

Changing Patterns of Thyroid Pathology and Trends of Surgical Treatment

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Summary:

Background: There were definite changes in pathologies involving thyroid gland all over the world with increasing incidence of thyrotoxicosis and differentiated malignancies.

Patients and methods: 224 patients were operated upon by the same surgeon during 15 years period. Those patients were divided into two groups (GI from June 1990 up to June 2000) and (GII from June 2000-June 2005).

Results: female to male ratio was 3.3:1. The most common presentation among both groups was Multinodular goiter (MNG) 76.8%. toxic goiter was recorded in 24% of patient with increase among GII patients. A significant effect of stress on the increasing incidence of thyrotoxicosis was elicited in more than 50% of patients with thyrotoxicosis. Malignant thyroid tumors constituted 8.5% of the diseases and they were mostly papillary carcinoma. There was increase incidence of malignant thyroid tumors among GII patients (2.65% in GI versus 13.5% in GII). The trend toward more radical surgery was evident among GII patients

Conclusion: thyroid malignancy and thyrotoxicosis are increasing in our country and stress factor might play a role in this rise. Due to the previous changes, the surgeon attitude had changed toward more radical surgery.

Keywords: thyroid diseases, thyrotoxicosis, thyroid malignancy, thyroidectomy , stressful life events,

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Introduction:

Thyroid diseases are common all over the world, but the incidence of different pathologies was variable depending on many factors like iodine deficiency or replacement. It was evident that there were changes in the pathology in developing countries where there is a definite increase in the incidence of differentiated thyroid cancer (1). Papillary carcinoma is the most prevalent endocrine malignancy, and the reported incidence of papillary carcinoma has more than doubled in many countries during the past half century (2, 3). In recent years, there have been also many reports about the possible association between stressful life events (SLEs) and onset of Graves disease (GD) (4,5). Surgery for differentiated thyroid malignancy should be more radical, but controversy remains regarding the best surgical approach for toxic Multinodular goiter (6) or for bilateral benign MNG (7). We tried in this study to outline some of the features of thyroid diseases in Iraq, and to elucidate whether there was a change in the behavior of the diseases and clinical types. The effect of stress on the incidence of thyrotoxicosis was studied and compared to the effect in other countries. Subsequently we tried to find the change in surgical management trends during this period of 15 years.

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Patients and methods:

This is a prospective review involving 224 patients with thyroid diseases operated upon by a single surgeon during 15 years period from June 1990 till June 2005. The patients were seen in the private clinic and the operated upon either in Baghdad teaching hospital or Hammad Shihab teaching hospital or in Private hospitals. About thirty patients were dropped from the study due to incomplete data. The patients were divided into two groups; group I (GI) included (105) patients managed during the period from June 1990 till June 2000 and group II (GII) included (119) patients managed between June 2000 till June 2005. For each patient a special form was filled with information including age, residency, and personal history, family history of thyroid disease, history of thyroid problem, results of physical examination, investigations, and the type of surgery performed with the results of histopathology. Special attention was given to the age, sex, history of stress in thyrotoxic patients, type of surgery and complications. Stressful life events (SLEs) were investigated as those events which put the patient under high stress like the death of one of the relatives, job loss, or severe psychological trauma. Hormonal assay including T3, T4, and TSH was done, while thyroid scan was done for few patients due to unavailability. Ultra sound study with Doppler (very late cases) was done to most patients in GII and few patients in GI because it was not available at the early years of the study.

Results:

The total number of patients was 224 patients with females constituted the majority (172 patients, 76.8%) as compared to male patients (52 patients, 23.2%), with more females in GII as compared to GI which was not statistically significant (tab.1).

Table 1: distribution of thyroid diseases by sex

	GI		GII		total	
	No.	%	No.	%	no	%
male	32	30.5%	20	16.8%	52	23.2%
female	73	69.5%	99	83.2%	172	76.8%
total	105		119		224	

Male: female =1:3.3. p=<0.005

The majority of patients in both groups were residents in Baghdad and central governorates of Iraq, as 97 patients (92.4%) in GI and 100 patients (84%) in GII were from these parts of the country. Clinically the most common presentation was multinodular goiter (MNG) which was the presenting type in 172 patients (76.8%) followed by clinically solitary nodule in 34 patients (13.2%) (table2). There was less cases of SN in GII as compared to GI while the opposite was true for MNG

Table (2) clinical presentations of goiter by study groups.

