Research Article

Screening For Islet Cell Antibodies In Non-Diabetic Siblings of Children With Type I Diabetes Mellitus

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Abstract
Type I Diabetes Mellitus (TIDM) is the most common chronic metabolic autoimmune disease. **Aim of the work:** To estimate serum levels of Islet cell antibodies (ICA) in first-degree relatives of type I diabetic children. **Subjects and Methods: Study Design:** This study was a prospective case-control hospital-based study carried upon 120 children randomly selected during the period from January 2016 till August 2016 after approval of the ethical committee of the Faculty of Medicine, Minia University. **Results:** This table shows insignificant differences between group I and group II regarding age, gender, residence, weight, height, and BMI centiles where ($P > 0.05$). Finally, ICA positivity had a significant moderate negative correlation with fasting C-peptide
Keywords: Type I Diabetes Mellitus, chronic metabolic, Islet cell antibodies

Introduction
Type I Diabetes Mellitus (TIDM) is the most common chronic metabolic autoimmune disease[(1)]**.** It is characterized by Hyperglycemia due to infiltration of lymphocytes in the pancreas causing destruction of insulin-producing beta-cells[(2)] **.**

Histological analysis of the pancreas from patients with TIDM shows immunological activity limited to insulin-containing islets, including infiltration by activated lymphocytes, antibodies and components of the complement system. These histological findings are consistent with TIDM being an immune-mediated disease[(3)]**.** Further evidence came from studies showing that TIDM is characterized by the presence of antibody (humoral) and T-cell (cellular) responses to islet proteins (antigens). Immune responses to these antigens predate the clinical onset of diabetes, giving further support for an immune etiology to TIDM[(4)]**.**

Early studies primarily of first-degree relatives followed over time demonstrate that islet cell autoantibodies may predict T1DM. First degree relatives of type 1 diabetic patients have provided an excellent study population for defining risk factors for the progression to T1DM because of the increased disease incidence in this group[(5)]**.**

Aim of the work
To estimate serum levels of Islet cell antibodies (ICA) in first degree relatives of type I diabetic children.

Subjects and Methods
Study Design:
This study was a prospective case control hospital based study carried upon 120 children randomly selected during the period from January 2016 till August 2016 after approval of the ethical committee of Faculty of Medicine, Minia University.
We had an oral approve from every caregiver of the studied children to be enrolled in this study.

Study Participants:
The studied children were grouped as following:
Group I: included 60 children with a first degree relative with T1DM who had regular follow up in the diabetes outpatient's clinic, Minia University Maternity and Children Hospital. They were 25 (41.67%) male and 35 (58.33%) female with a mean age of 7.1 ± 4.4 years old.

Group II: included 60 apparently healthy children with negative history of T1DM in their siblings, age and sex matched to the previous group. They were 27 (45%) male and 33 (55%) female with a mean age of 7.9 ± 3.6 years old.

The inclusion criteria:
Absence of diabetes as regaed criteria of ADA, (2018) which are:

The exclusion criteria:
- Presence of any chronic illness.
- Presence of any syndromes.
- History of any drug intake.
- Refusal to participate in the study.

Results

Table (1) Comparison between the studied groups as regard some demographic and clinical data.

Demographic Datum	GROUP I (FIRST DEGREE OF T1D) N=60	GROUP II (CONTROL) N=60	P-VALUE
Age (years): Mean ± SD	7.1 ± 4.4	7.9 ± 3.6	0.25
Gender: Males No (%) **Females No (%)**	25 (42.6%) 35 (58.4%)	27 (45%) 33 (55%)	0.71
Residence: Rural No (%) **Urban No (%)**	33 (55%) 27 (45%)	42 (70%) 18 (30%)	0.09
Weight centile (kg): **< 5th percentile No (%)** **5th: 95th percentile No (%)** **> 95th percentile No (%)**	 5(8.4%) 48 (80%) 7 (11.6%)	 4 (6.6%) 50 (83.4%) 6 (10%)	 0.56
Height centile (cm): **< 5th percentile No (%)** **5th: 95th percentile No (%)** **> 95th percentile No (%)**	 7 (11.6%) 45 (75%) 8 (13.4%)	 3 (5%) 51 (85%) 6 (10%)	 0.06
Body mass index (BMI) centile (kg/m2): **< 5th percentile No (%)** **5th: 95th percentile No (%)** **> 95th percentile No (%)**	 6 (10%) 47 (78.4%) 7 (11.6%)	 4 (6.6%) 51 (85%) 5 (8.4%)	 0.38

T1D=type 1 diabetes; NO=number; SD=standard deviation.
This table shows insignificant differences between group I and group II regarding age, gender, residence, weight, height and BMI centiles where (P > 0.05).

