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Research Article

A clinicopathological audit of thyroid malignancies - A 2 year study

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Abstract

Thyroid cancer is the commonest of all endocrine malignancies with annual world incidence of 0.5-10 cases /100000 population constituting 1 % of all malignancies .Most present as solitary thyroid nodules clinically indistinguishable from benign lesions posing great diagnostic trial. Histopathology plays a major role in diagnosis.

Aim: The objective of this study is to determine the overall incidence, frequency of variants and analyse with clinical presentation.

Material /Methods: All specimens of thyroid were grossed and processed methodically. Diagnosed cases of primary malignant neoplasms were analysed clinicopathologically.

Results- Papillary carcinoma formed the majority (83%) with 63% classical type. Solid and tall cell variants (4%) behaved in aggressive manner. Medullary and follicular carcinomas were rare (12%). 66% cases presented with solitary nodule. 71% comprised of less than 2cm in size. 22% of cases presented with metastases in lymphnode, liver, lung .Three cases of Non-Hodgkin's lymphoma and mesenchymal sarcoma ,confirmed by immunohistochemistry marker study ,were the least common(6%) . Fourteen cases of papillary carcinoma and three medullary carcinomas were discerned in the background of multinodular goitre (28%). Likewise, three papillary carcinomas and a lymphoma occured in Hashimoto's thyroiditis (7%).

Conclusion: Papillary carcinoma is most common type with predominantly classical variant having presentation at any age also with secondaries. It can be aggressive in solid and tall cell variant. Size is not a criterion for malignancy. Majority show female preponderance**.** Lymphomas and sarcomas are not uncommon.

Keywords: Primary thyroid malignancy, clinicopathology

1. Introduction

Thyroid cancer is the commonest of all endocrine malignancies. The overall world annual incidence can range from 0.5-10 cases /100000 populations. Most authors have reported a frequency of around 1 % of all malignancies to be all of thyroid origin. Most of the thyroid malignancies clinically present as solitary thyroid nodules clinically indistinguishable from benign neoplasms and nonneoplastic nodules and posing a significant diagnostic challenge. FNAC and histopathology play a key role in resolving this diagnostic challenge and help the clinicians in taking choice on management of these patients. Though FNAC is commonly used as a diagnostic tool for thyroid malignancies, it is associated with many shortcomings. Hence histopathology is considered a gold standard. The present study based on histopathological evaluation of thyroid malignancies is with the following objectives-to determine the overall incidence of thyroid malignancies**,** to assess the frequency of different thyroid malignancies, to assess age and sex incidence of thyroid malignancies and to analyse the clinical presentation of different types of thyroid malignancies.

2. Materials and methods

The study consisted of analysis of histopathology of thyroid malignancies reported in Department of Pathology from Jan 2011 to Dec 2013 along with clinical data. It is a prospective study. The specimens were received in 10% formalin. The clinical history with duration and progression of symptoms along with age and sex were noted. General, local and systemic examination findings were noted for hyperthyroidism or any other diseases. Thyroid function tests were routinely done along with other routine investigations. The specimens were grossed noting the dimensions, nodularity and capsular invasion.

Following parameters were noted-weight, shape, colour and consistency and nodularity of the specimen. Cut surface was studied for number, nodularity, consistency, texture, colour, cyst and hemorrhage, calcification, capsular invasion or hemorrhagic. Paraffin blocked tissue sections were stained with haemotoxylin and eosin and studied under light microscope. Special stains like reticulin, congo red were also carried out wherever necessary. Reticulin stain is positive in lymphomas and shows reticulin fibres surrounding the cells whereas in nonlymphomatous lesions, they surround follicles and groups of lymphocytes thereby distinguishing thyroid lymphoma from lymphocytic thyroiditis. Congored stain is done to confirm the presence of amyloid in medullary carcinoma thyroid using polarising microscope. Immunohistochemical staining technique was done by polymer detection technique from NOVACASTRA (LEICA) using mouse monoclonal antibody Desmin (RTU-DES-DER11), mouse monoclonal antibody CD 20(NCL-CD20-7D1), mouse monoclonal antibody CD45 (NCL-LCA-RP) and lyophilised mouse antihuman monoclonal antibody alpha smooth muscle actin (NCL-SMA).

3. Results

In this prospective study of thyroid malignancies of Department of Pathology, for a period of 2 years, there was total number of 59 cases out of 150 thyroidectomy specimens received .Hence incidence of thyroid malignancy cases was 39.3%. The distribution of these cases as per type of malignancy is given below.

