Thyroid cancer in Yemen

Yasser A. Abdulmughni, MBBS, FRCSI, Mohammed A. Al-Hureibi, MBBS, PhD, Khalid A. Al-Hureibi, MBBS, Mohammed A. Ghafoor, MBBS, MD, Ali H. Al-Wadan, MBBS, PhD, Yahia A. Al-Hureibi, MBBS, FACHARTZ.

ABSTRACT

Objectives: To evaluate the characteristics of thyroid cancer (TC) patients in regard to demographic distribution, histological variants, mode of presentation and modalities of diagnosis and treatment.

Methods: We retrospectively audited the records of 97 consecutive cases with histologically proved thyroid cancer between 1997 and 2001 presenting to the Kuwait University Hospital, Sana'a, Yemen.

Results: Patients with TC in this study comprise 17.7% of goiter patients who were admitted at the same period. Females constituted 89.7% (n=87), and males 10.3% (n=10). The average age of diagnosis was 38.4 years. More than two thirds were at the age of ≤40. Among patients with goiter, the percentage of carcinoma was higher in the following groups, males (37.9% versus 16.6%, p=0.028), patients aged ≥47 (25.8% versus 12.6%, p=0.001), patients with enlarged lymph nodes (9.3% versus 3.8%, p=0.020), and patients with recurrent disease after being operated for a presumably benign disease (8.2% versus 2.9%, p=0.012). The average period since patients noticed the swelling until seeking medical help was 4 years. Most patients (90%) came from highland areas. Multinodular swelling was the most common clinical finding (43.3%), and hoarseness was the most common symptom (17.5%). In histopathological examination, papillary carcinoma accounted for 93.8% of the cases and papillary microcarcinoma was found in 10 cases (10.3%). The papillary/follicular carcinoma ratio was 22:1. Hormone assay and ultrasonic imaging were the most commonly used investigations. Sub total thyroidectomy was the most common procedure used in treatment (39%).

Conclusion: Not all histological variants of TC are represented in this study. Papillary carcinoma formed the bulk of TC cases. Salt iodization program might have an effect on the incidence of thyroid malignancy, and on the papillary/follicular carcinoma ratio. Better level of expertise is needed in the field of fine needle aspiration and ultrasonography. A consensus has to be reached, which is based on our environment and capabilities, where TC has to be managed aggressively by experienced surgeons. Yemen is in real need of a national cancer registry to assess the problem on a national level.

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Thyroid malignancy is the most common endocrine malignancy.[1] Worldwide there are approximately 500 peer-reviewed studies published every year on thyroid cancer (TC). There was only one study came out of Yemen, which is nearly 12 years and it reported TC in multinodular goiter. It is a well known fact that thyroid carcinoma is more prevalent in areas with endemic adenomatous goiter, especially the follicular type.[2] The Republic of Yemen lacks a national cancer registry and there is no reliable data available, nevertheless a registry of patients who travelled abroad (1989-1993) for cancer treatment revealed that thyroid carcinoma represented 8.3% of the cancer cases in that series of 685 patients and was the third most common cancer in females.[3] However, this does not represent the real rate since that centre is not a referral one and not the only one where cancer patients diagnosed before leaving abroad for cancer treatment. National

From the Department of Surgery (Abdulmughni, Ghafoor, Al-Wadan), Department of Internal Medicine (M. Al-Hureibi), Department of Anesthesia (Y. Al-Hureibi), University of Sana'a, Sana'a, *Yemen*, and the Department of Surgery (K. Al-Hureibi), Hull Royal Infirmary, Hull, *United Kingdom*.

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Address correspondence and reprint request to: Dr. Yasser A. Abdulmughni, Assistant Professor, Department of Surgery, Faculty of Medicine, Sana'a University, PO Box 2481, Sana'a, *Yemen*. Tel. +967 73761714. Fax. +9671 440-777. E-mail: yabdulmughni@yahoo.co.uk

