

A Histopathological Audit of Thyroid Surgical Specimens

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Objective: This study was conducted to see the frequency of different morphological lesions encountered in surgically excised thyroid glands. **Study design:** Descriptive cross sectional study. **Place and duration of study:** The study was conducted at the Department of Pathology, King Edward Medical University, Lahore during a 2-year period commencing from 1st January 2005 to 31st December 2006. **Materials & methods:** All thyroid surgical specimens referred from the four major Surgical Units of Mayo Hospital, Lahore, to the Department of Pathology, King Edward Medical University, Lahore, during a 2-year period (2005-2006). Specimens from both sexes and all age groups were included in this study. **Results:** A total of 662 thyroid specimens were examined histologically. They constituted of 588 specimens (88.82%) from females and 74 specimens (11.17%) from males. The commonest lesion was Colloid Goiter (diffuse and multinodular) constituting 434 cases (65.55%). Next in frequency were tumours (benign and malignant) constituting 151 cases (22.80%). Benign tumours comprised of 113 cases (74.83%) and malignant constituted 38 cases (25.16%) out of 151 thyroid tumours. Follicular adenoma was the commonest tumour constituting of 108 cases (71.52%) followed by Papillary carcinoma constituting 27 cases (17.88%). Other non-neoplastic thyroid lesions included diffuse hyperplasia (3.62%), thyroiditis (2.26%), hyperplastic nodules (1.35%), colloid nodules (1.20%), completion thyroidectomy specimens (1.05%), colloid cysts (0.90%), colloid goiters with associated hyperplastic changes (0.60%), goiters with thyroiditis (0.45%) and a single case of dysmorphogenetic goiter (0.15%). **Conclusions:** Colloid goiter is the commonest lesion of the thyroid gland in both sexes and is the commonest cause of an enlarged thyroid gland. This is followed by Follicular adenoma which is the commonest benign tumour of the thyroid. Papillary carcinoma is the commonest malignant tumour seen in all age groups with a predominance in females.

Keywords: Colloid Goiter (CG), Follicular Adenoma (FA), Hurthle Cell Adenoma (HCA), Papillary carcinoma (PC)

Despite its structural simplicity, the thyroid gland can give rise to a large variety of pathological lesions, both neoplastic and non-neoplastic which usually present clinically as a diffuse swelling or enlargement called a "goiter" or as a discrete palpable "solitary nodule"^{1,2}. There is a well documented geographical dependency in thyroid diseases due to variation in the iodine content of the soil and water³, but "goiter" either diffuse or multinodular is the commonest lesion of the thyroid encountered in all hospital outpatients clinics worldwide^{4,5,6}. It is endemic in the mountainous regions of the world and in Pakistan an alarming high prevalence of goiter and iodine deficiency diseases (IDD) has been reported from the hilly areas of NWFP particularly upper Swat, Dir, Chitral, Mardan, Gilgit, Swabi and Peshawar^{7,8,9}.

The "solitary thyroid nodule" is defined as a discrete palpable swelling or lump within an otherwise normal palpable thyroid gland^{10,11}. These nodules are a source of concern for the patients and a diagnostic dilemma for physicians. Nodules either single or multiple occur spontaneously and are present in 4-7% of the adult population worldwide^{1,11}. Their incidence however, is significantly higher in the endemic goitrous regions, in females and with increasing age^{2,4,10}. Nodules are 10 times more frequent when the gland is examined at autopsy¹², during surgery^{2,10}, or by ultrasonography¹⁰. More than 80-85% of these nodules prove to be benign lesions like colloid nodules and adenomas on histological examination and only 10-20% are undoubtedly malignant^{13,14}, so the

critical significance of an isotopically cold, solitary thyroid nodule lies in its increased malignant potential when compared to a multinodular goiter^{15,16}.

Other lesions seen in a surgically excised thyroid specimens include hyperplastic nodules (toxic nodules) and diffuse hyperplasias (Graves disease), colloid cysts, inflammatory conditions like abscesses and thyroiditis including Hashimoto disease, granulomatous (De Quervain) thyroiditis and lymphocytic thyroiditis^{5,6,17}.

