



IMPROVE THE ABILITY TO PREDICT TYPE 1 DIABETES MELLITUS WITH THYROID DYSFUNCTION IN IRAQI CHILDREN

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Abstract:

T1DM and thyroid dysfunction are two of the most common metabolic diseases; the major purpose of this study is to investigate the epidemiologic behavior of T1DM patients who also suffer from thyroid disorders. The study population was represented by 60 type 1 diabetic patients who attended Al-Qadisiyah medical clinic in Al-Diwanyia City, Iraq, from January 2021 to July 2021, with ages ranged 1-16 years, each individual based on diabetes-associated antibodies (assessment of Glutamic acid decarboxylase antibodies, Zinc transport 8 autoantibody and nsulinoma-2 associated autoantibody) and determination of TSH, T3, and T4. Qualitative variables were expressed as absolute frequencies, and relative and quantitative variables as means+SD. The results found patients with diabetes mellitus were found to have TSH levels that were statistically considerably higher than those that are considered normal for healthy individuals, and the prevalence of GADA-Ab, IA-2ic-Ab, and ZnT8-Ab was as follows: 22 (42%), 14 (27%), and 16 (31%), respectively, in pediatric individuals with type 1 diabetes. In conclusion: An significant marker for the diagnosis of type 1 diabetes in children is a low level of thyroid-stimulating hormone in conjunction with the presence of the two autoantibodies (GADA-Ab and ZNT8-Ab).

Keywords: T1DM, thyroid disorder, GADA-Ab, ZNT8-Ab and IA-2ic-Ab

INTRODUCTION:

A chronic autoimmune condition known as type 1 diabetes mellitus (T1DM) is defined by eradicating the pancreas's beta cells (insulin-producing). The illness frequently affects Children and young people, and its prevalence is rising globally (Redondo et al., 2018; Patterson et al., 2019; Akerman and Ludvigsson, 2020).

Although the precise etiology of IDDM is unknown, it is thought to be an autoimmune condition in which the immunological process targets the beta cells. Viral infections, environmental triggers, and additional variables, including genetics, may also be at play (Colberg et al., 2016; Aronson et al., 2019). IDDM is currently incurable and is managed with lifetime insulin therapy, dietary changes, and frequent exercise. Serious problems, such as cardiovascular disease, kidney failure, and blindness, can result from improper blood sugar management (Lennerz et al., 2021).

The study by von Scholten et al. (2021) looked at the pathophysiology of type 1 diabetes study the role of beta cell autoimmunity. It also evaluated the disease's natural history. In addition, a summary of

the advancements made in diabetes research over the previous 60 years, including improvements in the identification, management, and prevention of IDDM, was provided by the National Institute of Diabetes, Digestive, and Kidney Diseases (2023).

In T1DM, the precise mechanism of beta cell apoptosis is still not well understood. It is thought that beta cell death is a result of both humoral and cellular immunological responses. By specifically identifying and eliminating beta cells, CD8+ cytotoxic T lymphocytes are expected to play a significant part in eliminating beta cells. The production of autoantibodies against beta cell antigens, B lymphocytes, and plasma cells also contribute to the death of beta cells (Kallionpää et al., 2012).

T1DM's pathogenesis involves a complicated interplay between immunological dysregulation, environmental stressors, and genetic predisposition (Kohil et al., 2021). Autoantibodies against beta cell antigens, such as glutamic acid decarboxylase, insulin, and islet antigen 2, are present in T1DM, which is largely an autoimmune illness (IA-2). The activation of autoreactive T cells, which recognize beta cell antigens



in the presence of HLA molecules, triggers the autoimmune response. As a result, cytokines, including interferon-gamma and interleukin-1, are released, causing inflammation and beta-cell death (Roep and Tree, 2014). The current work analyzes the epidemiologic behavior of T1DM patients who also suffer from thyroid disorders.

One of the most important serological indicators of diabetes mellitus type 1 (type 1 DM) is the presence of autoantibodies to pancreatic beta cell antigens. Insulin, islet cell antigen IA-2 or ICA-512, glutamic acid decarboxylase, and zinc transporter 8 are some of the antigens that these antibodies recognize.

