

Prevalence of differentiated thyroid cancer in 810 cases of surgically treated goiter in Yemen

Mansour Al-Jaradi,* Abdulkhalik Sallam,* Hikmat Jabr,* Angela Borda,† Myriam Decaussin-Petrucci,‡ Nicole Berger‡

BACKGROUND: In 1990, the World Health Organization (WHO) suggested that severe iodine deficiency exists in Yemen. Therefore, we looked at the prevalence of differentiated thyroid goiter in 810 cases consecutively treated by surgery for goiter.

METHODS: This was a retrospective study of 810 surgically operated cases of goiter over a 5-year period (1999-2003). All cases were evaluated on H&E stained sections from embedded, 10% buffered formalin fixed tissue blocks. Special stains and immunohistochemical analysis were done in Yemen and abroad. Most patients were older than 20 years of age and were from the high altitude areas (2000 to 2600 meters above sea level), where iodine deficiency disorders (IDD) are well documented.

RESULTS: In the 810 cases, 729 (90%) were females and the remaining 81 (10%) were males, with female-to-male ratio of 9:1. Differentiated thyroid cancer (DTC) was found in 170 (21%) cases, including 148 (86.4%) females and 22 (13.6%) males. Nearly 60% of the cases were in the age group of 21-40 years. Papillary carcinoma was the most common type of DTC (164 cases, 96.5%).

CONCLUSIONS: In a Yemeni population, which has a high prevalence of iodine deficiency, 21% of patients operated on for nodular goiter without pre-operative fine needle aspiration biopsy had thyroid cancer, mostly of the papillary type. In this study, males and elderly patients with goiter had a higher chance of having malignancy.

From *Sana'a University, Departments of Pathology and Pediatrics, Faculty of Medicine, Yemen; †University of Medicine and Pharmacy, Tirgu Mures, Romania; ‡Centre Hospitalier Lyon Sud, Service d'Anatomie Pathologique, Pierre Bénite, France

Correspondence:

Dr. Mansour Al-Jaradi FCPSP, Service d'Anatomie Pathologique, Centre Hospitalier Lyon Sud, Pierre Benite, 69495 Lyon cedex, France.

mansouraljaradi@yahoo.com

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In the USA, Pakistan and France, thyroid cancer accounts for 1.5%, 1.2% and 1% of cancer cases, respectively.^{1,2,3} In Yemen, there is no cancer registry, but there is a nationwide effort to establish a single cancer registry. The Republic of Yemen is located in the southern part of the Arabian Peninsula and is broadly divided into three regions, each with unique topographical and climatic conditions.⁴ Sixty percent of the terrain is highlands, 25% is coastal plain extending over 2500 kilometers (along the Red and Arabian Sea) and the remaining 15% in the east is desert.⁵ Yemen health authorities did not perceive iodine deficiency disorder (IDD) as a real health problem until 1991. Goiter is still a national problem in Yemen.⁶ In 1990, the first iodine nutrition status study was carried out in certain areas of the northern parts of the country by WHO, which concluded that IDD is a problem in Yemen.⁵

Of about 500 studies on thyroid cancer annually from around the world, only a few concern Yemen.⁷ Therefore, we determined the frequency and sex and age distribution of operated goiter and differentiated thyroid cancer (DTC) in cases of operated goiter, and the morphology of DTC.

Methods

A total of 810 surgically treated cases over a 5-year period (January 1999-December 2003) were reviewed in this retrospective study. The majority of the cases were from the Department of Pathology in Al-Kuwait University Hospital, and the rest were from the Department of Pathology in Al-Thawra Teaching Hospital (Sana'a, Yemen). All cases were handled by the standard method of fixing in 10% buffered formalin for at least 24 hours. All cases were studied macroscopically, with representative tissue pieces submitted for automatic processing machine (Shandon, Thermo Electron Corporation, Waltham, MA USA). Finally, tissues embedded in paraffin were cut by rotary and sliding microtomes and stained in haematoxylin and eosin stains. Histochemical special stains were used in Yemen and immunohistochemical stains were used in France.

The goiter in this study was defined as a nodular or diffuse enlargement of the thyroid gland of any cause.⁸ The diagnosis of goiter was made according to the classical description.^{9,10} The malignant lesions were classified according to the WHO classification.¹¹ Papillary carcinoma is defined as a tumor with strict specific diagnostic nuclear features, regardless of the structure (papillary, follicular or both). Follicular carcinoma is defined as a tumor with follicular architecture without cytological characteristics of papillary carcinoma, which is either minimally or widely invasive carcinoma, the former when there is partial capsular tumor invasion and the latter when there are complete capsular tumor invasion and vascular tumor emboli.¹²

More than one pathologist studied almost all of the cases, while the difficult cases were given for consultation to international experts in France (Hospital Lyon-Sud). All the cases were reported in duplicate (one copy for the patient and the other copy for the hospital archives).

Results

The majority of the 810 cases were females (729 cases, 90%) while 81 cases (10%) were males for a female-to-male ratio 9:1. The age of most of the 810 cases was between 21 and 40 years (Figure 1).

