

Mersudin Mulić*, Bilsana Mulić

NODULAR GOITRE EVALUATION IN THE REGION OF THE HEALTHCARE CENTER OF NOVI PAZAR

Summary: The term thyroid nodule refers to any irregular growth which forms a lump in the thyroid gland.

Objective: The evaluation of medical history, clinical, laboratory and ultrasonography findings in patients with the disorder of thyroid gland structure in the region of the Healthcare Center of Novi Pazar.

Methods: The study included 61 patients, 58 females and 3 males, with a disorder of the thyroid gland structure. Each patient underwent clinical examination and ultrasonography of the thyroid gland. In each patient the global function of the thyroid gland was assessed by measuring serum concentrations of triiodothyronine (T3), thyroxine (T4), thyroid-stimulating hormone (TSH), and titres of thyroglobulin (TGAb) and microsomal (TPOAb) antibodies.

Results: The frequency of the occurrence of a thyroid nodule is highest at the age 35-39 (16.39%) and at the age 55-59 (18.03%). By analyzing the ultrasound findings of the patients' thyroid glands, the following distribution was obtained: 13 (21.31%) patients had a diffuse and nodose struma, 17 (27.87%) had nodose struma, 20 (32.79%) had polynodose struma, 5 (8.19%) had cystic node, 3 (4.92%) had micronodular struma and 3 (4.92%) had a recurrence of nodules.

Conclusion: In the region of the Healthcare Centre of Novi Pazar, the frequency of thyroid nodule is highest at the age 55-59, and the most common disorder of the thyroid gland structure is polynodose struma.

Keywords: thyroid nodule, thyroid gland

* Mr. Med Sci Mersudin MULIĆ Specialist in Internal Medicine Subspecialist in Endocrinology.
Address: „Sutjeska” C/11.36300 Novi Pazar. E-mail: merko@ptt.rs

INTRODUCTION

Thyroid nodules are one of the most common diseases in medicine in general. They include all the changes in which limited, one or more, parts of the thyroid gland structurally (morphologically) differ from the normal, healthy tissue. Thyroid nodules can be cysts, adenomas, carcinomas, lobulations of the normal tissue or any other focal changes in the thyroid gland (1). The prevalence of nodules and struma detected by palpation is about 3% in the entire population, about 6.4% in women and 1.5% in men (2, 3). On the other hand, during the research which included the healthy population, nodules were detected by echosonography in 60% of the patients (4). Autopsy studies detected thyroid nodules in over 50% of the examined glands (5). The prevalence of thyroid nodules increases with age, iodine deficiency and exposure to ionizing radiation. The clinical significance of the nodules detected in this way has not been fully and thoroughly evaluated yet. Most nodules in the thyroid gland are completely asymptomatic and most likely will never cause any symptoms. If the cells in the nodus produce thyroid hormones independently, the nodus can give the symptoms of an increased thyroid gland (hyperthyroidism). A small number of patients complain of the pain which spreads from the nodus to the ear or the jaw. If the nodus is of a very large size, it may perform compression of the esophagus and trachea causing difficult swallowing and breathing. In some cases, the patient may complain of hoarseness and difficulty in speaking due to the compression of the larynx. However, in about 10 to 15% of nodules in the thyroid gland there is a carcinoma. For these patients, early detection and proper treatment is the condition for an exceptionally good prognosis in most cases. Therefore, the need to diagnose and continue the treatment of the nodules in the thyroid gland which can potentially be malignant has led to a widespread belief that all nodules greater than 1-1.5 cm should be thoroughly investigated. The main task of the doctor, therefore, is to identify the nodules that are of suspicious or malignant nature in order to begin a timely treatment of cancer, and to avoid unnecessary surgery of benign nodules (6). The evaluation aims to identify relatively rare cases of thyroid carcinoma among very common thyroid nodules (6).