MATERIALS AND METHODS

Study population with exclusion criteria:

The study of epidemiological behavior of hypothyroidism in patients with type 1 diabetes mellitus is descriptive and observational of a total of 60 type 1 diabetic patients who attended the outpatient medical consultation from January 2021 to July 2021. Those who used beta-blockers, amiodarone, steroids, products containing iodine, and those who underwent diagnostic procedures associated with the administration of iodinated contrast media in the previous two months, as well as stiff-person syndrome (Moersch-Woltman), brain stem encephalitis, autoimmune cerebellitis myelopathies, seizure disorders and blood pressure, were excluded from the study. Medical records were included after signing an informed consent to the patients about the research procedure.

Assessment of individuals:

The medical records collected in the Al-Qadysiya medical clinic in Al-Diwanyia city with thyroid diabetic patients were reviewed between Januarys 2021to July 2023 in Al-Diwanyia, Iraq. The physical examination information was recorded in a data collection sheet, as well as the results corresponding to the laboratory tests. Data on age, sex, and personal history were

collected. To measure blood pressure (BP), an auscultatory method was used, using a calibrated and properly validated stethoscope and sphygmomanometer to classify the individuals as hypertensive, the criteria of (7) Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC-7) were used.

Laboratory analysis:

Ten milliliter of blood was obtained after overnight fasting. The blood (5) ml was kept in the heparin tubes and frozen. The other (5) ml was kept in gel tubes without heparin, then left to clot before being centrifuged at 3000 RPM for five min to separate the serum for thyroid parameter and liver enzyme estimation. The values of the laboratory tests were collected in the tool designed for this purpose. Serum levels of TSH, T4, and T3 were quantified by the ECLIA method. Electrochemiluminescence immunoassay) with an Elecsys 2010 autoanalyzer from Roche S.A; the following diagnostic possibilities were considered according to the NHANES III criteria: clinical hypothyroidism, the presence of elevated TSH (>4.5 mIU/L). Glutamic acid decarboxylase antibodies (Medizym® anti-GAD/Eagle Bioscience, Canada), Zinc transport 8 autoantibody (Fast Zinc Transporter 8/ RSR Limited, United Kingdom) and nsulinoma-2 associated autoantibody (Medizym® anti-IA2/ Eagle Bioscience, Canada) were measured with ELISA.

RESULTS AND DISCUSSION:

Thyroid hormone's impact on type 1 diabetes

The TSH levels of patients with DM were significantly higher than those of the normal range (figure 1). This study is consistent with the findings of (Jun et al., 2017), (Shih et al., 2012). In addition, T3 and T4 levels were higher in the DM patients than in the normal value, which is agreed with (Rugge et al., 2012).