Table 1: Distribution of the various thyroid malignancies

	No of cases	%
Pap ca	49	83
Follicular ca	4	7
Medullary ca	3	5
Nonhodgkin's lymphoma	2	3
Leiomyosarcoma	1	2

The microphotographs of Papillary carcinoma, Hurthle cell carcinoma, medullary carcinoma, Nonhodgkin's lymphoma and leiomyosarcoma are shown in figures 1,2,3,4 and 5 respectively. As we can observe in the table 1, papillary carcinoma thyroid was the most common malignancy in this group (49 cases).

The duration of swelling of the various thyroid malignancies are shown in table 2.

Table 2: Duration of swelling for the neoplastic lesions

Duration	PTC	FC	MTC	NHL	LMS
Less than 2	18	0	0	0	1
2-5 years	26	2	1	2	0
5-10 years	1	1	1	0	0
More than 10 years	4	1	1	0	0
Total	49	4	3	2	1

PTC- Papillary thyroid carcinoma; FC-follicular carcinoma thyroid; MTC- medullary thyroid carcinoma; NHL-nonhodgkin's lymphoma; LMS- leiomyosarcoma

Although papillary carcinoma showed a wide age range from 15 to above 60 years, maximum number of patients were also in the age group of 21-30 years. Among the 49 cases of PTC in our study, 37 were females and 12 were males showing a ratio of about 3:1. All the cases of follicular carcinoma and medullary carcinoma were also encountered in females. The age and sex distribution are shown in table 3.

Table 3: The age and sex distribution of different thyroid malignancies

Age in years	PTC		FC		MTC		NHL		LMS	
	M	F	M	F	M	F	M	F	M	F
15-20	0	5	-	-	-	-	-	-	-	-
21-30	3	13	-	-	-	-	-	-	-	-
31-40	1	9	-	-	-	-	-	-	-	-
41-50	6	4	-	2	-	3	-	-	-	-
51-60	2	4	-	1	-	-	-	-	-	-
Above 60	-	2	-	1	-	-	2	-	1	-
Total	12	37	-	4	-	3	2	-	1	-

PTC- Papillary thyroid carcinoma; FC-follicular carcinoma thyroid; MTC-medullary thyroid carcinoma; NHL-nonhodgkin's lymphoma; LMS-leiomyosarcoma

Among the 49 PTC patients, 48 were euthyroid and one patient was hypothyroid .Both the NHL patients were hypothyroid. The distribution of thyroid status among the different thyroid malignancies is depicted in table 4.

Table 4: Distribution of euthyroid, hyperthyroid and hypothyroid cases among the thyroid cancers

Thyroid function	PTC	FC	MTC	NHL	LMS
Euthyroid	48	4	3	0	1
Hyperthyroid	0	0	0	0	0
Hypothyroid	1	0	0	2	0
Total	49	4	3	2	1

PTC- Papillary thyroid carcinoma; FC-follicular carcinoma thyroid; MTC-medullary thyroid carcinoma; NHL-nonhodgkin's lymphoma; LMS- leiomyosarcoma

The different types of papillary carcinoma in this group is distributed in the pattern shown in table 5.The follicular variant and solid variants are shown in figures 1a and 1 b.

Table 5: Distribution of the variants of papillary thyroid carcinoma

Type	Number	%
Classical type	31	63%
Follicular variant	12	24.4%
Microcarcinoma	2	4.0%
Solid variant	1	2%
Encapsulated variant	1	2%
Tall cell variant	1	2%
Columnar variant	1	2%

The distributions of secondary changes are shown in table 6.

Table 6: Distribution of hemorrhagic changes, cystic changes and calcification in the thyroid carcinomas

HE	PTC	FC	MTC	NHL	LMS
Absent	12	0	0	0	0
Present	37	4	3	2	1
Total	49	4	3	2	1
CYST	**PTC**	**FC**	**MTC**	**NHL**	**LMS**
Absent	39	4	3	1	1
Present	10	0	0	1	0
Total	49	4	3	2	1
CALC	**PTC**	**FC**	**MTC**	**NHL**	**LMS**
Absent	47	4	2	2	1
Present	2	0	1	0	0
Total	49	4	3	2	1

HE- haemorrhage, CYST-cystic change, CALC- calcification

Among the malignant tumors, majority (41, 71%) had a tumor size of less than 2 cm that included 38 cases of PTC, one follicular carcinoma and 2 medullary carcinoma cases.

