The Epidemiological Characteristics of Autoimmune Thyroiditis in the Tuzla Canton in the Period from 2015 to 2020

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ABSTRACT

Background: Bosnia and Herzegovina (B&H) is one of the countries of Southeast Europe with the lack of data about chronic autoimmune thyroid diseases (CAITD) epidemiology. Objective: This research aimed to assess incidence of CAITD in the Tuzla Canton of B&H during a 6-year period (2015–2020). Methods: We retrospectively evaluated 82,000 hospital records of inpatients and outpatients with possible thyroid symptoms residing in Tuzla Canton of B&H (total of 445,028 inhabitants). The study included patients with laboratory and clinical proof of autoimmune thyroid diseases (AITD). Incidence rates were calculated with age standardisation using European standard population. Trends in incidence were evaluated as moving three-year averages. Results: During the observed period, 1875 patients satisfied the diagnostic criteria for CAITD with male to female ratio of 1: 8.01. Median age of all cases was 46 years (interquartile range: 31 to 61) and women and men were on average the same age at the time of diagnosis. The overall standardized incidence was found to be 71.25 per 105 (%95 CI=63.36–79.15). The overall standardized incidence in men was 16.25 per 105 and 123.74 per 105 in women. In the end of the observed period, AITD prevalence was 427.52 per 105 and 123.74 per 105 in women and men respectively. Conclusion: There was a slight decline of incidence in our region during the observed period. This decrease might be the result of combination of various factors, mainly the Corona epidemics outbreak and emigration. On the basis of the lower incidence rate in the Tuzla Canton, one can assume that iodine prophylaxis carried out in order to eradicate goitre had satisfied expectations because there had not been any enormous increase in patients with AITD. Keywords: chronic autoimmune thyroid diseases, epidemiology, incidence, prevalence.

1. BACKGROUND

Autoimmune thyroid disease (AITD) has the highest incidence of all autoimmune diseases (1). It is estimated that AITD prevalence in general population is 2-5% (2). In more recent times, when AITD has become relatively easy to diagnose and treat, and fatal outcomes as a result of AITD are relatively rare, it can still have a significant effect on quality of life if it is not treated appropriately. Although the epidemiology of AITD has been well-described worldwide and in Western Europe (3-10), epidemiological data on AITD in the region of Southeast Europe are sparse. There are some incomplete reports from Croatia and Serbia (11, 12), but in Bosnia and Herzegovina (B&H) there are no epidemiological data available in relation to AITD. The most common form of AITD is chronic autoimmune thyroid disease (CAITD) which includes: Hashimoto’s thyroiditis (HT) and atrophic thyroiditis (AT) (13). Therefore, this research consists of a six-year retrospective analysis to determine the epidemiological characteristics of CAITD in the well-defined geographical area of the Tuzla Canton (TC) in North-Eastern B&H.

The TC is the most densely populated region in B&H, and according to the latest census from 2013 it had 445,028 inhabitants (14). The Tuzla University Clinical Centre (UCC) is the regional secondary and tertiary type university hospital, where diagnostics and treatment of patients with CAITD from this area are performed.

2. OBJECTIVE

This research aimed to assess incidence of CAITD in the Tuzla Canton of B&H during a 6-year period (2015–2020).

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3. PATIENTS AND METHODS

This epidemiological research is descriptive and retrospective-prospective cohort study. The data used in this study were obtained by evaluation of the hospital records of out-patients at the Thyroid Diseases Clinic of the Radiology and Nuclear Medicine Clinic of Tuzla UCC, in the period from 01.01.2015. to 01.09.2020. A total of 82,000 patients were included in the research. Patients who came for repeated check-ups were excluded. Each patient is presented only once on the basis of their unique registration number. The study did not include patients younger than 14 years or patients who, according to the widely accepted diagnostic criteria, did not have a concise confirmation of the type of ailment. In the end only patients with confirmed CAITD were included in the study. All patients were classified according to gender and age, as well as according to type of disease.