Thyroid cancer is a relatively rare malignancy representing only 1.5% of all human cancers but is the commonest endocrine cancer accounting for 92% of all endocrine malignancies⁽¹⁸⁾. Papillary carcinoma is the most frequent variety representing 70-80% of all thyroid cancers^{19,20}. Other malignant tumours include Follicular carcinoma, Medullary carcinoma, Anaplastic or Undifferentiated carcinoma and Non-Hodgkins Lymphoma^{20,21,22}. Multinodular goiters may also harbour an underlying cancer and the incidence of malignancy in these goiters ranges from 4-17% in different series²³.

The currently available diagnostic modalities for the investigation of thyroid lesions include Fine Needle Aspiration Cytology (FNAC), ultra-sound, scintiscan, thyroid function tests (TFT's) and histopathological evaluation of surgical specimens.

Materials and methods

All thyroid surgical specimens submitted to the Department of Pathology, King Edward Medical University, Lahore, during a 2-year period commencing

from 1st January 2005 to 31st December 2006 were included in this retrospective study. They were received from the four major Surgical Units of Mayo Hospital, Lahore and included specimens from both sexes and all age groups.

Relevant data and clinical information about each patient was retrieved from the computer files and biopsy forms. This included the name, age, sex, address and locality, biopsy number, history of previous thyroid surgery, family history of thyroid disease, any present or past medication etc. Relevant laboratory investigations like thyroid scans, Fine Needle Aspiration cytology reports etc if available were also noted.

Gross descriptive details of the excised thyroid specimens were noted like diffuse or nodular enlargement, presence of single or multiple nodules, cyst formation, haemorrhage, calcification, papillary structures, presence or absence of an intact capsule etc. In addition relevant information from the per operative surgical notes was also recorded like adherence of the thyroid to the adjacent structures, any new growth, and enlarged cervical lymph nodes. Microscopic details and the final diagnosis was noted from the Histopathology reports. In controversial cases, the blocks and slides were retrieved from the records and reviewed again to establish the final diagnosis. Results so obtained were compiled and compared with other similar local and international studies carried out on different pathological lesions of the thyroid gland.

Results

During a 2-year period commencing from 1st January 2005 to 31st December 2006, a total of 662 thyroid surgical specimens were referred for histopathological evaluation to the Department of Pathology, King Edward Medical University, Lahore. These included specimens from both sexes and all age groups. They comprised of excised cold solitary thyroid nodules, partial or subtotal thyroidectomy specimens, total thyroidectomy and completion thyroidectomy specimens. The latter consisted of a repeat surgery performed for cases diagnosed previously as thyroid cancer and comprised of complete removal of the remaining (residual) thyroid tissue, the adjacent cervical lymph nodes and any surrounding cervical tissue showing involvement by the tumour or any suspicious areas.

Our results were compiled and analysed as follows. Of the total 662 submitted specimens, 588 (88.82%) cases were from females and 74 (11.17%) cases were from males giving a female to male ratio of about 8:1 (Table I).

The commonest pathological lesion encountered was Colloid goiter (both diffuse and multinodular) which constituted 434 cases (65.55%) out of 662 specimens (Table I). There were 7 additional cases of Colloid goiter with associated findings of hyperplastic changes (4 cases) and subacute lymphocytic thyroiditis (3 cases) (Table I).

The other common lesions were thyroid tumours (benign and malignant) which constituted 151 cases

(22.80%) out of 662 cases. Benign tumours comprised of 113 cases (17.06% of the total thyroid lesions or 74.83% of the tumours) and malignant tumours numbered 38 cases (5.74% of the total thyroid lesions or 25.16% of the tumours (Table I and Table II). Ratio of benign to malignant tumours was 2.97:1 (Table II). Follicular adenoma (FA) was the commonest tumour constituting 108 cases (71.52% of the tumours) followed by Papillary carcinoma (PC) constituting 27 cases (17.88% of the tumours) out of 151 thyroid tumours. The frequency and sex distribution of the thyroid tumours (benign & malignant) is shown in Table II. Ages of these patients ranged from 13 years to 82 years.

