

RESEARCH ARTICLE

Histopathological Patterns of Thyroid Disease in Al-Madinah Region of Saudi Arabia

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Abstract

Objectives: This study aimed to characterize the histopathological pattern of thyroid lesions among Saudi patients and to highlight the age and gender variations of these lesions as base line data. **Materials and Methods:** We retrospectively analyzed the data from thyroid specimens received at the Department of Pathology, King Fahad Hospital, Madinah, Saudi Arabia from January 2006 to December 2013. **Results:** The 292 thyroidectomy specimens received during the study period came from 230 (78.8%) females and 62 (21.2%) males giving a female: male ratio of 3.7:1. Age of the patients ranged from 14 to 95 years with a mean age 39.7 years. Two hundred and eleven (72.3%) cases were found to be non-neoplastic and 81 (27.7%) cases were neoplastic. The non-neoplastic group included: colloid goiter, including both diffuse and nodular goiter (170 cases; 58.2%), nodular hyperplasia (28 cases; 9.6%), Hashimoto/chronic lymphocytic thyroiditis (12 cases; 4.1%), and Grave's disease (1 case; 0.3%). In neoplastic lesions, there were 7 benign tumors and 74 malignant tumors. Among the benign tumors, 5 were follicular adenomas and 2 were Hurthle cell adenomas. Papillary carcinoma was the commonest malignant tumor accounting for 87.8% of all thyroid malignancies, followed by lymphoma, follicular carcinoma and medullary carcinoma. The size of papillary carcinoma was more than 2 cm in 40 cases (76.9%). **Conclusions:** Non-neoplastic thyroid lesions were more common than neoplastic ones. Colloid goiter was the most common lesion. Follicular adenoma was the commonest benign tumor and papillary carcinoma was the commonest malignant lesion. There appears to be a slightly increased trend of papillary carcinoma diagnosis, most being diagnosed at an advanced stage.

Keywords: Thyroid diseases - histopathology - Saudi Arabia - Madinah.

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Introduction

Thyroid diseases are quite common. The incidence of thyroid diseases varies from one geographical region to another, mainly depending upon iodine deficiency status (Vanderpump, 2011). According to the American Cancer Society, about 60,220 new cases of thyroid cancers were estimated in 2013, out of which more than three quarters (45,310) were expected in females (Siegel et al., 2013). Although Thyroid cancer is reported to be rare in UK, it is one of the fastest growing tumors in both sexes (Cancer Research UK, 2011). In addition to these figures; a number of studies on thyroid disease are also available from all over the world including Gulf Cooperation Council (GCC) countries and Kingdom of Saudi Arabia (KSA), in the recent literature of past decade. Just to mention, some of the studies in the introduction section, these would be elaborated in greater detail during discussion while comparing with results of our present study figures.

During the last decade, from Europe, we have studies on thyroidectomies from Ireland (Chukudebelu et al., 2012), Belgium (Vincent, 2008) and Greece (Misiakos et

al., 2006; Griniatsos et al., 2009). Amphlett et al. (2013), observed the recent trends in the incidence, geographical distribution, and survival from thyroid cancer in Wales. From Turkey, Veyseller et al. (2009), looked into thyroidectomies for benign diseases, while Yildiz et al. (2014), studied the rising trends of papillary carcinoma of thyroid. Recent registry based studies are also available from Finland (Hakala et al., 2012) and Switzerland (Rapiti et al., 2014).

In a review of cancer epidemiology in the Pacific Islands, workers found thyroid carcinoma to be frequent in American Samoan females, Vanuatu and among populations born in French Polynesia. They also found thyroid cancer to be a major public health problem for Melanesians of New Caledonia, due to highest ever incidence reports in that population (Moore et al., 2010).

