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# Annual Incidence of Thyroid Disease in Patients Who First Time Visit Department for Thyroid Diseases in Tuzla Canton

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**ABSTRACT**

**Aim:** The aim of this paper was to evaluate the incidence of thyroid gland diseases in relation to age, sex, existing associated symptoms and thyroxine and thyroid-stimulating hormone levels, in correlation with morphological characteristics and corresponding clinical diagnosis for thyroid gland. **Methods:** Retrospective research was conducted in the period 1-Dec-2017 to 31-Dec-2017 and included a total of 500 subjects of both sexes aged 1 to 80 years. All subjects had clinical examination, which included anamnestic data, palpatory examination of thyroid gland, as well as functional status of thyroid gland. **Results:** The results of the research have shown that majority of subjects were females (78.6% vs. 21.4%). The largest number of subjects was in the age group 41 to 60 years. The average age of females was 43.22 years and 42.86 for males. The most common associated symptom for both sexes was related to cardiovascular system disorder (61.2%). Subclinical hypothyroidism was the most prevalent thyroid gland disease (12.8%), while diffuse enlargement of thyroid gland (4.60 %) was the most common in morphological classification. The mean value for free thyroxine for the overall sample was 14.39 pmol/L and 3,4 mlU/L for thyroid-stimulating hormone. Thyroid-stimulating hormone levels were highest in the age group 41-60 years (p=0.043). **Conclusion:** The overall incidence of thyroid gland diseases was 18.57% for females and 13.08% for males. Free thyroxine levels were highest in thyroid gland with nodular changes and subclinical hypothyroidism (p=0.0001). Thyroid-stimulating hormone levels had the highest value in a thyroid gland with diffuse changes and subclinical hypothyroidism (p=0.0001).

**Keywords: incidence, subclinical hypothyroidism, thyroid-stimulating hormone, thyroxine.**

## 1. INTRODUCTION

Thyroid diseases are common problem in the population. This small gland located in the neck plays an important role in regulating metabolism, as well as in functioning of a whole range of organs and organ systems. As there are various causes for these diseases, there are various causes for increased incidence, such as better diagnostics, radiation exposure (i.e. the Chernobyl accident as a cause of a greater number of malignant thyroid diseases in the exposed area). Incidence of thyroid diseases after radiation exposure in adults increases by 16-31% (1). The prevalence of thyroid disorders depends on a large number of factors, of which, the most important include: age, sex, geographic factors, ethnicity. The prevalence of thyroid disorders is higher in countries with iodine deficiency, where endemic goitre is also present (2). Nearly one third of the world's population lives in areas with iodine deficiency (3). In areas where daily iodine intake is <50μg, goitre is usually endemic, and when daily intake falls to <25μg, the congenital hypothyroidism is noticed. Goitre prevalence in the areas of serious iodine deficiency can be as high as 80%. Populations at a special risk have tendency to be remote and live in mountainous areas in southeast Asia, Latin America and Central Africa. Iodization programs have shown the value in decreasing the number of goitre and preventing development of goitre and cretinism in children. It can independently develop into nodular goitre

which can occasionally lead to thyrotoxicosis, and iodization programs can also cause thyrotoxicosis, especially in people older than 40 years with nodular goitre (4). In the areas of iodine sufficiency, most people with thyroid gland disorders have an autoimmune disease, ranging from primary hypothyroidism, Hashimoto thyroiditis and thyrotoxicosis caused by Graves' disease. Cross-sectional studies in Europe, USA and Japan have determined the prevalence of hyperthyroidism and hypothyroidism in various Caucasian communities (white race community) (4). Data from a large US population screening (5, 6) revealed differences in frequency of thyroid gland dysfunction in various ethnic groups, while studies from Europe found the effect of nutritional iodine in epidemiology of thyroid gland dysfunction (7). Studies on frequency of autoimmune thyroid gland disease were carried out only in a small number of developed countries (8). According to morphological criteria, thyroid diseases can be divided to tumor and non-tumor diseases. The pathology of thyroid nodules can be present at any age and is very common in clinical practice. The prevalence of thyroid gland nodules is larger in countries with iodine deficiency, where endemic goitre is also present (2). Causes for thyroid nodules are complex and still underexplored. One of the important factors in pathogenesis of nodular disease is thyroid-stimulating hormone (TSH), as a strong stimulator of thyroid growth. In a normal gland or in a diffuse goitre, thyroid nodules can be solitary or multiple. In a multinodular goitre, one nodule can be clinically dominant in growth, dimensions and functional characteristics. Nodules are divided into neoplastic, which include hyperplastic and inflammatory nodules (within acute bacterial, subcutaneous or Hashimoto's thyroiditis) and neoplastic which are divided to benign and malignant. Benign neoplastic nodules include adenomas and malignant include primary carcinomas (papillary, follicular, medullary and anaplastic), lymphomas and metastases in thyroid gland originating in another organ. According to the functional state, they are divided to euthyroid (normal function), hyperthyroid (overactive function), hypothyroid (underactive function). The findings are referred to as normal, high and low.