Regarding thyroid cancers, Papillary carcinoma was the commonest malignant tumour constituting 27 cases (71.05%) out of 38 cancers. Other malignant tumours included Follicular carcinoma (FC) constituting 4 cases (10.52%), Anaplastic thyroid carcinoma (ATC) constituting 3 cases (7.89%), Medullary thyroid carcinoma (MTC) and Non-Hodgkins lymphoma (NHL) comprising of 2 cases (5.26%) each, out of 38 malignant tumours (Table III). Out of 27 cases of Papillary carcinoma, 10 cases showed cervical lymph node metastasis at the time of initial surgery and 1 case (70 year old female) showed local extension of the tumour upto the overlying skin of the neck. 1 case of Non-Hodgkins Lymphoma in a 42 year old male also showed metastasis to the cervical lymph node.

Other findings in the excised thyroid specimens included 24 cases (3.62%) of diffuse thyroid hyperplasia, with 4 additional cases of colloid goiter showing associated hyperplastic changes (Table I). Thyroiditis was seen in 15 cases (2.26%) as the sole pathology and 3 cases of colloid goiter showed coexistent features of subacute lymphocytic thyroiditis. The breakup and frequency of the various morphological types of thyroiditis is shown in Table IV. All cases of thyroiditis were seen in females in the age range of 13 years to 48 years.

Table 1: Sex distribution and frequency of different thyroid lesions seen in surgically excised thyroid specimens (n=662)

Thyroid lesions	Male	Female	=n	%age
Colloid goiters	42	392	434	65.55
Benign tumours	13	100	113	17.06
Malignant tumours	08	30	38	5.74
Diffuse hyperplasia	04	20	24	3.62
Thyroiditis	0-	15	15	2.26
Hyperplastic nodules	02	7	9	1.35
Colloid nodules	02	6	8	1.20
Completion thyroidectomy	01	6	7	1.05
Colloid cysts	02	04	6	0.90
Colloid goiters with hyperplastic changes	0	04	4	0.60
Colloid goiters with thyroiditis	0	03	3	0.45
Dyshormonogenetic goiter	0	01	1	0.15
Total	74	588	662	100

Female to Male Ratio 8:1

Table II: Sex distribution and frequency of different morphological types of thyroid tumours (n = 151)

Types of thyroid tumours	Male	Female	=n	%age
Benign Tumours (n=113)(74.83%)				
Follicular adenoma	96	12	108	71.52
Hürthle cell adenoma	02	01	03	1.98
Hyalinizing trabecular adenoma	02	00	02	1.32
Malignant Tumours (n=38)(25.16%)				
Papillary carcinoma	23	04	27	17.88
Follicular carcinoma	04	00	04	2.64
Anaplastic thyroid carcinoma	01	02	03	1.98
Medullary thyroid carcinoma	01	01	02	1.32
Non-Hodgkins lymphoma	01	01	02	1.32
Total	130	21	151	100

Ratio of Benign to Malignant Tumours = 2.97:1

Female to Male Ratio of Benign Tumours = 7.69:1

Female to Male Ratio of Malignant Tumour = 3.75:1

Table III: Frequency of different morphological types of thyroid cancers (n = 38)

Types of malignant thyroid tumours	=n	%age
Papillary carcinoma	27	71.05
Follicular carcinoma	04	10.52
Anaplastic thyroid carcinoma	03	7.89
Medullary carcinoma	02	5.26
Non-Hodgkins lymphoma	02	5.26

Table IV: Morphological types of thyroiditis and their frequency (n=18)

Types of Thyroiditis	=n	%age
Subacute lymphocytic (painless) thyroiditis	8	44.44
Hashimoto thyroiditis (chronic lymphocytic thyroiditis)	3	16.66
Colloid goiter with associated subacute lymphocytic thyroiditis	3	16.66
De Quervain thyroiditis (granulomatous / painful) thyroiditis	2	11.11
Acute suppurative thyroiditis (thyroid abscess)	2	11.11

Discussion

Thyroid enlargement with either a solitary nodule, multiple nodules or diffuse involvement is a common clinical presentation in the Surgical Outpatients Clinics of Mayo Hospital, Lahore, where patients from all over Punjab and most parts of the Frontier Province are referred for opinion and surgical expertise. The present work was focused to evaluate the different types of morphological lesions observed in these surgically excised thyroid specimens.

