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TYPE 2 DIABETES AND HASHIMOTO THYROIDITIS-POSSIBLE ASSOCIATIONS AND CLINICAL CORRELATIONS - PRELIMINARY RESULTS

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Abstract

Background and aims*: The primary objective is to evaluate the possible relationship between Type 2 Diabetes (T2DM) and Hashimoto Thyroiditis (HT), since the only correlation described until now is between Type 1 Diabetes and HT based on the autoimmune mechanism. The secondary end-point is to evaluate if there is a correlation between the characteristics of Type 2 Diabetes and autoimmune thyroiditis and if the metabolic component may be a factor of association.* ***Material and method:*** *We designed a retrospective, observational research, enrolling patients from "Sanamed" Hospital from Bucharest. Between 2016 and 2017 in our clinic a number of 150 patients were enrolled, in the following groups: 50 only with T2DM, 50 only with HT and 50 with both T2DM and HT.* ***Results****: The main observations of the study were the following: the prevalence of obesity was higher in patients with T2DM ($p<0.001$) than in the group with HT ($p<0.001$); Dyslipidemia was higher in the HT group ($p<0.001$) than in the group of T2DM ($p<0.001$); Ischemic cardiac disease was more frequent in the HT group ($p<0.001$) than in the Diabetes group ($p<0.001$); in the group that had both T2DM and HT, the HbA1c was correlated with pre-existing Thyroid pathology ($p<0.001$), also Dyslipidemia was associated with hepatic steatosis ($p<0.001$).* ***Conclusions****: After assessing all the parameters we have reached the conclusion that there is an association between the characteristics of T2DM and HT, as well as an interaction between these two diseases, considering their metabolic component.*

key words: *type 2 diabetes, autoimmune thyroiditis*

Background and aims

The primary objective of this study is to evaluate a possible relationship between Type 2 Diabetes (T2DM) and Hashimoto Thyroiditis (HT), since the classical association described until now is between Type 1 Diabetes (T1DM) and HT, based on their common autoimmune mechanism. The association between those two autoimmune diseases was established throughout hormonal determinations and clinic appearance of the two illnesses. It is a well-established

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practice that after the onset of T1DM the next conditions to be checked are HT as well as celiac disease. In children, T1DM most frequently is associated with celiac disease and in adults it associates HT. T1DM and Autoimmune thyroiditis (AITD) occasionally co-exist and this forms the autoimmune polyglandular syndrome (APS) type 2 [1]. This is an autosomal dominant disorder and is often associated with other disorders, such as celiac disease, myasthenia gravis or premature ovarian failure [2,3]. AITD is not so often seen in the much rarer APS type I and there is no association between mutations in the AIRE gene, which causes APS type I, and sporadic AITD [4]. All of this proves an association of other autoimmune phenomena with AITD. A strongly association between T1DM and thyroiditis was made through the analysis of HLA molecules, DRβ-Tyr-26, DRβ-Leu-67, DRβ-Lys-71, and DRβ-Arg-74 [5,6]. Since all this was researched and it was published, we decided to see if there is any connection in between T2DM and thyroiditis; since it is very common encountered in the clinical practice.

The secondary end-point is to evaluate if there is an association between the characteristics of T2DM and autoimmune thyroiditis and if the metabolic component is a factor of association.

