Prevalence and Clinical Significance of Glutamic Acid Decarboxylase (GAD) Antibodies in Recently Diagnosed Type 2 Diabetes in the ADOPT Study Cohort

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Background and Aims: A number of patients with clinical type 2 diabetes mellitus (T2DM) are glutamic acid decarboxylase antibody positive (GAD+). The aim of this study was to assess the GAD status of patients enrolled in ADOPT. **Materials and Methods:** ADOPT (A Diabetes Outcome Progression Trial) is a randomised, double-blind, comparative drug trial in 4,293 drug-naive, recently diagnosed T2DM patients. The GAD status of these patients was evaluated at baseline in the context of anthropometric and biochemical characteristics. **Results:** Although BMI and age were similar, the 159 (3.7%) GAD+ patients tended to have a lower waist circumference, higher HbA_{1c}, and lower fasting insulin accompanied by decreased measurements of β-cell function (pro-insulin/C-peptide, Δ I30/Δ G30) during an OGTT. However, when β-cell function is corrected for insulin-resistance [Δ I 30/Δ G 30]/insulin, GAD+ and GAD- patients were similar.

Parameter	**GAD-positive***	**GAD-negative***	***P*-value**
Age (yrs)	59.0 (51.0, 65.0)	57.0 (50.0, 64.0)	*P* = 0.14
BMI (kg/m^2)	29.9 (27.3, 35.7)	31.1 (27.8, 35.3)	*P* = 0.26
Waist Circumference (cm)	103.0 (94.0, 113.0)	104.1 (96.0, 113.0)	*P* = 0.09
Fasting Glucose (mmol/l)	8.2 (7.6, 9.4)	8.2 (7.5, 9.1)	*P* = 0.37
HbA_{1c} (%)	7.5 (6.8, 8.0)	7.3 (6.7, 7.9)	*P* = 0.06
Fasting Insulin (pmol/l)	102.0 (64.6,150.0)	122.0 (86.1,186.6)	*P* = 0.03
Pro-insulin/C-peptide ([pmol/l]/[nmol/l])	43.8 (28.8, 62.1)	39.3 (27.1, 57.1)	*P* = 0.07
Δ I30/Δ G30 ([pmol/l]/[mmol/l])	26.4 (14.0, 51.9)	33.2 (18.7, 58.7)	*P* = 0.01
[Δ I30/Δ G30]/insulin ([[pmol/l]/[mmol/l]]/[pmol/l])	0.26 (0.16, 0.41)	0.27 (0.17, 0.43)	*P* = 0.49
*median (IQR)			

Consistent with increased fasting insulin as a surrogate for insulin resistance, GAD- patients had lower HDL (median [IQR] 1.20 [1.01, 1.42] vs. 1.26 [1.06, 1.48] mmol/l; $P < 0.05$]) and higher triglycerides (1.80 [1.29, 2.61] vs. 1.33 [1.12, 2.49] mmol/l; $P < 0.05$). **Conclusion:** Newly diagnosed patients with T2DM who are GAD+ appear otherwise phenotypically similar to GAD- patients. Although measures of β-cell function appear to be poorer in GAD+ patients,

when ambient insulin resistance is corrected for, β-cell function is similar. Nonetheless, the natural history and progressive nature of T2DM may be different in these two groups over time

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