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Original Research Article

Assessment of Endogenous Insulin Reserve through C-Peptide Levels and Its Association with Long-Term Glycemic Control in Type 2 Diabetes

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Abstract:

Background: Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and progressive β-cell dysfunction. C-peptide, co-secreted with insulin, serves as a robust indicator of endogenous insulin production, especially in the clinical assessment of β-cell functional reserve. While HbA1c remains a gold standard for monitoring long-term glycemic control, its correlation with basal and stimulated C-peptide levels may reflect the interplay between residual insulin secretion and glucose regulation. This biochemical relationship has potential implications for categorizing diabetic phenotypes and guiding therapeutic choices.

Objectives:

- To evaluate fasting and postprandial C-peptide levels in patients with T2DM.
- To assess the correlation between C-peptide levels (fasting and postprandial) and glycosylated hemoglobin (HbA1c).

Materials and Methods: A cross-sectional observational study was conducted over a period of 1 year. 120 diagnosed T2DM patients attending the outpatient and inpatient departments of the Biochemistry and Medicine units at Shri Ramkrishna Institute of Medical Sciences and Sanaka Hospital, Durgapur. Blood samples were collected after an overnight fast and 2 hours post-meal for estimation of C-peptide levels by chemiluminescence immunoassay (CLIA). HbA1c was measured using high-performance liquid chromatography (HPLC). Statistical analysis included Pearson's correlation and regression models to evaluate associations.

Results: Among 120 patients, mean fasting C-peptide was 1.86 ± 0.48 ng/mL, and mean postprandial C-peptide was 3.52 ± 0.65 ng/mL. HbA1c values ranged from 6.5% to 11.8% with a mean of 8.3 ± 1.1%. A statistically significant inverse correlation was found between HbA1c and both fasting ($r = -0.412$, $p < 0.001$) and postprandial ($r = -0.468$, $p < 0.001$) C-peptide levels. Patients with higher HbA1c (>9%) consistently showed lower C-peptide values, suggesting greater β-cell impairment.

Conclusion: Fasting and postprandial C-peptide levels inversely correlate with HbA1c, highlighting their utility in evaluating residual β-cell function and glycemic control in T2DM patients. These markers may support more individualized treatment plans based on endogenous insulin reserve.

Keywords: C-peptide, HbA1c, Type 2 Diabetes Mellitus, Glycemic Control, Insulin Reserve, β-cell Function.

Introduction

Type 2 Diabetes Mellitus (T2DM) represents a global epidemic, currently affecting more than 500 million people worldwide, with numbers projected to rise steeply in the coming decades. In India, the prevalence of T2DM has shown alarming growth due to rapid urbanization, sedentary lifestyles, and dietary changes, earning the nation the dubious title of the "diabetes capital" of the world. The disease is primarily characterized by insulin resistance and progressive pancreatic β-cell dysfunction, leading to chronic hyperglycemia and subsequent long-term vascular and metabolic complications [1,2].

In the clinical management of T2DM, the assessment of glycemic status and residual β-cell function forms the cornerstone of both diagnosis and long-term therapeutic planning. C-peptide, a 31-amino acid polypeptide, is released in equimolar amounts with insulin during the cleavage of proinsulin [3]. Unlike insulin, C-peptide has a longer half-life (~30 minutes), is not extracted by the liver, and shows greater stability, making it a more reliable indicator of endogenous insulin production [4].

Fasting C-peptide represents basal insulin secretion, while postprandial C-peptide reflects β-cell responsiveness to a glucose challenge. The combination of these two indices can offer critical insights into the functional reserve of pancreatic β-cells, which can guide decisions regarding the initiation of insulin therapy, switching to oral antidiabetics, or classifying diabetes subtypes, especially in cases where clinical presentation overlaps [5,6].

On the other hand, glycosylated hemoglobin (HbA1c) is a universally accepted biomarker for assessing long-term glycemic control, providing an average estimate of blood glucose levels over the previous 8–12 weeks. A higher HbA1c level reflects poor metabolic control and increased risk of diabetes-related complications. However, HbA1c alone does not offer any information about β-cell reserve or insulin secretory status, which are crucial for staging the disease and predicting therapeutic responsiveness [7,8].

Previous studies suggest that a low C-peptide level may indicate more advanced β-cell failure and poorer glycemic control, often associated with elevated HbA1c. Conversely, higher C-peptide values may be seen in the early or compensatory phases of T2DM. Despite these known physiological relationships, there remains a paucity of comprehensive Indian studies correlating both fasting and postprandial C-peptide levels with HbA1c among adult T2DM patients in routine clinical settings [9,10].

Moreover, in resource-limited settings where direct insulin assays are costly and less available, C-peptide estimation offers a practical and cost-effective alternative to stratify patients based on their endogenous insulin-producing capacity. This can play a critical role in minimizing overtreatment, personalizing diabetes care, and optimizing clinical outcomes.