## 2. METHODS

Retrospective research was conducted at the Radiology and Nuclear Medicine Clinic, Department for Thyroid Diseases, University Clinical Center Tuzla in the period 1-Dec-2017 to 31-Dec-2017. Research included a total of 500 subjects of both sexes aged 1 to 80 years, who were referred for examination for the first time. Subjects were divided into five groups according to their age: 1 to 15, 16 to 25, 26 to 40, 41 to 60 and 61 to 80. All subjects had clinical examination, taking into account anamnestic data, characteristics for thyroid gland diseases which are related to cardiovascular system disorders, menstrual disorders in women, difficulty swallowing and body weight changes. As a part of clinical examination, a palpatory examination was used, on the basis of which 4 categories were classified: normal findings, nodular changes in thyroid gland, multinodular changes in thyroid gland and diffuse enlargement of thyroid gland. In addition to that, by determining levels of free thyroxine (FT4) and thyroid-stimulating hormone (TSH), functional status of thyroid gland was determined for all subjects. FT4 concentrations with reference values ranging from 9.8-16.8pmol/L and TSH with reference values ranging from 0.63-4.19mlU/L, were determined by the DELFIA method (Dissociation-Enhanced Lanthanide Fluorescent Immunoassay) WALLAC Oy (LKB Pharmacia-Finland) on the WALLAC DELFIA fluorometer. The findings are referred to as normal, high and low, and the analysis of these hormones was compared to number of subjects, morphological characteristics and clinical diagnosis of thyroid gland diseases. Within clinical diagnosis and according to the FT4 and TSH levels, these were divided to: euthyroidism, subclinical hypothyroidism, subclinical hyperthyroidism, hypothyroidism and hyperthyroidism. Euthyroidism is defined by normal TSH and FT4 concentration. Diagnosis of subclinical hypothyroidism is based on higher TSH levels and normal FT4 levels. Subclinical hyperthyroidism is defined by lower TSH concentration with normal FT4 and FT3 concentrations. Diagnosis of clinical hypothyroidism is based on higher TSH levels and lower FT4 levels. Diagnosis of clinical hyperthyroidism is based on lower TSH levels and higher FT4 levels. Subjects who have previously been treated for thyroid gland disease and subjects who were on thyrostimulatory or substitution therapy, were excluded from the study.

Standard descriptive statistic methods were used in statistical data analysis: mean value, standard deviation, surface diagrams: histogram with circles, histogram with columns, Chi-squared test (x2), for calculation of significance of test differences, where $p<0.05$ will be considered statistically significant.

## 3. RESULTS

This paper presents and analyses retrospective research data which evaluated incidence of thyroid gland diseases in patients who were referred to the Radiology and Nuclear Medicine Clinic, Department for Thyroid Diseases for the first time. Research was conducted in the period 1-Dec-2017 to 31-Dec-2017 and included a total of 500 subjects of both sexes aged 1 to 80 years.

Cumulative and incidence rates were calculated for the total number of subjects, for normal results (euthyroidism) and for thyroid gland diseases (subclinical hypothyroidism, subclinical hyperthyroidism, hypothyroidism and hyperthyroidism) which has shown that 82.6% or 140 of 500 persons/year had thyroid gland with no abnormalities detected (euthyroidism) and 12.8% or 13.6 of 500 persons/year had subclinical hypothyroidism as shown in Table 1.