OBJECTIVE

The aim of the research is, by evaluating medical history, clinical, laboratory, and ultrasonography parameters, to assess the features of the thyroid structure in patients with disorders of the thyroid gland structure in the region of Novi Pazar. In our region, such studies have not been done in the past, and this is the first study that deals with the evaluation of the nodules in this area. For these patients, early detection and proper treatment are the conditions for a good prognosis. Therefore, it is necessary to timely diagnose and treat people with nodules in the thyroid gland and, in particular, to distinguish patients with the nodules that can be potentially malignant.

MATERIAL AND METHODS

The study involved 61 patients with an irregular thyroid gland structure in the region of the HC Novi Pazar. During the research, the following methodology was used:

1. Clinical examination in the assessment of the nodule size.
2. Ultrasound examination of the thyroid gland
3. Laboratory parameters for the evaluation of the thyroid function (measurement of serum concentrations of triiodothyronine (T-3), thyroxine (T-4), thyroid-stimulating hormone (TSH), and the titer thyroglobulin (TgAb) and microsomal (antiperoxidase, TPOAb) antibodies).
4. Questionnaire on life quality assessment (which included: full name, date of birth, gender, occupation, marital status, TV, TT, BMI, socioeconomic living conditions, pre-radiation of the neck region, the family history of cancer, as well as the question of why a patient came to see a doctor).
5. Statistical data processing

RESULTS

The study included 61 patients of whom 58 were female and three were male patients (Table 1).

Table 1

Gender	f	%
Male	3	4.92
Female	58	95.08
Toal	61	100.00

The youngest patient was 22 years old and the oldest was 76. The average age of females was 50.76 ± 13.4 years, while male patients were 54.33 ± 2.3 years of age. The prevalence and distribution of thyroid nodules according to the age of patients, taking a group interval of 5 years, is given in Table 2

Table 2

Age	f	%
20-24	1	1.64
25-29		
30-34	4	6.56

35-39	10	16.39
40-44	7	11.47
45-49	8	13.11
50-54	3	4.92
55-59	11	18.03
60-64	7	11.47
65-69	6	9.84
70-74		
75-79	4	6.56
80-84		
Total	61	100.00

Table 2 shows that the incidence of thyroid nodules in patients is highest at the age of 35-39 and 55-59.

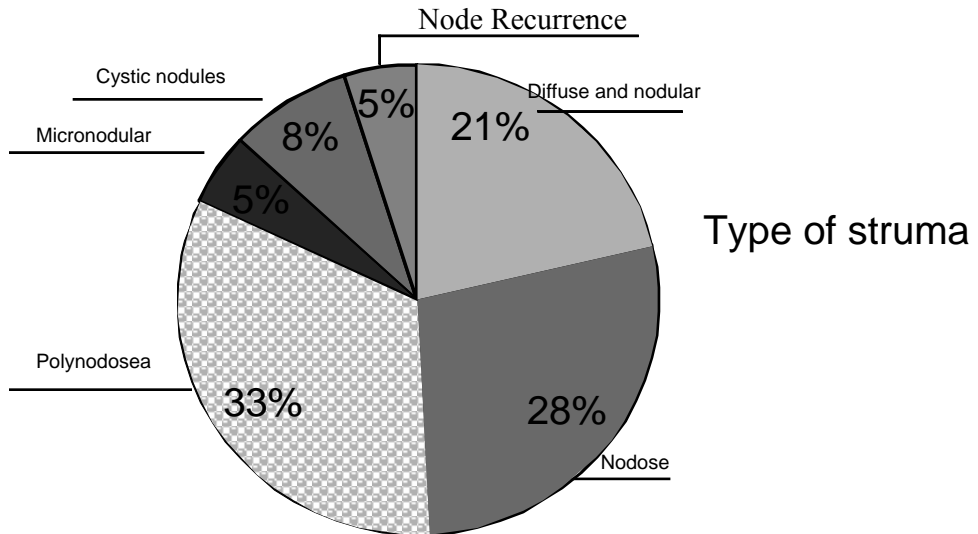
The analysis of the findings listed in the thyroid ultrasound examination revealed the following distribution, Table 3, Figure 1