Serum values of free triiodothyronine (FT3), free thyroxine (FT4), thyroid stimulating hormone (TSH), thyroid peroxidase antibodies (TPOAb), and thyroglobulin antibodies (TgAb) of all patients were recorded, with the following reference ranges: FT3: 3.1-6.8 pmol/l, FT4: 12.0-22.0 pmol/l and TSH: 0.27-4.2 mU/l, TPOAb: 0.0-34 IU/ml and TgAb: 0.0-115 IU/l. The analyses were conducted using electrochemiluminescence assay (ELCIA), Elecsys Cobas 411 (Roche Diagnostics, Mannheim, Germany).

The size of the thyroid gland was assessed on the basis of the palpable finding and visibility, in line with the classification proposed by the World Health Organization (WHO) (15): A - not visible and not palpable; B - not visible, palpable but normal size and consistency (both stages correspond to phase 0-A); C - not visible, but palpably enlarged gland (Phase 0-B); D - visibly extended neck and clearly enlarged thyroid gland (Phase 1); E - visible goitre on the neck in a normal position (Phase 2). The CAITD classification also includes separation into two forms of clinical disease: HT and AT (15).

Statistical analysis

Statistical analysis was performed using SPSS 15.0 (SPSS, Chicago, IL, USA). Descriptive statistics were used to describe the basic features of the data in a study, and a Student t-test and a Chi square test of independence. The year of diagnosis was used for the given incidence. To calculate the rate of incidence, presuming Poisson distribution of cases, a 95% confidence interval (CI) was taken.

4. RESULTS

During the six-year period, 1875 cases of CAITD were registered, of which 88.91% were female and 11.09% male patients. The ratio of women and men was 8.01:1. The mean age of all patients was 46 years (interquartile range: 31 to 61 years) with a range of 15 to 75+ years. The mean age of females (46.9±14.2 years) was about the same mean age as the male patients (46.1±15.2 years). The Student t-test did not find any significant difference in the mean ages of men and women for AT (t=0.726, df=1510, p=0.469) or HT (t=0.073, df=353, p=0.941). Autoimmune thyroiditis was recorded in 80.9% patients, while 19.1% had HT.

According to the data obtained, it may be seen that in the TC, 0.4 % of the population had CAITD. The total prevalence of patients with CAITD in the period from 2015 to 2020 was 427.52 (408.17, 446.87). The total prevalence of AT in all patients was 345.93 CI (328.53, 363.34) and for HT 81.77 (73.13, 90.04). The prevalence amongst women for AT was 599.44 (567.41, 631.46), for HT 142.96 (127.31, 158.6),
The incidence rate for the whole population is in the range as well as for the whole sample, is shown in the Figure 1. The annual incidence individually for both genders, (109.18, 138.30) and 16.25 (10.87, 21.70), for women and the total incidences of thyroid gland diseases were 123.74 and in total, respectively. The total incidence of thyroid gland diseases (AT+HT) per 100,000 inhabitants was 71.25 is much higher for the female population than for men, that is, for women, man, and in total 99.80 (86.69,112.82), 13.38, (9.06, 19.42) and 57.66 (50.54, 64.7), respectively. The mean incidence of HT in the same period was 23.82 (18.06, 31.38), 2.88 (1.03, 6.10) and 13.63 (10.44, 17.60) for women, man, and in total, respectively. The total incidence of thyroid gland diseases (AT+HT) per 100,000 inhabitants was 71.25 (63.56, 79.15). Observing it separately for women and men, the total incidences of thyroid gland diseases were 123.74 (109.18, 138.30) and 16.25 (10.87, 21.70), for women and men. The annual incidence individually for both genders, as well as for the whole sample, is shown in the Figure 1. The incidence rate for the whole population is in the range between 29.4/105 and 104/105. The highest incidence recorded was amongst women in 2017 (183.95/105).

The trend in the annual incidences of AITD as a moving three year average is shown in Figure 2. A decrease in incidence over the period in question is noticeable, and was confirmed by linear regression.

