting symptoms, site of the tumour, type of surgery, histopathological subtype and TNM staging and other laboratory investigations and treatment modalities. The patients were categorized according to their age (>30, 30-50, and <50 years). Histopathological slides belonging to all the study cases were retrieved and analysed. The grading and staging of excised specimens were based on the AJCC cancer staging protocol. Variables following normal distribution were expressed as mean (standard deviation), and variables that followed skewed distribution were expressed as median.

3. Results

Out of the 98 cases of thyroid carcinoma included in the study, 16 cases (16.3%) were below 30 years of age, 44 cases (44.9%) were 30-50 years of age and 38 cases (38.8%) were above 50 years of age (Table- 1). The mean age was 45.78. Female preponderance was noted, with 66 cases (67.3%) being females and 32 cases (32.65%) were males (table 2). The histopathology results revealed 90 cases (91.8%) to be papillary carcinoma, 1 case(1.02%) of medullary carcinoma, 1 case(1.02%) of Insular carcinoma, 5 cases(5.102%) of follicular carcinoma and 1 case(1.02%) of anaplastic carcinoma. Most of the cases were classified as T1 tumours (45.91%) under the TNM classification. 24 cases (24.49%) were graded as N1 (Metastasis to regional nodes). 3 cases (3.06%) exhibited distant metastasis. Majority of the cases (71.42%) were samples from a total thyroidectomy (Table- 3). The age distribution of different histological subtypes were tabulated in Table- 4. Comparison of age range and mean age of total thyroid carcinomas with other studies were mentioned in Table -5. The Histopathological images of various histological types of thyroid carcinomas are depicted in figures 1-5.

4. Discussion

GLOBOCAN 2020 database of cancer incidence and mortality by the WHO International agency for research on

Table 1: Demographic profile

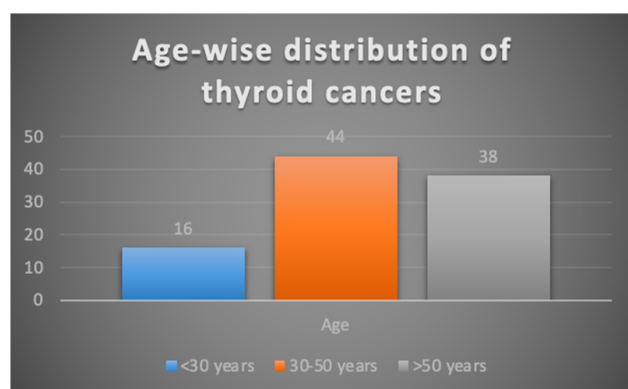
Variables	Entity	Number of Cases	Percentage
Age	<30	16	16.3265306
	30-50	44	44.8979592
	>50	38	38.7755102
Gender	Mean Age	45.78	
	Male	32	32.6530612
	Female	66	67.3469388
Histopathology	Papillary Ca	90	91.8367347
	Medullary Ca	1	1.02040816
	Insular Ca	1	1.02040816
	Follicular Ca	5	5.10204082
	Anaplastic Ca	1	1.02040816
Tumour size	T1(Tumor $\leq$ 2 cm in greatest dimension limited to the thyroid)	45	45.9183673
	T1a(Tumor $\leq$ 1 cm in greatest dimension limited to the thyroid)	26	26.5306122
	T1b(Tumor > 1 cm but $\leq$ 2 cm in greatest dimension limited to the thyroid)	19	19.3877551
	T2(Tumor > 2 cm but $\leq$ 4 cm in greatest dimension limited to the thyroid)	34	34.6938776
	T3(Tumor > 4 cm limited to the thyroid or gross extrathyroidal extension invading only strap muscles)	19	19.3877551
	T3a(Tumor > 4 cm limited to the thyroid)	19	19.3877551
	T3b(Gross extrathyroidal extension invading only strap muscles (sternohyoid, sternothyroid, thyrohyoid or omohyoid muscles) from a tumor of any size)	0	0
	T4(Includes gross extrathyroidal extension into major neck structures)	0	0
	Nx(Regional lymph nodes cannot be assessed)	55	56.122449
	N0(No evidence of regional lymph node metastasis)	19	19.3877551
Extent of nodal involvement	N1(Metastasis to regional nodes)	24	24.4897959
	N1a: (Metastasis to level VI or VII (pretracheal, paratracheal, prelaryngeal / Delphian or upper mediastinal) lymph nodes; this can be unilateral or bilateral disease)	8	8.16326531
	N1b*: Metastasis to unilateral, bilateral or contralateral lateral neck lymph nodes (levels I, II, III, IV or V) or retropharyngeal lymph nodes)	16	16.3265306
Distant metastasis	M0(No distant metastasis)	95	96.9387755
	M1(Distant metastasis)	3	3.06122449
Type of Surgery	Hemithyroidectomy	16	16.3265306
	Subtotal/Near-total thyroidectomy	11	11.2244898
	Total thyroidectomy	70	71.4285714
	Completion thyroidectomy	1	1.02040816

