

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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A number of patients with clinical type 2 diabetes mellitus (T2DM) are glutamic acid decarboxylase antibody positive (GAD+). The GAD status of the 4,293 patients enrolled in ADOPT (A Diabetes Outcome Progression Trial – a randomized double-blind comparative drug trial in drug-naïve, recently diagnosed T2DM patients) was evaluated in the context of anthropometric and biochemical characteristics. 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.

Parameter	GAD-positive*	GAD-negative*	P-value
Waist Circumference (cm)	103.0 (94.0, 113.0)	104.1 (96.0, 113.0)	0.09
Fasting Glucose (mmol)	8.2 (7.6, 9.4)	8.2 (7.5, 9.1)	0.37
HbA _{1c} (%)	7.5 (6.8, 8.0)	7.3 (6.7, 7.9)	0.06
Fasting Insulin (pmol/l)	102.0 (64.6, 150.0)	122.0 (86.1, 186.6)	0.03
Pro-insulin/C-peptide (pmol/nmol)	43.8 (28.8, 62.1)	39.3 (27.1, 57.1)	0.07
Δ I30/ Δ G30 (pmol/mmol)	26.4 (14.0, 51.9)	33.2 (18.7, 58.7)	0.01
$[\Delta$ I30/ Δ G30]/Insulin (pmol/mmol/pmol)	0.26 (0.16, 0.41)	0.27 (0.17, 0.43)	0.49

*median (IQR)

Consistent with increased fasting insulin as a surrogate for insulin resistance, GAD-patients had lower HDL [median (IQR) 46.5 (39.0, 55.0) vs 48.8 (41.0, 57.3) mg/dl; $P < 0.05$] and higher triglycerides [162.0 (114.2, 231.0) vs. 147.0 (99.0, 220.0) mg/dl; $P < 0.05$]. 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, with correction for the ambient insulin resistance β -cell function is similar. Nonetheless, over time, the natural history and progressive nature of T2DM may be different in these two groups.