Of the total number of female subjects (393) overall incidence of thyroid diseases was 18.57%, of which subclinical hypothyroidism was found in 13.7% female subjects. Of the total number of male subjects (107) overall incidence for thyroid diseases was 13.08%, where subclinical hypothyroidism was found in 9.34% subjects.

Cumulative incidence and incidence rates for palpatory examination of thyroid gland were calculated in relation to palpatory examination which has shown that largest number of subjects had diffuse enlargement of thyroid gland (Table 2).

By analyzing the anamnestic data and associated symp-

| Clinical diagnosis | Cumulative incidence (CI) | Incidence density(ID) |
|---|---|---|
| Euthyroidism | 82,6% | 140 |
| Sub.hipothyreoidism | 12.8% | 13.6 |
| Sub.hyperthyreoidism | 0.2% | 0.2 |
| Hypothyreoidism | 2.4% | 2.4 |
| Hyperhyreoidism | 2.0% | 2.02 |

Table 1. Incidence of euthyroidism and thyroid diseases

| Clinical diagnosis | Cumulative incidence (CI) | Incidence density(ID) |
|---|---|---|
| Palpator rest result | 90.60% | 165.6 |
| Normal palpatory exam | 4.40% | 4.49 |
| Nodular changes | 0.40% | 0.4 |
| Multinodular changes | 0.40% | 0.4 |
| Diffuse enlargement | 4.60% | 4.7 |

Table 2. Incidence of palpatory examination of thyroid gland

| | Age group | n | Meank rank | Chi Square | df | p-value |
|---|---|---|---|---|---|---|
| Parametar | 1-15 | 31 | 9663.50 | | | |
| | 16-25 | 70 | 19486.50 | | | |
| FT4 | 26-40 | 114 | 27194.50 | 01.10.00 | 4 | 43 |
| | 41-60 | 197 | 47575.50 | | | |
| | 61-80 | 88 | 21330.00 | | | |

Tabela 3. Kruskal-Wallis test for TSH in age group

toms for which patients were referred for examination, largest number of subjects out of the total sample had symptoms related to cardiovascular disorders, 306 of them (61.2%). 13% of subjects had difficulty swallowing, while 5.2% of subjects had body weight change as a dominant symptom. A statistically significant difference was found (p=0.0001) (Figure 1).

Of the total number of subjects examined by palpation, in 453 or 90.6% subjects palpatory test result was normal. In 23 subjects (4.60%) diffuse morphological changes in thyroid gland were found, while nodular changes in thyroid gland were found in 22 subjects (4.4%) and multinodular changes in thyroid gland were found in 2 subjects (0.40%). There was no statistically significant difference (p=0.376).

All subjects were evaluated for functional status of thyroid gland, by determining levels of serum free thyroxine (FT4) and thyroid-stimulating hormone (TSH) and in total number of subjects the mean FT4 value was 14.39 pmol/L and mean TSH value was 3.4mIU/L.

By comparing the FT4 hormone analysis to number of subjects in age groups by reviewing the mean reference range for certain age groups in values of continuous FT4

| | Clinical diagnosis | n | Meank rank | Chi Square | df | p-value |
|---|---|---|---|---|---|---|
| Parametar | Euthyroidism | 413 | 107756.50 | | | |
| | Subclinical hypothyreoism | 64 | 12234.50 | | | |
| FT4 | Subclinical hyperthyreoidism | 1 | 224.50 | 75909 | 4 | 0.0001 |
| | Hpothyreoidism | 12 | 80 | | | |
| | Hperthyreoidism | 10 | 4954.50 | | | |

Tabela 4. Kruskal-Wallis test for FT4 hormone in clinical diagnosis

| | Clinical diagnosis | n | Meank rank | Chi Square | df | p-value |
|---|---|---|---|---|---|---|
| Parametar | Euthyroidism | 413 | 90039.50 | | | |
| | Subclinical hypothyreoism | 64 | 29417.00 | | | |
| TSH | Subclinical hyperthyreoidism | 1 | 11.00 | 216.32 | 4 | 0.0001 |
| | Hpothyreoidism | 12 | 5727.50 | | | |
| | Hperthyreoidism | 10 | 55.00 | | | |

Tabela 5. Kruskal-Wallis test for TSH hormone in clinical diagnosis

variable, no statistically significant difference was found. FT4 levels were highest in the age group 41-60.