cancer registry if found would provide the actual rate of thyroid malignancy. The reported rate in the literature of thyroid carcinoma among all malignancies is approximately 1%.[4-6] The thyroid malignancy is quite common in the Middle East countries, such as Kuwait, where it accounts for the second most common cancer in females.[7] Among patients with thyroid swelling, it had been found in one series of Yemeni patients that approximately 30% of them had thyroid malignancy;[8] this is far much more than reported in other regions such as United States of America (5.8%), Libya (9.7%), and other areas. The management of thyroid carcinoma in the 1970's and 1980's was difficult due to the lack of the proper diagnostic tools, which made the differentiation between benign and malignant lesions impossible until surgical intervention and histopathological examination were carried out. Recently, new diagnostic tools were introduced in the course of diagnostic work up of thyroid swelling in Yemen, such as ultrasonic imaging, thyroid hormone assay, and fine needle aspiration cytology. This coincided with the national salt iodization program that was launched by the World Health Organization with the cooperation of the Ministry of Health to combat the iodine deficiency and associated disorders such as goiter. It has been recently a matter of debate how to manage thyroid carcinoma, and there were 2 opinions, one is supporting the aggressive approach and the other is favoring a more conservative one, since it is believed that aggressiveness will not affect the survival. In this paper we are trying to present a descriptive study of thyroid carcinoma in recent years in Yemen, and this is discussed in relation to age, sex, and geographical distribution. However, in the absence of national cancer registry, reasonable extrapolations can be derived. Therefore, we would like to compare our results with those reached previously before the launching of salt iodization program and before introduction of new diagnostic tools. Also, we would like to audit our local experience in the management of patients with thyroid cancer in Kuwait University Hospital (KUH), Sana'a, Yemen and try to combine this with views and experiences of others in terms of different lines of treatment and to come up with recommendations, which we believe, suit our capabilities and circumstances in Yemen in order to reach a departmental consensus to manage thyroid cancer in KUH.

Methods. We retrospectively examined the records of all patients who were diagnosed to have thyroid carcinoma from 1997-2001 in Kuwait University Hospital, which is a major referral hospital in the Capital Sana'a, Yemen. The following details were documented: 1) the distribution in regard to gender, age, and geographical areas; 2) the pattern of clinical presentation and diagnostic work up, 3) postoperative histopathological findings, and surgical procedures.

We studied 97 patients represent approximately 17.7% of patients who were admitted at the same period suffering from goiter and underwent postoperative histopathological examination. Females constituted 89.7% (n=87) and males constituted 10.3% (n=10). The average age at diagnosis is 38.42 ± 13.28 years, ranged between 14 and 70 years; more than two thirds of the patients were at the age of ≤40 (**Table 1**). The age difference between females and males was not statistically significant ($p>0.05$). Among patients with goiter, carcinoma was found more in males (37.9% versus 16.6%, $p=0.028$), patients aged 47 or more (25.8% versus 12.6%, $p=0.001$), patients with enlarged lymph nodes (9.3% versus 3.8%, $p=0.02$), and patients with recurrent goiter after being operated for a presumably benign condition (8.2% versus 2.9%, $p=0.012$). The average period since patients noticed any symptoms until seeking medical help was approximately 4 ± 3.56 years. For geographical distribution, more than 90% of patients came from highland areas, with an average altitude of 1000 meters above sea level. **Tables 2 and 3** summarize the most common clinical presentations and physical findings.

Results. In histopathological examination, the most common type of carcinoma was papillary, which accounted for 93.8% of the cases (**Table 4**). Papillary microcarcinoma accounted for 11% of cases of papillary carcinoma and approximately 10% of the total cases of thyroid malignancy in this series. For diagnostic examination and procedures, hormone assay and ultrasound were most commonly used (62% and 48% of cases). Most patients who underwent hormone assay (n=62) were euthyroid (88.7%). There was no significant difference between malignant and benign conditions in regard to ultrasonic findings ($p>0.05$). Of the 97 patients, 39 underwent fine needle aspiration

Table 1 - Intervals of patients diagnosed with thyroid carcinoma (N=97).

Age interval	Frequency	%
13-20	7	7.2
21-30	28	28.9
31-40	31	32
41-50	10	10.3
51-60	17	17.5
61-70	4	4.1
Total	**97**	**100**

Table 2 - Symptoms accompanying thyroid swelling.

Symptoms	Patients n	(%)
Hoarseness	17	(17.5)
Pain	15	(15.5)
Dyspnea	13	(13.4)
Thyrotoxic symptoms	8	(8.2)
Dysphagia	4	(4.1)
Symptoms of hypothyroidism	3	(3.1)

Table 3 - Physical findings.

Physical findings	Patients n	(%)
Multinodular swelling	42	(43.3)
Unilateral swelling	22	(22.7)
Solitary nodule	14	(14.4)
Diffuse swelling	14	(14.4)
Enlarged lymph nodes	9	(9.3)

Table 4 - Diagnosis by histopathology.

