World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

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Effect of duration of diabetic in glutamic acid decarboxylase autoantibodies and HbA1c in children with T1DM

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World Journal of Advanced Research and Reviews, 2023, 18(02), 870–876

Publication history: Received on 08 April 2023; revised on 15 May 2023; accepted on 18 May 2023

Article DOI: https://doi.org/10.30574/wjarr.2023.18.2.0909

Abstract

Background: a metabolic condition characterized by a failure in the metabolism of proteins, lipids, and carbohydrates that is brought on by problems with insulin production. When multiple autoantibodies, such as those against glutamic acid decarboxylase, are present against different insulin antigens, type 1 diabetes is present.

Objective: To estimate the Glutamic Acid Decarboxylase Autoantibodies and assessment of HbA1c in type 1 DM.

Methods: 40 children with diabetes participated, while 10 kids in the control group had blood sugar levels that were normal. HbA1c levels for each participant are measured as part of a quantitative ELISA test for the identification of circulating autoantibodies against glutamic acid decarboxylase in human serum.

Results: All the pathological samples showed an increase in the concentration of Anti-GAD compared to the control. Samples of patients with diabetes for 5 years or more showed a decrease in Anti-GAD concentration compared to patients with diabetes for less than five years, but the decrease was not significant

Conclusion: There was positive association between duration of type 1 Diabetes Mellitus and Glutamic Acid Decarboxylase Autoantibodies

Keywords: Anti-GAD; T1DM; HbA1C; Autoantibodies

1. Introduction

Diabetes mellitus (DM), a metabolic disorder caused by issues with insulin manufacturing, is defined by a sustained increase in blood glucose levels and a malfunction in the metabolism of carbohydrates, lipids, and proteins.[1] Insulin is required for cells to allow glucose entry because it binds to particular cellular receptors and allows glucose to enter the cell. It, through many mechanisms, transforms glucose into energy. The two primary kinds of diabetes are insulin dependent (Type 1) and non-insulin dependent (Type 2), which are named after these two mechanisms. In type 1 diabetes, there is typically either no insulin at all or not enough insulin, increased urine production, decreased appetite, and weariness are all indicators of both types of diabetes. Tests for glucose tolerance, glycosylated hemoglobin levels, and blood glucose levels are used to diagnose diabetes (glycohemoglobin or hemoglobin A1C).[2] In people with type 1 diabetes, the immune system produces antibodies inadvertently, harming body tissues. The immune system attacks the pancreatic beta cells in type 1 diabetes.3 Anti-glutamic decarboxylase antibodies, or GADA, are derived from these antibodies. These antibodies aid in identifying those who are most likely to acquire type 1 diabetes.[4] Glutamic acid decarboxylase antibodies (GAD-Abs) have been discovered in both neurologic and non-neurologic diseases, such as stiff person syndrome (ie. Type I diabetes) autoimmune disorders.[5] Anti-GAD and other antibodies against pancreatic

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antigens are frequently found several years before the onset of autoimmune-mediated diabetes, indicating a protracted "pre-diabetic" period of autoimmune activity.[6,7] Studies that use antibodies to determine who is at risk for developing autoimmune diabetes have mostly focused on relatives of type 1 diabetes patients.[8,9] On antibody profiling in the general population, there are little data. According to prospective epidemiological data, many people who acquire autoimmune diabetes, particularly latent autoimmune diabetes in adults (LADA), have antibodies prior to the development of the disease and typically also have a family history of the disease.

2. Material and methods

2.1. Statement of Ethics

As a mandatory step for taking samples from patients, is to get this study approved by the Ethical Committees, which include: the committee of Imam AL-Hussein Diabetes and Endocrinology Medical Center (no.108-on 24/4/2022), Karbala Health Directorate/Holly Karbala Governorate-Iraq. Written parental approval was obtained.

