The Clinical Characteristics and Treatment Outcomes in Patients with Autoantibody-Negative Ketosis-Prone Diabetes

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Introduction

Ketosis-prone diabetes (KPD), characterized by presentation with diabetic ketoacidosis (DKA) in patients lacking the typical features of autoimmune type 1 diabetes, is a heterogeneous syndrome. The objective of this study is to ascertain the presence of A−β+ (autoantibody-negative, β-cell functional reserve) KPD in Korean children and adolescents and to study their characteristics in this group.

Patients and methods

43 patients admitted with DKA (new onset diabetes) in the hospital were studied and followed up. A−β+ KPD (n = 19) was defined as presenting with unprovoked ketoacidosis in the absence of autoantibodies (A−) with recovery of beta cell functions (β+).

Table 1. characteristics of A−β+ and A+β− group

Characteristics	A−β+ (n = 19)	A+β− (n = 24)	*P* value
Age (years)	4.9 (12–16)	11.7 (8.0–12.7)	0.001
Male	11 (58)	9 (37.5)	0.12
Duration of Sx (days)	45 (30–90)	30 (10–60)	0.56
Weight loss (kg/week)	1.3 (0.2–2.5)	1.5 (3–2.6)	0.45
Family Hx of T2DM	12 (63)	12 (50)	0.28
BMI (kg/m2)	26.6 (23.1–30.4)	17.1 (14.5–21)	0.02
BMI-Z	1.6 (1.0–2.5)	-0.62 (-1.4–1.9)	0.01
Antibodies positive	0	24	NA
HbA1c (%)	9.9 (7.1–12.6)	11.8 (10.7–13.8)	0.53
C-peptide (ng/mL)	0.4 (0.3–0.5)	0.4 (0.2–0.5)	0.78
During DKA			
Glucose (mg/dl)	327 (287–435)	410 (343–692)	0.02
PH (arterial)	7.23 (7.1–7.3)	7.10 (6.8–7.2)	0.05
Bicarbonate (mol/L)	8.7 (4.2–13.6)	10.7 (7.5–15.1)	0.06
Treatment prescribed			
Use of insulin	19 (100)	24 (100)	NA
Insulin dose at discharge (U/kg)	0.7 (0.4–1.0)	0.8 (0.5–1.1)	0.81

Patients and methods

A+β−KPD (n = 24) was defined as presenting with ketoacidosis in the presence of autoantibodies (A+) with failure of recovery of beta cell functions (β−). Autoantibodies to glutamic acid decarboxylase (GAD), islet cell (ICA), insulin (IAA) were analyzed by Quantitative Sandwich Immunoassay method. A longitudinal evaluation of HbA1c, serum C-peptide level was similarly done at 3, 6 and 12 months of follow up.

Results

It was found that the A−β+ KPD patients presented with DKA at an older age (*P*= 0.001), with a higher BMI-Z (p= 0.01) as compared to A+β− patients (Table 1). Serial monitoring of the fasting C-peptide value in the A−β+ KPD patients done at 0, 3,6 and 12 months of follow up showed progressive improvement of beta cell secretory function (Figure 1). At the end of one year follow up, all 19 patients in the A−β+ KPD patients were off insulin. The HbA1c at 12 months of follow up it had significantly improved in the in the A−β+ KPD patients. The C-peptide values showed remarkable improvement in the A−β+ KPD patients in the contrast to the A+β−KPD patients (Table 2).

Table 2. Characteristics at 1-year follow up A−β+ and A+β− groups

Characteristics	A−β+ (n = 19)	A+β− (n = 24)	*P* value
BMI (kg/m2)	26.4(19.5–34.2)	19.1 (15.1–24.5)	0.01
BMI-Z	1.7 (0.64–3.1)	0.51 (-1.2–1.7)	0.01
HbA1c (%)	6.2 (5.2–7.1)	9.7 (6.1–13.6)	0.01
C-peptide (ng/mL)	3.4 (2.5–4.4)	0.4 (0.1–0.8)	0.01
Tx with insulin	0 (0)	24 (100)	NA
Tx with OHA	19 (100)	0 (0)	NA

Table 3. Multivariate analysis associated with β cell function recovery

Characteristics	β coefficient (95% CI)	*P* value
Age (years)	0.24 (0.81-1.47)	0.05
BMI-Z	0.45 (0.12-0.78)	0.008
Glucose at DKA	-0.01 (-1.50-2.40)	0.51
Autoantibody	Not entered	NA

Results

Baseline BMI-Z was negatively correlated with C-peptide at 1 year (Figure 2). Multivariate analysis indicated that age, BMI-Z were independently associated with beta-cell recovery (Table 3).