The commonest pathological lesions in our study were Colloid Goiters including diffuse and multinodular goiters which constituted 65-67% of our total surgical thyroid specimens. A study by Qureshi¹⁷ and colleagues at Lahore in 1990 showed multinodular goiters and colloid

goiters to constitute 38.31% and 17.04% cases (i.e. 55.35%) respectively. Another study conducted at Jinnah Post Graduate Medical Centre, Karachi⁽⁴⁾ in 1992 found the prevalence of goiter to be 74.1%, and a research by Sarfraz²² in the Northern areas of Pakistan which constitutes the goiter belt showed nonneoplastic thyroid disorders including goiters and solitary nodules to constitute 89.5% of their cases. A recent study by Imran⁶ in Lahore also showed multinodular goiters and diffuse colloid goiters to be the commonest pathology of the thyroid constituting 50.8% and 39.2% of lesions respectively. A study conducted in Spain by Diez J²⁴ concluded that the commonest lesion observed in enlarged thyroids of older age patients was also multinodular goiter comprising 75% of cases. Another study by Elahi⁽³⁾ reported a 60% prevalence of goiter among adolescent girls attributed to a deficiency of iodine in the diet and water supplies.

Minimal diffuse enlargement of the thyroid gland is seen in many teenagers of both sexes as a physiological response to the complex structural and hormonal changes occurring at the time of puberty. It usually regresses but occasionally may persist, enlarge and become nodular depending on many factors like sex, iodine intake and thyroid autoimmunity³. Iodine is an important element required by the body for the production of thyroid hormones which play a vital role in the metabolism of the body. Its deficiency causes a spectrum of disorders called Iodine Deficiency Disorders (IDD) which include goiter, stunted physical growth, mental retardation, impaired speech, hearing and movement disorders²⁵. Females suffering from iodine deficiency suffer miscarriages, stillbirths, decreased fertility and mentally retarded babies called Cretins⁹. In Pakistan, it is estimated that 20 million people are residing in the Northern endemic goitrous areas and 8 million of them are suffering from one or other forms of IDD²⁵. One million of these people are victims of mental retardation which affects school performance^{7,8,26}.

Dyshormonogenetic goiters (DG) are genetically determined thyroid hyperplastic disorders due to enzyme defects in thyroid hormone synthesis²⁷. There was a single case of this lesion in our study in a 19 year old girl who presented with a large recurrent multinodular goiter and previous thyroid surgery. Her thyroid profile revealed a hypothyroid clinical status. Gross examination of her surgical specimen showed multiple variable sized nodules and cyst formations. Histological examination exhibited variable architectural patterns ranging from microfollicular to cellular solid patterns, papillary formations and marked fibrosis. Other features included marked nuclear atypia, minimal colloid material and irregularity of the nodules. Ghossein and Rosai²⁷ reported 56 cases of DG occurring in 34 females and 22 males in the age range from newborn to 52 years. Common clinical presentation in their study was also hypothyroidism with enlarged multinodular thyroids. Vittal and friends²⁸ reported 37 patients of DG in 5 years

with an equal sex ratio and clinical picture of hypothyroidism and multinodular goiters.

Regarding thyroid tumours or neoplasms (benign and malignant), our 2 year study constituted a total of 151 tumours (22.80%) out of 662 thyroid surgical specimens. Nonneoplastic lesions like colloid goiters, thyroiditis, colloid nodules, hyperplastic nodules and cysts etc constituted 511 cases (77.19%). A study by myself⁶ in the recent past showed nonneoplastic thyroid lesions to constitute of 75.26% cases and tumours to constitute of 24.74% cases. A somewhat similar study by Qureshi and associates¹⁷ revealed neoplasms like adenomas and carcinomas to constitute of 28.9% cases and nonneoplastic lesions to comprise of 71.10% cases. In another study by Ahmad and co-workers², neoplasms constituted 31% cases and nonneoplastic lesions as 69% cases.