Comparison of TSH analysis to number of subjects in age groups by reviewing mean reference rage for certain age groups in values of continuos TSH variable, found statistically significant difference (p=0.043). TSH levels were highest in age group 41-60 (Table 3).

By comparing analysis of FT4 hormone and thyroid gland morphology findings with a review of mean reference range for certain morphology findings in values of continuous free thyroxine levels (FT4) variable, no statistically significant difference was found (p=0.373). Free thyroxine (FT4) levels were highest in a thyroid gland with nodular changes.

Comparison of FT4 hormone analysis with clinical diagnosis, by reviewing mean reference range for certain clinical diagnosis of thyroid gland in values of continuous free thyroxine (FT4) variable, statistically significant difference was found in the proportion of observed characteristics between these methods (p=0.0001). If only pathological clinical findings were considered, levels of FT4 hormone were highest in subclinical hypothyroidism (Table 4).

By comparing the analysis of thyroid-stimulating hormone (TSH) and morphological findings of the thyroid gland, reviewing the median rank for certain morphological tests for thyroid gland in values of continuous variable of TSH, there was no statistically significant difference (p=0.269). Levels of thyroid-stimulating hormone (TSH) were highest in a diffuse enlargement of thyroid gland.

By comparing analysis of thyroid-stimulating hormone (TSH) in clinical diagnosis, reviewing the median rank values for certain clinical diagnosis of thyroid gland in values of continuous variable of thyroid-stimulating hormone (TSH), there was statistically significant difference in the proportion of observed characteristics between these

methods (p=0.0001). If only pathological clinical findings were taken into consideration, the highest levels of TSH were in subclinical hypothyroidism (Table 5).

## 4. DISCUSSION

Thyroid diseases are common in adults and prevalence is increasing in all parts of the world. Ethnicity and geographical position also affect the prevalence of thyroid disorders along with age, gender and iodine concentration in a diet. Thyroid dysfunctions are considered as the most common endocrine diseases. The incidence of thyroid gland dysfunction has increased with time and varies between sites (characteristic associated with iodine level in diet (19, 20). Average prevalence of undiagnosed thyroid gland dysfunction in Europe was 6.71%. Prevalence of undiagnosed hypothyroidism and hyperthyroidism was 4.94% and 1.72% (21).

Several studies have attempted to determine the incidence of hypothyroidism in general population. Whickham survey documented the incidence of 3.5/1000 years in women and 0.6/ 1000 years in male population, while latest Danish results have documented the incidence of 0.27/1000 years and 0.4/1000 years. Our result of 2.7% in female population and 0.93% in male population is higher than Whickham's tracking and higher than Danish results. In the original Whickham survey in North-East Ireland, 8% of women and 3% of men had subclinical hypothyroidism. In a study in Colorado, 9.4% of subjects had high serum TSH concentration, of which 9.0% had subclinical hypothyroidism. Our result of 13.7% of women and 9.34% of men who had subclinical hypothyroidism is higher than Whickham tracking. TSH levels were highest in subclinical hypothyroidism which was confirmed in our study.

In subclinical hypothyroidism, there is still a debate as to what constitutes a normal serum TSH, particularly in older subjects. Recent targeted analyses have shown increased cardiovascular risk in younger persons and those with serum TSH >10mIU/L (29). Other data suggest that mild thyroid deficiency can be the only reversible cause of left ventricular diastolic dysfunction. Treatment in subjects who are symptomatic, pregnant, >65 years with evidence of heart failure appear justified (30).

Studies in elderly subjects have confirmed high prevalence of increased serum TSH in this age group, with approximately 10% of subjects over 60 years of age in one general practice in Birmingham, United Kingdom, with serum TSH levels over the reference range (22). In the Colorado study, the percentage of subjects with an elevated TSH concentration was greater for women than men in each decade of age, reaching statistical significance for each decade after age of 34 (P<01). According to the number of subjects, TSH levels in our study were highest in the age group 41-60. Whickham survey found annual mean incidence of hypothyroidism in women of 0.8/1000 years, with negligible results in men (23). Large population study in Tayside, Scotland identified 620 cases of hyperthyroidism with an incidence rate of 0.77/1000 per year in females and 0.14/1000 per year in males (24). The incidence increased with age and females were affected two to eight times more than males. In our study, incidence rate for hyperthyroidism in females was 1.78% and 2.8% in male subjects, which is higher than other results and females were two times more affected than males. Prevalence of subclinical hyperthyroidism in female population was 0.42% and 0.27% for men (21). In our study, incidence rate for females was 0.25% and 0.0% for males.

