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Original Article

Serum C-peptide levels as a predictor of beta-cell function in children with type 1 diabetes

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Abstract

C-peptide levels are important for assessing residual insulin secretion from β cells in individuals with Type 1 diabetes (T1DM). This study aimed to evaluate serum C-peptide levels in pediatric patients with T1DM and correlate them with various clinical and laboratory parameters. In a case-control study, 80 children aged 2–15 years with T1DM were enrolled, and an additional 80 non-diabetic healthy children were included as a control group. Laboratory data encompassed plasma glucose, C-peptide, hemoglobin A1c (HbA1c), pancreatic autoantibodies (anti-GAD), Thyrotropin, and Tissue transglutaminase antibodies-IgA (Anti-TTG-IgA). We conducted correlation analyses between C-peptide levels and clinical/laboratory parameters among children with T1DM. The chi-square test was employed, with a significance threshold set at $p \leq 0.05$. The mean age at diagnosis of T1DM was 8.11 years, with a mean disease duration of 3.84 years. The average HbA1c level was 10.94%. Twenty-seven out of eighty patients had a positive family history of diabetes, and the average GAD antibody level was 118.128 IU/ml. Serum C-peptide levels in children with T1DM were significantly lower than those in non-diabetic children (0.189 ng/ml *vs.* 2.960 ng/ml, respectively), indicative of reduced residual B-cell function. Correlation analyses revealed associations between C-peptide levels and age at diagnosis, disease duration, BMI, and fasting blood sugar, but not with HbA1c or anti-GAD levels. Patients with lower C-peptide levels tended to be diagnosed at a younger age and had a longer mean disease duration. Fasting C-peptide levels are valuable indicators for predicting beta-cell function in pediatric T1DM patients. Early initiation of treatment may be essential to preserve pancreatic beta-cell function.

Keywords: autoantibodies, B-cell function, control group, thyrotropin.

Introduction

Type 1 diabetes mellitus (T1DM) is characterized by a deficiency of insulin secretion, primarily due to the autoimmune destruction of pancreatic beta cells, leading to insulinopenia [1]. C-peptide, a fragment of pro-insulin, is co-secreted in equimolar amounts with insulin from pancreatic beta cells and serves as a reliable indicator of residual beta-cell function [2, 3]. Measuring C-peptide levels is considered the gold standard for assessing endogenous insulin secretion and plays a crucial role in managing diabetes mellitus (DM) [4, 5]; unlike children with type 2 DM, who typically present with elevated C-peptide levels at diagnosis, children with type 1 DM exhibit lower levels [6]. C-peptide testing offers advantages over insulin as a marker of beta-cell function, as it has a longer half-life (20–30 minutes, compared to insulin's 3–5 minutes), providing a more stable assessment of beta-cell response [2]. Moreover, C-peptide is not present in insulin medications, making it an ideal measure of beta-cell function even in patients on insulin therapy [7].

This study aimed to evaluate C-peptide levels in children with type 1 diabetes mellitus, reflecting the residual function of pancreatic beta cells and establishing correlations between C-peptide levels and specific

Table 1: Age at diagnosis of diabetes (years).

Sex \ Age	0–2	3–5	6–8	9–11	12–14	Total	P-value
Male	2 (5.88%)	4 (11.76)	13 (38.23%)	12 (35.29%)	3 (8.82%)	34 (42.5%)	
Female	2 (4.34%)	8 (17.39%)	18 (39.13%)	10 (21.17%)	8 (17.39%)	46 (57.5%)	0.1248
Total	4 (5.00%)	12 (15.00%)	31 (38.75%)	22 (27.50%)	11 (13.75%)	80 (100%)	

clinical and laboratory parameters. The findings are expected to guide the initiation of treatment at an earlier stage, potentially preserving pancreatic function.

Material and methods

Study design

A case-control study was conducted to assess C-peptide levels in children with type 1 diabetes mellitus (T1DM) who were registered and followed at Al-Mawani Teaching Hospital and Al-Faihaa Specialized Diabetes Endocrine and Metabolism Center (FDEMC) in Basrah, Iraq, from January 2021 to October 2021.

