



RESEARCH ARTICLE

The relationship between Anti-IA-2, Anti-TPO and T1DM

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Abstract

This study was conducted to find the relationship between antibodies for this antigens and T1DM which can be used for the early detection of T1DM in normal Iraqi patients. to study the importance of anti- TPO as a marker for autoimmune thyroid disease in T1DM patients to find the relationship between T1DM and autoimmune thyroid disease.

The study was carried out on 80 sample of men and women with age ranged from (20 – 60 years old), they are divided in to three groups: Group1 which have blood sugar above 180 mg / dL. Group 2 which have blood sugar ranged from 120–180 mg/dL. Group 3 which have blood sugar below 120 mg/dL. The statistical analysis results showed no significant difference in the presence of antibodies , glycated haemoglobin and blood sugar between men and women group inspite of some simple differences between the two groups. Significant ($p < 0.05$) elevation in the level of (anti-TPO) in T1DM patients compared with control group. No significant elevation in the level of (anti-IA-2) in the T1DM patients compared with control group. The results also showed that no positive results for (anti-TPO) present in the control group. One positive result for anti-IA-2 present in the control group.

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1.Introduction

Type 1 diabetes, results from a chronic autoimmune destruction of the insulin secreting pancreatic beta cells, probably initiated by exposure of genetically susceptible host to environmental agents. Autoimmune destruction of beta cells is thought to be completely asymptomatic until 80-90% of the cells are lost. During the preclinical phase, this autoimmune process is marked by circulating autoantibodies to beta cell as an antigens, these autoantibodies ,such as anti-insulin antibody (IAA), anti-glutamic acid decarboxylase (GAD) and anti-tyrosine phosphatase ICA-512 (IA-2), are present years before the onset of type1 diabetes and prior to clinical symptoms (Batstra *et al.*,2001) .

Hemoglobin A1c (HbA1c), the most abundant minor hemoglobin component in human erythrocytes, is formed by the binding of glucose with the N-terminal amino groups of the beta-chains of HbA (Taggar *et al.*, 2012). HbA1c level is more stable than the glucose measures such as fasting glucose it has been suggested to be a good marker for chronic hyperinsulinemia (Davidson *et al.*,2000) .

Thyroid disease is common in the general population, and the prevalence increases with age (Yalcin and Ozan, 2006). Hypothyroidism, because it slows down the body's processes, also affects insulin production, when a condition such as hypothyroidism is involved, the pancreas slows down its ability to turn blood sugar into energy, this is a complication that leads to diabetes (Venturi and egin, 2010). To find the relationship between anti- tyrosine phosphatase and T1DM for the early detection of diabetes in normal Iraqi patients, to evaluate anti- TPO Abs as markers of autoimmune thyroid disease in T1DM patients is the aim of the present study.

2. Materials and methods

2.1. Study population

This study included 80 individuals (50 men and 30 women) age ranged from 20 - 60 years old, they are divided into three groups: group 1 (chronic diabetic group), group 2 (early diabetic group) and group 3 (control group).

2.2. Laboratory investigations

2.2.1. Fasting Plasma Glucose (FPG)

Plasma glucose was measured by enzymatic colorimetric assay (Tietz *et al.*, 1995). using kits supplied by (Spinreact S, A. Spain).

2.2.2. Glycated hemoglobin HbA1c %

After collection of blood samples HbA1c was measured by boronate affinity assay .

2.2.3. Measuring of insulin level in the serum

The DRG Insulin ELISA Kit is a solid phase (ELISA) based on the sandwich principle.

2.2.4. Measuring of anti- IA2 in the serum

All samples were stored at -20c till tested. The test were done using Anti-IA-2 kit reagents manufactured by AESKULISA- Germany.

2.2.5. Measuring of Anti- Thyroid peroxidase (Anti- TPO)

Anti-TPO was measured in the serum of all samples using Anti-TPO kit reagents from Monobind, Inc.-U.S.A.

2.3. Statistical Analysis:

The Statistical Analysis System- SAS (2010) was used to effect of difference factors in study parameters. Least significant difference-LSD or T-test was used to significant compare between means in this study.

3. Results

The results of current study showed that there were no statistically significant differences in the Mean \pm SE values of parameters study between men and women. As shown in Table 1, the Mean \pm SE of blood sugar was higher in the diabetic patients compared to that of controls. Mean \pm SE of HbA1C was higher in the diabetic patients compared to that of controls. However, Mean \pm SE of insulin was higher in the control group compared with diabetic patients, a significant difference ($P < 0.05$) in the Mean \pm SE of insulin was observed among the three groups.