Table 2: Age groups of specific subtypes

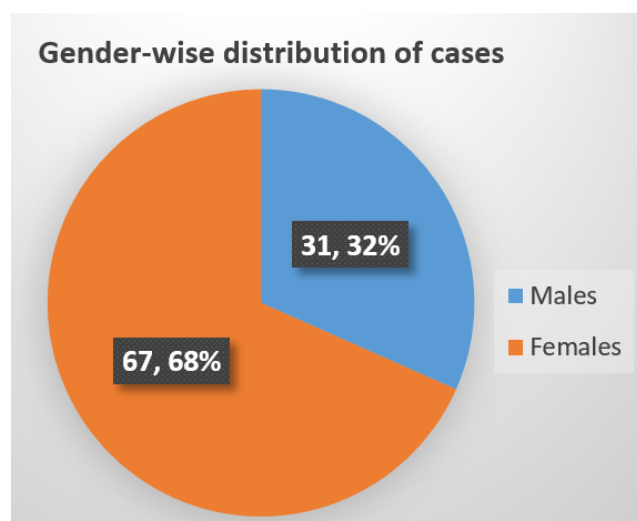
Subtype	Age Group			Total Cases
	<30	30-50	>50	
Papillary	16(17.78%)	39(43.33%)	35(38.89%)	90
Anaplastic	0	1(100%)	0	1
Medullary	0	0	1(100%)	1
Insular	0	0	1(100%)	1
Follicular	0	4(80%)	1(20%)	5

Table 3: Comparison of age range and mean age of total thyroid carcinomas

Entity	Cherit et al	Huber et al	Ponniah et al	Present Study
Age Range	21-76	19-84	10-85	18-85
Mean Age	43.8	44	34.5	45.41



Graph 1: Gender-wise distribution of cases

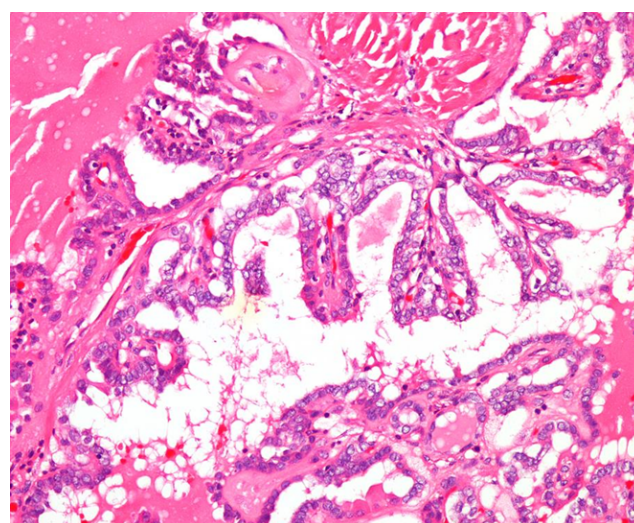
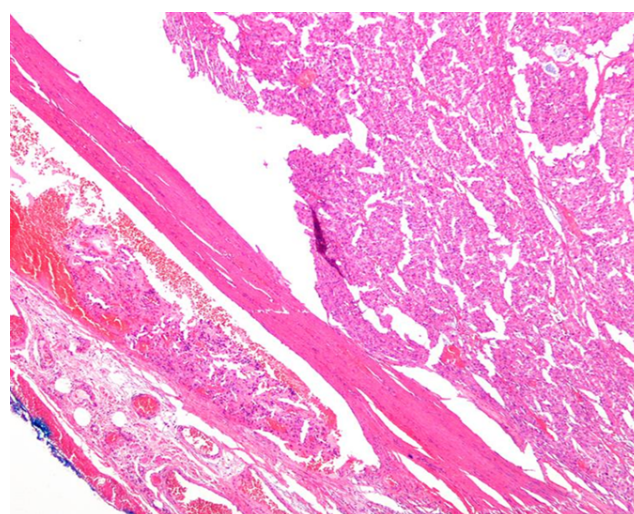