Sample size

The study included 80 diabetic children (34 boys and 46 girls) aged 2–15 years and 80 apparently healthy, non-diabetic children (38 boys and 42 girls) within the same age range.

Inclusion criteria

Participants were required to have a definite diagnosis of T1DM, as per the WHO criteria [8], which defines T1DM as a form of diabetes characterized by permanent insulinopenia and susceptibility to ketoacidosis, resulting from autoimmune destruction of the pancreas's beta cells (American Diabetes Association, 2010).

Exclusion criteria

Children with T1DM who had renal failure were excluded from the study, as C-peptide levels can be influenced by renal function (causing falsely elevated levels) [9]. Children who had experienced recent diabetic ketoacidosis within one week were also excluded.

Study procedures

Comprehensive patient histories were collected, including age at diagnosis, duration of DM, family history of T1DM and T2DM, and details of insulin therapy.

Table 2: Duration of diabetes (years).

Sex \ Age	0–2	3–5	6–8	9–11	Total	P-value
Male	14 (41.17%)	11 (32.35%)	5 (14.70%)	4 (11.76%)	34 (42.5%)	
Female	20 (43.47%)	15 (32.60%)	8 (17.39%)	3 (6.52%)	46 (57.5%)	0.6861
Total	34 (42.5%)	26 (32.5%)	13 (16.25%)	7 (8.75%)	80 (100%)	

Table 3: Doses of daily insulin at time of C-peptide determination (IU/kg body weight).

Sex \ Dose	0.5–1.0	1.1–1.5	>1.5	Total	P-value
Male	14 (41.17%)	11 (32.35%)	9 (26.47%)	34 (42.5%)	
Female	18 (39.13%)	23 (50%)	5 (10.86%)	46 (57.5%)	0.0046
Total	32 (40%)	34 (42.5%)	14 (17.5%)	80 (100%)	

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Table 4: C-peptide levels in the study population (ng/ml).

Level / Sex	<0.1		0.5		0.6–0.9		1–2		>2		Mean	
	P	C	P	C	P	C	P	C	P	C	P	C
Male	21	-	6	1	5	6	2	12	20	-	0.20	3.136
Female	32	-	9	1	4	6	1	20	14	-	0.177	2.850
Total	53	-	15	2	9	12	3	32	34	-	0.189	2.990

Note: P – patient; C – control.

Anthropometric measurements, such as weight and height, were recorded to calculate body mass index (BMI).

The C-peptide assay was conducted using fully automated chemiluminescence immunoassay kits on a Cobas e 411 analyzer series by Roche Diagnostics, Germany. C-peptide was measured in a random, non-fasting state at the time of T1DM diagnosis, reflecting stimulated levels.

The preservation of C-peptide, indicative of residual beta-cell function, was defined as a stimulated C-peptide level of ≥0.6 ng/mL (0.2 nmol/L) [10]. Subsequently, simple correlation analyses were performed to assess the relationships between C-peptide levels and various clinical and laboratory parameters in children with T1DM.

Results

The age of children with diabetes at the time of diagnosis ranged from 2 to 14 years, with a mean age of 8.11 years (Table 1).

The duration of the disease varied from 1 to 11 years (Table 2), with a mean duration of 3.84 years. Gender did not show significant differences concerning the age at diagnosis and the duration of diabetes (p=0.1248 and p=0.6861, respectively).

The mean BMI among the study participants was 18.50 kg/m^2, and the average Hb A1c level was 10.94%. A positive family history of diabetes was found in 27 out of 80 patients, and the mean fasting blood sugar (FBS) was 188.01 mg/dL. The study revealed a 50% positivity for anti-GAD antibodies (>30 IU/mL), with an average level of 118.128 IU/mL. Analysis of the total daily insulin dose at the time of C-peptide determination (IU/kg body weight) showed a statistically significant gender difference (p=0.0046) (Table 3).

The mean fasting serum C-peptide level in diabetic children was 0.189 ng/mL, while in the control group, it was 2.990 ng/mL. Female diabetic children tended to have a slightly lower mean C-peptide level than males (0.177 *vs.* 0.20 ng/mL), although this difference was not statistically significant (p=0.086) (Table 4).

