

A clinical epidemiologic study of thyroid carcinoma in patients under 25 years old in Tabriz, Iran (1995-2010)

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Abstract

Objective: To evaluate the epidemiology and prognostic factors of thyroid cancer among children and adolescents in Tabriz, Iran.

Methods: The retrospective descriptive-analytical study, assessing the tumour and characteristics of 356 patients with thyroid carcinoma aged 5-25, was conducted at the Department of Surgery, Imam Khomeini Hospital, Tabriz University of Medical Sciences from April 1995 to April 2010. All malignant neoplasms of the thyroid gland registered during the study period were studied, and their demographic and medical data was evaluated and, compared to identify the epidemiology and prognosis factors related to survival. SPSS 16 was used for statistical analysis.

Results: Of the total, there were 100 (28%) male and 256 (72%) female subjects, with their mean age being 12.6±8.4 years. In terms of the disease, there was no statistically significant difference between the two genders ($p=0.65$). The five-year survival rate was 345 (97%) in patients aged 5-25 years. Gender was not a statistically significant marker ($p=0.82$).

Conclusion: The study indicated an increase in cases of thyroid cancer incidence. It also underlined the need for standardisation of diagnostic, classification and registration criteria which shall be a fundamental requirement for future studies of thyroid carcinoma in young people.

Keywords: Thyroid cancer, Epidemiology, Incidence. (JPMA 62: 1265; 2012).

Introduction

Thyroid cancer is rare, causing less than 1% of cancer deaths.¹ Yet its epidemiology is of interest for several reasons. Upward trends of thyroid cancer have been reported in recent decades in various registration areas (e.g. Nordic countries, and USA),^{2,3} although lack of increase in mortality rates⁴ and changes in the definition of several areas of thyroid pathology⁵ limit the interpretation of temporal changes. Thyroid cancer is rare in children; especially before the age of 10 years.⁶ Cancer affecting the thyroid gland is one of few that are more frequent in females than in males, with a ratio of almost 3, already seen in later childhood,⁷ which may suggest the importance of hormonal factors in its etiology. Thyroid cancer comprises a group of tumours with remarkably different features. Papillary thyroid carcinoma (PTC), follicular thyroid carcinoma (FTC) and Hurtle cell carcinoma (HCC) are tumours of the thyroid follicular cell that are often collectively referred to as 'differentiated thyroid carcinoma' (DTC). However, the unique characteristics of these tumours may be overlooked when classified together as DTC. Though the management of these tumours has many similarities, important diagnostic, therapeutic and prognostic differences exist

between the three tumour types.⁸ The other two major forms of thyroid cancer are medullary thyroid carcinoma (MTC), a tumour of the thyroid C cell that secretes calcitonin; and anaplastic thyroid carcinoma (ATC), which usually arises from well-differentiated thyroid cancer.⁹ The best known cause of thyroid carcinoma is ionising radiation, recently demonstrated by the spectacular increase in thyroid cancer incidence in areas in the vicinity of the Chernobyl accident of 1986, especially in the childhood population.¹⁰ At first, the increase was suspected to be largely related to opportunistic screening for these tumours and registration of non-malignant tumours. The extent of the geographical differences, however, in conjunction with the reported histological types of the tumours, removed any doubt about the reality of the association,¹¹ although some of the increase may still have resulted from early diagnosis of tumours that would otherwise have presented at later ages. Consensus exists that PTC accounts for the vast majority of the increase in thyroid cancer.¹² It is the most common type of thyroid cancer, accounting for 80% of cases with a 5-year survival rate of 90-95%.^{12,13} Treatment for well-differentiated thyroid carcinoma typically consists of surgical resection with or without the addition of radioactive

iodine ablation. With the exception of the anaplastic type, thyroid carcinomas have a good prognosis. Survival of children diagnosed with thyroid cancer cases in 1978-1989 and included in the EUROCARE study was 97%,¹⁴ and similar results were also reported from the US.¹⁵ These favourable figures may be partly counter-balanced by the late effects that were reported to be more common in patients diagnosed at a young age than in adulthood.¹⁶ The aim of this study was to provide a broad overview of the epidemiology and prognostic factors of thyroid cancer. These variables are critical for the clinician to consider when tailoring an individual treatment and follow-up plan for patients with thyroid cancer.

