

Sherine I. Salama¹ (MSc).
Layla S Abdullah (MD, FRCPC),
Mohamed H. Al-Qahtani (PhD)²
Jaudah A. Al-Maghrabi^{1,2}
Professor (MD, FRCPC, FCAP)

Department of Pathology¹,
King Abdulaziz University
Hospital, Faculty of Medicine,
Center of Excellence in Genomic
Medicine Research²,
Jeddah, Saudi Arabia

HISTOPATHOLOGICAL PATTERN OF THYROID LESIONS IN WESTERN REGION OF SAUDI ARABIA

BACKGROUND: Partial or complete thyroidectomies are frequently encountered by the practicing pathologist and the possibility of neoplastic disease is of major concern in patients with thyroid nodules. Pathological evaluation of those specimens ranged from non-neoplastic lesion to highly aggressive malignancy. **OBJECTIVE:** This study aimed to document the frequency of different patterns of thyroid diseases as presented to pathology departments at King Abdul-Aziz University Hospital (KAUH) and King Faisal Specialty Hospital and Research centre (KFSHRC) within the last twelve years. **MATERIAL AND METHOD:** All specimens presented to pathology departments at KAUH (1997-2008) and KFSHRC (2000-2008) as thyroidectomies (partial or complete) were retrospectively reviewed and categorized according to their histological appearance. **RESULTS:** The total number of the studied cases was 845 cases. The age of the patients ranged between 9 and 93 years. One hundred seventy eight were males and 667 were female (male to female ratio; 1:3.7). The reviewed cases were classically categorized into two main groups; Non- neoplastic (494; 58.5%) and Neoplastic (351; 41.5%). The non-neoplastic group includes: Multinodular Goiter (311 cases; 36.8 %), hashimoto/chronic lymphocytic thyroiditis (64 cases; 7.6 %), single hyperplastic nodule (51 cases; 6 %), Grave's disease (8 cases; 0.9 %), miscellaneous (58 cases; 6.9%). The neoplastic group includes benign category represented by "Adenomas" and includes 94 cases (11% of all cases, and 26.8 % of neoplastic cases) and the malignant category includes 256 cases, representing 30.3 % of all studied cases and 73% of the neoplastic category. Two hundred and nine cases (81.6 % of malignant) were papillary carcinoma. **CONCLUSION:** Thyroid lesions are more common in Saudi female. The majority of the thyroid nodules in Saudi are non-neoplastic. Papillary carcinoma is the commonest type of thyroid cancer in Saudi society. Thyroid neoplasm is rare in Saudi children.

INTRODUCTION

Diseases of the thyroid are of great importance because most are amenable to medical or surgical management. They include conditions associated with excessive release of thyroid hormones (hyperthyroidism), those associated with thyroid hormone deficiency (hypothyroidism), and mass lesions of the thyroid⁽¹⁾. Thyroid surgical specimens, including partial or complete thyroidectomies are frequently encountered by the practicing pathologist⁽²⁾. From a clinical standpoint, the possibility of neoplastic disease is of major concern in patients who present with thyroid nodules. Fortunately, the overwhelming

majority of solitary nodules of the thyroid proved to be localized, non-neoplastic conditions (e.g. nodular hyperplasia, simple cyst or foci of thyroiditis)⁽¹⁾. An estimated 4% of the adult population is affected by one or more palpable thyroid nodules, most of these nodules are benign⁽³⁾. Overall, thyroid nodules are more common in women, in older individuals, in those with history of radiation exposure, or those with certain diets rich in goitrogens or deficient in iodine⁽¹⁾. This study aimed to document the frequency prevalence of different patterns of thyroid diseases as presented to pathology department at KAUH and KFSHRC.

MATERIAL AND METHOD

All specimens presented to pathology departments at KAUH (1997-2008) and KFSHRC (2000-2008) as thyroidectomies (partial or complete) were retrospectively reviewed and categorized according to their histological appearance. The clinical data of the studied cases were reviewed.

RESULTS:

The total number of the studied cases was 845 cases (table 1). The reviewed cases were classically categorized into two main groups; Non- neoplastic (494; 58.5%) and Neoplastic (351; 41.5%).

The largest group was that of "Multinodular Goiter" (MNG), it involved 311 cases (36.8 % of the whole reviewed specimens and 63 % of non-neoplastic cases), 84 case (27%) were right thyroidectomy specimens, 77 (24.8%) were left thyroidectomy specimens, while 150 (48.2 %) were total thyroidectomies. Of these cases; 57 (18.3%) were males while, 254 (81.7%) were females with male to female ratio 1: 4.5. The age of the studied cases ranged from 13 to 93 years with mean age of 39.4 years. Twenty seven cases were associated with a dominant hyperplastic nodule, twenty one other cases were associated with lymphocytic thyroiditis, while 6 cases with Hurthle cell hyperplasia.

The second group of the non-neoplastic category included the autoimmune thyroid lesions (hashimoto/chronic lymphocytic thyroiditis) which contain 64 cases (7.6 % of all specimens, and 13% of non-neoplastic cases). Only three cases were in males while the rest were females (93.5%). Seventeen cases (40%) were left thyroidectomies, 16 (34.8%) cases were right thyroidectomies, while 13 cases (28.2%) were total thyroidectomies. The age of the cases ranged from 19 to 70 years, with mean age of 40.3 years.