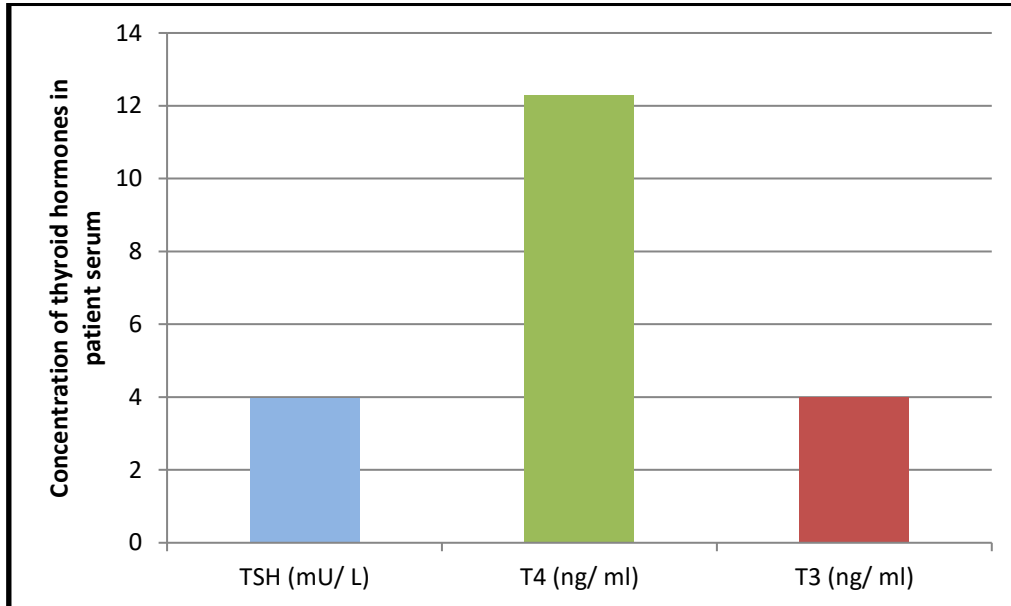


Figure (1): Effect of diabetic mellitus on the serum Thyroid hormones

T3 is the active form of thyroid hormone, which does the metabolic effects of thyroid hormone (Wu et al., 2005). T4 is a hormone that is converted into T3 in many organs. High TSH levels increase in DM cases (Crunkhorn & Patti, 2008). T3 and T4 can regulate the metabolism by increasing oxygen consumption, protein production, and the consume energy rate.

Figure (2) displays the frequency of GADA-Ab, IA-2ic-Ab, and ZnT8-Ab among n-positive and -negative patients. In Type 1 DM children patients, the rate of GADA-Ab, IA-2ic-Ab, and ZnT8-Ab was 22 (42%), 14 (27%), and 16 (31%), respectively.

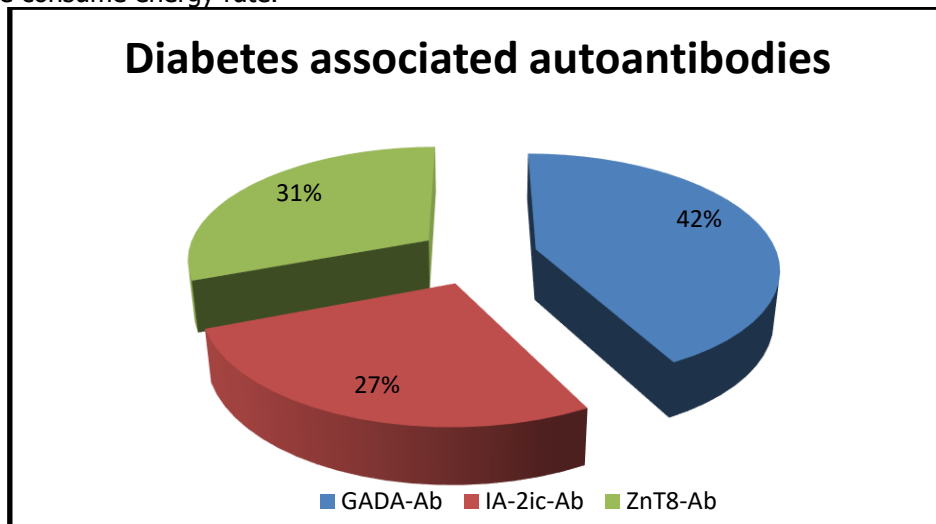


Figure (2): autoantibodies associated with Type 1- Diabetes mellitus

Glutamic acid decarboxylase (GAD) is a neural enzyme that helps to produce gamma-aminobutyric acid (GABA). Antibodies targeted toward the 65-kD isoform of GAD (GAD65) are seen at high titers in a number of autoimmune neurologic illnesses, including stiff-person syndrome (Moersch-Woltman), brain stem encephalitis, autoimmune cerebellitis myelopathies, and seizure disorders (Butler et al., 1993 & Ludvigsson,

2009). A key serological predictor of propensity to type 1 diabetes, GAD65 antibody is also the predominant pancreatic islet antibody. In addition, predisposition to autoimmune diseases such as vitiligo, Addison disease (idiopathic adrenocortical failure), pernicious anemia, premature ovarian failure, and thyroid disease (e.g., thyrotoxicosis, Hashimoto thyroiditis, hypothyroidism, Grave disease, Hashimoto thyroiditis) can be

determined by measuring GAD65 autoantibody levels (Kakleas et al., 2015). A significant autoantigen in T1D, (insulinoma-associated protein 2) is a receptor-tyrosine phosphatase-like protein found in the secretory granule membranes of neural and endocrine cells (Takeyama et al., 2009).