Material and methods

We designed a retrospective, observational research on patients attending visits to "Sanamed Hospital"- Clinic from Bucharest. During 2016 and 2017 in our clinic a number of 150 patients were enrolled in one of the following three groups: 50 patients having only T2DM, 50 having only HT and 50 having both T2DM and HT. For the positive diagnosis of T2DM, the American Diabetes Association's diagnostics criteria were followed: HbA1c ≥6.5% (48mmol/mol) or fasting plasma glucose ≥ 126mg/dL (7.0mmol/L). For thyroiditis, TPO antibodies were measured and a value above 8IU/L was considered to be positive and indicated the presence of AITD. Several other biological parameters ware analyzed such as TSH and Free T4, in all the participants in the study. The patients were evaluated form a clinical point of view as well; the presence or absence of the following conditions was established: obesity, dyslipidemia, arterial hypertension, cardiac ischemic disease, metabolic syndrome, hepatic steatosis or preexistent thyroid pathology. The three groups were divided as follows taking into consideration the gender: for the T2DM group 26 (52%) were females and 24 (48%) were males, for the group with HT 48 (96%) were females and 2 (4%) were males, respectively for the last group, 48 (96%) were females and 2 (4%) were males.

Results

Out of the results it was considered to be statistically significant the following: the incidence of Obesity was higher in the lot with T2DM (32%) than in the lot with HT (21%) as shown in Figure 1 below, the differences being statistically significant ($p<0.001$).

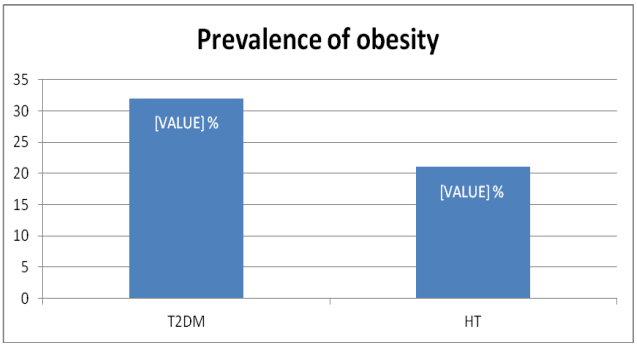

Figure 1. *The prevalence of obesity.*

Dyslipidemia was higher in the HT group (59%) when compared with the group of patients with T2DM (36%) as shown in Figure 2 below.

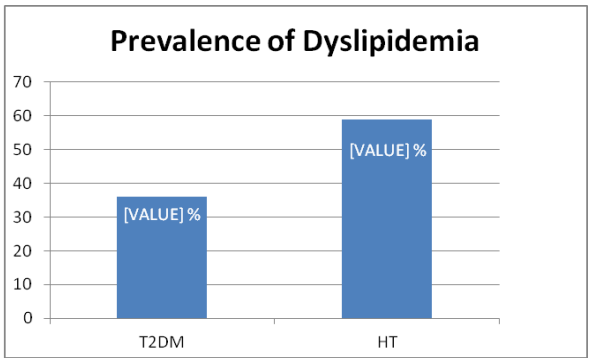

Figure 2. *The prevalence of dyslipidemia.*

Ischemic cardiac disease was more frequent (p<0.001) in the HT group (49%) than in the T2DM group (38%) as shown in Figure 3.

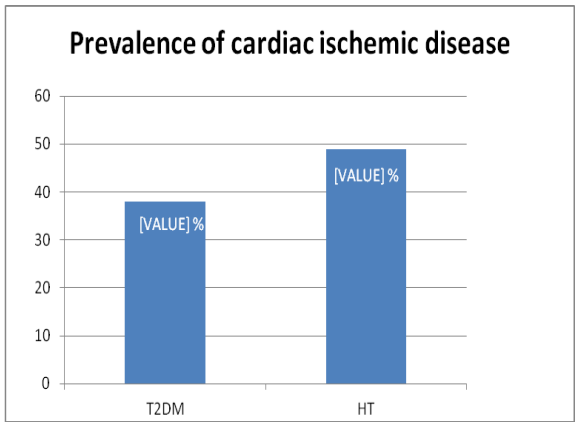

Figure 3. *The prevalence of cardiac ischemic disease.*

In the group that had both T2DM and HT, the value of HbA1c was associated with pre-existing Thyroid pathology (r=-0.28, p<0.001), also Dyslipidemia was correlated with Hepatic Steatosis (r=0.34, p<0.001); Ischemic Cardiac Disease was correlated with the value of TPO antibodies (r=-0.25, p<0.01).