Table 3

Struma	f	%
Diffuse and nodular	13	21.31
Nodose	17	27.87
Polynodose	20	32.79
Micronodular	3	4.92
Cystic nodules	5	8.19
Node recurrence	3	4.92
Total	61	100.00

13 patients were diagnosed with diffuse and nodular struma, 17 patients had a single thyroid nodule. Most patients (20 of them) had multinodular struma, 3 patients had micronodular struma and cystic nodules were found in 5 patients. In 3 patients there was the recurrence of nodules in the remaining lobe after lobectomy. It is evident that there is the highest percentage of multinodular struma (about 33%).

Figure 1. The distribution of patients according to the morphological findings



The distribution of patients according to the value of the findings of T3, T4, TSH is shown in Table 4.

Table 4

T3	fN	%
1 – below RR		
2 – within RR	47	77.05
3 – above RR	14	22.95
Total	61	100.00
T4	fN	%
1 – below RR		
2 – within RR	47	77.05
3 – above RR	14	22.95
Total	61	100.00
TSH	fN	%
1 – below RR	14	22.95
2 – within and above RR	47	77.05
Total	61	100.00

RR: reference range

T3 findings in 77% of patients (47 of them) were within the normal range, and 23% (14 of them) had T3 values above the reference range.

The distribution of patients in relation to the values of the findings of thyroglobulin and microsomal antibodies is shown in Table 5.

Table 5. Distribution of patients according to the values of laboratory tests for thyroglobulin and microsomal antibodies

Thyroglobulin antibodies	fN	%
2 – within RR	49	80.33
3 – above RR	12	19.67
Total	61	100.00
Microsomal antibodies	f	%
2 – within RR	46	75.41
- above RR	15	24.59
Total	61	100.00

The values found for the level of thyroglobulin antibodies in 49 patients (80%) were within the reference range and in 12 patients (20%) they were above the reference range. The values found for the level of microsomal antibodies in 46 patients (75%) were within the reference range and in 15 patients (25%) they were above the reference range.

DISCUSSION

Thyroid nodules are often discovered during clinical examination, especially if it was supplemented with echotomographic assessment of the thyroid gland. In countries like the U.S., where iodine deficiency is corrected with iodine prophylaxis, thyroid nodules are clinically evident in about 4-7% of the entire population. The prevalence is higher in countries affected by high or severe iodine deficiency, where the disease is endemic (7). The incidence of sub-clinical (non-palpable) nodes detected by means of thyroid ultrasonography reaches 50% in women older than 50. In our series of patients, ultrasound examination showed that there were 21.31% patients with diffuse and nodular struma, whereas 27.87% of patients had only nodular struma. The sum of these two categories shows that in our area, too, the percentage of nodes detected by means of echotomographic assessment is around 49%, which indicates that the incidence of nodular changes in the study population of Novi Pazar and the surrounding area is at the global level.

In our study, we discovered elevated antithyroglobulin antibodies in 12 patients, which could speak in favor of the existence of inflammation of the thyroid gland, 3 patients with diffuse and nodular struma, 3 patients with nodular struma, 3 patients with polynodose struma and 3 patients with node recurrences. A similar result was obtained when testing the presence of high titer antimicrosomal (peroxidase) antibodies – there was an increase in 15 patients, or 25% of the study population, which could indicate the presence of Hashimoto's thyroiditis. Radionuclide examination shows that scintigraphy isoactive "hot" nodules represent 3-20% of thyroid nodules and their incidence is higher in countries with iodine deficiency. About 10% of nodules in this group were malignant. They are 3 to 4 times more common in women, particularly after the age of 40. In most cases, warm nodules are benign. Cold nodules make more than 80% of all thyroid nodules and up to 17% of them may be malignant.