Patients and Methods

The cross-sectional retrospective study covered the record of all 5-25-years-old patients of all malignant neoplasm of the thyroid gland who registered between 1995 and 2010 with the Department of Surgery, Imam Khomeni Hospital, Tabriz University of Medical Sciences, Iran. For each case, the information available included basic demographic data (age, gender etc.), information on the tumour (date of incidence, site, morphology and basis of diagnosis), general characteristics, personal and family history of thyroid diseases, relevant medical conditions (metabolic and immunological disorders), diagnostic and therapeutic procedures (X-rays and radiotherapy), history of residence in endemic goiter areas and follow-up (date of last contact and vital status). Patients were counted as having thyroid disease only if the diagnosis had been made at least a year before cancer discovery. Five histological groups were considered; PTC, FTC, MTC, ATC and other carcinomas. Stages included local disease (tumour confined to the thyroid); regional disease (lymph node involvement); or distant disease (metastatic spread to distant organs). Operative therapies were defined as follows: (1) partial thyroidectomy included lobectomy and isthmusectomy; (2) total thyroidectomy was restricted to cases in which the entire thyroid was removed or a near-total thyroidectomy was performed; (3) the operative approach not otherwise specified (NOS); and (4) no operative therapy was treated as such where indicated. SPSS, version 16 was used for

statistical analysis. The association between two variables was estimated using chi square test, with $p \leq 0.05$ being the cutoff value for statistical significance.

Results

Of the 356 patients whose records were studied, 100 (28%) were male and 256 (72%) female. The age of the patients ranged from 5 to 25 years and the mean age being 12.6 ± 8.4 years. Compared with women, men had greater likelihood of loco-regional lymph node involvement (46% vs. 38%), and more than twice the rate of distant metastases. There was a family history of thyroid cancer in 48 (13.4%) patients of which 30 (8.4%) were female and 18 (5%) were male; the difference was not statistically significant ($p = 0/64$). There was no history of obvious radiation to any of the patients. Neck mass was the most prevalent symptom of the patients that existed in 314 (88.2%), while pain was the least prevalent symptom that existed in only 32 (8.9%) patients; 24 (6.7%) patients were symptom-free (Table-1). In terms of histology, PTC was the most common ($n=281$; 78.9%), followed by FTC ($n=35$; 10%) MTC ($n=18$; 5.1%), other carcinomas ($n=20$; 5.5%) and ATC ($n=2$; 0.6%) (Table-2). In Isotope scan, 232 (65.1%) patients had cold nodules, 68 (19.1%) had hot nodules, and 56 (15.7) patients had normal nodules. The prevalence of lymph node metastases at initial surgery were seen in 46 (46%) of the males and 102 (39.8%) of the females. Lymph node metastases existed only in PTC. Most patients ($n=227$; 64%) underwent radical dissection and total thyroidectomy, while the remainder ($n=129$; 36%) underwent other types of surgery. For tumours $<1\text{cm}$, the extent of surgery did not affect recurrence or survival rates. On the other hand, patients with tumours $\geq 1\text{cm}$ had a 24% higher risk of recurrence if lobectomy alone was carried out ($p = 0.04$) (Table-3). Mortality records during the period showed relatively stable or slightly improved mortality rates for thyroid cancer patients. However, over the same period, mortality rates measured in terms of relative survival showed an overall significant decline in the trend for women ($p < 0.05$) and an increase in mortality rates among men ($p < 0.05$). The 5-year survival of patients was encountered in 345 (97%). No significant differences in

Table-1: Symptoms on the basis of gender.

First symptom	Male (%)	Female (%)	All the patents (%)	P value
Neck mass	76 (21.3)	240 (67.4)	314(88.7)	0.32
Dysphagia	8(2.2)	40(11.2)	48(13.4)	0.14
Dyspnoea	7(1.9)	48(13.4)	55(15.3)	0.08
Dysphonia	6(1.6)	30(8.4)	36(10)	0.24
Pain	8(2.2)	24(6.7)	32(8.9)	0.38
Symptom-free	2(0.5)	14(3.8)	16(4.3)	0.06
Others	32(8.9)	84(23.5)	116(32.4)	0.54

Table-2: Distribution of the patients according to gender and histological type.

