

BRIEF REPORT

CLINICAL CHARACTERISTICS OF THYROID
CANCER IN MANIZALES, COLOMBIA, 2008-2015Nelson E. Arias-Ortiz ^{1,a}, Eduardo A. Guzmán-Gallego ^{2,a}¹ Grupo de investigación en Promoción de la Salud y Prevención de la Enfermedad, Universidad de Caldas, Manizales, Colombia.² Universidad de Caldas, Manizales, Colombia,^a Physician

ABSTRACT

A study was conducted to describe the cases of thyroid cancer in Manizales, Colombia. This study describes the characteristics of patients; and tumors according to size, laterality, focalization, nodal involvement, contiguous invasion, metastasis and TNM staging. A total of 672 cases were analyzed, 84.8% of which were women between 40 and 64 years of age. From the population, 34.1% were cases diagnosed in early stages and 15% of the tumors were >20 mm in size. Nodal and adjacent tissue involvement was present in 33% and 3% of the cases, respectively. Distant metastasis was documented in 1% of the cases. Papillary carcinoma was present in 82% of cases. Thyroid cancer in Manizales is more frequent in adult women. Tumor size and being at the early stages are factors that suggest improvement in early detection.

Keywords: Cancer; Thyroid neoplasms; Epidemiology (source: MeSH NLM).

INTRODUCTION

Thyroid cancer (TC) is the most frequent malignant endocrine disease, derived from epithelial cells in 90% of cases, such as papillary, follicular, anaplastic and medullary cells. Worldwide, it ranks 16th among the most common cancers, representing 2% of all the new cases ⁽¹⁾. In several Latin American countries, this neoplasia is among the 10 most frequent cancers in both genders, being much more frequent in women ⁽²⁾. Colombia has population-based incidence data for 5 cities according to national estimates of cancer incidence based on mortality ^(3,4). The latest thyroid cancer calculated incidences were 16.0 and 0.7 per 100,000 in women and men, respectively, which places this cancer as the third most common one in women after breast and cervix ⁽¹⁾.

Manizales, capital of the department of Caldas, is a Colombian Andean city with nearly 430,000 inhabitants ⁽⁵⁾ and has a population-based cancer registry indexed by the International Agency for Research on Cancer (IARC). This registry actively searches for new cases of malignant neoplasias among the population living in urban and rural areas. The information sources are hospitals and clinics, imaging and endoscopy centers, clinical laboratories and histopathology laboratories, as well as official mortality data. The registry is operated by the University of Caldas, in agreement with the National Institute of Cancerology of Colombia, and complies with the quality standards recommended by the IARC ⁽⁶⁾. TC incidence data have been published in volumes 10 and 11 of *Cancer Incidence in Five Continents*, a world reference publication about descriptive cancer epidemiology. According to information from this registry, the incidence of TC went from 12.3 and 3.2 per 100,000 in women and men, respectively, in the period 2003-2007; to 23.2 and 4.6 from 2008 to 2012, representing an average annual percentage increase of 13.4% and 7%, respectively ⁽²⁾. These rates are significantly higher than those reported by other cities with population records in the country: Bucaramanga reported

Citation: Arias-Ortiz NE, Guzmán-Gallego EA. Clinical characteristics of thyroid cancer in manizales, Colombia, 2008-2015. Rev Peru Med Exp Salud Publica. 2020;37(2):287-91. doi: <https://doi.org/10.17843/rpmesp.2020.372.4892>

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Received: 18/10/2019
Approved: 15/04/2020
Online: 16/06/2020

14.4 and 2.5; Cali, 13.5 and 3.2; and Pasto, 11.8 and 2.6, for women and men, respectively, per 100,000 inhabitants ⁽²⁾.

The objective of this research was to describe the characteristics of TC cases in Manizales, Colombia during the period 2008-2015.

THE STUDY

Observational, descriptive, retrospective, cross-sectional study based on population-based data. Information was collected on the total number of patients with TC (topographic code C73X of the International Classification of Diseases in Oncology, 3rd edition, first revision, ICD3.1) between January 1, 2008 and December 31, 2015, without applying exclusion criteria. Histopathological reports were reviewed in order to extend the microscopic descriptions of the tumors.