From Africa, similar works were done in Zambia (Mirzakarimov et al., 2012) and Nigeria (Ariyibi et al., 2013). There are a number of studies from Asia, just to cite some of the recent works on histopathological patterns of thyroid diseases in Pakistan (Sushel et al., 2009; Khanzada et al., 2011; Fahim et al., 2012) and Bangladesh (Rahman

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et al., 2013); and thyroid cancers from Beijing, China (Yang et al., 2013). In a study from India, on adolescent and young adults, thyroid cancer was found to be one of the five most common cancers (Kalyani et al., 2010); whereas in Iranian population, thyroid cancer is the 7th most common cancer in females with an overall 5-year survival rate of 88% (Khayamzadeh et al., 2011). In a study spanned over 25 years, on the incidence of common cancers in Hong Kong, a number of cancers including thyroid cancers were found to be on an increase throughout the study period (Xie et al., 2012). A study from Nepal on head and neck carcinomas reported that the most common site of primary lesion was larynx, followed by the thyroid (Lasrado et al., 2012).

From the GCC countries and region around KSA, two epidemiological studies have reported thyroid cancers to be second commonest tumor in the GCC countries except Bahrain and Kuwait (Al-Zahrani and Ravichandran, 2007; Al-Hamdan et al., 2009). In two excellent review articles covering cancer epidemiology in Arab world and South East Asia, researchers also concluded thyroid carcinoma to be second commonest cancer in Saudi females (Salim et al., 2009, Salim et al., 2010). These findings have recently been confirmed in the KSA by Hussain et al. (2013). From other Arab countries, Abdulkareem (2010), did a prospective study on thyroid biopsies in Iraq. Darwish et al. (2006), from Bahrain did a histopathological study on the pattern of thyroid diseases, while in Yemen, Abdumughni et al. (2004), did a retrospective histopathological work on thyroid carcinoma. Al-Zaher et al. (2008), shared their thyroid carcinoma perspective and experience from a tertiary care hospital in the United Arab Emirates. Sokouti et al., (2013) studied the clinical and histopathological features of thyroid cancer on patients under 25 years in Tabriz, Iran. Thyroid cancer has been reported to be one of the top five commonest cancers in females, from Jordan (Ismail et al., 2013), Oman (Nooyi and Al-Lawati, 2011), Yemen (Ba Saleem et al., 2010), Turkey (Eser et al., 2010) and Qatar (Bener et al., 2008).

In KSA, a number of histopathology-based articles on thyroid lesions are present in the recent literature i.e. from the Western region (Qari, 2004; Salama et al., 2009), Jeddah (Alamoudi et al., 2011), Aseer region (Refeidi et al., 2010) and Eastern province (Al-Amri, 2012). Investigators also found that there are significant clusters of thyroid carcinoma in the Eastern and Riyadh regions of KSA (Al-Ahmadi and Al-Zahrani, 2013).

Finally there is one article from Madinah (Al-Bouq et al., 2006), which was the work done by colleague Surgeons on a data which is now more than a decade old (April 2000 to July 2003). This study in addition to demographic data, also included clinical aspects and surgical complications related to thyroidectomies. Thus our study is a completely different histopathology-based study, including new data and tumor parameters (such as size and capsular / lymphovascular invasion) of the thyroidectomy specimens in Al-Madinah Al-Munawwarah region, which is a now rapidly growing and developing city. Our present study is a larger scale study spread over eight years and we will also compare the pathological data from the previous study to observe any change in the

trend or patterns of thyroid lesions during the last decade.

Materials and Methods

This was a retrospective study of thyroid specimens received at the Department of Pathology, King Fahad Hospital, Madinah, Saudi Arabia from January 2006 to December 2013. All patients presenting with thyroid enlargement, who underwent any type of thyroid operation (i.e. lobectomy, subtotal thyroidectomy, or total thyroidectomy) were included in this study. Demographic data including patients' age, sex and the histopathologic diagnosis were collected from pathology reports and analyzed by software program SPSS 17. The thyroid diseases were classified on histological grounds into: colloid goiter (both diffuse and nodular goiter), adenoma (both follicular and hurthle cell type), all types of thyroiditis and carcinoma including all subtypes that is follicular, papillary and medullary carcinoma.

Results

A total of 292 thyroid specimens were received in the department of Pathology, King Fahad Hospital, Madinah, Saudi Arabia from January 2006 to December 2013. There were 230 (78.8%) females and 62 (21.2%) males giving a female: male ratio of 3.70:1. The age of the studied cases ranged from 14 to 95 years with a mean age 39.7 years. The majority of the thyroid diseases (n=224; 76.7%) were seen in the age group 21-50 years. The young age group (≤ 20 years) and the elderly age group above 60 years constituted 4.8% and 10.3% respectively (Table 1, 2).