In 3 cases the tumor size was more than 4cm. The tumor size among the thyroid malignancies in our study group ranged from 0.5cm to 7.5 cm.

Significantly most of the papillary carcinomas during presentation were less than 2 cm (66 %) highlighting an early presentation. In the remaining 11 cases, tumor size ranged from 2 to more than 4 cm (20%). Size of follicular carcinoma ranged from 1.5 to 4 cm. Thus majority of the epithelial malignancies presented with a small tumor. The lymphomas and leiomyosarcoma were fairly large on presentation (more than 5 cm). Among the 58 thyroid malignancies, only 13 cases presented with lymphnode and distant metastases. One solid variant of papillary carcinoma presented with bone metastases and two follicular carcinomas presented with lung and liver metastases.

Figure 1a: Microphotograph of follicular variant of papillary carcinoma

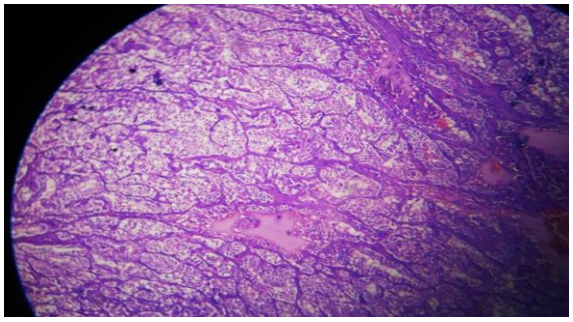


Figure 1 b: Microphotograph of solid variant of papillary carcinoma

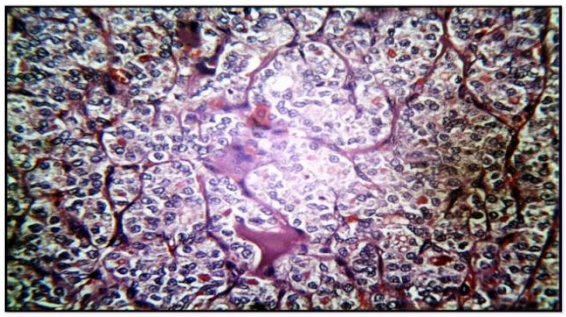


Figure 2: Microphotograph of Hurthle cell carcinoma

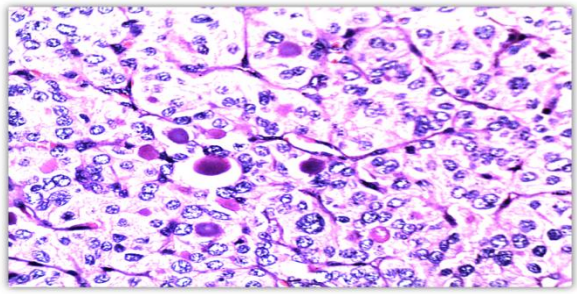


Figure 3: Microphotograph of medullary carcinoma thyroid(Hand E X10)

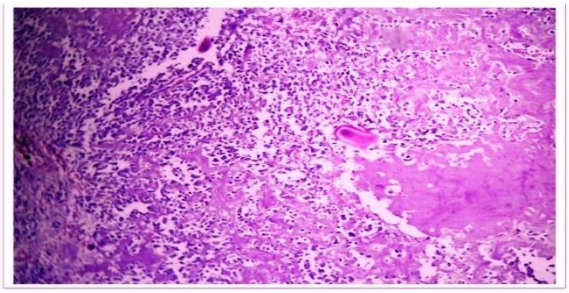


Figure 4: Microphotograph of Nonhodgkin's lymphoma thyroid (H and E, X 40)

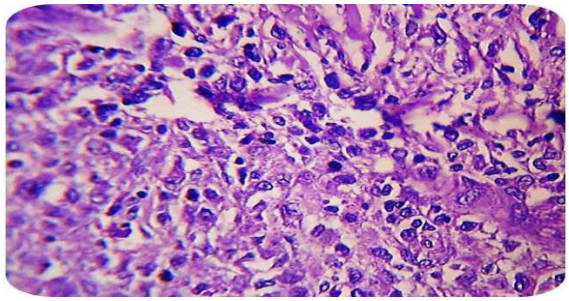
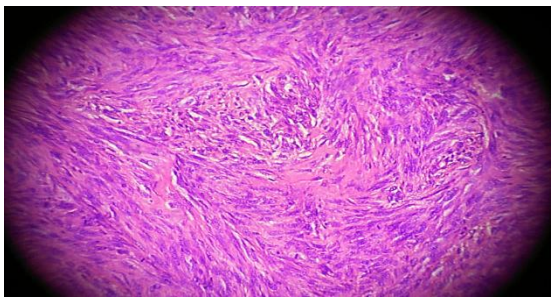