	Males (%)	Females (%)	Pvalue
Histological type			
Papillary	71 (71)	210 (82.1)	0.24
Follicular	14 (14)	21 (8.2)	0.48
Anaplastic	0 (0)	2 (0.6)	0.028
Medullary	9 (9)	9 (3.5)	0.18
Other	6(6)	14 (5.5)	0.52

Table-3: Different types of surgery.

Treatment	N (%)	Male (%)	Female (%)	Pvalue
Total Thyroidectomy	106 (30)	32 (32)	74 (28.9)	0.62
Lobectomy	10 (3.3)	4 (4)	6 (2.3)	0.48
Radical dissection +				
Total Thyroidectomy	227 (64)	70 (70)	157 (61.3)	0.58
Complementary	13 (3.6)	5 (5)	8 (3.1)	0.36

survival were observed between boys (n=3; 3%) and girls (n=8; 3.1%) (p= 0.82). The incidence of recurrence was in 54 (15.1%) patients of whom 42 (11.7%) were female and 12 (3.4%) were male. Recurrence was observed in PTC and FTC, and was not observed in MTC cases.

Discussion

As the results showed, thyroid cancer is on the rise. The reason for this increase is not clear, but it seems to be multi-factorial, with increased rates of detection only representing part of the equation. The clinician must, therefore, have a complete understanding of the various prognostic factors and how they contribute to the outcome, so that the patient can be counselled accordingly about treatment and long-term surveillance decisions. In our study, the overall rate for all thyroid cancers was seen to have increased irrespective of any possible misclassification between histology groups.

From the clinical point of view, PTC and FTC in children and adolescents differ from those occurring in adults: they are more advanced upon presentation (higher frequency of extra-thyroidal spread), the recurrence rate is higher while the prognosis is better.^{13,17} In our study, the incidence of thyroid cancer had a significant increase than previous studies done in Tabriz.^{13,18} Because the detection methods between the two studies were not different, one possibility for this difference could be the long-term effects of the Chernobyl accident. Exposure to ionising radiation is associated with an increased risk of a wide range of cancers. Epidemiological studies of cancer following Chernobyl have so far concentrated on two diagnostic groups: thyroid cancer and leukaemia.¹⁸ In countries closest to the site of the accident, studies of thyroid cancer have predominated.

There were good reasons to expect that there would be an increase in the risk.¹⁹ Much of the initial deposit of radioactive material consisted of iodine, which is readily taken up by the thyroid gland. The thyroid in young people, especially in infants, is particularly vulnerable to radiation and there is convincing evidence for a carcinogenic effect even of doses as low as 0.1 Gy.²⁰ Young age at the time of the accident has been associated with greater severity of the disease as indicated by extra-thyroidal tumour extension, lymph node involvement and distant metastases.²¹ Several studies have reported the epidemiological and clinical features of post-Chernobyl carcinoma.^{22,23} In one study,¹³ 472 patients presenting with post-Chernobyl carcinoma, aged less than 21 years at diagnosis, were compared with those of 369 subjects from the same age group presenting with a sporadic carcinoma, observed in Italy and France. Mean age at the time of the accident was 4.4±3.4 years. The female-to-male ratio was significantly higher in the two countries (2.5:1), compared with the ratio of patients from Belarus (1.6:1). Most of the tumours were papillary. Extra-thyroidal extension and lymph node metastases were more frequent in Belarus compared to Italy and France. Other studies are in contrast with the effect of Chernobyl accident in the rise of thyroid cancers. A recent French study has concluded that no increase of thyroid cancers in eastern France could be related to the fallout from Chernobyl.²⁴

Conclusion

Numerous factors affect the outcome for patients with differentiated thyroid carcinoma, including age, gender, tumour histology, and presence of extra-capsular extension, tumour size, presence of lymph node or distant metastases, and oncogene expression of the tumour. The priority must be accorded to matters such as diagnosis, treatment and prevention.

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