2.2. Topics of Research and Clinical Parameters

The study was performed between April 2022 and July 2022., a total of 50 male children (from 40 T1D patients and 10 controls, blood and urine samples) were obtained, the age of all was between 5–15 years. The patients were divided into four categories: group A children who are normal weight and have a urinary tract infection; group B children who are overweight with urinary tract infection; group C children who are normal weight without a urinary tract infection; group D children who are overweight but without a urinary tract infection. All T1D patients required the beginning of insulin replacement therapy right away. Patients exhibited either decreased C-peptide secretion or at least one positive typical pancreatic islet autoantibody (anti-GAD antibodies [GADA], anti-zinc transporter 8 antibodies [ZnT8A], or anti-insulinoma associated protein-2 antibodies [IA-2A]).10 Samples were collected in Karbala (Imam Hassan Center for Endocrinology and Diabetes) and Al-Hilla (Turkish Hospital). In accordance with World Health Organization (WHO) guidelines, diabetes was identified.11 In order to estimate the levels of glucose and HbA1c, blood samples from patients and controls were collected. Autoantibodies were assessed in persons who had been diagnosed with diabetes. A basal and bolus regimen was used to treat diabetic children, which comprised giving them rapid-acting insulin with meals and a background of slower-acting, longer-lasting insulin. Insulin was injected once before bed. Healthy children in the control group had normal HbA1c readings and normoglycemia.

With the HROCHE COBAS Integra400 plus, HbA1c was calculated. Using commercial ELISA kits, autoantibodies to glutamic acid decarboxylase antibodies (GADA) were quantified (Elabscience, U.S.A.). Weight (kg)/squared height was used to determine the body mass index (BMI) (m). Using the Centers for Disease Control and Prevention's growth curves, BMI percentiles were calculated.12

The bacterial isolates from urine were identified using the Vitec 2 automated compact system, a GN-ID card, and 64 biochemical tests.

2.3. Statistical Analysis

The statistical program for social sciences (S.P.S.S.) version 25 was used to enter and evaluate data from the study samples. The outcomes were reported as mean Standard Error (Mean S.E.). An independent-sample T-test was used in the statistical analysis to determine whether differences in the quantitative data were significant. One sign P 0.05, two signs P 0.01, three signs P 0.001, and four signs P 0.0001 were used to denote the probability levels.

3. Results

In comparison to the control, the concentration of Anti-GAD increased in every patient sample. We discovered that the concentrations of anti-GAD were lower in overweight individuals compared to normal weight people in the pathological samples. As indicated in figure 1. Samples of patients with diabetes for 5 years or more showed a decrease in Anti-GAD concentration compared to patients with diabetes for less than five years, but the decrease was not significant, as shown in figure 2.