In this study, non-neoplastic lesions were more common found 72.3% (n=211) cases. The most common cause of goiter was colloid goiter including diffuse and nodular goiter and accounts for 58.2% of the whole reviewed specimens and 80.6% of all non-neoplastic lesions (Table 1). Of these cases 136 (80%) were females and 34 (20%) were males with female to male ratio 4:1. Most of the patients (n=132; 77.6%) were between 21-50 years of age (Table 2). Twenty-eight cases (9.6%) of nodular hyperplasia, 12 cases (4.1%) of hashimoto/chronic lymphocytic thyroiditis and 1 case (0.3%) of Grave's

Table 1. Age and Sex Distribution of 292 Patients with Thyroid lesion

Thyroid Lesion	No. (%)	M/F	Age (Year)
Non-Neoplastic	211 (72.3%)	41/170	39.7
Colloid goiter	170 (58.2%)	34/136	39.3
Nodular hyperplasia	28 (9.6%)	3/25	36.9
Hashimoto thyroiditis	11 (3.8%)	2/9	48.6
Lymphocytic thyroiditis	1 (0.3%)	Male	24
Grave's disease	1 (0.3%)	Male	40
Neoplastic	81(27.7%)	20/61	40
Adenoma	7 (2.4%)	1/6	31.1
Follicular adenoma	5 (1.7%)	All female	31.6
Hurthle cell adenoma	2 (0.6%)	1/1	30
Carcinoma	74 (25.3%)	19/55	41.7
Papillary	65 (22.3%)	15/50	42.2
Lymphoma	4 (1.4%)	All female	26.5
Follicular	3 (1%)	2/1	39
Medullary	2 (0.6%)	All male	50

Table 2. Age Distribution of 211 Patients with Non-Neoplastic Thyroid Lesions

Age	Colloid goiter	Hyperplastic nodule	Hashimoto thyroiditis	Lymphocytic thyroiditis	Grave's disease	Total
≤20	7	-	-	-	-	7 (3.3%)
21-30	38	11	2	1	-	52 (24.6%)
31-40	60	5	3	-	1	69 (32.8%)
41-50	34	10	4	-	-	48 (22.7%)
51-60	16	-	-	-	-	16 (7.6%)
>60	15	2	2	-	-	19 (9%)
Total	170 (80.6%)	28 (13.4%)	11 (5.2%)	1 (0.4%)	1(0.4%)	211 (100%)

Table 3. Age Distribution of 81 Patients with Neoplastic Thyroid Lesions

Age	Follicular adenoma	Hurthle cell adenoma	Papillary carcinoma	Follicular carcinoma	Medullary carcinoma	Lymphoma	Total
≤20	1	1	3	1	-	1	7 (8.6%)
21-30	2	-	17	1	-	2	22 (27.2%)
31-40	1	1	15	-	1	1	19 (23.5%)
41-50	1	-	13	-	-	-	14 (17.3%)
51-60	-	-	8	-	-	-	8 (9.8%)
>60	-	-	9	1	1	-	11 (13.6%)
Total	5 (6.2%)	2 (2.5%)	65(80.2%)	3 (3.6%)	2(2.5%)	4(2.5%)	81 (100%)

disease were found (Table 1).

Neoplastic lesions were found in 27.7% (81 cases) of thyroid diseases and seen mainly adenomas and carcinomas. Seven cases of adenoma (8.6% of the neoplastic category and 2.4% of all studied cases) were found with a female: male ratio 6:1. Five cases of follicular adenoma and two cases of Hurthle cell adenoma were diagnosed. The age of the cases ranged from 20 to 44 years with a mean age 31.1 years (Table 1).

Seventy-four cases of malignant neoplasms were found, representing 91.4% of the neoplastic category and 25.3% of all thyroid lesions. The female: male ratio was 2.9:1. Papillary carcinoma was the commonest malignant tumor in this study seen in 80.2% (n=65) of all neoplastic lesions (Table 1). Of these cases 15 (23.1%) were males and 50 (76.9%) were females with a female: male ratio 3.3:1. Most of the patients (n=45; 69.2%) were between 21-50 years of age (Table 3). Twenty cases (30.7%) were follicular variant, 10 cases (15.4%) were papillary microcarcinoma, 2 cases were tall cell variant (3.1%), while the rest were conventional (classic) type of papillary carcinoma. The size of the tumor was less than 2 cm in 15 cases (23.1%) and more than 2 cm in 40 cases (76.9%). Capsular invasion and lymphovascular involvement were seen in 9 cases (13.8%) and 7 cases (10.7%) respectively.