Fifty one cases (6%) were a single hyperplastic nodule, 8 cases (0.9%) were diagnosed as Grave's disease, and 58 cases (6.9%) were miscellaneous cases diagnosed as scar tissue, simple cyst, single colloid nodule, thyroglossal duct cyst and foreign body giant cell reaction.

The second group of the examined cases was that of neoplastic nature. The benign category represented by "Adenomas" included 94 case (11% of all cases, and 26.8% of neoplastic cases). Twenty eight cases (29.8%) were males, while 66 cases (70.2%) were females. The male to female ratio was 1: 2.4. The age of the cases ranged from 11 – 93 years with mean age of 44.8 years. These cases were presented clinically as single nodules, 54 (57.4%) were on the right while 40 (42.6%) were on the left side. Thirteen cases (13.8%) were diagnosed as Hurthle cell adenoma, in which the neoplastic cells acquire striking eosinophilic granular cytoplasm. Only 1 case (1.1%) was designated as "Atypical adenoma" which demonstrated increased cellularity, variation in cell size and nuclear morphology with increased mitotic activity with intact overlying capsule.

The malignant cases were 256, representing 30.3 % of all studied cases and 73% of the neoplastic category. Two hundred and nine cases (81.6 %) were papillary carcinoma, 13 cases (5.1%) were follicular, 13 cases (5.1%) were medullary, 7 cases (2.7%) were anaplastic (undifferentiated) while 5 case (2%) was diagnosed as Hurthle cell carcinoma. Six cases (2.3%) were lymphomas (5 Non-Hodgkin and 1 MALT lymphomas), one case (0.4%) was plasmacytoma, one case (0.4%) was diagnosed as squamous cell carcinoma and one case (0.4%) of the malignant cases was metastatic carcinoma.

The papillary carcinoma (PTC) covered wide age range; from 9 to 93 with a mean age of 39.2 years. Males represented 22% (46 cases)

while females comprised 78% (163 cases). The male to female ratio was 1: 3.5. The cases were slightly more presented in the right than in the left lobes (84 case in the right and 71 in the left lobe) while 54 cases (25.8%) were presented as total thyroidectomies. Most cases were solitary mass in the thyroid gland/lobe, some were multifocal (23 cases), 31 cases were encapsulated lesion while seven cases were presented as a cyst. Thirty eight cases were not detected grossly and only diagnosed incidentally after microscopic evaluation of nodular lesion. 46 cases (22%) were follicular variant, 38 cases (18%) were papillary microcarcinoma, one case was tall cell variant (0.5%) while the rest were conventional (classic) type. Eighteen cases (8.6%) arise in a background of autoimmune thyroiditis (hashimoto/lymphocytic) whereas 25

cases (12%) in MNG. Lymph node metastasis was encountered in 27 cases (13%). All cases revealed the characteristic nuclear features of papillary carcinoma.

The age range of *follicular carcinoma (FTC)* was 17 – 86 years. The mean was 41 years. Male to female ratio was 1 : 1.4 . 7 cases arise in the right lobe while 6 cases on the left. Six of the cases were designated as minimally invasive whereas, the other half were widely invasive. There were 13 cases of medullary carcinoma (MTC). Three cases (23%) involved both lobes, 5 (35.5%) cases involved the left lobe, while the remaining 5 cases (35.5%) involved the right lobe. The age ranged from 24 to 68 with a mean of 50.2 years. Male to female ratio was 1:1.6.

Table (1) Different patterns thyroid diseases

Total number of cases: 845					
Category	no.	%	Category	No.	%
Non- Neoplastic	494	58.5	Neoplastic	351	41.5
-Goiter	311	36.8	*Adenoma	94	11
-Hashimoto/Lymphocytic thyroiditis	64	7.6	*Carcinomas:		
-Hyperplastic nodule			-Papillary	209	24.7
-Grave's/diffuse hyperplasia	51	6	-Follicular	13	1.5
-Miscellaneous conditions	8	0.9	-Medullary	13	1.5
	58	6.9	-Undiff./anaplastic	7	0.8
			-Hurthle cell	5	0.6
			-Lymphoma	6	0.7
			-Plasmacytoma	1	0.1
			-Squamous cell ca.	1	0.1
			-Metastatic carcinoma.	1	0.1

DISCUSSION:

The burden of thyroid diseases in the general population is enormous. The epidemiology of thyroid diseases in iodine- sufficient areas deals mainly with sporadic goiter, thyroid autoimmune diseases, and thyroid cancer. As reported in North America ⁽⁴⁾ 50% of people in the community have microscopic nodules, 15% have palpable goiter and 3.5% have occult papillary carcinoma. The incidence of *Multinodular goiter* (MNG) differs according to the countries and seems to be widely dependant on the iodine status. Many authors ⁽⁵⁾ confirmed the notion that thyroid disease are more prevalent in females. The females in our MNG series (n=311) represent 81.7% , while in similar study in Yemen they represent 92.5%. The mean age of our study (39.4 years) was concurrent with the age in the Yemanien study (35.2 years) ⁽⁶⁾. According to some published articles from different countries ⁽⁷⁻¹²⁾ in order to establish the incidence of carcinoma, 7 -17 % of the patients operated for goiter, during the histopathological examination, a pattern of MNG associated to carcinoma was evidenced. In comparison to our study, only 25 cases (12%) of MNG proved histologically to harbor malignancy. In accordance with published works, in our study the histopathological type of carcinoma more frequently associated to MNG was shown to be the papillary. ⁽¹³⁾.

