

# Histopathological findings in goiter: A review of 624 thyroidectomies

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## Abstract

**OBJECTIVES:** To identify the histopathological patterns of goiter in thyroidectomy specimens and their frequency in relation to age and gender of the patients.

**METHODOLOGY:** We present a retrospective data of 624 thyroidectomy specimens diagnosed over a period of six year (2007–2012) at the Department of Pathology, Holy Family Hospital, Rawalpindi, Pakistan.

**RESULTS:** A total of 624 consecutive thyroidectomy specimens were selected. Patient's age ranges from 11–89 years, 541 females and 83 males. There were 512 (82%) non-neoplastic lesions, which includes; 475 (76.1%) multi-nodular goiter (MNG), 16 (2.6%) Hashimoto thyroiditis, 11 (1.8%) colloid goiter, 4 (0.6%) toxic goiter, 2 (0.3%) chronic lymphocytic thyroiditis, 2 (0.3%) tuberculous thyroiditis and 2 (0.3%) miscellaneous. From 112 (18%) neoplastic lesions, 43 (6.9%) were adenomas (41 females and 2 males) and 69 (11.0%) were carcinomas (58 females and 11 males). Peak age for thyroid malignancy was 3<sup>rd</sup> to 4<sup>th</sup> decades. The histological subtypes of thyroid carcinomas includes, 35 (5.6%) follicular variant of papillary carcinoma (FVPC), 15 (2.5%) well-differentiated tumor of uncertain malignant potential (WDT-UMP), 6 (1%) medullary carcinomas, 6 (1%) papillary carcinomas, 3 (0.5%) anaplastic carcinomas, 2 (0.3%) follicular carcinomas and 2 (0.3%) other carcinomas. Twenty-nine (4.6%) neoplastic lesions were associated with MNG, includes; 2 (3.5%) follicular adenomas, 3 (0.5%) WDT-UMP and 4 (0.6%) FVPC.

**CONCLUSIONS:** MNG is common and FVPC is the common thyroid cancer seen in females. The overall frequency of thyroid cancer is 11%. Follicular adenoma and FVPC appears to be associated with long standing MNG of iodine deficiency.

## INTRODUCTION

The enlargement of thyroid gland called “goiter” may be diffuse, nodular or multi-nodular. Dietary deficiency of iodine is responsible for majority of the cases of goiter worldwide. As reported by World Health Organization (WHO), in 2007 about 2 billion individuals had insufficient iodine in their diet and among these one third being school age children (De Benoist *et al.* 2008). However, in the last decade, improved iodine in diet resulted in decreased number of iodine-deficient countries from 54 in 2003 to 32 in 2011 but still 1.88 billion people worldwide, including 241 million school children, have insufficient iodine in their diet (WHO 2007; UNICEF 2011).

The areas of the world which are naturally iodine deficient, in their soil, water and food includes; Western Pacific, South-East Asia, Africa, China and Kazakhstan. In some areas iodine deficiency goiter is endemic and northern areas of Pakistan is one of them.

Clinically goiter presents as small to large, single or multi-nodular, unilateral or bilateral slow growing painless swellings. In northern mountainous rural areas of Pakistan, low socioeconomic status, lack of public awareness and sparse health facilities delay patient visit to the hospital. This results in long standing, huge goiter over a period of time, thus making the surgical procedure more difficult. Thyroidectomy (lobectomy, subtotal or total) is performed after clinical examination and cytological diagnosis made by fine needle aspiration and the specimens are submitted to the department of pathology for histopathological diagnosis. The development of malignancy is of great concern in patients especially having long standing MNG or having dominant thyroid nodules (Gandolfi *et al.* 2004; Tollin *et al.* 2000).

The aim of this study is to identify the histopathological patterns of goiter in thyroidectomy specimens and their frequency in relation to age and sex of the patients.

## MATERIAL AND METHODS

This is a retrospective review of record of 624 consecutive thyroidectomy specimens submitted and diagnosed between 1<sup>st</sup> January 2007 and 31<sup>st</sup> December 2012 at the Department of Pathology, Holy Family Hospital (HFH), Rawalpindi, Pakistan. The HFH is a public sector, tertiary care teaching hospital, affiliated with Rawalpindi Medical College, Rawalpindi. The HFH is 1000 bedded and provides health services to more than 4.5 million populations of the Rawalpindi city and adjacent rural areas. It is a referral center for the northern most part of Punjab, receiving patients from Rawalpindi, Islamabad, Murree, Azad Jammu Kashmir, Attock, and Chakwal districts.

The clinical data and histopathological diagnosis was retrieved from the laboratory record register. The surgical specimens comprised of lobectomy and subto-

tal, near total or total thyroidectomies. The consultant pathologists identified the histopathological patterns and these were categorized into non-neoplastic and neoplastic (benign and malignant) lesions. Cases of thyroid malignancy presenting for follow up and recurrent MNG were not included in this study.