Diagnosis	Frequency	(%)
Papillary carcinoma	91	(93.8)
Follicular carcinoma	4	(4.1)
Anaplastic carcinoma	1	(1)
Lymphoma	1	(1)
Total	**97**	**(100)**

Table 5 - Frequency of surgical procedures.

Procedure	Frequency	(%)
Subtotal thyroidectomy	38	(39)
Lobectomy	21	(21)
Hemithyroidectomy	13	(13)
Near total thyroidectomy	8	(9)
Total thyroidectomy	8	(9)
Incisional biopsy	7	(7)
Total thyroidectomy with dissection	1	(1)
No surgical intervention	1	(1)
Total	**97**	**(100)**

cytology before surgery. Indirect laryngoscopy is carried out routinely for all patients who are due to undergo thyroid surgery. Subtotal thyroidectomy was the most common procedure performed; it was carried out for 39% of the patients (**Table 5**). There were 2 (2.2 %) cases that developed postoperative complications, one patient developed hypoparathyroidism after undergoing subtotal thyroidectomy, and the other had a recurrent laryngeal nerve injury after undergoing hemithyroidectomy.

Discussion. As Kuwait University Hospital is a major referral hospital and it is the only free of charge main hospital in the City, it serves a great portion of the population in Sana'a. In general, women are nearly 8 times more likely to be affected with TC, although in patients with goiter, men are more likely to have TC if they present with goiter. Patients took a long time to seek consultation for the first time, and this can be explained by educational and cultural backgrounds. According to the results, one has to be cautious when encountered with patients with goiter who present after the age of 47, with a recurrent goiter, or with enlarged lymph nodes; especially that the diagnostic tools in our setting, such as ultrasonic imaging and fine needle aspiration cytology, were not helpful in differentiating benign from malignant lesions, another thing which adds to the difficulty in the diagnosis of malignant lesions is the presence of malignant disease inside a multinodular swelling, which is dealt with usually as a benign condition. In this series 43% of the cases presented with a multinodular swelling which contained malignancy inside it. The reported incidence of malignancy among patients with goiter varies widely; in some series it was found to be 5.4% and 5.8%.[9,11] Nevertheless, in some areas it is as high as 30.7%.[12] Patients with thyroid malignancy in this series represent of 17.7% of patients with goiter who presented at the same period of study. This malignancy rate is much less than that reported previously in Yemen (30%).[8] This difference might be attributed to the improvement in the intake of dietary iodine. A national iodization program has been launched in 1995 by the WHO and Ministry of Health. This raised the percentage of households who consumed iodized salt from 22-60%.[13] After implementing the program of salt iodization, the total goiter rate has dropped from 32% in 1991 to 16.8% in 1999.[14] The evidenced role of goiter as a strong risk factor for thyroid cancer,[15] and the reported decreasing incidence of thyroid carcinoma in some areas following iodine supplementation,[16] might explain the change in malignancy rate after salt iodization.

If iodine prophylaxis program is improved further, until we can reach the non-endemic rate of goiter