Benign tumours constituted 74.83% cases and malignant tumours constituted of 25.16% cases in our study, giving a benign to malignant tumour ratio of 2.97:1. A study by Sarfraz²² in the northern areas of Pakistan, comprised of 65.5% benign tumours and 34.5% malignant tumours. The commonest benign tumour seen in the thyroid gland is the Follicular adenoma. It presents clinically as a discrete solitary cold nodule. Morphologically it is characteristically surrounded by a well developed, thin capsule. Invasion of the capsule and blood vessels is the key feature distinguishing a malignant Follicular carcinoma from benign Follicular adenoma²⁹. Therefore, thorough circumferential sampling of all encapsulated follicular lesions is the key to accurate diagnosis of Follicular carcinoma³⁰. Follicular adenomas were seen in 108 cases (16.31%) out of 662 thyroid surgical specimens. They constituted the second commonest lesion of the thyroid after colloid goiters. A study conducted by Chaudry and Majeed¹³ also found follicular adenomas in 17.8% of surgically excised cold solitary nodules. According to Qureshi¹⁷ et al there were 100 cases (20.3%) of Follicular adenoma in their 487 surgical specimens.

Hürthle Cell tumours (HCT's) are derivatives of the follicular epithelium and characterized histologically by large cells with an abundant granular eosinophilic cytoplasm and distinct cell borders. The criteria for distinction between a Hürthle cell adenoma and Hürthle cell carcinoma are the same as for Follicular adenoma and Follicular carcinoma based on capsular and/vascular invasion³¹. Hyalinizing Trabecular Adenoma (HTA) is a controversial entity; some have considered it a variant of Papillary carcinoma and others consider it a nonspecific entity that may be seen in a variety of thyroid lesions³². It has a distinctive histology reminiscent of that seen in paragangliomas and Medullary carcinoma, showing a prominent trabecular arrangement forming cords or trabecular with an occasional small abortive follicle and prominent hyaline fibrosis³³. We reported 3 cases of HCA (2.02%) and 2 cases of HTA (1.35%). Study by Qureshi¹⁷

quoted 3 cases(3%) of HCA out of 100 cases of adenomas and a similar study by Guadagni et al³⁴ reported HCA to constitute 6.37% of thyroid neoplasms.

Although thyroid enlargements and solitary nodules are common, thyroid cancer is relatively rare. A review of different studies shows variable figures regarding the incidence of malignancy in isolated solitary thyroid swellings. Although many of these nodules are benign, there is a substantial risk of malignancy usually quoted as 20-30%^{11,14,15,16}. According to Mazzaferri¹⁰, of all nodules removed surgically an estimated 42 to 77% are nonneoplastic colloid nodules, 15 to 40% are adenomas and 8 to 17% are carcinomas. A study by Ahmad and associates² shows 23.75% of thyroid nodules to be malignant²⁰. According to him, a thyroid nodule in a male patient should raise a higher suspicion of cancer than that found in a female. His study concluded that 31.25% of thyroid nodules in males were malignant when compared to 21.87% of malignant nodules in females.

In our study thyroid cancers constituted 38 cases (5.74% of the 662 excised thyroid lesions). In a study of 113 thyroidectomy specimens by Ahmad², malignant tumours were seen in 4.4% (5 cases) cases, whereas 95.6% (108 cases) showed lesions like colloid nodules, follicular adenomas, hyperplastic nodules and thyroiditis. Study by Qureshi¹⁷ revealed 42 cases (8.6%) of thyroid cancer out of 487 cases. Another study by Sarfraz²² showed thyroid cancer in 21 cases (3.61%) out of 581 thyroid surgical specimens. In our study, thyroid cancer was seen in 30 females and 8 male cases giving a sex ratio of 3.75:1. In Jensen's study²¹, a female preponderance of 3:1 was noted. Figures from different studies in Pakistan reveal a female to male ratio of 2.6:1¹⁹ and 3.2:1²² for thyroid cancers.