Other types of thyroid carcinoma were lymphoma (Hodgkin/non-Hodgkin); 4 cases (1.4%), follicular carcinoma; 3 cases (1%), and medullary carcinoma; 2 cases (0.6%). No cases of anaplastic carcinoma were seen in our study.

Discussion

Both the neoplastic and non-neoplastic diseases of thyroid are common all over the world, with a varying frequency and incidences depending upon iodine deficiency status (Vanderpump, 2011). Numerous epidemiological and hospital based researches are available. Although

it is reported to be rare in some developed countries like UK, however it is one of the fastest growing tumor in both sexes (Cancer Research UK, 2011). Similarly a number of studies on thyroid disease are also available from all over the world including GCC countries (Darwish et al., 2006; Abdulkareem, 2010) and KSA (Qari, 2004; Salama et al., 2009; Refeidi et al., 2010; Alamoudi et al., 2011; Al-Amri, 2012), in the recent literature. There is only one article from Madinah (Al-Bouq et al., 2006), which was the work done on a decade-old data (April 2000 to July 2003). In our present larger study, in addition to demographic data, we have also included details of histopathological features including size of tumor and capsular / lymphovascular invasion, wherever available. We have also compared the two pathological data from the region for any change in the frequency and patterns of thyroid lesions during the last decade.

Thyroid diseases have historically been known primarily to affect the female sex. Similar are the finding in our study and recent literature from around the world ranging from 71.5% females in a study of 358 thyroidectomies from Pakistan (Fahim et al., 2012) to as high as 88.7% females from Zambia (Mirzakarimov et al., 2012). Intermediate figures of 77.46% from Ireland (Chukudebelu et al., 2012), 82.4% from Bangladesh (Rahman et al., 2013) and 84.8% from Turkey (Veyseller et al 2009) have also been reported in the studies from last couple of years. Within the Middle East region, we have figures of 76.36% females in 110 thyroidectomy cases from Bahrain (Darwish et al., 2006) and 78.9% females in 845 thyroidectomy cases from Western region of KSA (Salama et al., 2009). In the study of Thyroid diseases from Madinah, Al-Bouq et al., (2006) found 84.65% females in their total 189 cases; this figure is much higher than the figures of 78.8% females in our present study.

Regarding age range of thyroidectomies, Chukudebelu et al. (2012) from Ireland in their 1003 consecutive thyroidectomies reported the age range of patients from

4-87 years and the mean age was 51 years; while a group from Pakistan in their 358 thyroidectomy specimens found an age range between 10 to 70 years with a mean of 32 years (Fahim et al., 2012). Veyseller et al. (2009) from Turkey in 323 thyroidectomy specimens found an age range of 13 to 80 years with a mean age of 42.6 years. In a study from Greece, there were 264 patients between the ages of 18 and 89 who underwent thyroid surgery (Misiakos et al., 2006). Hussain et al. (2005) from Karachi, Pakistan in 662 cases reported an age range from 12 to 70 years. Similarly, Liu Q et al. (1998) from Chicago, USA, in their 106 patients who underwent total thyroidectomy for benign disease found an age range of 16-82 years with an average of 46 years. Whereas on the malignant side, a study from Kazakhstan report peak incidence of thyroid cancer in 70 years and older population (Igissinov et al., 2011). From the GCC countries, we find a study of 110 cases from Bahrain, quoting the age range of different disorders of thyroid separately i.e. for colloid goiter was 19-67 years, malignancy 21-82 years, follicular adenoma 20-69 years, primary thyrotoxicosis 20-42 years and Hashimoto's thyroiditis 20-56 years. Colloid goiter had a peak at age group 31-40 years (Darwish et al., 2006). From KSA Salama et al., (2009) in their 845 cases, have reported an age range of patients between 9 and 93 years. Al-Bouq et al (2006) from Madinah, in their study of 189 thyroidectomies, found a peak frequency of goiter in third and fourth decade of life.