Thyroid ultrasonography can distinguish three different types of nodes: cystic, solid or mixed (containing solid and cystic component). Cystic nodules (10-20% of all nodules) are almost always benign (malignancy rate is of about 10%). In our study, 5 cystic nodules were found among the study population of Novi Pazar and the surrounding area, which is 8.19% of the study population. Discovered data indicate that the presence of nodes in examined material is lower than the world average. Thyroid malignancy is found by means of ultrasonography in about 10% of cold nodules that are solid or mixed. Since hot and cystic nodules can be tentatively considered as neoplastic diseases, the prevalence of thyroid malignancy is approximately 5%. As neck ultrasonography is a routine procedure in the diagnostics, the detection of micro nodes is increasing. Generally, micro nodes have no clinical significance and, in the absence of other clinical findings, they do not call for further examination or treatment. Most often, it is recommended that ultrasound is repeated at regular intervals, i.e. in 6 to 12 months. In our examined material, micronodular changes were observed in 3 patients or 4.91% of the study population.

When diagnosing benign lesions, it is equally important to note clinical signs or symptoms, such as compression of the trachea, esophagus, or recurrent laryngeal nerve, which all require surgical treatment. Normally, it is considered that the elderly are 1.5 to 2 times more likely to have malignant nodules than those aged 20 to 60, but this has not been confirmed yet (8).

A thyroid nodule is more suspicious of malignancy when detected in older men (over 60), and in children and adolescents (under the age of 20). In our series of patients, thyroid nodules were detected in only 3 male patients, accounting for 4.92% of the study population. The highest incidence of nodes was found in the age group of patients between 55 and 59. The second group in terms of incidence of thyroid nodes in our study is the group of patients between 35 and 39 years of age. In the study, in which the correlation between suspicious clinical findings and histological diagnosis was required, a benign disease was found in 29% of patients with palpable cervical

lymph nodes, in 50% of patients with solid nodules, in 29% of patients with a visible fixation of nodes, and in 17% of patients with vocal cord paralysis. Thus, the available data indicate that the clinical characteristics may increase the likelihood that an evaluation of a nodule greater than 1 cm in diameter is of malignant nature and this may be helpful in interpreting cytopathological findings of unspecified nature (9).

General clinical examination is important to detect signs and symptoms of hypo- or hyperthyroidism and health conditions where a surgical procedure is contraindicated. Two groups of researchers have investigated the concentration of TSH in patients with thyroid nodules and both confirm that the higher TSH is related to an increased risk of malignancy. In general, the concentration of TSH above the upper limit of the reference range is linked to the 2 to 3 times greater risk of the nodule being cancerous. So far, there are still no prospective and controlled studies that address this issue (10).

In our study, it is shown that 47 patients or 77.05% of the patients had the normal value of T3. 14 or 22.95% of patients had elevated T3 values. None of the subjects had lower levels of thyroid hormones. Elevated serum T3 in the patients could indicate the existence of hot nodes in the thyroid gland with increased functionality. T4 measurement showed normal values in 47 patients, or 77.05% of the study population. None of the patients had lower levels of T4. 14 patients, or 22.95% of the study population, had elevated serum T4. TSH was normal in 47 patients, or 77.05% of the study population. TSH reference values below the range were found in 14 patients, or 22.95% of the study population. Together, given the existence of elevated T3 and T4 values with supreme TSH values, hyperthyroidism was indicated in 14 patients, who make up 22.95% of the study population among the entire population of Novi Pazar and the surrounding area.

The distribution of the patients in our study based on the conclusion of ultrasound examination is given in Table 3 in the work results section. The most frequent finding in the ultrasound scan in our patients was the existence of polynodular goiter (32.79%), the second most common was the presence of nodular goiter (27.87%), while the third group, in terms of frequency, combined diffuse and nodular goiter (21.31%).