We compared results for thyroid dysfunction in Europe and other parts of the world. National Health and Nutrition Examination Survey (NHANES III) provided reference on prevalence of thyroid dysfunction in the United States (25). Unknown hypothyroidism and hyperthyroidism were found in 4.6% and 1.3% of US sample. Comparing these results with current results from Europe, Europeans have surpassed Americans for 0.34% for unknown hypothyroidism and 0.42% for unknown hyperthyroidism. According to the Colorado study research, number of Americans with subclinical disease supersedes Europeans for 3.4%, while Europeans have 0.9% of clinical dysfunction. Information from Asia is scanty. Reported prevalence of thyroid gland function in Japanese, among the others, was about 10%, which is higher than in Europe (26). As usual, the main cause for thyroid gland dysfunction among Japanese was subclinical hypothyroidism (5.8%), followed by subclinical hyperthyroidism (2.1%). The prevalence of thyroid gland dysfunction in Australia was estimated in the elderly sample, but not in general population (27). Authors reported the prevalence of undiagnosed thyroid gland dysfunction of 3.6%, which is approximately half of what has been found in Europe. The Colorado study included 14 symptoms related to thyroid gland diseases (28). One of the symptoms is fatigue, which was also confirmed in our study, with largest number of subjects having cardio vascular disorders, of which 65 or (51.4%) were male subjects and 251 (63.8%) were female subjects. The most common thyroid gland disease is simple (diffuse) goitre. Epidemiological studies used ultrasonography to estimate the size of the thyroid gland, which led to greater estimates of goitre prevalence than in studies in which the goitre was estimated by physical examination (4). The largest prevalence was in women in premenopause and female to male ratio was at least 4:1 (29). In our study, female to male ratio was 10.5:1. In the Framingham study with 5234 subjects, the prevalence of solitary thyroid gland nodule was 3%, and 1% for multinodular goitre, while in our study with 500 subjects, prevalence of subjects with nodular changes in thyroid gland was 4.4% and 0.4% for multinodular changes in thyroid gland.

## 5. CONCLUSION

In a retrospective study which involved 500 subject of which the largest number were females in the age group 41 to 60, statistically significant difference was found with regard to sex. The average age for females was 43.22 years and for males 42.86 years. The most common associated system for both sexes was related to cardiovascular system disorders (61.2%), with a statistically significant difference (p=0,0001). Of the total number of subjects referred for examination 82.6% or 140 of 500 persons/year had thyroid gland with no abnormality detected (euthyroidism). Of total number of female subjects (393) the total incidence for thyroid diseases was 18.57%, where subclinical hypothy-

roidism was found in 13.7% of female subjects. Of the total number of male subjects (107) total incidence for thyroid diseases was 13.08%, where subclinical hypothyroidism was found in 9.34% subjects.

Subclinical hypothyroidism was the most common thyroid gland disease (12.8%), while the diffuse enlargement of thyroid (4.60%) was the most common disease in morphologic classification. The mean value for free thyroxine for the overall sample was 14.39 pmol/L and 3.4 mlU/L for the thyroid-stimulating hormone. Thyroid-stimulating hormone levels were highest in the age group 41-60, with a statistically significant difference (p=0.043).

Free thyroxine levels were highest in a thyroid gland with nodular changes and subclinical hypothyroidism (p=0.0001). Thyroid-stimulating hormone levels had the highest value in a thyroid gland with diffuse changes and subclinical hypothyroidism (p=0.0001). Statistically significant difference was found in both cases.


- **Author's contribution:** Each author gave substantial contribution to the conception or design of the work and in the acquisition, analysis and interpretation of data for the work. Each author had role in drafting the work and revising it critically for important intellectual content. Each authorgave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
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