Gender and age were described as patient variables. Histological type, number of lesions, size, laterality, involvement of adjacent tissues and lymph nodes, and distant spread were reviewed as tumor variables. Based on the combination of these variables, the clinical stage at the time of diagnosis was described using the TNM system of the American Joint Committee on Cancer (AJCC), 8th edition. To classify the tumors according to their size, the 20 mm cut-off point was used to classify small lesions, as suggested by Herránz González-Botas J, Barro CV and Vidal JM ^(7,8).

Trends of the numerical variables were described by calculating medians and interquartile ranges. Categorical variables are presented by using absolute and relative frequencies. The Mann-Whitney U test (sum of ranges) and the Chi-square test contained in the Stata 14.2[®] statistical package were used to test for possible differences in tumor characteristics by gender, since the variables follow non normal distributions.

This research project was approved by the Bioethics Committee of the University of Caldas and classified as risk-free research in accordance with the regulations in force in Colombia (Resolution 8430 of 1993, art. 11).

FINDINGS

A total of 672 incident cases were analyzed. Median age at diagnosis was 51.1 years old and the interquartile range (IQR) was 21.4 years old. The most affected age groups ranged from 40 to 64 years old; and the period 45-49 years old, predominated. Females were affected the most, representing 84.8% of total cases (n=570). A female/male ratio of 5:1 was found. The predominant histological result was papillary carcinoma with 81.7% of the cases.

KEY MESSAGES

Motivation for the study: Thyroid cancer is the most common malignant endocrine disease, derived from epithelial cells.

Main findings: From the total, 82% of cases were early stage papillary carcinomas, predominantly in women aged 40-65 years, measuring <20 mm.

Implications: Early stages and small sizes suggest improvement in early diagnosis. The predominance in women, the possible cohort effect and the increase at the expense of papillary carcinoma, suggest actual increase in incidence.

Most cases (85%) corresponded to small tumors (<20 mm); however, 40% of the cases had missing data regarding this variable. Larger lesions were found in men compared to women (p=0.004). The size of papillary carcinomas was apparently smaller than that of other histological types. Unspecified carcinomas were also smaller, suggesting that they may correspond to papillary carcinomas that were not histologically verified. Characteristics of thyroid cancer cases by gender are presented in Table 1.

Most cases had unifocal tumors (50.2%), unilateral tumors (52.4%), and nodal involvement was found in one third of the cases (positive nodes 33%, 60% in anatomical group III). Only 3.2% of cases presented invasion into the larynx, trachea and pharynx; distant metastases occurred in 1.0% of cases.

Regarding the clinical-pathological stage of the disease, complete data for staging were found in about 60% of cases, from which 82.6% correspond to stage I and 12.4% to stage II.

DISCUSSION

This study describes the characteristics of the cases of TC in Manizales (Colombia) and points out the higher frequency in women, in age groups between 40 and 64 years old, with small lesions diagnosed at an early stage and with predominance of papillary carcinoma. There were gender differences in favor of women in: age median at diagnosis, median tumor size, and number of nodes involved.

The case distribution found by age group is consistent with a study in Cataluña (Spain) and with a case series reported by Chala and collaborators, in Manizales (Colombia) ^(9,10). The female/male ratio 5:1, the predominance of the histological

Table 1. Characteristics of thyroid cancer cases in Manizales, Colombia, 2008-2015

Characteristic	Men		Women		p-value ^b
	n	%	n	%	
Age ^a	55.9	45.0-66.1	50.5	40.1-61.3	0.020
Size in mm ^a	19	10-40	13	8-20	0.004
Laterality					
Unilateral	48	47.0	304	53.3	0.733
Bilateral	8	7.8	44	7.7	
No data	46	45.1	222	38.9	
Tumor foci					
Single	43	42.2	294	51.6	0.241
Multiple	12	11.8	54	9.5	
No data	47	46.1	222	38.9	
Ganglion compromise					
Yes	33	32.3	166	29.1	0.309
No	29	28.4	193	33.9	
No data	40	39.2	211	37.0	
Number of ganglions ^a	4.2	0-24	2.2	0-47	0.038
Nearby tissue compromise					
Yes	4	3.9	18	3.2	0.558
No	53	52.0	333	58.4	
No data	45	44.1	219	38.4	
Metastasis					
Yes	1	1.0	6	1.04	0.941
No	53	52.0	345	60.5	
No data	48	47.1	219	38.4	
Total	102	15.2	570	84.8	

^a Median (interquartile range), ^b p values of the test applied to the cases with data available for each variable, i.e. excludes the category without data so as not to affect the results..

papillary type and the difference in average size of the tumors between men and women found in this study are consistent with what is reported by Herránz J⁽⁷⁾.