The graphic presentation of incidence by gender and age shows that the highest incidence was in the 45-54 year age group in both genders (Figure 3). The Student t-test did not find any significant difference in the mean ages of men and women with AT (t=0.726, df=1510, p=0.469) or in patients with HT (t=0.726, df=1510, p=0.469).

Figure 3. Incidence of CAITD by age and gender

Figure 4. Distribution of sex and type of diseases

Although the ratio of woman and men in the observed population was not evenly distributed, in the two-dimensional frequency panel, the Chi-square test of independence was conducted (Figure 4) in order to test the connection between gender and the type of thyroid gland diseases. The results suggest that gender is not a significant criterion of distribution into individual groups according to the type of AITD (Pearson chi2 (1) = 0.2579, p=0.612).

5. DISCUSSION

Endocrinology is facing its greatest challenges today in relation to the problem of the incidence of AITD. According to research conducted in the United Kingdom (UK) (2) 2-5% of the general population is affected by an autoimmune response to thyroid components, and in Scotland alone (5) hypothyroidism is found in 2-3% of the general population. While the total prevalence of AITD in the Republic of Croatia was 5.29% in 2015 (12), the results of this study indicate a significantly lower prevalence in the TC, where it amounted to 0.42% amongst the general population. No epidemiological research into AITD in B&H has been conducted so far, but it is possible to draw comparisons with data from the review paper on AITD, which provides results from the UK, Spain, Scotland and Sweden (7). Statistical data from 2008 in the UK indicate annual incidence of hypothyroidism of 250/100,000 in women and 80/100,000 in men (9, 16). Similar results were recorded in research conducted by Flynn et al. (5) in the UK where the incidence for men was more than 80/100,000 and for women more than 400/100,000. The results obtained in our study indicate that the incidence in the TC is lower, that is, per 100,000 inhabitants the number of cases of CAITD in women was 123.74, in men 16.25, and in total 71.25. The deviations are even greater knowing that this study included all patients with CAITD (with different hormonal status), while the studies from UK, Scotland and Sweden only analysed the incidence of hypothyroid patients. It is possible that the cited studies have a higher rate of incidence due to the type of study conducted (prospective study - screening conducted), and that a larger number of subclinical cases were included in the incidence rate. Our research only included patients who sought medical help due to their symptoms, and had had CAITD confirmed. Also, this study only analysed patients with high TPOAb and TgAb values, while the other studies mentioned analysed functional disorders, where it is possible that not all patients with hypothyroidism had AITD. The lower incidence of CAITD recorded in the TC may had also been influenced by the possibility of the choice by a certain number of patients to attend private clinics, and who were, not entered into a joint IT system. Consequently, these patients were not included in the statistical analysis.

