ORIGINAL ARTICLE

# Frequency of thyroid cancer in patients operated at Cantonal Hospital Zenica, Bosnia and Herzegovina, in the period 2007- 2014

**Nermin Hrnčić[1], Amna Goga[1], Selma Hrnčić[2], Marijana Filipovska-Mušanović[3], Haris Hatibović[1], Đenad Hodžić[1]**

[1]Ear, Nose and Throat Department, Cantonal Hospital Zenica, [2]Cantonal Institute for Occupational Health and Sports Medicine Zenica-Doboj Canton; Zenica, [3]Public Health Centre Kakanj; Bosnia and Herzegovina

## ABSTRACT

**Aim** To determine frequency and type of thyroid cancer (TC) as well as gender and age distribution of patients operated at the Department of Ear, Nose and Throat (ENT), Cantonal Hospital Zenica, Bosnia and Herzegovina.

**Methods** A retrospective analysis of data obtained from an operating protocol and disease history of patients operated in the eight-year period (2007- 2014) was made according to the frequency and type of thyroid cancer, as well as age and gender of the patients. $\chi 2$ test was used for statistical with $p<0.05$.

**Results** A total of 818 surgeries of the thyroid gland were conducted, in 714 (87.29%) female and 104 (12.71%) male patients. Malignancies were diagnosed in 74 (9.05%) patients, of whom 64 (86.49%) were females and 10 (13.51%) were males, resulting in the gender prevalence of 8.96% and 9.62%, respectively. The most often presented type was papillary carcinoma, in 48 (out of 74, 64.86%) patients, followed by follicular carcinoma in 10 (13.51%), medullary carcinoma in four (5.41%), Hurthle cell carcinoma in four (5.41%) patients, while anaplastic carcinoma was found in one (1.35%) patient. The number of diagnosed malignancy varied from 0% (in 2007) to 13.91% (in 2014) ($p=0.05$).

**Conclusion** The prevalence of thyroid cancer is low, but has an increasing trend. A large number of unnecessary surgeries on thyroid gland was performed. Preoperative diagnostic procedures for diseases of the thyroid gland in Cantonal Hospital Zenica should be improved in order to avoid unessential surgeries.

**Key words:** thyroidectomy, malignant disease, thyroid nodule

**Corresponding author:**
Nermin Hrnčić
Department of Ear, Nose and Throat,
Cantonal Hospital Zenica
Crkvice 67, 72000 Zenica,
Bosnia and Herzegovina
Phone: +387 32 405 133;
Fax: +387 32 226 576;
E-mail: nhrncic@yahoo.de

**Original submission**:
07 January 2016;
**Revised submission:**
29 January 2016;
**Accepted:**
12 May 2016.
doi: 10.17392/846-16

Med Glas (Zenica) 2016; 13(2):113-117

## INTRODUCTION

Thyroid carcinomas (TC) are rare tumors with the rate of 1% of all malignoma (1). It is the most common endocrine carcinoma and includes about 5% of all thyroid nodules (2). In general population it is considered that 20-50% of people have nodules in the thyroid gland (3). About 8% of the adult population have palpable nodules (4). Majority of the nodules are benign and only 10% harbor malignancy (5). In an autopsy series from Malmoe, Sweden, comprising 821 thyroid glands, the reported nodule prevalence was 49.5% (3). Some statistics indicate that one quarter of the population (13-35%) has papillary thyroid carcinoma (PTC), detected in 3-9 cases per 100000 yearly mostly by accident (3). Thyroid cancer is 2-4 times more frequent in females than in males (2). Also, the incidence of TC has been on the continuous rise in the last 20 years (1). There is a report describing overall prevalence of TC in 53 856 patients from the United States with approximately 79% of cases with papillary carcinoma (PTC), 13% of follicular carcinoma (FTC), and approximately 3% of Hurthle cell carcinoma. Medullary thyroid cancer (MTC) accounts for about 4% of thyroid carcinomas (6). Anaplastic carcinomas, lymphoma and metastatic disease make a small portion of thyroid malignancies (6). There are many reports showing an increasing incidence of TC (7-9).

There are different methods of diagnostic evaluation but it always begins with history and clinical examination (10). The diagnostics continues with laboratory tests (thyroid hormone, thyroid antibodies, thyroglobulin, and calcitonin) and then is expanded to ultrasonography (US), thyroid scintigraphy, fine needle aspiration biopsy (FNAB) (10). The evaluation and management of cold thyroid nodules remains the area of controversy (11). In most centers, FNAB has supplanted imaging studies as the routine initial procedure for differentiating benign from malignant nodules (12). Cytological diagnosis is reliable and inexpensive, and it results in better selection of patients for surgery (12).

