COMMENTS AND RESPONSES

Accuracy and Predictive Value of Classification Schemes for Ketosis-Prone Diabetes

Response to Balasubramanyam et al.

We have read with interest the study by Balasubramanyam et al. (1). They described a new classification scheme (Aβ classification) based on C-peptide levels and the presence or absence of β-cell autoantibodies to predict long-term β-cell function and insulin independence in patients who presented with diabetic ketoacidosis (DKA). They reported a sensitivity of 99.4%, a specificity of 95.9%, and a positive likelihood ratio (LR) of 24.55 in the total cohort of 294 subjects. In the subset of 138 subjects presenting with DKA as new-onset diabetes, 99.1%, 95.5%, and 21.79 sensitivity, specificity, and positive LR, respectively, were observed.

To evaluate the performance of this new classification in a Caucasian-Spanish population, 40 consecutive adult patients (23 of whom were male) aged <40 years and presenting with DKA as diabetes onset were included. The mean ± SD age, BMI, and A1C at diagnosis were 25.4 ± 5.0 years, 21.9 ± 4.6 kg/m^2, and 10.9 ± 3.5%, respectively. Glutamic acid decarboxylase and tyrosine phosphatase antibodies were measured as previously described (2). At onset and 12 months later, plasma C-peptide was measured before and 6 min after intravenous injection of 1 mg glucagon (NovoNordisk, Gentofte, Denmark). C-peptide was determined using a radioimmunoassay (2). β-Cell function 12 months after the DKA episode was defined as preserved or absent, as described (1). To predict 12 months' β-cell function in our group of subjects, the new classification had a sensitivity of only 20%, a specificity of 80%, and a positive LR of 1. Based on the classification used and new terminology introduced by Balasubramanyam et al., the proportion of subjects of our population in each of the four groups was as follows: 72.5% A+β− (type 1A); 7.5% A−β− (type 1B); 12.5% A+β+ (type 2A); and 7.5% A−β+ (type 2B). These results were clearly different compared with the 74% of type 2B and the 6% of type 1A reported in the original paper (1).

In conclusion, the Aβ classification recently introduced in the literature barely predicts β-cell function 12 months after the onset of type 1 diabetes diagnosed in DKA in a Caucasian-Spanish population. Likewise, the proportion of subjects in each group defined by the classification is markedly different from data reported by Balasubramanyam et al. (1). While in their study, the higher proportion of new-onset diabetes corresponded with A−β+ (ketosis-prone diabetes [KPD], type 2B), in ours the vast majority of subjects corresponded with A+β− (KPD type 1A). These big differences can be explained by different factors. First, there are major ethnic differences between both populations. In our case, all of the subjects were Caucasian and from a Mediterranean area, whereas in the study by Balasubramanyam et al., 89% were non-Caucasian, mainly of African-American or Hispanic origin. Second, the high predictive value of Aβ classification was driven mainly by the presence of positive β-cell function following diabetes onset and DKA rather than by the presence of islet autoantibodies. In our group, the proportion of subjects with preserved β-cell function after 12 months of follow-up was only 20%, whereas the proportion of subjects with positive β-ell autoantibodies was 85%.

In summary, the accuracy and performance of classification schemes addressed to KPD may extremely differ when applied to different ethnic groups. This points to the heterogeneity of the disease from an epidemiological, pathogenic, and clinical presentation point of view in different populations (3,4).

Cristian Fernández, md
Marga Giménez, md
Gonzalo Díaz, md
Ignacio Conget, md, phd

From the Endocrinology and Diabetes Unit, Institut d'Investigacions Biomèdiques August Pi i Sunyer, Hospital Clínic i Universitari, Barcelona, Spain.

Address correspondence to Dr. I. Conget, Endocrinology and Diabetes Unit, Villarroel 170 , 08036 Barcelona, Spain. E-mail: iconget@clinic.ub.es.

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