### Statistical analysis

Data entered into Statistical Package of Social Sciences (SPSS) version 16, for statistical analysis. The quantitative variable like, age is expressed as mean  $\pm$  S.D. (standard deviation) and qualitative variables like, histopathological diagnosis are represented by frequencies and percentages.

## RESULTS

A total of 624 thyroidectomy specimens received, were analyzed. The non-neoplastic lesions were seen in age ranging from 10 to 90 years in males and females. The neoplastic benign lesions were present in age ranging from 10 to 70 years in females and 21 to 50 years in males, whereas the malignant neoplasms were seen in age ranging from 10 to 70 years in both genders (Table 1). The mean age of the patients who underwent thyroidectomy was  $37.20 \pm 13.25$  years for males and  $35.01 \pm 11.76$  years for females. There were 83 males and 541 females with female to male ratio 6.5:1.

Out of the total 624 cases, the non-neoplastic thyroid lesions were 512 (82%) and neoplastic were 112 (18%) (Table 2). The histopathological patterns of non-neoplastic group reveals 475 (76.1%) MNG, 16 (2.6%) Hashimoto's thyroiditis, 11 (1.8%) colloid goiter, 4 (0.6%) toxic goiter, 2 (0.3%) chronic lymphocytic thyroiditis, 2 (0.3%) tuberculous thyroiditis and 2 (0.3%) miscellaneous which includes; one each case of a colloid cyst and a dermoid cyst. All cases of Hashimoto's thyroiditis were found in females in the age group 15–48 years.

The histopathological pattern of benign neoplastic lesions reveal, 43 (6.9%) adenomas; { (39)6.2 % follicular and (4)0.6 % Hurthle cell adenomas}. There were, 41 females and 2 males. The malignant neoplasms 69 (11%) were thyroid carcinomas (Table 3), 58 females and 11 males with female to male ratio 5.2:1. The peak age for thyroid cancer was 3<sup>rd</sup> to 4<sup>th</sup> decades (Table 4). The histological subtypes of thyroid carcinomas includes, 35 (5.6%) follicular variant of papillary carcinoma (FVPC), 15 (2.5%) well-differentiated tumor of uncertain malignant potential (WDT-UMP), 6 (1.0%) medullary carcinomas, 6 (1%) papillary carcinomas, 3 (0.5%) anaplastic carcinomas, 2 (0.3%) follicular carcinomas and a single case each of clear cell and Hurthle cell carcinoma. Twenty-nine (4.6%) out of the total cases showed neoplastic lesions in association with MNG. The histologic subtypes of such neoplastic lesions includes; 22 (3.5%) follicular adenomas, 3 (0.5%) WDT-UMP, 4 (0.6%) FVPC. One case of papillary carcinoma was associated with Hashimoto's thyroiditis.

**Tab. 1.** Age distribution and histological categories of 624 thyroidectomy specimens.

Age (years)	Female cases 541 (86.7%)			Male cases 83 (13.3%)			Total	%
	Non-neoplastic	Benign Neoplasms	Malignant Neoplasms	Non-neoplastic	Benign Neoplasms	Malignant Neoplasms		
10-20	54	5	4	5	0	1	69	11.1
21-30	119	15	20	16	1	3	174	27.9
31-40	154	14	16	21	0	2	207	33.2
41-50	92	5	10	12	1	2	122	19.6
51-60	25	1	6	6	0	2	40	6.4
61-70	2	1	2	2	0	1	8	1.3
71-80	1	0	0	0	0	0	1	0.2
81-90	2	0	0	1	0	0	3	0.5
Total	449	41	58	63	2	11	624	100

## DISCUSSION

Diseases of the thyroid gland either of non-neoplastic or neoplastic nature usually presents clinically as diffuse or nodular goiter. Their evaluation is of great clinical importance as most are well managed and treated by medicine or surgery.

In present study, the frequency of non-neoplastic and neoplastic thyroid lesions is 82% and 18% respectively. The non-neoplastic lesions are common in 3<sup>rd</sup> to 5<sup>th</sup> decades of life in females as compare to males. MNG is common and constitute 76.1% of the total cases, comparable from 63% to 93.5%, in various international studies (Bekele & Osman 2006; Bouq *et al.* 2006; Bukhari & Sadiq 2008; Hussain *et al.* 2005; Nzegwu *et al.* 2010; Rahman *et al.* 2013; Salama *et al.* 2009; Sushel *et al.* 2009; Tollin *et al.* 2000; Tsegaye & Ergete 2003). Hashimoto thyroiditis is the next common lesion and comprised of 2.6% of total cases, all being females. One case of Hashimoto's thyroiditis showed papillary carcinoma supporting the view that Hashimoto's thyroiditis is a risk factor for the development of papillary carcinoma, as reported in literature (Sulimani 1996; Tamimi 2002; Tsegaye & Ergete 2003).