C-peptide levels below 0.6 ng/mL were observed in 68 patients (85%), while only 12 (15%) had levels above 0.6 ng/mL. Simple correlation analysis revealed that C-peptide levels were positively correlated with the age at diagnosis, duration of the disease, BMI, and FBS, but not with Hb A1C and anti-GAD antibodies. Screening for celiac disease yielded negative results, and Thyrotropin (TSH) levels were within the normal range in the study population (Table 5).

Discussion

This study examined the serum C-peptide levels in children with T1DM to assess residual beta-cell function. The results showed that C-peptide levels in diabetic children were significantly lower compared to non-diabetic children evaluated using the same method for C-peptide determination (0.189 *vs.* 2.990 ng/mL),

Table 5: C-peptide level in relation to some clinical/laboratory variables.

Variable	C peptide <0.6 ng/ml	C peptide >0.6 ng/ml	P-value
Mean age at diagnosis (year)	7.81	10	0.010
Mean duration of DM (year)	4.057	2.636	0.002
Mean FBS (mg/dl)	185.338	204.545	0.028

Table 5: Continued.

Variable	C peptide <0.6 ng/ml	C peptide >0.6 ng/ml	P-value
Mean HbA_1C %	10.928	11.018	0.555
Mean BMI (Kg/m²)	18.743	15.238	0.021
Mean GAD ab (IU/ml)	113.781	145.363	0. 217

reflecting diminished residual B-cell function. Among the diabetic patients, 85% had C-peptide levels below 0.6 ng/mL, while only 15% had levels above this threshold. This finding was higher than that presented by Novac *et al.*, where 65% of patients had C-peptide levels below 0.6 ng/mL and 35% had levels above it [11].

The presence of even very low residual beta-cell function has been associated with improved glycemic control, a reduced incidence of hypoglycemia, and a decreased risk of vascular complications in T1DM patients [12]. Previous research has also suggested that C-peptide may slow the progression of microvascular damage in type 1 diabetes [13].

In this study, patients with C-peptide levels below 0.6 ng/mL were diagnosed at a younger age compared to those with levels above 0.6 ng/mL (7.81 *vs*. 10 years, p=0.010). This observation is consistent with findings by Suh J *et al.* [14] and Novac *et al.* [11]. Recent studies confirmed that the rate of C-peptide secretion falls over time is significantly related to the age of disease onset, with younger age predisposing to far more rapid C-peptide decline [15]. Additionally, the mean disease duration was longer in patients with lower C-peptide levels (4.05 years) than those with higher levels (2.63 years, p=0.002). This is in line with a study by Fawwad *et al.* [16], which found that individuals with longer T1DM duration tended to have slightly lower C-peptide levels compared to those measured at or near the time of diagnosis.

Several other studies have demonstrated low but still detectable C-peptide secretion a long time after the diagnosis. Most patients are insulin "micro secretors", and some maintain clinically relevant endogenous secretion for many years after diagnosis [17, 18].

The study population exhibited an average Hb A1c level of 10.94%, similar to the result (10.6%) reported by Alsaheel *et al.* [19]. The American Diabetes Association recommends an Hb A1c target of <7% for many children with type 1 diabetes [20].

Regarding anti-GAD antibodies, the study showed a 50% positivity rate (>30 IU/mL) with an average level of 118.12 IU/mL. However, the level of anti-GAD antibodies did not correlate with C-peptide levels (p=0.217). High anti-GAD antibody levels, especially in higher titers, indicate declining beta-cell function in the years following DM diagnosis [21, 22].

The limitation of this study is the small-sized sample. The findings can serve as a foundation for future research.

Conclusion

Fasting C-peptide levels serve as valuable indicators for predicting beta-cell function in children with T1DM. The study revealed significant correlations between C-peptide levels and the age at diagnosis, disease duration, BMI, and FBS, but not with Hb A1C and anti-GAD antibodies. Early initiation of treatment should be considered to help preserve pancreatic beta-cell function.

Conflict of interest

The authors declare no conflict of interest.

Ethical approval

The study protocol received approval from the College Council and Ethical Committee at Basrah College of Medicine and Al-Zahraa College of Medicine, University of Basrah, with reference number 7/39/4300 on 13/11/2020.

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