Hashimoto thyroiditis (HT) is an autoimmune inflammatory disease characterized by widespread lymphocyte infiltration, fibrosis, and parenchymal atrophy and oxyphilic changes. HT affects approximately 5% of the population, is usually diagnosed in the fourth to sixth decade of life and is approximately 15 times more common in women ⁽¹⁴⁾. Historically, the presence of HT was thought to increase the risk of developing thyroid lymphoma. In 1955, Dailey and colleagues ⁽¹⁵⁾ reported an increased association between HT and PTC, but not lymphoma. Since this initial report, the causal association of the two diseases

remains controversial ⁽¹⁶⁾, with various authors reporting no association between HT and PTC while others describe a variable frequency as high as 38%⁽¹⁴⁻¹⁶⁾ . Sulimani et al reported that 10 out of 81 patents with thyroid carcinoma had coexisting Hashimoto's thyroiditis documented histologically ⁽¹⁷⁾. This association was recently owed to the common RET/PTC gene rearrangement shared between the two condition in close to 95% of cases ⁽¹⁸⁾. This has led to the proposal by one of these groups to consider these cases as being affected by PTC even if not microscopically seen ⁽¹⁹⁾. In a study carried out in university of Texas ⁽¹⁶⁾, primary thyroid malignancy was identified in 25.1% of cases of HT; PTC was the most common histological type identified (87.6%), followed by FTC (10.4%), medullary (0.5%), and anaplastic (1.5%). These results were in concordance to our study in which 25 cases of the HT (39%) showed primary malignancy; 18 cases of them (72%) were PTC, while one case was medullary (4%). All 6 cases of lymphomas in our series were in background of HT.

The epidemiology of *follicular adenoma* (FA) is difficult to analyze because of the lack of consistent criteria for distinguishing hyperplastic nodules and adenomas. Solitary thyroid nodules occur in 4-7% of adults in iodine sufficient areas. In iodine deficient areas, the rate can rise to 50%. In our study as well as internationally females are more commonly affected than males ⁽²⁰⁾. Whereas, the risk for progression to malignancy in males is relatively greater ⁽²¹⁾. Many histologic variants of FA have been recognized. In our study ; 13 cases (13.8%) were Hürthle cell variant, 1 case was atypical variant, whereas, the rest were the conventional type. In the context of Hürthle cell neoplasm, the mean age of our study cases was less than that in literature ⁽²²⁾ (38.4 versus 46.7 years) while, the females predominance in our study was in concordance with the literature.

Papillary thyroid carcinoma (PTC) is the most common type of thyroid malignancy. Most tumors manifest in age 20 – 50 years, the mean age at the time of diagnosis is approximately 40 years. The female to male ratio 4:1.⁽²⁰⁾ The age in our study was in concordance to literature (mean 39.2 years), whereas, the female to male ratio 3.5:1). PTC is described as the most common pediatric thyroid malignancy^(20, 23-28) but only one case was encountered in a child. The youngest patient in our series was 9 years old. Among the multiple histological variants described in literature, the only variants diagnosed in our study were; follicular (22%), papillary microcarcinomas (18%) and one case (0.5%) was tall cell variant. Involvement of cervical lymph nodes is very common in PTC. This metastasis may not be clinically apparent because of their small size and normal nodal consistency⁽²⁹⁾. That may explain our small number of cases presented with nodal metastasis in our study (13%).

After exclusion of the follicular variants of other tumors, *follicular carcinoma (FC)* becomes relatively rare tumor, it accounts for 10-15% of clinically evident thyroid malignancy. It is more in women, and tends to occur in patients in the fifth decade^(20, 29). FC represents 5.1% of the malignant cases in our study with female to male ratio 2.3 : 1. The age was more than that encountered in PTC (mean 41 years).

Medullary thyroid carcinoma (MTC) comprises 5 – 10% of all thyroid malignancies. The mean age at presentation is 50 years^(20, 29). This is in concordance to our study in which MTC comprises 5.1% with mean age of 50.2 years, which may indicate that all our cases were sporadic forms.

Only 7 cases (2.7%) in our malignant series were undifferentiated (anaplastic) carcinomas, all were elderly. Three were females and the other four were males. The background of PTC was evident in one case.

In conclusion, thyroid lesions are relatively a common disease in Saudi Arabia. Thyroid lesions are more common in female. The majority of the thyroid nodules are either non-neoplastic or benign neoplasm. Papillary carcinoma is the commonest type of cancer in Saudi society. Thyroid neoplasm is very rare in Saudi children.

DISCLOSURE:

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