In this study, thyroid neoplasms constitute 112 (18%) of the total thyroid cases as compare to 18.5%, 21%, 26% and 41.5% reported from, Bangladesh, Ethiopia, Pakistan (Karachi, Southern Punjab) and Saudi Arabia (Hussain *et al.* 2005; Nadeem *et al.* 2013; Qari 2004; Rahman *et al.* 2013; Salama *et al.* 2009; Tsegaye & Ergete 2003). Of these 43 (6.9%) were thyroid adenomas reflecting its lowest incidence in Rawalpindi area as compare to 10.1%, 10.2%, 11% and 12.8%, reported from, Italy, Bangladesh, Pakistan (Karachi, Southern Punjab), Saudi Arabia and Ethiopia (Gandolfi *et al.* 2004; Hussain *et al.* 2005; Nadeem *et al.* 2013; Rahman *et al.* 2013; Tsegaye & Ergete 2003; UNICEF 2011). Histologically, 39 (6.3%) are follicular and 4 (0.6%) Hurthle cell adenomas. The frequency of thyroid adenoma is

**Tab. 2.** Histopathological patterns of 624 thyroidectomy specimens.

Histological Diagnosis	N (%)
<b>NON-NEOPLASTIC LESIONS (n=512)</b>	
Multi-nodular goiter	475.0 (76.1%)
Hashimoto thyroiditis	16.0 (02.6%)
Colloid goiter	11.0 (01.8%)
Toxic goiter	4.0 (00.6%)
Chronic lymphocytic thyroiditis	2.0 (00.3%)
Tuberculous thyroiditis	2.0 (00.3%)
Miscellaneous (one Colloid cyst & one Dermoid cyst)	2.0 (00.3%)
<b>NEOPLASTIC LESIONS (n=112)</b>	
<b>Benign Neoplasms (n=43)</b>	
Follicular adenoma(22 have associated MNG)	39.0 (06.2%)
Hurthle cell adenoma	4.0 (00.6%)
<b>Malignant Neoplasms (n=69)</b>	
Follicular Variant of papillary carcinoma (04 have associated MNG)	35.0 (05.6%)
Well-differentiated tumor of Uncertain Malignant Potential (03 have associated MNG)	15.0 (02.5%)
Medullary Carcinoma	6.0 (01.0%)
Papillary Carcinoma ( includes one micropapillary carcinoma)	6.0 (01.0%)
Anaplastic Carcinoma	3.0 (00.5%)
Follicular Carcinoma	2.0 (00.3%)
Others ( one Clear cell & one Hurthle cell carcinoma)	2.0 (00.3%)
<b>TOTAL</b>	<b>624 (100%)</b>

N = Number of cases and in bracket percentages are shown.

**Tab. 3.** Histopathological patterns of 69 malignant neoplasms.

Type of malignant tumor	Female (58)	Male (11)	Total (69)
Follicular Variant of papillary carcinoma	31	4	35 (50.7%)
Well-differentiated tumor of Uncertain Malignant Potential	12	3	15 (21.7%)
Medullary Carcinoma	6	0	6 (8.7%)
Papillary Carcinoma	4	2	6 (8.7%)
Anaplastic Carcinoma	2	1	3 (4.4%)
Follicular Carcinoma	1	1	2 (2.9%)
Others (1 Clear cell & 1 Hurthle cell carcinoma)	2	0	2 (2.9%)

**Tab. 4.** Age and gender distribution of types of thyroid cancers.

Age Years	WDT-UMP	FVPC	PTC	MTC	FC	AC	HCC	CCC	Total
10–20									
M	1	-	-	-	-	-	-	-	1
F	-	2	1	1	-	-	-	-	4
21–30									
M	1	2	-	-	-	-	-	-	3
F	2	17	1	-	-	-	-	-	20
31–40									
M	-	1	1	-	-	-	-	-	2
F	6	8	1	-	1	-	-	-	16
41–50									
M	-	1	-	-	1	-	-	-	2
F	3	2	1	2	-	-	1	1	10
51–60									
M	-	-	1	-	-	1	-	-	2
F	-	2	-	2	-	2	-	-	6
61–70									
M	1	-	-	-	-	-	-	-	1
F	1	-	-	1	-	-	-	-	2
Total	15	35	6	6	2	3	1	1	69

WDT-UMP; Well-differentiated tumor of uncertain malignant potential, FVPC; Follicular variant of papillary carcinoma, PTC; Papillary thyroid carcinoma, MTC; Medullary thyroid carcinoma, FC; Follicular carcinoma, AC; Anaplastic carcinoma, HCC; Hurthle cell carcinoma, CCC; Clear cell carcinoma.