A high incidence of 200/100,000 was recorded by Sundbeck et al. in a study conducted in 1991 in Sweden (17). Such a high incidence was primarily the result of the limitations of that study, because only older women were included in the research and the autoimmune aetiology was not traced. If the results of the research from Scotland conducted in 2017 are compared to the results of the present study for the same year in B&H, limiting it to the region of the TC, and if only women in our study are analysed, the highest
incidence was recorded in 2017. This is not a major deviation from the results from Scotland, however it only relates to 2017. It is possible that, due to the increasing life expectancy in Scotland, there is a greater possibility of diagnosing hypothyroidism, with the consequent higher incidence rate. The research from Spain showed a much lower incidence of hypothyroidism due to AITD, where for men the rate was 2.2/100,000 and for women 45.4/100,000. This is significantly lower than in other published research and much lower than even in our research as well. This study had an exclusively selected list of out-patients with no screening, and this was without the major effect on incidence of patients with subclinical hypothyroidism. The post-hoc evaluation of changes probably underestimated the incidence rate, because a prospective study would have included the subclinical cases. Although the United States of America began the first prophylaxis of thyroid diseases by using iodinated salt in 1917, in former Yugoslavia, of which B&H was a part until the early 1990’s, using did not begin until 1950’s. The prophylaxis had a positive effect and endemic goitre vanished from these regions, however the incidence of AITD increased (19, 20). It is assumed that higher levels of iodine reduced the incidence of hyperthyroidism at the cost of a higher rate of hypothyroidism (18, 19). The total incidence of hyperthyroidism noticed in Ireland was lower, while it was higher than in Denmark, where a mild or moderate lack of iodine was observed (20). The International Council for Control of Iodine Deficiency Disorders recommend a daily intake of 150 μg iodine for adolescents and adults (21). In order to provide this daily intake, in 2007 they recommended the iodization of cooking salt in the amount of 15-40 mg/kg. In most cases, the population of the TC uses iodized cooking salt produced locally which contains 20–30 mg/kg of potassium iodate. Iodized cooking salt differs from region to region, so in neighbouring Croatia, locally produced salt contains 25.5–38.5 mg/kg potassium iodate, while in salts from Slovenia, Spain, and Australia contains 20 mg/kg, 60 mg/kg, and 76 mg/kg of potassium-iodate in cooking salt, respectively (22, 23). The guidelines in the recommendations for iodization of cooking salt have changed due to the effect of iodization on the occurrence of goitre and AITD, and a minimum of 30 mg of potassium iodate in 1 g cooking salt is recommended, which in our region is categorized as an optimum supply, but at the lower limit (24). On the other hand, the guidelines for salt iodization have also changed in order to reduce the intake of salt and to prevent cardiovascular diseases. A higher concentration of iodine in salt is recommended, still maintaining a sufficient intake of iodine (25). However, it may be presumed that most people continue to use an equal quantity of salt which now has higher iodine content. This could be one of the major causes for increase in the incidence of AITD in developed countries who have successfully reduced the incidence of CVDs.

As shown in the Figure 2 there was a decrease in incidence in 2019. This was due the reduced number of visits the doctors in 2020 due to the COVID-19 pandemic. The greater ratio of female patients with AITD (8.01:1) is not surprising. The domination of female patients is a well-established fact, which has been reported in several studies (7, 26–28). As a result, female gender is a firmly established risk factor for all types of AITD. The higher probability of women developing the disease may be explained by disrupted inactivation of the X chromosome, the role of sex steroids and foetal microchimerism (27). Another cause of the higher incidence of AITD in women is the interaction of thyroid hormones and sex hormones during the menstrual cycle, pregnancy and menopause (28). Thyroid problems can occur at any time, but some research has shown that in women autoimmune processes most often occur in menopause. The results of this research indicate that although women suffer from CAITD more often, gender does not determine the type of AITD. According to the figures from the annual report of primary health care teams in Croatia for 2016, thyroid disorders account for 32.52% of endocrine diseases, and 1.7% of total morbidity. They are registered most often in the 20–64 age groups (68.96 %) (27). These figures are in accordance with the results from our study, according to which in the TC patients of both genders aged between 45 and 54 years most often suffer from CAITD.

This study also has its own limitations that should be highlighted. The data were collected at the largest centre for thyroid disorders in the TC, where almost all patients from the region are treated. However, some patients are treated elsewhere in the B&H, and the data from these institutions are not available for analysis. Intensive emigration of the residents of TC may also lead to the decrease in the incidence, although this remains only on assumptions. Despite the limitations, this research provides beneficial information of great local and regional importance in view of the fact that there are no data on the epidemiology of AITD from B&H in existence. In addition, bearing in mind that the incidence of AITD differs in countries with different legislation governing the iodization of cooking salt, it demonstrates the possible correlation of cooking salt iodization with the incidence of CAITD in our region, which should be further considered in the subsequent studies.

6. CONCLUSION

From the results of this study it can be concluded that the incidence of AITD in our region in the 2015–2020 period showed a significant decrease in the later years of the study. Due to the suspicion that the apparent trend of decreasing incidence of AITD might be a consequence of emigration and the worldwide problem of the Corona virus, it would be valuable to continue to monitor the incidence of AITD in the TC in the years to come. If the incidence of AITD does indeed decrease in the future, it would be a good basis for future research to presume that the legislation on iodization of cooking salt, in line with the guidelines of the WHO, has met the expectations in our country, that is, that it would reduce the incidence of goitre without an (significant) increase in AITD.

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