Risk factors for TC include low alimentary iodine intake, genetics, certain familial syndromes (e.g. familial polyposis coli, Gardner syndrome), obesity (women), ionizing radiation (especially in childhood, children tend to get papillary cancer), reproductive and hormonal status (higher risk associated with high parity and late menarche) (13).

Epidemiology of TC in the developed world is sufficiently described (2,6,14). In Bosnia and Herzegovina and other Balkan countries there are only a few reports (15,16). The aim of this retrospective study was to review hospital records in order to assess data on TC prevalence as well as characteristics (age, gender, type of TC) of patients operated at the Department of Ear, Nose and Throat (ENT), Cantonal Hospital Zenica, Bosnia and Herzegovina.

## PATIENTS AND METHODS

### Patients and study design

A retrospective analysis of data obtained from operating protocols and disease history of patients with the diagnosis of multinodular goiter or suspicions of malignancy of thyroid gland operated at the Ear, Nose and Throat (ENT) Departtment of Cantonal Hospital Zenica in the eight-year period (January 01, 2007- December 31, 2014) was conducted.

### Methods

Indications for surgery including multinodular goiter, big goiter with compression syndrome or suspicions of TC were assessed at the Departtment of Nuclear Medicine and patients were referred to ENT department for surgery. Majority of patients were diagnosed with multinodular goiter. Depending on an extent of the disease in the entire gland, or only a portion of the gland, more or less extensive surgery was planned, e.g., biopsy, lobectomy, isthmectomy, enucleation of cysts, subtotal thyroidectomy, and total thyroidectomy with or without neck dissection. Total thyroidectomy with or without neck dissection in all patients with histologically verified TC was performed. Histopathological examination was done at the Pathology Department of the Cantonal Hospital Zenica. Immunohistochemistry was performed at the Institute of Pathology at Clinical University Center in Sarajevo or Tuzla.

All patients with histological confirmation of TC were selected. Age, gender, number and type of operation were recorded. Histologically, tumors are classified according to the WHO classification into 4 main types: papillary (PTC), follicu-

lar (FTC), medullar (MTC) and anaplastic) (17). Adenocarcinoma and squamous cell carcinoma (SCC) in the thyroid gland were considered as metastases from other organs (17).

### Statistical analysis

Age, gender and type of TC as well as annual prevalence were analyzed using $\chi 2$ test with statistically significance limit of $p < 0.05$.

## RESULTS

In the eight-year period 818 surgeries on the thyroid gland were performed. There were 714 (87.29%) females and 104 (12.71%) males. Three oldest patients at the time of surgery were 79 years old (without malignancy); the youngest patient was a 12-year old girl operated due to suspicion of MTC, but after lobectomy no malignancy was found on histopathological examination.

Among 818 surgeries there were 385 total thyroidectomies, 379 lobectomies, 28 subtotal thyroidectomies, 15 cyst enucleations, and 11 other types of surgeries (biopsy, isthmectomy).

The number of operations had an increasing trend during the 2007-2014 period (the lowest number was recorded in 2008 with 62 patients, and highest in 2012 with 156 patients). The number of diagnosed malignancy varied from 0% (in 2007) to 13.91% (in 2014) with cutoff statistically significant difference (p=0.05). Every year a large number of operations was done on patients without the malignant disease (86.09% and 100% in 2014 and 2007, respectively) (Table 1).

**Table 1. Number of surgeries and prevalence of thyroid carcinoma (TC) in the period 2007-2014**

| | | No (%) of patients | |
|---|---|---|---|
| Year | No. of surgeries | With TC | Without TC |
| 2007 | 77 (9.41) | 0 | 77 (100) |
| 2008 | 62 (7.58) | 6 (9.68) | 56 (90.32) |
| 2009 | 69 (8.44) | 6 (8.70) | 63 (91.30) |
| 2010 | 91 (11.12) | 12 (13.19) | 79 (86.81) |
| 2011 | 98 (11.98) | 8 (8.16) | 90 (91.84) |
| 2012 | 156 (19.07) | 11 (7.05) | 145 (92.95) |
| 2013 | 150 (18.34) | 15 (10.00) | 135 (90.00) |
| 2014 | 115 (14.06) | 16 (13.91) | 99 (86.09) |
| **Total** | 818 (100) | 74 (9.05) | 744 (90.95) |

Among 818 surgeries there were 74 (9.05%) verified malignancies by histopathology, of which 64 (86.49%) were found in females, and 10 (13.51%) in males (female:male 6.4:1) resulting in gender prevalence of 8.96% and 9.62%, respectively, without statistically significant difference (p=0.83).