Graph 2: Gender-wise distribution of cases

cancer has found that thyroid cancer has been among the ninth cancer incidence worldwide.^{1,2} In 2023, an estimated 43,720 adults (12,540 men and 31,180 women) in the United States will be diagnosed with thyroid cancer. Women are 3 times more likely to have thyroid cancer than men, our study also recorded a female preponderance of 68.37%.³⁻⁵

Age range of our study was 18-85yrs with mean age of 45.78 years, which was found to be concordant to two other studies from our review of literature. Comparison with another study from South India (Ponniah et al.) showed that there was a higher incidence of thyroid carcinoma in a relatively older age group.⁶

Thyroid cancer can occur at any age, but the risk peaks earlier for women (3rd and 6th decades) than men (7th

**Figure 1:** Histology of papillary carcinoma, classic subtype (H&E x 200x)**Figure 2:** Histology of Follicular carcinoma (H&E x 200x)

and 8th decades). In our study the mean age affected was 43.66 years for females and 49.19 years for males. So in our study group, the incidence of thyroid cancer was much earlier in females as expected. Incidence of thyroid carcinomas is three times more in virtually all geographic locations in females than in males. However the reasons are unclear. Several studies have attributed that female sex hormones play a role in the etiology of thyroid malignancies. Pregnancy and hormonal treatment have also

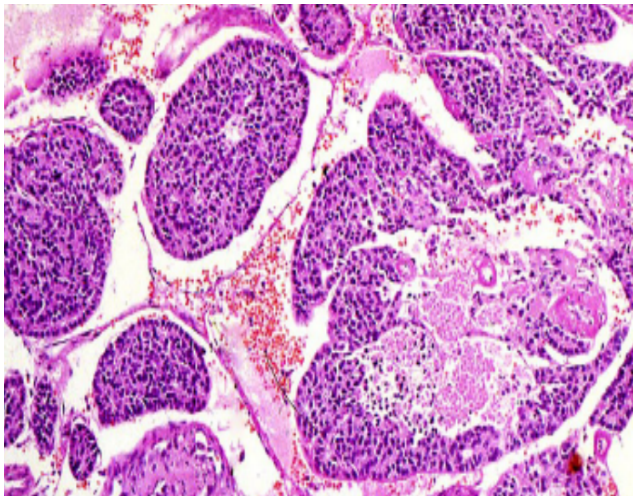


Figure 3: Histology of poorly differentiated carcinoma (H&E x 200x)

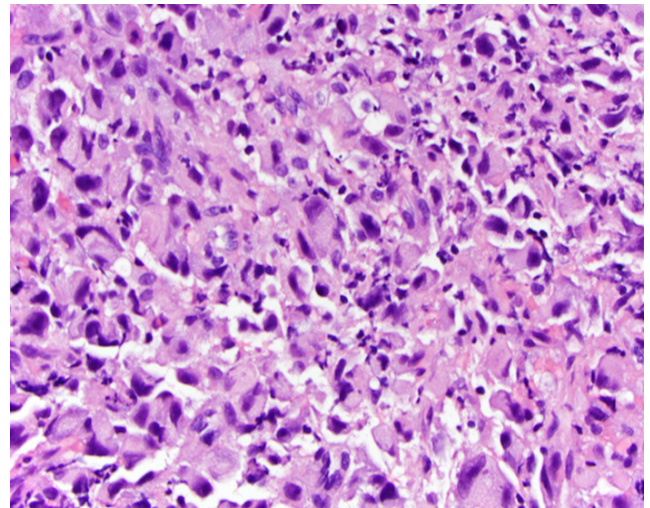


Figure 5: Histology of Anaplastic carcinoma thyroid (H&E x 200x)