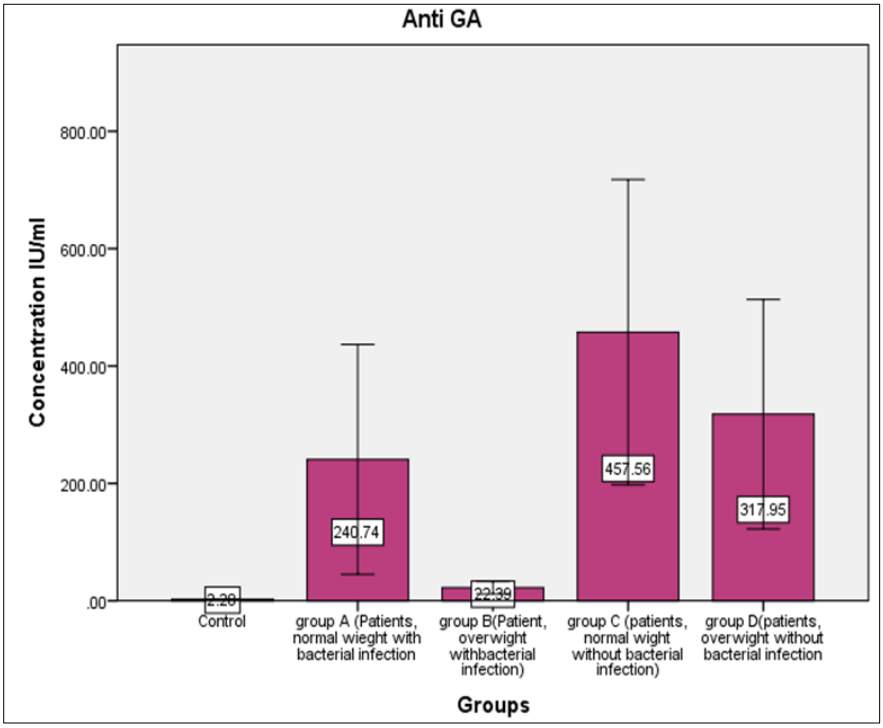

Figure 1 Concentration of Anti-GAD in control group and patients' groups

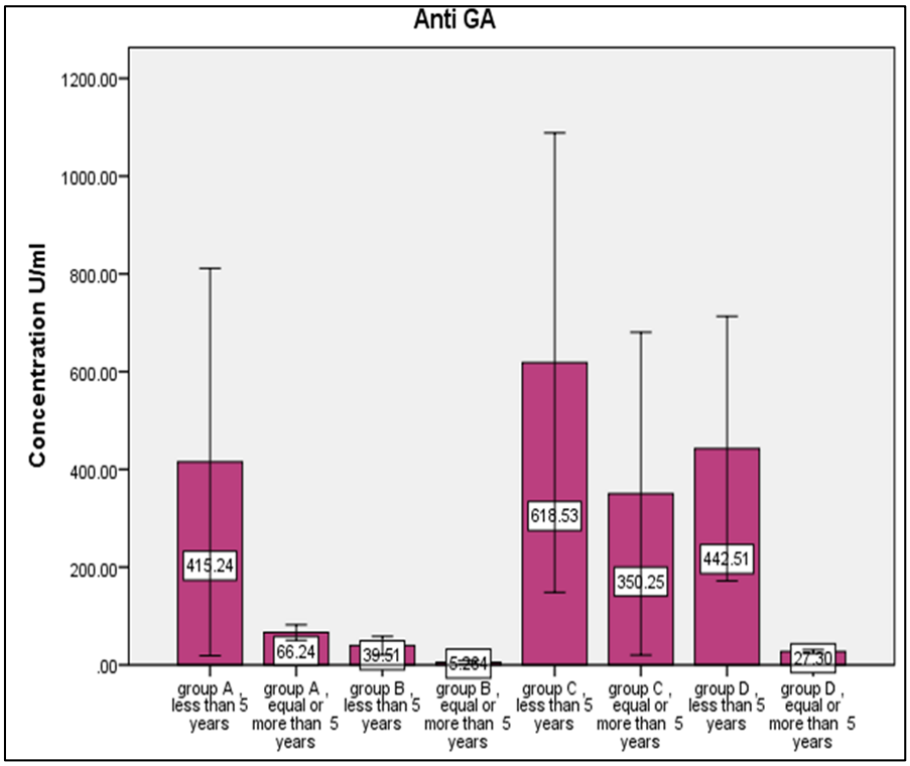

Figure 2 Concentration of Anti-GAD (U/ml) in duration disease categories of patient's groups

All studied samples showed a significant ($P < 0.0001$) increase in the HbA1C levels compared to the control. When comparing the pathological samples, we find that the HbA1C levels decreased in group A of normal-weight patients with a bacterial infection compared to group B of overweight patients with a bacterial infection. Also, there were decreased

HbA1C levels in group C of normal-weight patients without bacterial infection compared to group D of overweight patients without bacterial infection, but the differences were not significant. As shown in figure 3.

