

Association of detectable C-peptide levels with glycemic control and chronic complications in individuals with type 1 diabetes mellitus: A systematic review and meta-analysis

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Abstract

Aims

Multiple studies have addressed the association between detectable levels of C-peptide and [glycemic](#) control, as well as the development of chronic complications of [type 1 diabetes mellitus](#) (T1DM), including both macrovascular and [microvascular diseases](#). We aimed to summarize the available evidence on the [clinical significance](#) of detectable levels of C-peptide in T1DM.

Method

A systematic search was performed on online databases using the following key terms: T1DM, C-peptide, [diabetes mellitus complications](#), and [glycemic](#) parameters. We pooled standardized mean difference (SMD) and odds ratios (OR).

Results

Of the 1519 articles retrieved from the initial search, 38 (12 cohort and 26 cross-sectional studies) met our eligibility criteria. Individuals with T1DM in the detectable C-peptide group, compared with the undetectable C-peptide group, had lower mean [HbA1c](#) [pooled SMD (95 % confidence interval (95 % CI): -0.08 (-0.13 to -0.02), $I^2 = 0$ %, p.value: 0.005] and daily insulin dose [-0.41 (-0.65 to -0.18), $I^2 = 83$ %, p.value < 0.001]. They also showed lower odds for [retinopathy](#) [pooled crude OR (95 % CI): 0.53 (0.41 to 0.69), $I^2 = 65$ %, p.value < 0.001] and [nephropathy](#) complications [0.62 (0.55 to 0.70), $I^2 = 19$ %, p.value < 0.001]; however, the two groups were similar regarding [neuropathy](#) [0.92 (0.65 to 1.31), $I^2 = 0$ %, p.value: 0.31].

Conclusions

The available evidence suggests that individuals with T1DM in the detectable C-peptide group may experience better clinical outcomes.

Introduction

Type 1 diabetes mellitus (T1DM) is a condition characterized by the loss of β -cell mass in pancreatic islets caused by an autoimmune response.¹ The novel ultrasensitive method for measuring C-peptide levels allows for the detection of lower levels of this biomarker than previously possible in individuals with T1DM, even long after diagnosis.^{2,3}

Many studies have reported detectable levels of C-peptide in individuals with T1DM years after their initial diagnosis, indicating the presence of endogenous insulin secretion by residual autoimmune-resistant β -cells.^{4, 5, 6} Previous studies have explored the risk factors and determinants associated

with detectable C-peptide levels in T1DM. In this regard, some human leukocyte antigens (HLA) serotypes, including HLA DR3, DR4, and DQ8, along with early age at diagnosis, long-standing disease, higher HbA1c at the time of diagnosis, and male gender, are inversely associated with detectable C-peptide levels in individuals with T1DM.^{2,7}

Increasing numbers of studies have assessed whether detectable C-peptide levels are correlated with lower glucose level fluctuations and better glycemic control in individuals with T1DM.^{8,9} Additionally, some studies have addressed the association between detectable C-peptide levels and chronic complications of T1DM, including macrovascular and microvascular diseases.^{10,11}

Nevertheless, current evidence regarding the clinical importance of detectable C-peptide levels in individuals with T1DM is scattered, making it difficult to utilize these data in clinical decision-making. Thus, as the first systematic review and meta-analysis in this area, our goal is to provide a clear and cohesive summary of the key findings from the existing evidence on the clinical significance of detectable C-peptide levels in individuals with T1DM.

Section snippets

Materials and methods

We conducted a systematic review of the literature following a standardized methodology and reported our findings according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Since our study was a systematic review of existing literature, we were exempt from obtaining institutional ethics committee approval. We included all original studies assessing C-peptide levels in individuals with T1DM.

Results

In the initial search, a total of 1519 articles were identified. Following the removal of duplicates (238 articles) and those that did not meet the inclusion criteria based on title/abstract (1127 articles) or full text (116 articles), 38 articles were considered eligible for this study. These 38 articles consisted of 12 cohort studies (mean/median follow-up duration of 0.5 years to 20 years) and 26 cross-sectional studies. Please refer to Fig. 1 for a visual representation of this process.

Discussion

This systematic review includes a total of 38 articles investigating the relationship between C-peptide status and critical parameters in individuals with T1DM. Individuals with T1DM in the detectable C-peptide group exhibited better glycemic control, as evidenced by their lower HbA1c levels and a reduced daily insulin requirement. Regarding microvascular complications, detectable C-peptide was associated with a lower risk of retinopathy and nephropathy; however, there was no association

Conclusions

This study represents the first systematic review exploring the correlation between C-peptide levels and critical parameters in individuals with T1DM. Individuals who exhibit detectable C-peptide levels may experience enhanced control over their glycemic parameters, including reduced HbA1c levels, decreased daily insulin requirements, and decreased likelihood of DKA. Moreover, the presence of detectable C-peptide likely correlates with a lowered risk of hypoglycemic incidents. Detectable

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CRedit authorship contribution statement

Mahin Seifi Alan: Writing – original draft, Visualization, Validation, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Amirhossein Tayebi: Writing – original draft, Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **Elmira Jafari Afshar:** Writing – original draft, Methodology.

Sanaz Seifi Alan: Writing – original draft, Visualization, Resources, Investigation. **Mahnaz Seifi Alan:** Writing – original

Declaration of competing interest

The authors declare no conflicts of interest.

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[Fasted C-peptide distribution and associated clinical factors in adults with longstanding type 1 diabetes: analysis of the Canadian study of longevity in type 1 diabetes](#)

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