	Group I (GI)		Group II (GII)		Total	
	No.	%	No.	%	No.	%
Solitary nodule	22	21	12	10.1	34	15.2
Diffuse goiter	8	7.6	10	8.4	18	8
Multinodular goiter	75	71.4	97	81.5	172	76.8
Total	105		119		224	

Thyrotoxicosis was present in 54 patients (24%) being more frequent among GII patients (table 3). In GI thyrotoxicosis was present in 21% of the patients while in GII it constituted about 27% of the patients, this difference was not statistically significant. Toxic MNG was present in 18 patients (82.2%) in GI, while it was less common in GII as it was found in 21 patients (65%). on the other hand toxic DG was higher in GII as it was found in 9 patients (28.2%) compared to 3 patients (13.65%) in GI. There was no difference between the two groups regarding the occurrence of toxic SN as it was found in only one patient (4.5%) in GI and in two patients (6.2%) in GII. (Tab4)

Table (3) thyrotoxicosis among GI and GII.

	GI		GII		total	
	No.	%	No.	%	No.	%
Toxic	22	21	32	27	54	24
Non toxic	83	79	87	73	170	76
Total	105		119		224	

The occurrence of thyrotoxicosis in GI was comparable in males (10 patients, 45.5%) and females (12 patients, 54.5%), while in GII it was much higher

in females (28 patients, 87.5%) as compared to male patients (4 patients, 12.5%). In general male: female ratio was about 1:3

Most of the patients with toxic goiter were below 40 years of life (46 patients, 82.1%) with no much difference between the two groups (GI and GII).

Table (4) distribution of thyrotoxicosis by sex, type of goiter and groups

	male	female	MNG	Solitary N	Diffuse G	Total
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
GI	10 (45.5)	12 (54.5)	18 (82.6)	1 (4.5)	3 (13.6)	22 (21)
GII	4 (12.5)	28 (87.5)	21 (65.6)	2 (6.2)	9 (28.2)	32 (27)

Definite history of stressful life events was linked to the establishment of thyrotoxicosis in 7/22 patients with thyrotoxicosis (31.2%) in GI, as compared to the much higher prevalence in GII as it was present in 15/32 patients with thyrotoxicosis (46.9%) in GII. Thyroid malignancy was diagnosed in 19 patients (8.5%). The majority of whom were females (13 patients -68.4%). Most of malignant tumors were papillary carcinomas (17 patients, 89.5%). Malignant tumors of thyroid were much more common among GII patients (table 5) (p=<0.005). All the malignant tumors in GI were papillary carcinomas and all of them were diagnosed postoperatively because there was no facility to do FNA at that time. One patient in GI presented with solitary nodule with no lymph nodes metastasis while the other two patients presented as MNG and one of them had lymph nodes metastasis.

Table (5) types of malignant thyroid tumors by groups.

Type of tumor	GI= 105		GII = 119		Total= 224	
	No.	%	No.	%	No.	%
Papillary Ca.	3	2.65	14	11.8	17	7.14
Follicular Ca	-		1	1.68	1	0.44
Lymphoma	-		1	1.68	1	0.44
Total	3	2.65	16	13.44	19	8.5

Other types of malignant tumors were diagnosed in GII. Follicular carcinoma was recorded in one patient and non Hodgkin's lymphoma in other patient and two patients had follicular variant of papillary carcinoma. Metastasis of papillary carcinoma to the cervical lymph nodes in GII was recorded in seven patients; four of them presented primarily with palpable cervical lymph nodes which were proved to be metastatic papillary carcinoma. In one patient with follicular carcinoma the metastasis was to the pelvic soft tissue as he presented with large gluteal soft tissue mass and FNA yielded adenocarcinoma. Thorough investigations proved the mass to be metastatic follicular carcinoma of thyroid origin. Cases of malignant tumors in both groups were equally distributed between central part of Iraq and southern parts as there were 9 patients from the central part of

Iraq and another nine patients from the southern part of Iraq. Only one patient with malignancy was from the northern part. All the patients involved in this study underwent surgical treatment and the types of surgery were either subtotal thyroidectomy, near total thyroidectomy, or total thyroidectomy. The most common operation was subtotal thyroidectomy in both groups (80.75%), more commonly used in GI (93.3%). Near total thyroidectomy was more common in GII (29.9%) ($p < 0.005$), while total thyroidectomy was used only in 4 patients (3.4%) in GII (tab.6).