Among the 170 cases of DTC, papillary carcinoma was the most common histological type (164 cases, 96.5%). Only a few cases were follicular carcinoma (6 cases, 3.5%). The majority of DTC cases were females (148 cases, 86.4%). In the DTC cases, the female-to-male ratio was 6.7:1. More than half of the DTC cases (101 cases, 59.4%) were between

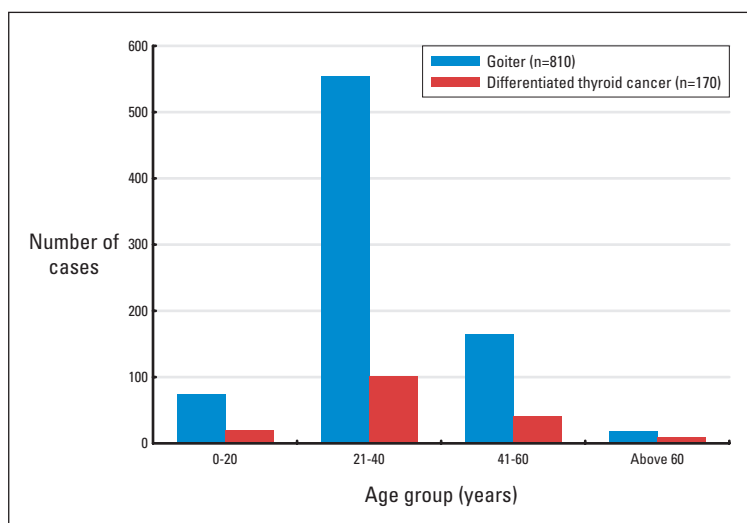


Figure 1. Age distribution of 170 cases of differentiated thyroid cancer (DTC) from 810 cases of surgically operated goiter in a Yemeni population.

21 and 40 years of age (Figure 1). Almost a quarter of the cases (41 cases, 24.1%) were between 41 and 60 years of age.

Within age groups, the frequency of DTC cases as a percentage of the surgically treated cases was about 25% in both the 21-40 year and 41-60 year age groups. The highest frequency of DTC (50%) was in the >61 year age group and the lowest frequency was in the 0-20 year age group (18.2%). In examining the frequency of DTC in relation to sex, in 729 (90%) female cases surgically treated for thyroid enlargement, there were 148 (20.3%) DTC cases. In males, the number of DTC cases among the 81 (10%) surgically treated for thyroid enlargement was 22 (27.2%).

Discussion

In 1990, the WHO survey study suggested that IDD is severe in Yemen. Endemic goiter is more common in mountainous areas and more than 60% of the area of Yemen is mountainous.⁵ Abnormal irradiation exposure was not reported in any of the cases included in this study. Head and neck therapeutic irradiation is not yet available in Yemen. In our study, most patients were older than the age of 20 years and were from the high altitude areas (2000 to 2600 meters above the sea level), where IDD is well documented. With the exclusion of parafollicular cells, which give rise to modularly carcinoma, follicular cells are the origin of differentiated thyroid cancers. However, undifferentiated thyroid cancers are excluded by definition.^{9,10,11}

Well-differentiated thyroid cancer encompasses both papillary carcinoma, which is the most common type and follicular carcinoma.¹³ Papillary carcinoma is generally a solid and infiltrative tumor with the exception of the rare encapsulated and cystic forms. Microscopically, the classic type may be associated with the follicular form, but both must reveal nuclear enlargement and the frequent specific diagnostic nuclear features (ground glass appearance, nuclear groove and nuclear pseudo-inclusion).¹² Follicular carcinoma is an encapsulated, solitary and fleshy tumor in the beginning. It simulates the benign counterpart follicular adenoma, but in due time the capsule becomes thick and ruptures with the progressive growth of the tumor.¹² In this study, the majority of the 810 cases surgically operated for goiter were females (90%), with female-to-male ratio of 9:1. This finding is similar to studies published in Yemen and India,^{14,15} and it is comparable with female-to-male ratios reported for Turkey (1:3.4), Italy (1:5.5), and France (1:7.4).^{16,17,18} More than two-thirds of cases were younger than 40 years old, which is similar to another study published in Yemen.¹⁵ While the incidence of DTC in the operated cases was 21%, which is comparable with other studies published in Yemen (17.7%) and Saudi Arabia (21.3%).^{15,19}

The majority of DTC cases were papillary carcinomas (96.5%); only 6 (3.5%) were follicular carcinomas. This is similar to study a series of 252 operated cases for differentiated thyroid cancer, wherein 96.8% of the cases were papillary carcinomas, and 3.2% were follicular carcinomas.²⁰

We also looked in depth at the incidence of DTC in operated cases for goiter in relation to sex and concluded that males seem to have a greater risk of having

DTC (27.2%) than females (20.3%). There was a relatively higher risk (50%) of having DTC among aged patients. The sex distribution of DTC in this study was 86.6% female and 13.6% male for a female to male ratio 6.7:1. This ratio is similar to a study published in South Africa, and comparable with other studies that reported a female-to-male ratio in Germany (5.5:1), in Spain (4:1) and India (1.1:1).^{21,22,23,24} The age distribution of 170 cases of differentiated thyroid cancer revealed that the highest numbers of cases were between 21 and 40 years (59.4%); this finding is similar to another study, which reported an incidence of 65% in the same age group in Saudi Arabia.¹⁹

In conclusion, the majority of cases surgically treated for thyroid enlargement were females. More than two-thirds of the cases were younger 40 years of age. Papillary carcinoma was the most common type of differentiated thyroid cancer, which was relatively more common in females. However, the frequency of DTC in surgically treated goiter was relatively higher in males, as well as among the young and the old population. These data indicate that males and the youngest and oldest age groups with goiter had a substantially higher risk of developing malignancy. Future epidemiological studies are recommended to ascertain risk factors for malignancy other than IDD. Yemen is in urgent need for a better level of expertise and diagnostic facilities in diagnosing tumors. Finally, the constitution of a national tumor registry is needed to assess the incidence and prevalence of thyroid cancer on a national level.

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