Table (2): Comparison between the studied groups as regard some family history variables.

VARIABLE	GROUP I N=60	GROUP II N=60	P-Value
Birth order 1st No (%)	12 (20%)	22 (36.6%)	
2nd No (%)	22 (36.6%)	19 (31.7%)	0.17
3rd No (%)	13 (21.7%)	7 (11.7%)	
More No (%)	13 (21.7%)	12 (20%)	
Family size: Mean ± SD	5.3 ± 1.3	5 ± 0.7	0.11
Father occupation: Farmer No (%)	20 (33.4%)	27 (45%)	
Worker No (%)	25 (41.6%)	18 (30%)	0.51
Employee No (%)	10 (16.6%)	9 (15%)	
None No (%)	5 (8.4%)	6 (10%)	
Mother occupation: House wife No (%)	56 (93.4%)	51 (85%)	
Works No (%)	4 (6.6%)	9 (15%)	0.14
Father education: Educated No (%)	22 (36.6%)	15 (25%)	
Illiterate No (%)	38 (63.4%)	45 (75%)	0.17
Mother education:Educated No (%)	23 (38.4%)	15 (25%)	
Illiterate No (%)	37 (61.6%)	45 (75%)	0.12
Family history of T1D in distant relative:			
+ve No (%)	25 (41.6%)	7 (11.6%)	
-ve No (%)	35 (58.4%)	53 (88.4%)	0.18
Consanguinity: +ve No (%)	24 (40%)	20 (33.4%)	
-ve No (%)	36 (60%)	40 (66.6%)	0.45

This table shows insignificant differences between group I and group II regarding family history variables where (P > 0.05).

Discussion

As regards T1D, autoimmunity is considered the major factor in the pathophysiology. In a genetically susceptible individual, viral infection may stimulate the production of antibodies against a viral protein that triggers an autoimmune response against antigenically similar beta cell molecules[6].

The aim of this study was to screen for Islet cell antibodies in nondiabetic siblings of children with T1D.

Concerning the results of this study, Table (1) showed insignificant differences between group I and group II regarding age, gender, weight, height, and BMI centiles. In this study 33 (55%) of the group, I children were from rural families and 27 (45%) were urban. This disagreed with Borchers et al.,[7] who stated that higher socioeconomic status and the increase in the degree of urbanization are among the environmental factors that play a role in the rising incidence of T1D.

Table (2) showed insignificant differences between group I and group II regarding family history, family size, birth order, parental education, or occupation. In this table, as regard birth order, 12 (20%) were 1st birth order, 22 (36.6%) were 2nd birth order, 13 (21.7%) were 3rd birth order and 13 (21.7%) were more than 3rd birth order.

We found that 24 (40%) of group I results from a consanguineous marriage. This disagrees with Lebenthal et al.,[8], who suggested that there was a relatively high degree of familial clustering among patients with T1D.

This was in agreement with **American Diabetes Association [9]** where it was stated that in siblings the relative expected insulin deficiency, due to the slightly expected B-cell

destruction, decreases the body ability to convert glucose into glycogen, which in turn makes it difficult to remove excess glucose from the blood, this lead to slightly increasing in plasma glucose.

Moreover, in table (5), HbA1c% was significantly higher in the first degree of T1D than the control group. This was in agreement with (Svensson et al., 2005) who found that increased plasma glucose causes red blood cells hemoglobin to join with glucose in the blood, becoming 'glycated'.

Regarding Islet cell antibodies, table (6) showed that group I had significant higher percentage of ICA positivety than the control group (P=0.004). This was in accordance with Watkins et al.,[10] and Salama et al., (2016) who found that islet cells antibodies were significantly higher among the relatives of the diabetics compared to healthy controls.

Moreover, Watkins et al., (2014) stated that ICA positivity can detect individuals at greater risk for T1D.

Recommendations

- There must be a wide immunogenetic screening of non-diabetic siblings of T1Dpatients to identify individuals at risk of T1D.
- There must be an extensive study on different antibodies rather than ICA
- Further follow-up of those with positive antibodies to predict progression of their levels or progression to overt clinical diabetes.

References

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