Table (6): Types of surgical operations in GI and GII.

procedure	GI		GII		TOTAL cases	
	No.	%	No.	%	No.	%
Subtotal thyroidectomy	98	93.3	83	69.75	181	80.8
Near total thyroidectomy	7	6.6	32	26.9	39	17.4
Total thyroidectomy	-	-	4	3.4	4	1.8

The incidence of complications varied between the two groups (tab.7). Simple wound Haematoma was the commonest complication and it was more common among GII patients. Other mild complications like stitch abscess or granuloma were less common. Serious complications in the form of recurrent laryngeal nerve palsy occurred in five patients; four of them were in GII. Two of those in GII had bilateral recurrent laryngeal nerve palsy following surgery for third time recurrent goiter in one patient and following near total thyroidectomy for non Hodgkin's lymphoma in the other patient. Both patients were managed by temporary tracheostomy for few weeks with eventual cure. Temporary hypocalcaemia was detected in 6 patients; five of them were among GII. They were managed by supplementation of calcium for few days. Only two patients required One Alpha tab. (alphacalcidol) for few weeks with resultant cure. Three of those with temporary hypocalcaemia developed symptoms of hypocalcaemia following surgery for toxic goiter recurrent goiter were seen mostly in GI, while it could not be assessed in GII because many patients failed to show for follow up. Recurrent thyrotoxicosis was equally distributed among the two groups.

Table (7): distribution of postoperative Complications by groups

Complications	GI	GII	Total
	No. (%)	No. (%)	No. (%)
Wound Haematoma	1 (0.95)	9 (7.5)	10 (4.5)
Unilat. Rec. lary. nerve palsy	1 (0.95)	2 (1.7)	3 (1.3)
Bilat. Rec. lary. Nerve palsy	-	2 (1.7)	2 (0.9)
Superior lary. Nerve injury	-	4 (3.4)	4 (1.8)
Hypocalcaemia	1 (0.95)	5 (4.2)	6 (2.7)
Stitch granuloma	4 (3.8)	1 (0.85)	5 (2.2)
Recurrent goiter	3 (2.85)	unknown	-
Recurrent thyrotoxicosis	2 (1.9)	2 (1.7)	4 (1.8)
Keloid	2 (1.9)	2 (1.7)	4 (1.8)

Discussion:

In the present study thyroid diseases were more common in females as compared to males ; a finding consistent with many previous studies (8,9,10,11,12,13,14). This female preponderance did not change during the study period. The possible explanation for this result is the increase need for iodine by females especially during puberty, pregnancy and lactation, and possibly the dietary iodine deficiency which is the case in many countries among which is Iraq. The most common clinical presentation was Multinodular goiter (MNG) in the form of colloid MNG or Toxic MNG in both groups, although in recent years there was a slight increase in the occurrence of diffuse goiter especially diffuse toxic goiter (Grave's disease) , but there was also increase in the occurrence of MNG. This high occurrence of MNG in Iraq is nearly similar the neighboring countries like Turkey (15). In South Korea, as a representative of Asia, a national study adopted WHO classification revealed adenomatous goiter as the most common followed by follicular adenoma and lastly carcinoma (18, 19). These findings were not supported by the European figures; a higher incidence of solitary nodules (about 50%) was registered as compared to MNG (40%) (9). In Africa, different studies revealed different results. In a study carried in Uganda diffuse colloid goiter was twice as common as nodular goiter (12) while in Guinea the studies showed solitary nodule to be the most common clinical diagnosis (11). In Ethiopia MNG made up the majority of thyroid diseases (54.2%) (18). these differences can be explained by different levels of iodine in the diet which might play a role in the pathogenesis of nodular goiter. Thyrotoxicosis was common among patients in the present study; in addition there was a significant increase incidence of thyrotoxicosis over the years of the study especially among female patients. A similar increase in thyrotoxicosis was also detected in other countries especially in Africa like Nigeria (13),