Figure 1. Serial C-peptide levels between A-β+ group and A-β- group

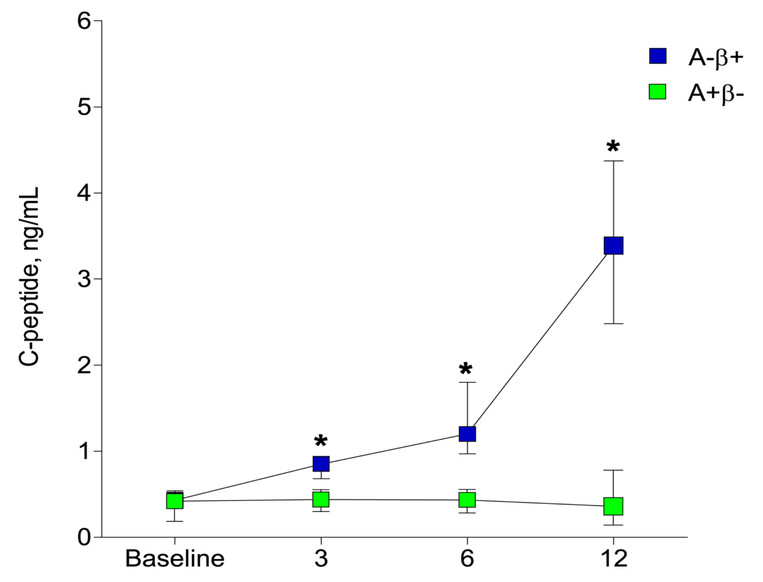
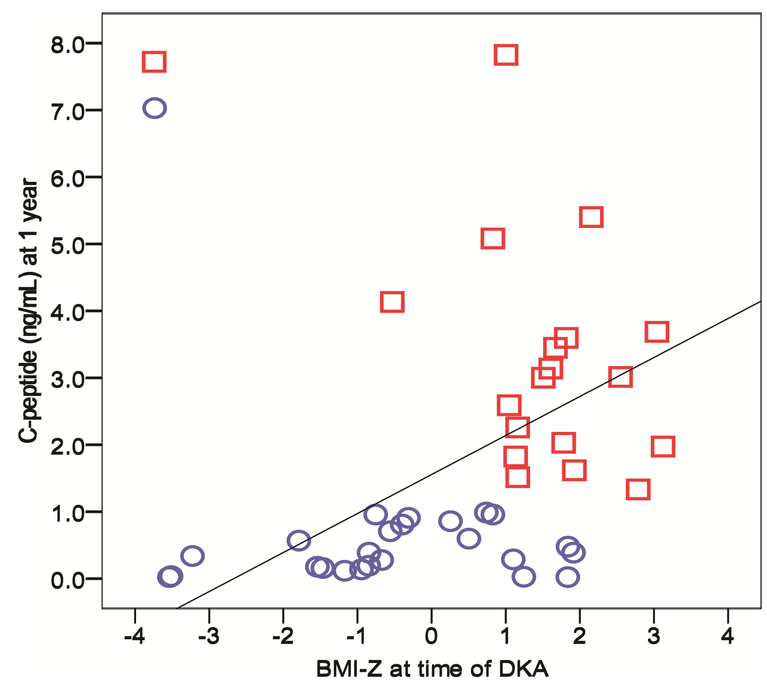


Figure 2. Correlation between baseline BMI-Z and C-peptide at 1 year



Conclusion

Our data showed that 19 out of the 43 patients who were admitted with DKA at diagnosis for diabetes characteristics of A−β+ KPD which suggested a prevalence rate of 38.8 %. A−β+ KPD patients had a greater mean BMI and higher frequency of obesity, significantly older age than the A−β+ KPD.