Glutamic acid decarboxylase autoantibodies role in reclassifying diabetes of adulthood in Basrah

Abstract

Aim: To determine the prevalence and phenotypic characteristics of diabetes subtypes based on glutamic acid decarboxylase autoantibodies (GADA) status in those newly presented diabetic to the Al-Faiha Specialized Diabetes, Endocrine and Metabolism Center (FDEMC) in Basrah, Southern Iraq.

Methods: The study design is cross-sectional and includes adult diabetic patients if they are free of insulin treatment for at least 6 months from diagnosis and to be 30 years of age and over from the period of January 2013 to March 2013.

Results: Of our diabetics with age 30 years and more, 26.4% were GADA-positive. The only significantly higher variables seen more among GADA-positive diabetes groups were normal weight and current insulin uses. GADA-positivity was not associated with gender, age, BMI, family history, smoking, hypertension, duration of diabetes, or specific HbA1c in the current study.

Conclusion: A quarter of adults diabetic in Basrah were GADA positive. GADA positivity means more likely to be normal weight diabetics and currently on insulin use.
status in those newly presented diabetic (regardless the duration of diabetes) to the Al-Faiha Specialized Diabetes, Endocrine and Metabolism Center (FDEMC) in Basrah, Southern Iraq.

**Subjects, Materials and Methods**

**Setting**

FDEMC is a tertiary referring center in Basrah Southern Iraq. The ethics committee in the Basrah College of Medicine approved the study.

**Design**

The study design is cross-sectional and includes adult diabetic patients if they are free of insulin treatment for at least 6 month from diagnosis and to be 30 years of age and over for the period of January 2013 to March 2013. Diabetes was designated according to standard criteria, and LADA was defined as patients aged at time of diagnosis 30 years or more with GADA-positive who did not require insulin treatment for at least 6 months after diagnosis [16]. Participants were classified according to the following definitions: type 1 diabetes, insulin-dependent <6 months from diagnosis; LADA, GADA-positive, age ≥ 30 years and insulin-independent ≥6 months from diagnosis; type 2 diabetes, GADA-negative and insulin-independent ≥6 months from diagnosis.

**Exclusion criteria:** Patients with incomplete data, current pregnancy, renal disease with a raised creatinine level.

All patients were given informed consent form. Data were collected on clinical characteristics (age, gender, symptoms, family history of diabetes, anthropometric features: height, weight, BMI, biological parameters like glycosylated hemoglobin (HbA1c), immunological markers (GADA).

**Variables**

Current smoking was defined as smoking all or part of a cigarette within the 30 days preceding the enrollment.

Family history of diabetes was defined as having diabetes in any of the following family members: parents, grandparents (either paternal or maternal), and siblings.

Height and weight were measured without shoes and heavy clothes. BMI was calculated as weight in kilograms divided by the square of height in meters.

Hypertension was defined as systolic blood pressure 140 mmHg or more and or diastolic blood pressure 90 mmHg or more on two occasions in seated patients for at least 5 minutes or history of hypertension and currently on drugs.

**Biochemical tests**

Blood (10mL) was collected for determination of biochemical parameters. HbA1c was determined by high-pressure liquid chromatography (HPLC) using D-10 Hemoglobin Testing System from Bio-Rad Laboratories, Inc., Hercules, CA 94547.

**Antibody Measurement**

Estimation of GADA.GADA were determined by GAD kit (Diametra, Italy). The kit was used for an in vitro qualitative ELISA test for detection of circulating autoantibodies against GAD antigens. (Sensitivity: 92.3%; Specificity: 98.6%). The intra-assay variability is ≤ 7.6%,and inter-assay variability is ≤8.2%. The upper normal limit for anti-GAD is 4 unit/ml. Subjects were considered positive for GADA if the value was 5 U/ml or higher.

**Statistical Analysis**

For continuous variables, the comparisons between GADA group and others were based on the t test as univariate analysis. Similarly, for categorical variables, the x2 test was used. Data were considered significant at P<0.05. Statistical analysis was performed using SPSS-15 statistical software.

**Results**

Total enrolled patients were 760 (Table 1). They were divided into two groups (GADA- positive diabetes and GADA- negative). GADA-positive diabetes constituted 26.4% of this cohort (57.2% men). Mean age of GADA- positive diabetes group was 40.8±8.1 years, which was not statistically different from that GADA-negative. The mean BMI was 27.1±24.8 kg / m2 with no significant difference from GADA-negative. Of those GADA-positive diabetes, 53.3% was having normal weight vs. 32.3% GADA-negative (P<0.0001). Family history was positive in 59.7% and current cigarette smoking was seen in 18.9% of GADA-positive patients, respectively, but none of these statistically different from GADA-negative. About 13.4% of GADA-positive were hypertensive, which is again not statistically different from those GADA-negative.

There was no difference between two groups in the duration of diabetes or onset of starting insulin, but 78.6% of GADA-positive were currently on insulin (P<0.0001). Again, presenting HbA1c not different between the two groups.

GADA-positive diabetes, according to age group is present in (Table 2). About 45.7% of the patients were in the age group 30-39 year. No significant difference in GADA positivity in all age groups (P value=0. 595).

**Discussion**

Of our diabetics with age 30 years and more, 26.4% were GADA-positive. The only significantly higher variables seen more among GADA-positive diabetes groups were normal weight and current insulin users in this study. GADA-positivity was not associated with gender, age, BMI, family history, smoking, hypertension, duration of diabetes, or specific HbA1c in the current study.

The family history among patients with LADA are conflicting among studies. Some people suggest that LADA patients are unlikely to have a family history of type 2 diabetes [17], while Carlsson et al indicate presence of family history as an important risk factor for the development of LADA [18].