6.5% in females and is 0.3% in males, with female to male ratio 20:1. They are common in 3<sup>rd</sup> to 4<sup>th</sup> decades of life (Table 1).

There are 69 thyroid carcinomas, 58 in females and 11 in males. The common histologic types seen in females are FVPC (45%), WDT-UMP (17.4%), medullary carcinoma (8.7%) and papillary carcinoma (5.8%) (Table 3). All cases of medullary carcinomas are present in females. On the other hand, common histologic types of thyroid cancers in males are; FVPC (5.8%), WDT-UMP (4.3%) and papillary carcinoma (2.9%).

The incidence of thyroid cancer in Pakistan is 1.2% (Nadeem *et al.* 2013) of all malignant neoplasms. In the present study, the frequency of thyroid cancer is 11% as compared to 14.4% to 15.3%, reported in other studies done in Pakistan (Bukhari & Sadiq 2008; Nadeem *et al.* 2013; Anwar *et al.* 2012). Various international studies reported that the incidence of thyroid cancer varies from one geographical area (Nigeria, Ethiopia, Bangladesh, USA, India, KSA) to another ranging from 7%, 8.2%, 8.3%, 8.8%, 12%, 30.3% to 37.5% (Abdulkareem *et al.* 2014; Bhartiya *et al.* 2014; Botrugno *et al.* 2011; Qari 2004; Rahman *et al.* 2013; Salama *et al.* 2009; Tsegaye & Ergete 2003). The peak age for thyroid cancer is 3<sup>rd</sup> to 4<sup>th</sup> decades of life in both genders, with female to male ratio of 5.2:1 (Table 4). We observed that the frequency of thyroid cancer decreases as age advances. No case of thyroid malignancy is seen in the 1<sup>st</sup> decade of life.

Of all the thyroid cases the incidence of papillary carcinoma in our study is 6.6% (5.6% FVPC and 1% classical papillary carcinoma), as compared to 6.1%, 10.6%, 9.8%, 13.8%, 22.2% and 24.7% reported from Ethiopia, Pakistan (other regions), Italy, and Saudi Arabia (Anwar *et al.* 2012; Bekele & Osman 2006; Gandolfi *et al.* 2004; Memon *et al.* 2010; Mulaudzi *et al.* 2001; Nadeem *et al.* 2013; Qari 2004). Five cases of FVPC are of diffuse type and all others encapsulated. The next in frequency are medullary carcinoma (1%), anaplastic carcinoma (0.5%), and follicular carcinoma (0.3%) (Table 2). In our study the incidence of follicular carcinoma is very low as compared to Africa and Nigeria where follicular carcinoma is more common (Abdulkareem *et al.* 2005; Desai & Islam 1992). Encapsulated neoplasms with follicular pattern are seen in 0.6% of the cases, such lesions showed equivocal nuclear features and we categorized them as WDT-UMP as proposed (Williams 2000), some pathologist report them as atypical follicular adenoma (Salama *et al.* 2009).

Most of the thyroid cancers clinically, presents as MNG. It is important to note that, 29 (4.6%) of the total cases showed neoplastic lesions in association with MNG. The histologic subtypes of such neoplastic lesions includes; 22 (3.5%) follicular adenomas, 3 (0.5%) WDT-UMP and 4 (0.6%) FVPC. Similar findings have been reported in the literature (Anwar *et al.* 2012; Memon *et al.* 2010; Qari 2004) suggesting that long standing MNG is a risk factor for thyroid cancer.

This study may contribute in gathering some baseline data of thyroid diseases in Pakistan and the load of thyroidectomies in one of the tertiary care teaching hospital. Although the preoperative diagnosis of thyroid neoplasms by fine needle aspiration biopsy has been helpful in cutting down the load of unnecessary thyroidectomies but some time difficulties occurs in the assessment of follicular neoplasms (Wojtczak *et al.* 2012).

In conclusion, this study shows that non-neoplastic and neoplastic thyroid lesions are more common in

females with female to male ratio 6.5:1. The venerable age for thyroid cancer in both genders is 3<sup>rd</sup> to 4<sup>th</sup> decade. MNG in iodine deficient areas of prolong duration appears as a risk factor for the development of follicular adenoma, WDT-UMP and FVPC. Therefore, it is highly important to prevent the development of MNG by public awareness programs, use of iodized salt and non-goitrogenic diet. Regular in time checkup of thyroid swelling of any nature is recommended.

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## Conflict of interest

Authors have no financial interest in this manuscript and no conflict of interest to disclose.

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