Figure 5: Microphotograph of Leiomyosarcoma thyroid (Hand E X 10)



4. Discussion

In the present retrospective study of thyroid malignancies reported in the Department of pathology of Yenepoya Medical college consists of 59 cases .As usual the commonest tumor was papillary carcinoma (49,83%) which matches well with most of other sources of data in which incidence of papillary carcinoma is 70-80% of all thyroid malignancies[1]. The incidence of papillary thyroid carcinoma was comparable to study by Salama *et al*[2]. The follicular carcinoma cases were comparable to other studies as shown in table 7. Also the incidence of medullary carcinoma was comparable to study by Salama *et al*[2] and Ahmed *et al*[3]. This can be attributed to relatively small number of cases in our study when compared to other authors. In the present study, anaplastic carcinoma and poorly differentiated carcinoma were not reported (0%) in contrast to the general incidence of 2-10% and 4-10% respectively in other studies. The incidence of Nonhodgkins lymphoma in this study (4%) is also comparable to other data[1]. Both the cases of lymphoma were confirmed by histopathology and subsequent immunohistochemical study as mature B cell lymphoma (CD45, CD20). In contrast to the major studies in the literature, there was a case of leiomyosarcoma in our group which contributed to 2 % of all cases .As such the overall incidence of malignant mesenchymal tumors is extremely rare in thyroid. The case was of a 75 year old patient who presented with hard mass which was diagnosed as spindle cell tumor in FNAC and later confirmed as leiomyosarcoma by histopathology and immunohistochemistry (Desmin,SMA Positive).

Table 7: Showing comparison of incidence of thyroid malignancies with other study

Authors	PTC	FC	MTC	AC
Bukhari *et al*[4]	138(13.8%)	3(0.3%)	7(0.7%)	1(0.1%)
Ahmed *et al* [3]	6(6%)	1(1%)	1(1%)	-
Sushel C *et al*[5]	11(7.85%)	3(2.1%)	-	1(0.71%)
Salama SI *et al*[6]	209(24.7%)	13(1.5%)	13(1.5%)	7(0.8%)
Present study	49(32.7%)	4(2.6%)	3(2%)	-

PTC-Papillary thyroid carcinoma; FC-follicular carcinoma thyroid;
MTC- medullary thyroid carcinoma; AC- anaplastic carcinoma

The incidence of thyroid malignancies in our study group was a little higher as compared to other studies as shown in table 7 and 8. This may be attributed to a shorter period and a smaller number of cases studied in our group when compared to studies by other authors and a relatively less number of colloid goitres encountered in this coastal region. Compared to the percentage obtained by other authors where the percentage of thyroid malignancy is less, duration of the study is high and they had a relatively higher number of cases.

Table 8: Comparison of incidence of thyroid malignancies in different studies

Authors	No of years	Percentage
Htwe *et al* (Malaysia)[7]	5 years	6.7
Othman *et al*[8]	11 years	7.5
Olatoke *et al*[9]	5 years	10.8
Htwe *et al*(Myanmar)[10]	3 years	26.3
Present study	3 years	39.3

The incidence of papillary thyroid carcinoma was comparable to studies by other authors which is shown in table 9.

Table 9: Comparison of incidence of papillary carcinoma thyroid

Authors	Percentage
Bukhari *et al* [4]	90.2
Hay ID[11]	90
Ahmed Z *et al* [3]	57.9
Abdulmughni *et al*[12]	93.8
Larijani *et al*[13]	69.9
Present study	71

In the present study, among the 49 cases of papillary carcinomas, 31 cases (63%) were of classical type, and remaining (37%) were different variants of papillary carcinoma. The histological variants encountered were –follicular variant (24.4%), micro carcinoma (4%), solid variant (2%), encapsulated variant (2%), tall cell variant (2%) and columnar variant (2%). Among the variants of papillary thyroid carcinoma, classical type papillary carcinoma formed the major group. The number of classical PTC was 63 % which is comparable to study by Muzaffar *et al*[14] in which it is 70.7%.The follicular variant in our study is 24.4% and the tall cell and the encapsulated variants in our study are each 2%. These were comparable to study by Muzaffar *et al* where its 1.2%.But the columnar variant was higher in his study which was 7.3% but in ours it is slightly less, i.e. 2%. From our study it was decerned that nuclear features played a vital role in diagnosis of papillary carcinoma of thyroid especially in its variants.