(<5%), this might have a great effect on the overall incidence of thyroid carcinoma. Hormone assay was carried out for 62% of patients; most of them were euthyroid. It is regarded that hormone assay is not informative in malignancy, since patients can be euthyroid, hyper-or hypothyroid. Approximately half of the patients (n=49) underwent ultrasonic imaging, in fact ultrasonic imaging was not able to differentiate between malignant and benign lesions; the findings were not significantly different in both groups with benign and malignant goiter ($p>0.05$); although the ultrasound can aid in distinction of solitary nodule from a multinodular goiter, this distinction is somewhat academic as most now feel that the risks of a dominant nodule in a multinodular goiter are the same as the risks of a solitary nodule.[17] In addition to that, although ultrasound differentiates solid from cystic lesions; but it has been found that solid lesions are not more prone to be lesions, instead, they have the same propensity if not higher than solid lesions to be malignant.[18] In this series, approximately two thirds of the patients (**Table 3**) presented with a unilateral or bilateral multinodular swelling rather than a solitary nodule, which makes the role of ultrasound questionable. Maybe the most beneficial role of ultrasound would be in case of localizing of fine-needle aspiration biopsy (FNAB) in case of small or non-palpable nodules, which are difficult to localize for sampling. In spite of the existence of suspicious ultrasonic features in thyroid nodules, this needs experienced radiologist and these features are not definitive; hence, should be weighed in the whole clinical picture. In our centre FNAC is still a non-established diagnostic tool, whether due to its unavailability or due to lack of expertise. Thyroid scan is not yet available in Yemen, that if exists would be a useful tool to detect cold nodules that are more prone to be malignant. The main histopathological finding was papillary carcinoma (93.8 %), which is higher than the reported rate in the Western and developed countries (70-80%),[19] similarly, the low incidence of follicular carcinoma (4.1%) is much <15-25% reported in international literature,[20] this pattern as opposing to that reported should be investigated. The ratio of papillary to follicular carcinoma is much more less than what reported previously (1.7/1),[8] in this study its 22 to 1, this might be attributed to the correction of the status of iodine deficiency since follicular carcinoma is found more frequently in iodine deficient areas,[2] whereas papillary carcinoma was found to be more in iodine excessive areas;[21] hence, this might explain the alteration in papillary carcinoma ratio compared to the time before initiation of salt iodization program. This assumption is supported by other studies that showed that ratio of papillary/follicular carcinoma increased after iodine deficiency is being corrected.[22] Ten percent of the cases were found to have papillary microcarcinoma, and this contributes to the difficulty in the diagnosis and raises the question of extent of surgical resection of such tumor, which if not associated with distant metastasis, has a rather benign course.[23] Although, surgical treatment is the key management of thyroid cancer, determining of the optimal surgical procedure has been controversial; several opinions currently exist regarding the management of differentiated thyroid carcinoma, these include extent of surgical resection and postoperative thyroxin suppression. The most common surgical procedure was subtotal thyroidectomy (39%), more aggressive procedures were carried out less frequently, and this is because of the failure to identify malignant cases preoperatively. Therefore, most procedures were carried out for presumably benign conditions. Another possible reason for the low percentage of radical procedures is the fear to injure the recurrent laryngeal nerves and parathyroid glands, and this is due to the lack of good experience in thyroid surgeries. Radioactive iodine treatment is not available to treat postoperative residual disease. Conservative treatment might not be justified due to the multifocality of the papillary carcinoma, which is considered as an indication of total thyroidectomy. The study shows that we do not have a uniform protocol for the management of TC. In fact many papers suggest that total lobectomy or at the most subtotal thyroidectomy constitutes adequate therapy for papillary carcinoma and questioned whether total thyroidectomy worth the price in papillary or minimally invasive follicular carcinoma, since it achieves very similar results without the high risk of complications associated with the more radical procedures.[24-32] While accepting the efficacy of the above conservative approach, we think it would be more useful for us to adopt in our environment a more aggressive approach as of the following reasons: 1. To remove completely the primary site of malignancy 2. The multifocality of the disease in many cases 3. To lower the probability of recurrence especially in the light of the indolent behavior of the disease and the loss of follow up in many cases. The risk of recurrent laryngeal nerve injury and hypoparathyroidism, which are the main complications of thyroidectomy, can be kept to the minimum by confining the practice of thyroid surgery to dedicated and competent surgeons. Suppression with thyroxin is reasonable since we do not have I^{131} for ablation; also the current literature is in agreement that all patients with differentiated thyroid carcinoma will benefit from thyroxin suppression treatment, which improves the survival rate.[33] Not all histological variants of TC are represented in this study. Papillary carcinoma formed the bulk of TC cases. Patients took long times to present. Salt iodization program might have an effect on the incidence of thyroid malignancy, and on the papillary/follicular carcinoma ratio. Better level of expertise is needed in the field of fine needle aspiration and ultrasonography to avoid making wrong surgical decisions for presumably benign conditions. A consensus has to be reached, which is based on our

environment and capabilities, where TC has to be managed aggressively by experienced surgeons. Additional researches on the epidemiological risk factors for thyroid cancer, particularly for gender, and region, is needed to explain the elevated rate of thyroid malignancy among patients with goiter. The numbers involved in this study are not significant to make absolute conclusions on a national level and we still lack the knowledge on the real extent of the problem of thyroid cancer in Yemen. The establishment of national cancer registers could overcome this problem, and this can be established by the Ministry of Health where all health institutions would provide relevant information regarding all patients with a confirmed diagnosis of thyroid cancer, and subsequent treatment.

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