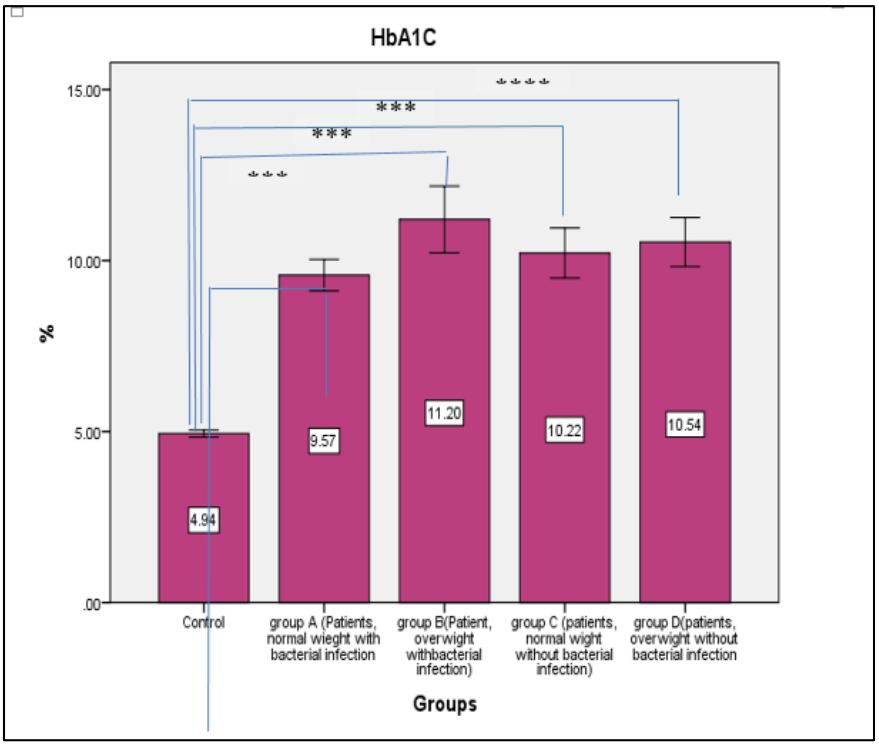

Figure 3 Percentage of HbA1C in control group and patients' groups.

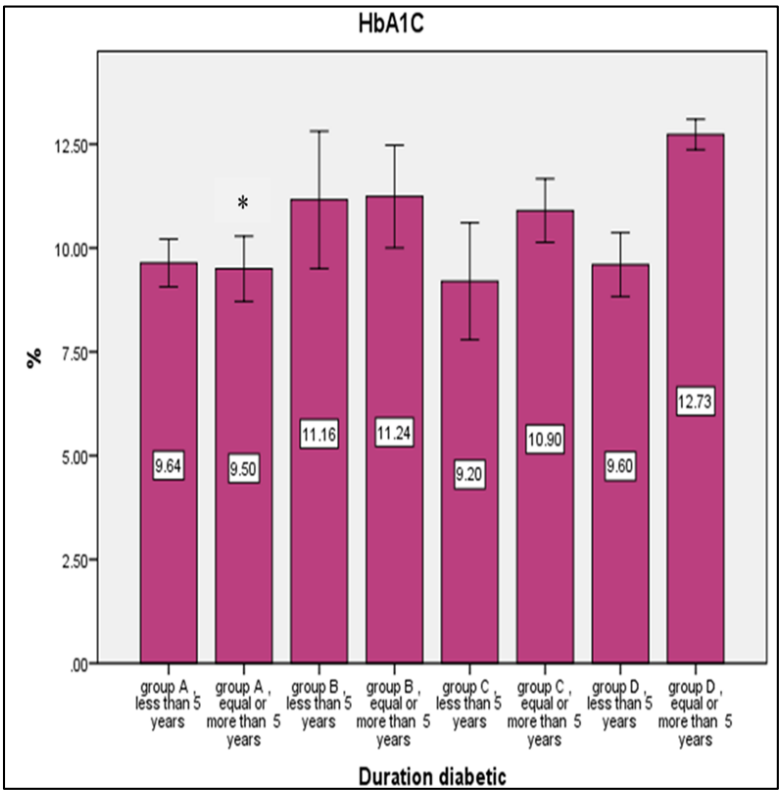

Figure 4 Percentage (%) of HbA1C in duration disease categories of patient's groups

All studied samples showed an increase in the HbA1C levels in the first four years of diabetic disease, except for group A, compared to the HbA1C levels in samples infected with diabetes for more than five years or equal, but it did not reach significance. There was a significant decrease in patients group A (5 years or more) compared to patients group D (5 years or more), as shown in figure (4).