Mean \pm SE of anti-GAD and anti-IA-2 was higher in the control group than in the early diabetic group . It was found that Mean \pm SE of anti-TPO was higher in the diabetic patients than in the control group, a significant difference ($P < 0.05$) in the anti-TPO was observed among the three groups.

It was found that 14 person of chronic diabetic group (46.67 %) were positive for anti-IA-2, six persons (20 %) of early diabetic group (No:30) were positive for anti-IA-2 while one person (5%) of control group (No:20) was positive for anti-IA-2. Our data showed that one person of chronic diabetic group (3.33%) was positive for anti-TPO. 2 persons (6.67 %) of early diabetic group (No:30) were positive for anti-TPO. However, no one of control Group was positive for anti-TPO.

Table 1: Comparison between different groups in parameters study

| Parameters | Mean \pm SE | | | LSD Value |
|-------------|---------------------------|-------------------------|------------------------|-----------|
| | Chronic diabetic (No: 30) | Early diabetic (No: 30) | Control group (No: 20) | |
| Blood sugar | 310.67 \pm 12.72 | 145.10 \pm 2.15 | 96.75 \pm 2.25 | 24.246 * |
| HbA1C | 11.76 \pm 0.28 | 7.06 \pm 0.22 | 5.48 \pm 0.13 | 0.639 * |
| Insulin | 21.86 \pm 3.51 | 25.85 \pm 3.54 | 45.17 \pm 3.19 | 10.122 * |
| Anti-IA-2 | 37.79 \pm 5.53 | 22.25 \pm 6.57 | 28.20 \pm 11.47 | 21.394 NS |
| Anti-TPO | 33.57 \pm 11.97 | 30.16 \pm 4.65 | 21.86 \pm 1.23 | 24.028 * |

* (P<0.05), NS: Non-significant.

4. Discussion

This study investigated the existence of anti-GAD, anti- insulin, anti- IA-2 and anti-TPO in T1DM patients and in normal individuals. To achieve these objectives anti- GAD , anti- IA-2, anti- insulin, anti-TPO antibodies, Insulin, HbA1C and glucose levels were measured for 80 patients in Baghdad city. As T1DM is often associated with other endocrine autoimmune disorders, so circulating autoantibodies could be hallmark of clinical or sub clinical autoimmune polyendocrine disease.

Many studies postulated that the detection of thyroid antibodies might reflect the developing of other autoimmune disease such as T1DM. This led to suggestion that the search for anti-TPO antibodies could be a good prognosis for other autoimmune disease especially T1DM.

The present study in general is important in order to identify all these antibodies which could be a good prognosis for T1DM. the frequency of these autoantibodies in a population is an important step for a better understanding and diagnosis of type1 diabetes.

Among the effect of gender of patients on parameters study, our data reported that there is a non significant difference between males and females in all parameters study related to T1DM with a little difference between their mean. This result is similar to the result of Berwary *et al.*(2013) who found that T1DM can be observed among males and females. Also in agreement with the finding of Soltesz *et al.*(2007); found that T1DM is common amongst both of males and females with a very little difference. The present study showed that the mean blood sugar and HbA1C was higher in diabetic patients when compared with control group with significant difference between these two groups. This finding is similar to the findings of Izzat *et al.*, (2011) found that mean fasting and random blood sugar and HbA1c was higher in patients than control group. Also in agreement with Lundgren *et al.*(2012) . The results reveal a significant difference between the serum glucose in T1DM patients and non-diabetes individuals, and agreed Berwary *et al.*(2013) who showed that The result of statistical analysis shows that there is a significant difference in the mean value of serum glucose between T1DM patients and control group.

This fact may be explained by the decreased production of insulin by pancreatic beta cells in T1DM patients that leads to accumulation of glucose in the blood . When blood glucose enters the erythrocytes, it glyicates the amino terminals of hemoglobin. The fraction of hemoglobin glyicated, normally about 5%, is proportionate to blood glucose concentration. Since the half- life of an erythrocyte is typically 60 days, the level of glyicated hemoglobin reflects the mean blood glucose concentration over the preceding 6-8 weeks. Measurement of HbA1c therefore provides valuable information for management of diabetes mellitus (Murray *et al.*,2012).

The present study data reported that the mean serum insulin was significantly (P<0.05) lower in diabetic patients

compared to control group. This result agreed with (Oram et al.,2013; Wang et al.,2012) that approximately 75% of patients with long-duration type 1 diabetes produce very low levels of insulin, the reason for this lowering is that type 1 diabetes leads to absolute insulin deficiency due to the progressive autoimmune destruction of beta cells.