The median age in all patients with TC was 51 year with a range spanning from 14 to 75 years. In female patients the median age was 52 years, and in male patients it was 50 years. The majority of patients with malignant disease aged over 41 years, 58 (78.38%) (Table 2).

**Table 2. Age and gender distribution of patients with thyroid carcinoma**

| | No (%) of patients | | |
|---|---|---|---|
| Age (years) | Males | Females | Total |
| 1-20 | 1 (10.00) | 2 (3.13) | 3 (4.05) |
| 21-30 | 0 | 4 (6.25) | 4 (5.41) |
| 31-40 | 2 (20.00) | 7 (10.94) | 9 (12.61) |
| 41-50 | 1 (10.00) | 13 (20.31) | 14 (18.92) |
| 51-60 | 3 (30.00) | 19 (29.69) | 22 (29.73) |
| 61-80 | 3 (30.00) | 19 (29.69) | 22 (29.73) |
| **Total** | 10 (13.51) | 64 (86.49) | 74 (100) |

The largest proportion of patients had PTC tumor type, 48 (64.86%) (five males and 43 females), of which eight were micro carcinoma; 10 patients (13.51%) had FTC (one male and nine females); four (5.41%) patients had MTC (all females); four (5.41%) patients had Hurthle cell carcinoma (all females); one male patient (1.35%) had anaplastic type of TC. Of the remaining seven patients three had adenocarcinoma (one male and two females) and four had squamous cell carcinoma (SCC) (two males and two females) (Table 3). The distribution of TC type according to gender has shown statistically significant difference (p=0.03).

**Table 3. Distribution of thyroid cancer (TC) according to histopathology of tumor and patient gender**

| | No (%) of the patients | | |
|---|---|---|---|
| Histopathological type of tumors | Females | Males | Total |
| Papillary TC | 43 (67.19) | 5 (50.00) | 48 (64.86) |
| Follicular TC | 9 (14.06) | 1 (10.00) | 10 (13.51) |
| Medullar TC | 4 (6.25) | 0 | 4 (5.41) |
| Hurthle cell TC | 4 (6.25) | 0 | 4 (5.41) |
| Squamous cell carcinoma | 2 (3.13) | 2 (20.00) | 4 (5.41) |
| Adenocarcinoma | 2 (3.13) | 1 (10.00) | 3 (4.05) |
| Anaplastic TC | 0 | 1 (10.00) | 1 (1.35) |
| **Total** | 64 (86.49) | 10 (13.51) | 74 (100) |

## DISCUSSION

The results of this study related to frequency of each histopathology type of thyroid cancer do not differ from the published literature; follicular and anaplastic TC were noticed less frequently,

while Hurthle cell carcinoma was slightly more common in our study (6,10,18). Data from this study on gender and age distribution are similar to those of the relevant literature: TC was more frequent in females than in males (2), and the diagnosis of all carcinomas increased significantly from the age of 40 (18).

There are two sets of data on the incidence of TC in the literature. In institutions where FNAB is routinely performed preoperatively, the incidence of TC is much higher, because this procedure has high sensitivity and specificity (19,20,21). The second group of data report incidentally discovered TC in the patients undergoing surgery without suspicion of malignancy, usually with the diagnosis of multinodular goiter. The data from our study do not differ from the published literature (22-25).

In our institution the FNAB is not performed routinely because of the lack of cytopathologists. In most cases the diagnostic process ends with ultrasonography (US) or scintigraphy. Relying on such a diagnostic evaluation, majority of our patients were sent to surgery with the diagnosis of multinodular goiter without suspected malignancy. A small number of patients was referred to surgery with suspected malignancy after US or scintigraphy, and even then in many cases the diagnosis was not confirmed by histopathological analysis. Consequently, a large number of patients could avoid surgical treatments if the diagnostic procedures were satisfactory. Additionally, money could be saved because the cost of FNAB diagnostic procedures is much lower than the cost of unnecessary surgical treatment (11). Due to better diagnostic evaluation, a large number of patients with suspected TC are referred to surgery, and this is the reason for a very extensive type of surgery. In our daily practice each TC and even microcarcinoma undergo total thyroidectomy. An analysis of autopsy material from Malmoe (Sweden) showed high prevalence of undiagnosed TC suggesting a large number of microcarcinomas and slow growing well-differentiated TC, which do not require surgery, or operations may not be too extensive (2,18, 25-27).

In conclusion, a lot of unnecessary surgeries on thyroid gland were performed. One of ten patients operated in our institution has TC. The development of a strategy for better preoperative diagnostic procedures is necessary to avoid unessential surgeries. This would reduce costs, and more importantly, ensure better health care for our patients and getting closer to standards of the developed countries.