In our study out of 38 malignant cases, Papillary carcinoma was the commonest variety constituting 27 cases (71.05%). Follicular carcinoma was reported in 4 cases (10.5%), Anaplastic thyroid carcinoma in 3 cases (7.89%), Medullary thyroid carcinoma in 2 cases (5.26%) and Non-Hodgkins Lymphoma also in 2 cases (5.26%). These figures are somewhat similar to the study by Shah and Muzaffar¹⁹, who reported their figures of Papillary carcinoma as 69%, Follicular carcinoma as 11.6%, Medullary carcinoma as 9.7%, Anaplastic carcinoma as 5.9% and NHL as 2.9%. According to Ahmad and friends¹⁶, Papillary carcinoma was reported in 58%, Follicular carcinoma in 21.05%, Anaplastic carcinoma as 15.78% and NHL in 5.26% cases. A similar study by Jensen²¹ reported Papillary carcinoma as 68%, Follicular carcinoma as 18%, Medullary carcinoma as 4%, Anaplastic Cancer as 1.4% and NHL as 1%.

The term "thyroiditis" refers to a group of inflammatory diseases affecting the thyroid. Hashimoto thyroiditis the commonest is an autoimmune disease manifesting as goiter, hypothyroidism and elevated antithyroid antibody titres³⁵. In the United States and other countries with an adequate dietary iodine intake, this form

is the most frequent cause of hypothyroidism and goiter affecting 2% of females^{36,37}. A rare but serious complication of this disorder is Non-Hodgkins lymphoma³⁷. Subacute thyroiditis (SAT) encompasses two distinct syndromes: subacute granulomatous thyroiditis (SAGT) and subacute lymphocytic thyroiditis (SALT)³⁸, the former is a self limited painful viral infection^{36,38}. SALT is typically painless, often occurs in the postpartum period (postpartum thyroiditis) and is probably of autoimmune origin^{39,40}. Acute suppurative thyroiditis is another type caused by bacterial infection occurring on a preexisting nodular goiter³⁷. Riedel's struma (fibrous thyroiditis) a rare form with a prevalence of only 0.05% in patients with thyroid disease³⁶, is characterized by extensive extracervical fibrosclerosis and mimics cancer⁴¹. Another rare but well defined entity is "drug-induced thyroiditis", caused by amiodarone, interferon α , interleukin 2 and Lithium^{36,40}.

In our study, subacute lymphocytic thyroiditis (SAT) was the commonest thyroiditis constituting 8 cases (44.44%). Hashimoto thyroiditis was the next common type (3 cases) followed by De Quervain thyroiditis and acute suppurative type constituting 2 cases each. Subacute thyroiditis was also the commonest type seen in the study by Qureshi et al¹⁷ constituting 23 cases (45%) out of 51 cases in their 5 year study. Hashimoto thyroiditis was second on their list constituting 14 cases (27.4%), followed by Riedel's struma comprising of 13 cases and acute suppurative thyroiditis constituting 1 case. Study by Imran⁶ showed thyroiditis in 9 cases (3.6%) out of 250 thyroid specimens. Hashimoto thyroiditis constituted of 6 cases, De Quervain thyroiditis 1 case, Riedel's thyroiditis 1 case and tuberculous thyroiditis 1 case. Analysis of 20 cases of thyroiditis in the study by Intenzo³⁸ showed Hashimoto thyroiditis to be the commonest constituting of 14 cases, subacute granulomatous thyroiditis to consist of 3 cases, postpartum thyroiditis of 2 cases and subacute lymphocytic thyroiditis of 1 case.

Conclusions

Colloid goiter is the commonest lesion observed in thyroid surgical specimens worldwide. Common cause of this condition in our geographical locale appears to be a relative or absolute deficiency of dietary iodine. Universal Salt Iodination (USI) programme is a major sustainable and cost effective strategy for eliminating this preventable disorder and other iodine deficiency related problems.

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