In patients with diabetes mellitus, the existence of autoantibodies against IA-2 (IA-2A) confirms the presence of autoimmune, type 1 diabetes, impaired insulin production, and further phenotypes are the direct effects of inhibiting IA-2 activity. These results are consistent with a general influence on neurosecretion and hormone release (Yi et al., 2015). The autoimmune response against beta cells is caused

by (T1D), an organ-specific form of autoimmune disease. Zinc transporter 8 (ZnT8) is a recently discovered autoantigen in type 1 diabetes. It is an islet-specific gene product that is localized to the insulin granules of beta cells (Kawasaki, 2014).

The study found the most number of patient have intersectional operation; all elements that belong into both test was (GADA-Ab and ZNT8-Ab) it was found 9 patient had matched intersection between the two test Figure 3, whereas the study recorded intersectional operation as 6 and 4 match intersection between (GADA-Ab and IA-2A) and (ZNT8-Ab and IA-2A), respectively.

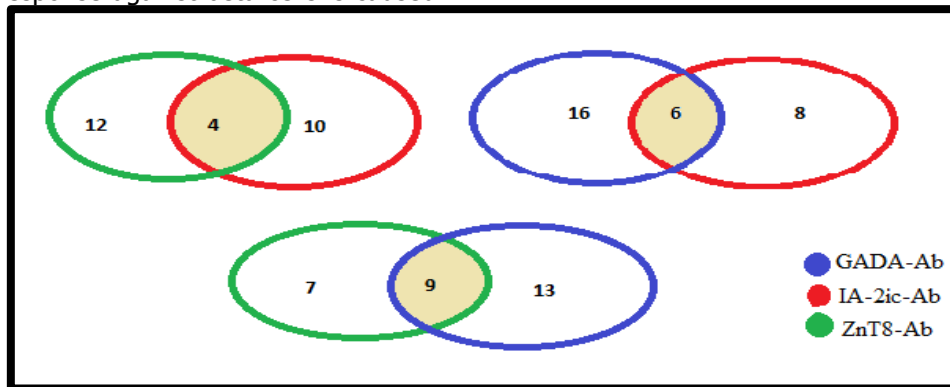


Figure (2): intersection between two sets of test for detection of diabetes associated autoantibodies

The concentrations of thyroid hormones were measured in the serum of patients with type 1 diabetes, and these concentrations were compared with the antibodies of the studied groups; as shown in Table 1, the groups of patients that carried autoantibodies to both tests (GADA-Ab and ZNT8-Ab) showed the lowest concentration of thyroid stimulating

hormone TSH level compared to the other groups, in contrast to the group of patients who carried antibodies to both test (GADA-Ab and IA-2A), where the levels of thyroid hormones were higher than other groups. Mostly, the study did not notice any significant differences in T and 4 T concentrations for all the studied groups with their antibodies.

Table (1): Concentration of thyroid hormones with the distribution of autoantibodies in patients has type 1 DM

Intersection autoantibodies	N	TSH Mean ±SD	T4 Mean ±SD	T3 Mean ±SD
GADA-Ab and ZNT8-Ab	9	1.487±0.26	11.9.3±2.46	3.67±0.35
GADA-Ab and IA-2A	6	2.698±0.17	12.55±1.89	4.12±.62
ZNT8-Ab and IA-2A	4	2.557±0.11	11.57±2.01	3.85±0.55
P value	-	0.042	0.673	0.24



Thyroid problems can affect as much as one-third of patients with type 1 diabetes (Boord et al., 2001). When the thyroid gland isn't working as it should, it can have a domino effect on the rest of the body, a condition known as thyroid illness. In addition, autoimmune disorders can bring on thyroid dysfunction in some cases. In autoimmune diseases, the immune system inappropriately attacks healthy tissue and organs. When this occurs, the immune system mistakenly targets and destroys thyroid cells, causing the thyroid to malfunction (McGrogan et al., 2008 & Vanderpump, 2011).

Thyroid disease and type 1 diabetes share more similarities than other autoimmune disorders because they both affect hormone-producing glands critical to the body's regulation of its use of energy (Weckman et al., 2014).

In conclusion: It can be considered that the decrease in thyroid stimulating hormone with the presence of the two autoantibodies (GADA-Ab and ZNT8-Ab) in children is a key marker for detecting T1D in the patients.

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