Many centers prefer almost total thyroidectomy for papillary nodules suspected of neoplasia, the findings of follicular changes or atypical images with a lower risk degree identified as indeterminate cytological findings (11, 12). Measurement of serum TSH by means of an ultra-sensitive process, thyroid ultrasonography, thyroid scintigraphy and ^{99m}Tc FNB can be considered the first line of examination. In countries where iodine deficiency is improved, many doctors believe FNB choice test and additional testing should be based on the results of FNB. If the nodules are shown as hot in scintigraphy, further examination generally depends on the presence of hyperthyroidism, and the size of the nodule. In the cases of cystic forms, FNB is performed for therapeutic purposes (contents evacuation) and as a diagnostic procedure it is used to detect a small percentage of cystic carcinomas. If a

nodule is cold in thyroid scintigraphy and mixed or solid in thyroid ultrasonography, the decision on further treatment will depend on the results of FNB.

CONCLUSION

1. The incidence of thyroid nodules in the Healthcare center of Novi Pazar is highest at the age between 55-59 with 18.03%.

2. The most common form of the disorder of the thyroid gland structure in the Healthcare center of Novi Pazar is multinodular goitre with 32.7%.

3. Adequate examination is the "gold standard" in the evaluation of patients with nodules in the thyroid gland.

4. Fine needle aspiration biopsy is performed because it is the first diagnostic tool in the evaluation of patients with solitary pulmonary nodule due to its simplicity and accuracy.

5. Methods and tests performed during this study may be useful in the evaluation of patients with a nodus and performed in accordance with local protocols and findings.

LITERATURE

1. DeGroot LJ, Pacini F. Thyroid Nodules. <http://www.thyroidmanager.org/Chapter18/18-nodulesframe.htm> 1-5-2006. 13-2-2009.
2. Tunbridge WM, Evered DC, Hall R et al. The spectrum of thyroid disease in a community: the Whickham survey. *Clin Endocrinol (Oxf)* 1977; 7(6): 481-493.
3. Vander JB, Gaston EA, Dawber TR. The significance of nontoxic thyroid nodules. Final report of a 15-year study of the incidence of thyroid malignancy. *Ann Intern Med* 1968; 69(3): 537-540.
4. Tan GH, Gharib H. Thyroid incidentalomas: management approaches to nonpalpable nodules discovered incidentally on thyroid imaging. *Ann Intern Med* 1997; 126(3): 226-231.
5. Mortensen JD, Woolner LB, Bennett WA. Gross and microscopic findings in clinically normal thyroid glands. *J Clin Endocrinol Metab* 1955; 15(10): 1270-1280.
6. Janković R. Surgery of thyroid and parathyroid glands. Institute for textbook publishing and teaching aids, Belgrade, 2001.
7. Belfiore A., La Rosa G.L., La Porta G.A., Giuffrida D., Milazzo G., Lupo L., Regalbutto C., Vigneri R. Cancer risk in patients with cold thyroid nodules: relevance of iodine intake, sex, age, and multinodularity. *Am J Med* 1992; 93: 363-369
8. Yang J, Schnadig V, Logrono R, Wasserman PG. Fine-needle Aspiration of Thyroid Nodules: A Study of 4703 Patients With Histologic and Clinical Correlations *CANCER (CANCER CYTOPATHOLOGY)* 2007, 111 / 5, 306-315

9. Gerhard R Cunha Santos G da: Inter- and intraobserver reproducibility of thyroid fine needle aspiration cytology: an analysis of discrepant cases *Cytopathology* 2007, 18, 105–111
10. K. Boelaert, J. Horacek, R. L. Holder, J. C. Watkinson, M. C. Sheppard, and J. A. Franklyn: Serum Thyrotropin Concentration as a Novel Predictor of Malignancy in Thyroid Nodules Investigated by Fine- Needle Aspiration *J Clin Endocrinol Metab* 2006, 91: 4295–4301
11. Delbridge L Symposium on Evidence-Based Endocrine Surgery (2): Benign Thyroid Disease *World J Surg* 2008, 32:1235–1236
12. White ML, Doherty GM, Gauger PG: Evidence-Based Surgical Management of Substernal Goiter *World J Surg*, 2008, 32:1285–1300