The studies on LADA in the Middle East were scanty. We come across one study from Iran, where, among 500 patients with type 2 diabetes GADA positivity was reported in 14.2%. GADA positivity was more associated with 50–59 Years, but not associated with hypertension, family history of diabetes, and cigarette smoking [19].
Table 1: Comparative analysis between GADA-positive diabetes and GADA-negative groups.

<table>
<thead>
<tr>
<th></th>
<th>GADA positive diabetes</th>
<th>GADA negative diabetes</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%)</td>
<td>201 (26.4)</td>
<td>559 (73.6)</td>
<td></td>
</tr>
<tr>
<td>Gender (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>115 (57.2)</td>
<td>294 (52.6)</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>86 (42.8)</td>
<td>265 (47.4)</td>
<td></td>
</tr>
<tr>
<td>Age at recruitment years (mean±SD)</td>
<td>40.8±8.1</td>
<td>41.3±9.1</td>
<td>0.502</td>
</tr>
<tr>
<td>BMI (kg/m²) (mean±SD)</td>
<td>27.1±24.8</td>
<td>27.5±5.4</td>
<td>0.703</td>
</tr>
<tr>
<td>Overweight (%)</td>
<td>57 (28.9%)</td>
<td>203 (36.6%)</td>
<td></td>
</tr>
<tr>
<td>Obese (%)</td>
<td>35 (17.8%)</td>
<td>173 (31.2%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Normal weight (%)</td>
<td>105 (53.3%)</td>
<td>179 (32.3%)</td>
<td></td>
</tr>
<tr>
<td>Family history (%)</td>
<td>120 (59.7)</td>
<td>393 (70.3)</td>
<td>0.006</td>
</tr>
<tr>
<td>Current cigarette smoking (%)</td>
<td>38 (18.9)</td>
<td>119 (21.3)</td>
<td>0.474</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>27 (13.4)</td>
<td>123 (22.0)</td>
<td>0.009</td>
</tr>
<tr>
<td>Duration of diabetes years (mean±SD)</td>
<td>6.7±4.5</td>
<td>6.2±5.3</td>
<td>0.231</td>
</tr>
<tr>
<td>Onset of starting insulin years (mean±SD)</td>
<td>4.0±3.8</td>
<td>4.0±4.4</td>
<td>0.957</td>
</tr>
<tr>
<td>Current insulin use (%)</td>
<td>158 (78.6)</td>
<td>337 (60.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HbA1c at recruitment % (mean±SD)</td>
<td>11.4±2.5</td>
<td>11.1±2.6</td>
<td>0.497</td>
</tr>
</tbody>
</table>

Table 2: Age ranges between GADA-positive diabetes and GADA-negative groups.

<table>
<thead>
<tr>
<th>Age range</th>
<th>GADA-positive diabetes (%)</th>
<th>GADA-negative diabetes (%)</th>
<th>Total (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-39</td>
<td>84 (41.8)</td>
<td>263 (47.0)</td>
<td>347 (45.7)</td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>84 (41.8)</td>
<td>202 (36.1)</td>
<td>286 (37.6)</td>
<td>0.595</td>
</tr>
<tr>
<td>50-59</td>
<td>19 (9.5)</td>
<td>57 (9.5)</td>
<td>76 (10.0)</td>
<td></td>
</tr>
<tr>
<td>60-69</td>
<td>6 (3.0)</td>
<td>20 (3.6)</td>
<td>26 (3.4)</td>
<td></td>
</tr>
<tr>
<td>≥70</td>
<td>8 (4.0)</td>
<td>17 (3.0)</td>
<td>25 (3.3)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>201</td>
<td>599</td>
<td>760</td>
<td></td>
</tr>
</tbody>
</table>

While in Saudi Arabia, of patients with type 2 DM, 8/99 patients were GADA positive [20]. Furthermore, in a small cohort from Turkey GADA-positive cases were seen in 31% among 54 initially diagnosed type 2 diabetic patients [21].

Different data reported from Africa, where the prevalence range 14% in Nigeria to 13.5% in Ghana to 7.3% in Tanzania [22-24].

Furthermore, in Asia, GADA were detected in 16.1% of Chinese type 2 diabetic patients [25]. And the prevalence of GADA-positive diabetes cohort from three largest hospitals in Sri Lanka was 5.4% (n = 54; 95% CI 4.0 – 6.8). The prevalence of GADA positivity was much higher among those who were young and had a lower BMI compared with those who were older and more obese [26]. GADA positivity among men and women was 7.4% and 4.0%, respectively (p = 0.028). Compared with those that tested negative for GADA, GADA-positive participants had been diagnosed at a younger age, were leaner, had a lower frequency of hypertension, presented.

European data are exemplified in LADA in South Wales study, were the predictors of associations with increasing levels of GADA: younger age at presentation, increasing IA-2 concentration, decreasing C-peptide concentration, presence of other autoimmune disorders, lower BMI and increasing HbA1c [27]. Factors not statistically significant included: symptom at presentation, family history of diabetes and family history of other autoimmune disorders. Multivariate analysis revealed that, out of the above, higher GADA levels were associated with higher IA-2, higher HbA1c, younger age and lower BMI. Ethnic background was not included in the analysis as 98.4% of the sample population were Caucasian [27].

Conclusion

A quarter of adults diabetic in Iraq are GADA positive. GADA positivity means more likely to be normal weight diabetics and currently on insulin use.

Acknowledgment

The authors would like to acknowledge all the medical staff of Al-Faiha Specialized Diabetes, Endocrine and Metabolism Center (FDEMC).

Duality of interest

The authors declare that there is no duality of interest associated with this manuscript.

References


Copyright: © 2015 Mansour AA, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.