Regarding staging at the time of diagnosis, most patients were in early stages of thyroid cancer, a figure that is almost twice of what was reported in La Coruña (Spain), where 47% of patients aged 45 years and older were stage I⁽⁷⁾. This result would support the hypothesis of overdiagnosis in the population of Manizales.

Several reports have described a dramatic increase of thyroid cancer incidence in recent decades, predominantly small papillary carcinomas, even though mortality rates related to thyroid cancer have not changed substantially^(1,11). This phenomenon has been observed in different populations around the world, especially in women. Although the reasons for this are not completely clear, it is attributed to the improved and increased use of diagnostic techniques, especially soft-tissue neck ultrasound⁽⁹⁾. The incidence in-

crease is more visible in women, mainly in the 45-49 year age group, which may be related to the greater use frequency of health services by women of these ages compared to men.

Increasing TC incidence in Manizales may not be something new. According to previous data from the Population Registry of Cancer of Manizales, the incidence of TC in women, doubled between 2003-2007 and 2008-2012 and became the second most common malignant neoplasia in women; a significant increase in incidence in men was also observed⁽²⁾.

Some authors have suggested that improved early detection, associated with improved diagnostic techniques, and greater access to medical care by the population are the most plausible reasons for the notable incidence increase. Among arguments presented in the literature, we can find: the diffusion of advanced medical procedures, such as ultrasound; the increased incidence of microcarcinomas; the increase in incidental diagnoses (thyroidectomies for benign diseases,

greater detail in anatomopathological studies; the incidental discovery of thyroid nodules during other procedures, such as carotid ultrasound); the high frequency of small and asymptomatic thyroid cancers in autopsies; and greater thoroughness in cancer registries⁽¹²⁻¹⁶⁾.

However, some studies indicate that this increase is explained by improvements in health services and by an actual incidence increase⁽¹⁵⁻¹⁷⁾. The arguments supporting this controversy are the simultaneous increase of large tumors; the lack of decrease in the incidence of larger and advanced stage tumors as a result of a supposed improvement in early detection; the predominant increase in only the histological papillary type (and not all other types as would be expected as a result of diagnosis improvement); the non-uniform distribution of the increase in incidence by age and gender (predominance in women and presence of cohort effect); the lack of increase in incidence for other tumors as a result of supposedly greater thoroughness of cancer records; and the lack of decrease in mortality as a result of supposedly greater early detection, and conversely, a slight increase especially in men.

On the other hand, the focused increase in female population and certain age groups (possible cohort effect) could also be explained by differential exposures between men and women to unknown risk factors, for example, to substances with potential endocrine disrupting behavior and possible thyroid carcinogenic inducing effects^(18,19). The increase almost exclusively at the expense of the histological papillary type can also be interpreted as an argument in favor of a possible real increase in incidence combined with artificial increase due to improved diagnosis⁽²⁰⁻²²⁾. In addition, the

predominance of tumors smaller than 2 cm and in early stages, also supports conclusions in this sense.

One of the strengths of this study was the fact that it worked with population-based data with international quality standards⁽⁶⁾ indexed in the IARC⁽²⁾. However, important limitations in data completeness were observed for some tumor variables that are not routinely collected by the registry. The results of this study serve as a basis for further research exploring exposure to possible risk factors through more complex designs. Research opportunities arise regarding the study of the possible association between thyroid carcinomas and the massive use of ultrasound as an initial study method that would favor the disease overdiagnosis in the population.

As a conclusion, in Manizales the TC affected mainly women. The histological papillary type was more frequent in women than in men. At the time of diagnosis, the early stages were predominant. There were gender differences in favor of women of median age at diagnosis, median tumor size, and number of nodes involved. Some of the characteristics of the patients and the tumors make plausible the hypothesis of an overdiagnosis scenario whose magnitude should be the subject of future research.

Funding: The authors declare no conflict of interest in the publication of this article.

Conflicts of interest: Los autores declaran no tener conflictos de intereses en la publicación del artículo.

Authorship contributions: NEAO and EAGG participated in the conception of the article, data collection, writing and approval of the final version.

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