Ethiopia (18), and Uganda (20). The increasing occurrence of thyrotoxicosis in these countries was attributed to the increasing use of iodized salt to combat endemic goiter, a cause which might play a role in Iraq where iodized salt was introduced during the last two decades. Despite that, we feel that stressful life events (SLEs) might be a more significant trigger for thyrotoxicosis especially among patients who already had goiter. This study was carried over a very stressful period in the history of Iraq, characterized by war and economic sanction. These events put a severe burden on Iraqi people, so we propose, as suggested previous workers in the field from different countries also subjected to the stress of similar events as in Serbia, Nigeria, or Portugal that stressful life conditions might be the cause of increase incidence of thyrotoxicosis (4, 5, 12, 13, and 14). The current study demonstrated that increase occurrence of thyrotoxicosis was mainly among patients with diffuse goiter (Grave's disease), a fact that was stressed upon by Matos –Santos et al (4, 5) in two studies proving a relationship between SLEs and diffuse goiter. They attributed the association between Grave's disease and stress to the effect of SLEs on immune system of the patients. They also demonstrated that SLEs do not seem to have any conclusive relationship with the onset of toxic MNG. In Serbia which had passed through similar war conditions and stress, Panskovic N , et al also reported increase incidence of Graves disease and he also put SLEs as one of the provoking factors . another finding in the present study, which we couldn't detect in other studies, the fact that most of the patients with thyrotoxicosis were below the age of 40. This finding might also support the assumption of the effect of stress on the development of thyrotoxicosis, as people in this age group are usually suffer more than other age groups from the stress of life events. The increasing occurrence of thyrotoxicosis in female patients in the present study might also support this assumption. Due to the situation of war and military action, women became increasingly responsible for daily life activities which put them under higher stress as compared to the normal situation where they had amore relaxed life style. The second important finding of the current study was the changing incidence of malignant tumors of thyroid gland. Papillary thyroid carcinoma (PTC) is the most prevalent endocrine malignancy, and the recorded incidence of PTC has been more than doubled in many countries, especially in the West, during the past half century (2, 3, and 8). In Ireland, studies showed a breakdown of thyroid carcinoma over a 10 year period in which also papillary carcinoma was the most common thyroid malignancy (22). In Ukraine the results of studies following Chernobyl accident showed an increase in papillary microcarcinoma (19).The present study had shown a statistically significant rise in the cases of thyroid

malignant tumors over the period of the study and papillary carcinoma was the most frequently detected type. In other Asian countries as in Sirelanka (1) a similar preponderance of papillary carcinoma was reported with decreasing incidence of anaplastic carcinoma which was attributed to the use of iodized salt, but a similar conclusion can not be made from the present study as anaplastic carcinoma was not reported .The occurrence of thyroid carcinoma in Korea was reported to be high and the most common type was papillary carcinoma accounting for about 80% of cases of thyroid carcinomas (10, 23). In Africa, the picture is different as in Nigeria where the overall occurrence of malignant thyroid tumors is similar to the results of this study, but the most common type was the well differentiated follicular carcinoma (21). In Ethiopia ,the incidence of malignant thyroid tumors was about 21% and papillary carcinoma was the most common type in one study(24), while in another study the incidence of differentiated thyroid carcinoma was much less (2.7%) (11). in countries neighboring to Iraq, as in Turkey, an increased prevalence of carcinoma was reported after Chernobyl disaster (9). In Saudi Arabia which is another neighboring country to Iraq, they reported a similar incidence of thyroid carcinoma to ours and again papillary type was the commonest but they reported a higher incidence of other types of carcinoma. Their results also showed malignant tumors to be more common in male patients rather than females (11, 25). For patients included in the present study there was no difference in the distribution of malignant thyroid tumors related to Iraqi governorates. The lower frequency in patients from the northern parts of Iraq is not factual because during that period of the study the political situation did not permit free movement of patients from the northern parts to Baghdad. During the last decade there was a change in the behavior of surgery towards more radical surgery as Near total thyroidectomy (NTT) or Total thyroidectomy (TT) especially for toxic MNG and even for large non toxic MNG (2). It was found that TT and NTT are safe and effective approach in these conditions and in thyroid carcinoma (7). Due to the changes of the pathologies of thyroid gland, and the change in the behavior of surgeons allover the world toward more radical surgery, there was a real change in the extent of surgical excision of the gland. During the early period of this study the surgery most commonly conducted was subtotal thyroidectomy (STT), but with time there was a significant increase in the use of more radical procedures especially Near total thyroidectomy and to lesser extent Total thyroidectomy. This change in the attitude towards more extensive surgery was mostly due to the increase in the incidence of thyroid carcinoma among the second group. It was also observed that although recurrent MNG was not very common among the first group, the more radical

surgery for GII patients was associated with no recurrence at least during the study period. In fact the increasing use of TT and NTT in our practice was following the changing practice in the West (15, 26), but in the developing countries, the most common surgical procedure employed is still STT (10). This change in the behavior does not seem to be associated with rise in the complications (15, 26), as it is also evident in the present study through the comparison of complications in both groups. In conclusion, the definite rise in the incidence thyrotoxicosis could be due to increasing stressful life conditions affecting Iraqi population but this should be studied more thoroughly well in future studies involving more patients to be more representative. The rise in the number of malignant thyroid tumors especially papillary carcinoma may be due also to stress, or changing type of diet, or to exposure of Iraqi people to depleted Uranium or other pollutants. This again needs further studies to prove. The changing behavior toward more extensive surgery is safe and better for managing carcinoma, toxic goiter and large MNG.

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