The results also demonstrated that mean anti- IA-2 antibodies were higher in chronic diabetic patients than in the early diabetic patients and control group . Our results agreed with the results of Farhan et al.(2013) who showed that mean \pm SE anti- IA-2 in T1DM patients was (0.014 \pm 0.003). But mean \pm SE anti- IA-2 in Healthy controls was (0.0035 \pm 0.0021) , we observed that the mean of anti- IA-2 in control group was higher than that of early diabetic patients . Because these antibodies appear during the preclinical period of β -cell destruction before the clinical manifestation of diabetes, they have proven invaluable for predicting an individual's risk for developing diabetes. On the other hand the present study showed that among diabetic group the mean serum anti-TPO level was significantly ($P<0.05$) higher than that of control group. This result agreed with Ardestani *et al.*(2011) that T1DM patients had higher levels of thyroid autoantibodies than non-diabetic ones.

Conclusion

We concluded that the level of IA-2 antibodies in control group was higher than that of early diabetic group, this means the possibility of this parameters could be a hidden factor for a future diabetes for our control. Anti IA-2 antibodies can be used as early detection of T1DM. Thyroid peroxidase antibody was evident in many T1DM patients while it is within normal level in the control group. We recommended to study the relationship between T1DM and other antibodies such as anti-insulin and anti-GAD antibodies.

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References

- Ardestani,S,K and Keshteli,A.H. (2011):Thyroid Disorders in Children and Adolescents with Type 1 Diabetes Mellitus in Isfahan, Iran. Iran J. Pediatr., December; 21(4): 502–508.
- Batstra, M.; Anstoot, H.and Herbrink (2001): Prediction and diagnosis of type 1 diabetes using B-cell autoantibodies. Clin. Lab., 47:497-507.
- Berwary, N. J. A., Abdul-Majid,.F-A., Hamdan, S., Khangholi, S., Waheda. N.E. (2013): Type 1 Diabetes Mellitus (T1DM): Induced by Environmental, genetic and immunity factors. Life Sci. J.,10(3) 638.
- Davidson, M.B.; Schriger, D.L.; Peters, A.L. and Lorber, B.(2000): Revisiting the oral glucose tolerance test criterion for the diagnosis of diabetes. J. Gen. Intern .Med.,15:551–5.
- Farhan, J.; Alghasham, A.; Zafar,U.; Abdel-Raheim, M.A.; Meki and Rasheed,Z. (2013):Impact of anti-glutamic acid decarboxylase-65, anti-insulin and anti-tyrosine phosphatase autoantibodies on disease activity in type 1 diabetes patients. J. Diab. Res.& Clin. Metab., 12:552-5.
- Izzat,A.M.; Noor, T.T. and Aufira, S.N. (2011) : Study of the prevalence of anti Glutamic Acid Decarboxylase antibody in Iraqi children and adolescent with type 1 Diabetes mellitus. AJPS., Vol. 10, No.2.
- Murray,R.K.;Bender,D.A.;Botham,K.M.;Kennelly,P.J.;Rodwell,V.W. and Weil, P.A.(2012): Harpers illustrated biochemistry.29th edition. Mc Graw-Hill Companies.PP: 55.

Oram, R.A.; Jones, A.G.; Besser, R.E. *et al.*(2013):The majority of patients with long-duration type 1 diabetes are insulin microsecretors and have functioning beta cells. *Diabetologia*. Oct 12.

Soltesz, G., C. ;Patterson, C. and Dahlquist, G.G.(2007) : Worldwide childhood type 1 diabetes incidence – what can we learn from epidemiology? *Pediatr. Diab . 8(6): p. 6-14.28.*

Taggar ,J.S.; Coleman, T.; Lewis, S. and Szatkowski, L.(2012) :The impact of the Quality and Outcomes Framework (QOF) on the recording of smoking targets in primary care medical records etc *BMC Public Health. , 4;12(1):329.*

Venturi, S; Donati, FM; Venturi, A and Venturi, M (2000): "Environmental iodine deficiency: A challenge to the evolution of terrestrial life?". *Thyroid : official journal of the American Thyroid Association, 10 (8): 727–9.*

Wang L, Lovejoy NF, Faustman DL.(2012): Persistence of prolonged C-peptide production in type 1 diabetes as measured with an ultrasensitive C- eptide assay. *Diabetes Care., 35(3):465-470.*

Yalçın, B. and Ozan, H. (February 2006) : "Detailed investigation of the relationship between the inferior laryngeal nerve including laryngeal branches and ligament of Berry". *Journal of the American College of Surgeons., 202 (2): 291–6.*