We found non-neoplastic diseases to be more common than neoplastic lesions. Our findings are consistent with all the recent studies on thyroidectomy specimen, that have reported that non-neoplastic lesions are more common than the neoplastic lesions (Chukudebelu et al., 2012; Fahim et al., 2012; Mirzakarimov et al., 2012; Rahman et al., 2013). In addition to some of the studies from across the world, the researchers from the region and KSA also report predominance of benign diagnoses in the thyroidectomy specimens (Al-Bouq et al., 2006; Darwish et al., 2006; Salama et al., 2009; Abdulkareem, 2010).

Within the group of non-neoplastic lesion in the thyroid specimen, there is a consensus in all the remote and recent studies, that colloid goiter is the commonest lesion. A group working in an endemic area of Greece, report 54.9% nodular goitre in their 264 cases of total thyroidectomies specimens (Misiakos et al., 2006). From Zambia, Mirzakarimov et al. (2012), in their 239 thyroid specimens found 172 cases (71.96%) of colloid goiter. From Bangladesh, Rahman et al. (2013), found colloid goiter in 92.05% of all non-neoplastic diagnosis in 108 thyroidectomy specimens. Similarly, recent works from Pakistan report colloid and multinodular goiter as the commonest in their experiences (Hussain et al., 2005; Khanzada et al., 2011; Fahim et al., 2012). Within the Arab world, Abdulkareem (2010) from Iraq report 59% colloid goitre (nodular and diffuse); while Darwish et al., (2006) from Bahrain in their 110 cases report 55 cases (45.5%) of nodular goiter and concluded it to be the most common thyroid disease. From Western KSA, Salama et al., (2009), studied 845 cases of thyroidectomies and found 311 cases (36.8 %) of multinodular goiter, which was the commonest diagnosis in their study.

Only few groups of investigators have mentioned the frequency of other non-neoplastic thyroid lesions in the recent literature. Misiakos et al. (2006), from Greece after reporting 54.9% nodular goitre, mentions 14.7% hyperplastic nodules and 3.8% Hashimoto thyroiditis in their series of 264 cases. From Zambia, in contrast to the commonest colloid goitres (71.96%), only 1.2% thyroiditis, 8.1% thyroid cysts and 3.8% toxic goitre were reported (Mirzakarimov et al., 2012). Similarly Rahman et al. (2013), from Bangladesh, found only three cases (2.77%) of thyroiditis and four cases (3.7%) of thyroglossal duct cyst in their 108 case series. Hussain et al. (2005), from Pakistan in their total 662 cases, found 26 cases of thyroiditis (lymphocytic thyroiditis was seen in 22 (3.32%) as compared to 4 cases (0.06%) Hashimoto's thyroiditis). Regionally from Bahrain, after the common disease of nodular goiter and neoplastic lesions, primary thyrotoxicosis was found in 8% cases (age range 20-42 years) and Hashimoto's thyroiditis in 7% cases having an age range of 20-56 years (Darwish et al., 2006). Salama et al., (2009) from Western KSA while studying the histological patterns of thyroid lesions, after the commonest diagnosis of multinodular goiter (311 cases; 36.8 %) found the following breakdown of lesser frequent diagnoses: 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%).

Within the neoplastic lesions, malignant lesions predominated over benign adenomata in our study. Recently, Chukudebelu et al. (2012), from Ireland in their 1003 consecutive thyroidectomies found that 742 were benign lesions and 261 were malignant, of which papillary carcinomas accounted for 75.1%, follicular carcinomas 13.4%, Hurthle cell carcinoma 1.5%, medullary thyroid carcinomas 3 %, undifferentiated carcinomas 3%, others (lymphoma and squamous cell carcinomas) 4%. A group from Nigeria, in their 1,207 cases series found, 174 cases (14.4%) of thyroid gland neoplasms. Seventy six (43.7%) cases were benign and 98 (56.3%) cases were malignant. Follicular adenoma accounted for 89.5% of benign thyroid neoplasms with a peak in the 5th decade. Papillary carcinoma was the most common malignant thyroid neoplasm in this study with a peak in the 3rd decade (Ariyibi et al., 2013). From Eastern Province of KSA; Al-Amri (2012), studied total of 143 patients with thyroid tumors who underwent thyroidectomy. Their median age was 37.5 years. Females were predominantly affected (81%) with female to male ratio of (4:29). Thyroid carcinoma accounted for (75%) while benign tumors for (25%). The most common thyroid epithelial cancer was papillary type (74%). Non-epithelial cancer in the form of thyroid lymphoma accounted for (4.89%) of the cases. Our results are consistent with the international remote and recent data regarding the pattern and frequency of neoplastic diseases of thyroid, including the predominance of papillary carcinoma. A study from Iran on cancers in elderly population, concluded that incidence rates of breast and thyroid cancers in old women were greater than in elderly men (Akbari et al., 2011). In a chinese study of 1,685 cases, 222 had thyroid carcinomas and frequency