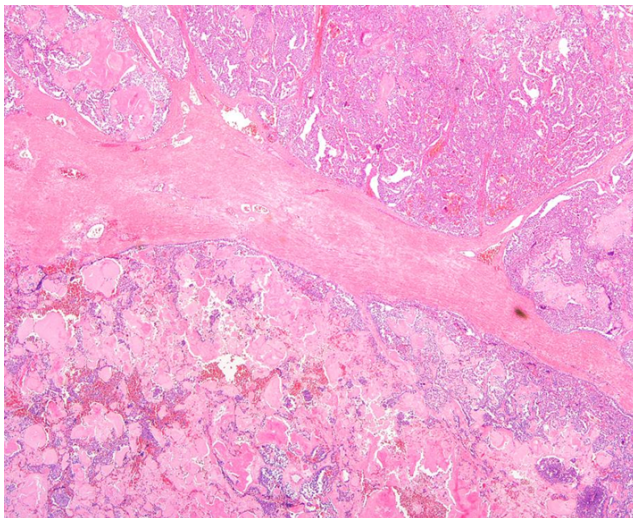


Figure 4: Histology of Medullary carcinoma thyroid (H&E x 200x)

been associated with thyroid malignancies among females. The hormone-related factors probably act as promoters of tumor growth and proliferation.^{7–9}

Iodine has an essential role in production and regulation of thyroid hormones. Both deficiency and excess intake of iodine are considered to be risk factors of thyroid cancer. Chronic hyper secretion of Thyroid stimulating hormone (TSH) is associated with thyroid follicular cell hyperplasia and hypertrophy and this association leads on to an increased risk of neoplastic transformation. Long term intake of excessive amounts of iodine can also affect the functioning of the thyroid follicular epithelial cells which eventually may elevate hormone levels.

In the literature, numerous histopathological variants of thyroid carcinoma have been described, each with distinct

behaviors. According to various studies, classical papillary carcinoma is the most prevalent variant,¹⁰ followed by papillary microcarcinoma and the follicular variant of papillary carcinoma, in descending order of frequency. In our study, we also found classical papillary carcinoma to be the most common (91.84%), followed by the follicular variant of papillary carcinoma (5.1%). Insular, anaplastic and medullary carcinomas were the least commonly encountered types in our research.^{11–14}

Histologically, classic PAPCA can present as a fairly circumscribed lesion limited to thyroid with papillary architecture and cells having the characteristic nuclear features including nuclear enlargement, clearing, grooving, overlapping, intranuclear cytoplasmic inclusions etc. Follicular carcinomas usually have a thick capsule with solid and trabecular arrangement of thyroid follicles and evident capsular and vascular invasion. Medullary carcinomas arising from the C-cells have propensity for multifocality and usually have round, plasmacytoid, polygonal or spindled and arranged in nests, cords or follicles. Numerous lymphocytes and plasma cells may be seen admixed. Occasionally amyloid may also be noted. Insular and anaplastic types are high grade with high propensity to invade adjacent structures.

Symptoms like hoarseness, dysphagia, and airway obstruction are occasionally associated with thyroid carcinoma. The presence of a hard, fixed nodule during a physical examination can raise suspicion of malignancy. But PAPCA can remain asymptomatic and present with extra thyroid lesions or evidence of metastasis too. One clinical challenge lies in determining which asymptomatic thyroid nodules warrant surgical intervention. Factors such as patient age, sex, and history of irradiation can offer some clues but only affect the likelihood of malignancy. Thyroid

function tests typically appear normal in thyroid cancer patients and are valuable for excluding other disorders. Ultrasound can identify cystic lesions, which, if smaller than 4 cm and without internal echoes, are usually benign. Fine-needle aspiration biopsy is the most cost-effective and accurate method for diagnosing papillary, medullary, and anaplastic thyroid cancers. However, it isn't particularly helpful in distinguishing between follicular or Hurthle cell adenomas and carcinomas.^{5,15,16}

5. Conclusion

In our demographic study, we observed that thyroid carcinomas tend to peak in incidence during the fourth decade of life, with a higher prevalence among females. The majority of cases in our study were identified as papillary carcinomas. The TNM staging for all the cases were analyzed. Most of the cases were samples from a total thyroidectomy. A thorough review of literature and appropriate comparisons were also done. As a result, a complete demographic profile regarding thyroid carcinomas in our tertiary health care centre was obtained and also helps us understand how the trends in our hospitals differ when compared to similar studies from other centre. This understanding is essential for making informed decisions about the most suitable treatment approaches, predicting patient prognosis, and assessing clinical outcomes.

6. Human Subjects

Consent was obtained or waived by all participants in this study. Sri Ramachandra Institutional Ethics Committee issued approval CSP/21/AUG/97/407. The tissue in paraffin blocks can be subjected to research purposes since SRIHER is an academic institution. Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue.

7. Source of Funding

All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

8. Conflicts of Interest

In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work.

9. Other Relationships

All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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