## FUNDING

No specific founding was received for this study.

## TRANSPARENCY DECLARATION

Competing interests: none to declare.

## REFERENCES

1. Salkić A, Brkić F, Cickusić A, Cickusić E, Altumbabić H. Thyroid cancer in Tuzla region of Bosnia and Herzegovina: a 10-year study (1999-2008). Coll Antropol 2012; 36:53-7.
2. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T, Thun MJ. Cancer statistics, 2008. Cancer J Clin 2008; 58:71–96.
3. Members of the Guideline Development Group. Diagnosis and management of metastatic malignant disease of unknown primary origin. NICE 2010; 2:4-6.
4. Yeung MJ, Serpell JW. Management of the solitary thyroid nodule. Oncologist 2008; 13:105–12.
5. Layfield L. Fine-needle aspiration in the diagnosis of head and neck lesions: a review and discussion of problems in differential diagnosis. Diagn Cytopathol 2007; 35:798–805.
6. Hundahl SA, Fleming ID, Fremgen AM, Menck HR. A National Cancer Data Base report on 53,856 cases of thyroid carcinoma treated in the U.S., 1985-1995. Cancer 1998; 83:2638-48.
7. Jossart G, Clark OH. Well-differentiated thyroid cancer. Curr Probl Surg 1994; 21:933–1012.
8. Brennan MD, Bergstralh EJ, van Heerden JA, McConahey WM. Follicular thyroid cancer treated at the Mayo Clinic, 1946 through 1970: initial manifestations, pathologic findings, therapy, and outcome. Mayo Clin Proc 1991; 66:11-22.
9. Nel CJ, van Heerden JA, Goellner JR, Gharib H, McConahey WM, Taylor WF, Grant CS. Anaplastic carcinoma of the thyroid: a clinicopathologic study of 82 cases. Mayo Clin Proc 1985; 60:51–58.
10. Amra Jakubović Čičkušić. Ultrazvučna dijagnostika u bolestima štitne žlijezde, Tuzla: Princom, 2015.
11. Giuffrida D, Gharib H. Controversies in the management of cold, hot, and occult thyroid nodules. Am J Med 1995; 99:642-50.
12. Mazzaferri EL. Management of a solitary thyroid nodule. N Engl J Med 1993; 328:553–9.
13. Hrnčić N, Ramaš A, Altumbabić H, Hodžić Đ, Hatibović H, Šehanović E, Salkić N. Papillary thyroid carcinoma in a female patient with squamous cell carcinoma of the larynx. Med Glas (Zenica) 2014; 11:241-3.
14. Meurisse M, Claeys N, Paesmans M, Nguyen Dang M, Degauque C, Delmelle M, Larsimont D, T'Hooft-Andry M, Verhest A, Hamoir E, Andry G, Squifflet JP. Belgian registry of thyroid cancer. Preliminary epidemiological characteristics revealed by a retrospective study (1988-1995). Belgian Thyroid Cancer Study Group. Ann Endocrinol (Paris) 1997; 58:163-71.