Below, in Table 1 there is a description of all the numeric parameters evaluated.

Discussions

The study that we have conducted resulted from the frequent encounter of the association between T2DM and HT in the clinical practice as well as in the literature reviews; for instance in a study conducted by Radaideh et al. in Jordan investigating the prevalence of thyroid dysfunction and autoimmunity in T2DM, the following results were revealed: 5.9% of the patients with T2DM had prior diagnosed thyroid dysfunction; 12.5% was the total prevalence of thyroid disorder in the diabetic population of this study; also TPO antibodies were evaluated and the results showed that in the diabetic population this was positive in 8.3% versus the control group in which the level was at 10.3% [7].

Table 1. The parameters of the studied group.

	Minimun	Maximum	Mean	Standard deviation
BMI (kg/m2)	20.20	49.30	32.25	6.65
HbA1c (%)	5.58	11.40	7.31	1.37
FPG (mg/dL)	96.00	226.00	155.76	40.10
TSH (uUI/mL)	0.07	14.94	2.93	2.73
Free T4 (pmol/L)	1.00	25.10	14.13	4.62
TPO antibodies (IU/L)	5.80	1362.94	245.14	284.03

BMI – Body Mass Index; HbA1c – Hemoglobin A1c; FPG – Fasting Plasma Glucose; TSH – Thyroid Stimulating Hormone; TPO – Thyroid Peroxidase

Another study conducted by Papazinfiropoulou et al. also wanted to establish the prevalence of thyroid disorder in T2DM population, in this study the discovered that the prevalence was 12.3%, significantly higher in the female population (p<0.001) [7]. This was also the findings in our study, in the group of patients with T2DM 52% were females, in the group with HT 96% were females and in the

group of patients that had both T2DM and HT 96% were females.

In the same study it was shown that patients with thyroid pathology had higher body mass index (BMI) in comparison with the patients without thyroid dysfunction. Since T2DM is a risk factor for cardiac diseases and the most frequent complications are cardiac, we also wanted to evaluate if the risk is higher in patients that have both T2DM and HT; the same thing was followed also in Villano Mh et al. [7] and the conclusion that the combination of this will enhance the cardiac failure in patients having these combined pathologies. In our study we evaluated the presence of Cardiac ischemic disease and found out that in the group that had HT it was more frequent (49%) with a statistically significant value of $p<0.001$, rather than in the group that only had T2DM (38%). This condition also associated strongly with the presence of Hepatic steatosis ($p<0.01$) and the value of ATPO ($p<0.01$) in the group that had both T2DM and HT.

Another parameter that was evaluated in our study was ATPO, as part of the method to determine the presence of HT. This was also studied in other trials, for instance in Ravishankar et al. it was positive in 29.4% of the patients with T2DM [8].

Dyslipidemia was also assessed because of data shown in the literature in Ravishankar et al. and in Pasupathi et al. it was shown that levels of cholesterol, triglycerides, HDL-C and LDL-C were out of ranges along with the values of Hba1c in patients that had both T2DM and thyroid dysfunction [8]. In the study we have conducted dyslipidemia was more frequent in the group that had HT (59%) than in the T2DM lot (36%); which is consistent with the data from the literature.

Overall, the study that we have conducted shows that the population that was studied is in consistence with the data from the literature. This was one of the first studies conducted on this topic in Romania and it leads the way for more investigations to be made. Many more aspects of these two diseases and the association in between the two of them can be analyzed, starting with the immune component that was not determined in this study.

Conclusions

After assessing all the parameters, we have reached the conclusion that there is a significant association between the characteristics of Type 2 Diabetes and Autoimmune Thyroiditis.

We are looking forward to finalizing this study in order to be able to provide more evidence capable of leading us to the above conclusion, that there is a connection in between this to diseases.

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