Detection of variants of papillary carcinoma has prognostic significance in some subtypes[15]. For eg, 10 % of follicular variant presented with metastases in contrast to 27% in classical type. Similarly tall cell[16] and solid variant are associated with more aggressive behaviour than other types. The solid variant of our group presented with bone metastasis. The tall cell variant of papillary carcinoma thyroid is known to be having more aggressive clinical features than classical variant and had worse prognosis with increased age similar to our case.[1,2,3,4,5] The incidence of Hurthle cell variant of follicular carcinoma is almost similar to general data (about 30%).In the Memorial Sloan –Kettering Cancer centre series[17], and the earlier series from Mayo clinic, Hurthle cell carcinoma obtained a higher degree of distant metastasis than follicular thyroid cancer. Hurthle cell carcinomas are more aggressive than conventional follicular carcinomas showing high rate of extrathyroidal extension, local relapse and lymphnode metastases. At the age of 40 years, 10% of patients with PTC, 25% of patients with follicular thyroid carcinoma and 35% of patients with Hurthle cell carcinoma develop distant metastasis.[18] Follicular carcinoma is usually unifocal,10-15% of patients present with metastatic disease mostly involving the lung followed by bone[18]. One of the 3 cases of medullary carcinoma was diagnosed as oxyphilic variant which is a rare variant of medullary carcinoma which presented with lymphnode metastases. About one half of patients with medullary carcinoma will have metastasis at the time of diagnosis, particularly when one does not include those having prophylactic thyroidectomies due to RET germline mutations.

The age distribution of various thyroid malignancies in this group matches fairly well with the general data. The papillary carcinomas were encountered between 15-85 years with a peak between 20-50 years. It is also observed that the 12 cases of follicular variant of papillary

carcinoma belong to the age group of 25-60 years. The mean age of follicular variant was 37.2 years in a study[14]. The 4 cases of follicular carcinoma were encountered in age group of 50-70 years which is also correlating with other studies[19]. The medullary carcinomas were encountered between 30 and 50 years as seen in other studies groups.[20]

The incidence of leiomyosarcoma in literature has been only 0.014% [21,22] . So far only 20 cases are reported. In our small group of 58 malignancies in our study, one case of leiomyosarcoma was encountered which is significant. Even thyroid lymphomas are rare. Our study had two cases. One of the cases had a background of hashimotos thyroiditis. In a study by Foppiani[23], more than one half of patients with thyroid NHL have biochemical or ultrasonographic features of Chronic Lymphocytic Thyroiditis (nearly 50% presenting with hypothyroidism. The overall sex distribution of thyroid malignancies in this group was approximately 2.8:1 which matches well with the general data which ranges from 2.5:1 to 4:1[1].

On pathological scrutiny, 21 patients (42%) had pre-existing thyroid disease. Among these, 17 patients had colloid goitre (28%), and 4 had Hashimotos thyroiditis (7%). One of the 2 patients of NHL had associated Hashimotos thyroiditis which is generally encountered as a predisposing disease for NHL. In a study incidence of malignancy was 11.6% for nontoxic group and no case was detected in non toxic group[24].

From this study we can conclude that papillary carcinoma is the most common malignancy with predominantly classical variant having presentation at any age also with secondaries. The variants of the papillary thyroid carcinoma have higher metastatic potential than classical type. Nuclear features play a vital role in diagnosis of papillary carcinoma of thyroid especially in its variants. They can be aggressive in solid and tall cell variant; also the follicular variant showed a much higher aggressive behaviour than classical type. Size of the tumor is not a criterion for malignancy. Most of the thyroid malignancies show female preponderance.

As observed in the present study, as many as 28% of malignancies were encountered in a background of colloid goitre. All thyroidectomy specimens operated for colloid goitre must be evaluated carefully to rule out a focus of malignancy as a second disease. Similarly, all follicular lesions of thyroid should be carefully evaluated in order to differentiate between possibilities of follicular adenoma, follicular carcinoma, follicular variant of papillary carcinoma and adenomatous nodule in a colloid goitre. As in small group of 59 cases of thyroid malignancies, we have encountered a rare case of leiomyosarcoma, therefore a malignant mesenchymal tumor although rare should be considered as a possibility.

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