15. Scheiden R, Keipes M, Bock C, Dippel W, Kieffer N, Capesius C. Thyroid cancer in Luxembourg: a national population-based data report (1983–1999) BMC Cancer 2006; 6:102.
16. Zivaljevic V, Paunovic I, Diklic A, Krgovic K, Kalezic N, Kazic M, Tatic S, Savic D, Stojanovic D, Perunovic R. Acta Chir Belg 2008; 108:328-32.
17. Trimboli P, Ulisse S, Graziano FM, Marzullo A, Ruggieri M, Calvanese A, Piccirilli F, Cavaliere R, Fumarola A, D'Armiento M. Trend in thyroid carcinoma size, age at diagnosis, and histology in a retrospective study of 500 cases diagnosed over 20 years. Thyroid 2006; 16:1151-5.
18. Šimunović D, Cvjetko I, Gladić V, Elez M, Glasnović M, Leniček T, Vučić M, Lechpammer M, Čupić H, Strnad M, Kusić Z, Krušlin B, Belicza M. Possible effects of the 1990-1995 war in Croatia on thyroid cancer epidemiology. Acta Clin Croat 2000; 39:155-60.
19. Leonard N, Melcher DH. To operate or not to operate? The value of fine needle aspiration cytology in the assessment of thyroid swellings. J Clin Pathol 1997; 50:941-3.
20. Miseikyte-Kaubriene E, Ulys A, Trakymas M. The frequency of malignant disease in cytological group of suspected cancer (ultrasound-guided fine-needle aspiration biopsy of non palpable thyroid nodules). Medicina (Kaunas) 2008; 44:189-94.
21. Mikosch P, Gallowitsch HJ, Kresnik E, Jester J, Würtz FG, Kerschbaumer K, Unterweger O, Dinges HP, Lind P. Value of ultrasound-guided fine-needle aspiration biopsy of thyroid nodules in an endemic goitrearea. Eur J Nucl Med 2000; 27:62-9.
22. Gandolfi PP, Frisina A, Raffa M, Renda F, Rocchetti O, Ruggeri C, Tombolini A. The incidence of thyroid carcinoma in multinodular goiter: retrospective analysis. Acta Biomed 2004; 75:114-7.
23. Pezzolla A, Lattarulo S, Milella M, Barile G, Pascazio B, Ciampolillo A, Fabiano G, Palasciano N. Incidental carcinoma in thyroid pathology: our experience and review of the literature. Ann ItalChir 2010; 81:165-9.
24. Slijepcevic N, Zivaljevic V, Marinkovic J, Sipetic S, Diklic A, Paunovic I. Retrospective evaluation of the incidental finding of 403 papillary thyroid microcarcinomas in 2466 patients undergoing thyroid surgery for presumed benign thyroid disease. BMC Cancer 2015; 15:330.
25. Pelizzo MR, Rubello D, Berbardi C, Gemo G, Bertazza L, Schievano E, Fedeli U. Thyroid surgical practices shaping thyroid cancer incidence in North-Eastern Italy. Biomed Pharmacother 2014; 68:39-43.
26. Carlini M, Giovannini C, Mercadante E, CAstaldi F, Dell´Avanzato R, Zazza S. Incidental thyroid microcarcinoma in benign thyroid disease. Incidence in a total of 100 consecutive thyroidectomies. Chir Ital 2006; 58:441-7.
27. Sission JC. Medical treatment of benign and malignant thyroid tumors. Endocrinol Metab Clin N Am 1989; 18:359-87.

# Učestalost karcinoma štitne žlijezde kod pacijenata operisanih u Kantonalnoj bolnici Zenica u periodu od 2007. do 2014. godine

**Nermin Hrnčić[1], Amna Goga[1]; Selma Hrnčić[2], Marijana Filipovska-Mušanović[3], Haris Hatibović[1], Đenad Hodžić[1]**

[1]Kantonalna bolnica Zenica, ORL odjel, [2]JU Zavod za medicinu rada i sportsku medicinu Zeničko-dobojskog kantona, Zenica [3]JU Dom zdravlja Kakanj

## SAŽETAK

**Cilj** Utvrditi učestalost i vrstu, te spolnu i dobnu distribuciju karcinoma štitne žlijezde u pacijenata operisanih na Odjelu za bolesti uha, grla i nosa Kantonalne bolnice Zenica.

**Metode** Napravljena je retrospektivna analiza podataka dobijenih iz operativnih protokola i historijâ bolesti pacijenata u periodu od 2007. do 2014. godine. Analizirana je učestalost i tip karcinoma, te spolna i starosna dob pacijenata. Za statističku obradu korišten je $\chi 2$ test uz $p \leq 0.05$.

**Rezultati** Ukupno je izvedeno 818 operativnih zahvata na štitnoj žlijezdi. Operisano je 714 (87.29%) žena i 104 (12.71%) muškarca. Dijagnosticirano je 74 (9.05%) maligniteta, 64 (86.49%) kod žena i 10 (13.51%) kod muškaraca. Zabilježena je učestalost karcinoma kod 9.62% (10/104) muškaraca i kod 8.96% (64/714) žena. Najčešće je bio zastupljen papilarni karcinom, u 48 od 74 (64.86%) pacijenta, folikularni karcinom kod 10 (13.51%) pacijenata, a po 4 (5.41%) pacijenta imala su medularni i Hurthle *cell* karcinom, dok je 1 (1.35%) pacijent imao anaplastični karcinom. Broj dijagnosticiranih karcinoma varirao je od 0% (2007. god.) do 13.91% (2014. god.) (p=0.05).

**Zaključak** Učestalost karcinoma štitne žlijezde je niska, ali ima tendenciju porasta. Napravljen je veliki broj nepotrebnih hirurških zahvata na štitnoj žlijezdi. Preoperativne dijagnostičke procedure za bolesti štitne žlijezde u Kantonalnoj bolnici Zenica trebaju biti poboljšane ako se želi smanjiti broj nepotrebno urađenih operativnih zahvata.

**Ključne riječi:** tireoidektomija, maligna bolest, čvor u štitnoj žlijezdi