Data results show in Table 1, the bacterial pathogens that cause UTI belongs to gram negative and gram-positive bacteria. *Escherichia coli* 31%, *Pseudomonas stutzeria* 20%, *Streptococcus thoraltensis* 17%, *Kocuria rosea* 12%, *Streptococcus gallolyticus* 11%, *Staphylococcus haemolyticus* 6%, and *Kocuria kristinae* 3%.

Table 1 Bacterial etiology of UTI in diabetic individuals

No.	Types of bacteria	Number of strains	%
1	*Escherichia coli*	11	31
2	*Pseudomonas stutzeria*	7	20
3	*Kocuria rosea*	4	12
4	*Staphylococcus haemolyticus*	2	6
5	*Streptococcus gallolyticus*	4	11
6	*Kocuria kristinae*	1	3
7	Streptococcus thoraltensis	6	17
		∑=35	

4. Discussion

The results showed an increase in the antibodies in the pathological samples compared to the control, and this is consistent with the previos study.[13] The level of antibodies was lower in overweight diabetic patients compared to normal weight diabetic patients, and this is consistent with the study.[14] As the duration of diabetes increased, the data revealed a drop in Anti-GAD levels, and this finding is consistent with the study.[15] Islet cell autoantibodies were more common in patients who developed the condition earlier, and these autoantibodies gradually diminished and disappeared. In recent years, community samples have been used in numerous studies on anti-GAD antibodies. They foresee the need for insulin even before diabetes manifests itself clinically. They can also forecast the need for insulin in those with type 2 diabetes. A subpopulation of diabetic individuals known as latent-onset auto-immune diabetes mellitus in adults (LADA) has also been defined by their characteristics. Anti-GAD is known to be positive in more than 70% of kids with type 1 diabetes who just got the disease, and its level seems to go down as the disease progresses and as there are fewer remaining beta cells. For a more accurate knowledge and diagnosis of type 1 diabetes, it is crucial to know how frequently these autoantibodies are present in a community.[16]

Recent research has found that sex and age at onset affect the diagnostic sensitivity of GAD65, IA-2, and insulin autoantibodies.Boys who develop diabetes before the age of 10 are less likely to have GAD65 antibodies, while both boys and girls have diagnostic sensitivity of 80% in older kids, teenagers, and young adults. Patients with other related autoimmune disorders, such as thyroiditis, had greater and more frequent GAD65 antibody titers.[4] It is known that anti-GAD is positive in more than 70% of kids with type 1 diabetes who just got the condition, and that its level seems to go down as the disease progresses and as there are fewer remaining beta cells.[17]

The American Diabetes Association has recommended glycated hemoglobin (HbA1c) as a possible substitute for fasting blood glucose for the diagnosis of diabetes. HbA1c is a vital biomarker of long-term glycemic control because it can reflect the total glycemic history of the past two to three months. In addition to serving as a reliable marker of chronic hyperglycemia, HbA1c also shows a significant link with the possibility of long-term effects from diabetes. A stand-alone risk factor for people with and without diabetes developing coronary heart disease and stroke is high HbA1c, which has also been acknowledged. The useful information from a single HbA1c test has made it a reliable biomarker for the diagnosis and prognosis of diabetes.[18] All patient categories had significantly higher HbA1c values than the control group, according to the data, with overweight and bacterially infected diabetes patients experiencing the largest increases. High HbA1c levels in obese children can be tested to look for early indications of insulin sensitivity and resistance.[19]

5. Conclusion

In contrast to individuals with positive Anti-GAD antibodies, those with negative Anti-GAD antibodies had higher BMI ratios.

The decrease in the percentage of Anti-GAD antibodies with the progression of the period of diabetes

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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