of thyroid cancer showed a progressive decrease from the younger to the older patients (Yang et al., 2011).

Regarding the parameters of advanced disease and aggressiveness in the papillary carcinoma, we looked into the size of tumor at the time of diagnosis and features like capsular and lympho-vascular invasion, in the histopathology reports. Our cases were diagnosed in an advanced stage in contrast to the findings from recent studies from Europe, which conclude that there is a trend of decreasing size of thyroid carcinoma at the time of diagnosis (Griniatsos et al., 2009; Hakala et al., 2013). However our results are consistent with the findings of research group from KSA, which also conclude large tumor size and advanced stages of papillary thyroid carcinoma at the time of diagnosis (Al-Nuaim et al., 1996).

Comparing our recent study in the Madinah region with the previous study done about 8 years back on the diseases of thyroid (Al-Bouq et al., 2006), there is slightly increased trend of papillary carcinoma diagnosis during the two compared study periods. In the previous study, total cases of papillary carcinoma diagnosed in the period between April 2000 and July 2003, were 34 out of total 189 cases (17.98%), while in our study period of January 2006 to December 2013; 65 cases of papillary carcinoma were diagnosed out of total 292 thyroidectomies (22.26%). Our finding regarding increased trend of papillary carcinoma diagnosis is also consistent with that of Yang et al. (2013), from Beijing who found histologically confirmed 4594 primary tumors out of 4883 cases accounting for 94.08% of total cases. Papillary carcinoma was the most common subtype accounting for 77.31% (3775/4883) of total cases. They concluded that among all the pathological types of thyroid cancer, the proportion of papillary carcinoma has risen from 51.55% (50/97) in 1995 to 87.63% (673/768) in 2010. Similarly in a recent study from Turkey, Yildiz et al. (2014), report 216 thyroid carcinoma which account for 13.6% of their thyroidectomies and concluded that there is a significant increase in the frequency of papillary and micropapillary carcinoma while comparing their two study periods. Within the KSA, Hussain et al. (2013), from Riyadh report that a total of 2292 patients with thyroid cancer were treated from 2000 to 2010. Thyroid cancer constitutes about 9% of all malignancies. Papillary adenocarcinoma was the most common histological subtype followed by follicular variant of papillary carcinoma. Median age at diagnosis was 40 for females and 44 years for males. They concluded that thyroid cancer incidence rates have increased exponentially between 2000 and 2010 and there is significant geographical variation in the incidence of thyroid cancer throughout the Kingdom. Thyroid cancer has become the second most common cancer among young Saudi women. In addition to being consistent with the hospital based histopathological studies that papillary carcinoma is the commonest malignancy of thyroid and its frequency is increasing. Our findings also conform to the recent registry based studies from Finland (Hakala et al., 2012) and Wales (Amphlett et al., 2013); regarding the increasing trend of papillary carcinoma in Europe. Wang et al., (2013) in their study found incidental papillary carcinoma in 147 out of their 709 cases and concluded

that these are more common in females.

Thus in conclusion, the histological spectrum of thyroid diseases in the thyroidectomy specimens from Al-Madinah region is similar to that seen around the globe and the region. Non-neoplastic thyroid lesions are more common than neoplastic ones, with colloid goiter being the most common lesion. Follicular adenoma is the common benign tumor and papillary carcinoma is the commonest malignant lesion. There appears to be a slightly increased trend of papillary carcinoma diagnosis which is being reported at an advanced stage in our region.

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