In this context, the present study was conducted to systematically analyze the fasting and postprandial C-peptide concentrations in patients with T2DM and to assess their correlation with HbA1c levels. The study aims to provide evidence on the clinical utility of C-peptide in evaluating glycemic status and β-cell function, which may ultimately support individualized diabetes management strategies in Indian clinical practice.

Objectives: The present study was undertaken with the aim to evaluate the relationship between endogenous insulin secretion, as measured by fasting and postprandial C-peptide levels, and long-term glycemic control reflected by HbA1c in patients with Type 2 Diabetes Mellitus (T2DM).

Primary Objectives:

1. To estimate fasting C-peptide and postprandial C-peptide levels in adult patients diagnosed with Type 2 Diabetes Mellitus.
2. To measure glycosylated hemoglobin (HbA1c) in the same patient population.

Secondary Objective:

1. To determine the correlation between C-peptide levels (both fasting and postprandial) and HbA1c values in T2DM patients, thereby assessing the relationship between β-cell function and long-term glycemic control.

Materials and Methods

Study Design and Setting: This was a hospital-based, observational, cross-sectional study conducted in the Department of Biochemistry at Shri Ramkrishna Institute of Medical Sciences and Sanaka Hospital, Durgapur, West Bengal, India. The study was carried out in collaboration with the Department of General Medicine, where eligible patients were recruited.

Study Duration: The study was conducted over a period of one year

Study Population: Patients diagnosed with Type 2 Diabetes Mellitus as per the American Diabetes Association (ADA) criteria and attending the outpatient or inpatient departments during the study period were considered eligible for participation.

Inclusion Criteria

- Adults aged 30–65 years.
- Diagnosed with Type 2 Diabetes Mellitus for a minimum duration of 1 year.
- Patients who had not received insulin therapy in the past 3 months.
- Willingness to give written informed consent for participation.

Exclusion Criteria

- Patients with Type 1 Diabetes Mellitus or latent autoimmune diabetes in adults (LADA).
- Patients on exogenous insulin therapy or GLP-1 analogs.
- Individuals with chronic kidney disease (eGFR < 60 mL/min/1.73 m^2).
- Patients with hepatic dysfunction, malignancies, acute infections, or severe systemic illnesses.
- Pregnant or lactating women.

Sample Size: A total of 120 patients with Type 2 Diabetes Mellitus were included in the study using convenience sampling based on hospital attendance and eligibility.

Data Collection Procedure: After obtaining informed written consent, detailed demographic and

clinical data were recorded, including age, sex, duration of diabetes, BMI, and history of antidiabetic medications.

Venous blood samples were collected under the following conditions:

- Fasting C-peptide: Blood sample collected after 8–10 hours overnight fasting.
- Postprandial C-peptide: Sample collected 2 hours after a standard breakfast meal.
- HbA1c: Blood collected in EDTA vials for analysis.

Biochemical Parameters and Assay Methods

- C-peptide levels (fasting and postprandial) were estimated using chemiluminescence immunoassay (CLIA).
- HbA1c was measured by high-performance liquid chromatography (HPLC) method, standardized to the National Glycohemoglobin Standardization Program (NGSP).

All samples were processed in the central clinical laboratory of the institution under strict quality control protocols.

Statistical Analysis: Data were compiled in Microsoft Excel and analyzed. Descriptive statistics were presented as mean ± standard deviation for continuous variables and percentages for categorical variables. The correlation between fasting and postprandial C-peptide levels with HbA1c was evaluated using Pearson's correlation coefficient (r). A p-value of <0.05 was considered statistically significant.

Results

A total of 120 patients diagnosed with Type 2 Diabetes Mellitus were included in the present study. The majority were in the age group of 45–60 years, with a slight male predominance. Clinical variables including BMI, duration of diabetes, fasting blood glucose, postprandial blood glucose, and treatment regimen were documented. The mean values of fasting and postprandial C-peptide levels were assessed and compared with HbA1c levels. Correlation analysis was performed between these parameters to determine the relationship between β-cell functional reserve and long-term glycemic control.

Table 1: Distribution of Study Population by Age Group

Age Group (Years)	Frequency	Percentage (%)
30–40	14	11.7
41–50	36	30.0
51–60	52	43.3
>60	18	15.0

Table 2: Gender-wise Distribution of Study Participants

Gender	Frequency	Percentage (%)
Male	68	56.7
Female	52	43.3

Table 3: Body Mass Index (BMI) Distribution

BMI Category (kg/m²)	Frequency	Percentage (%)
Normal (18.5–24.9)	28	23.3
Overweight (25–29.9)	49	40.8
Obese (≥30)	43	35.9

Table 4: Duration of Diabetes Among Patients

Duration (Years)	Frequency	Percentage (%)
<5	24	20.0
5–10	58	48.3
>10	38	31.7

Table 5: Distribution Based on Antidiabetic Therapy

Treatment Type	Frequency	Percentage (%)
OHAs Only	84	70.0
Insulin + OHAs	26	21.7
Lifestyle Modification	10	8.3

Table 6: Distribution of Fasting C-Peptide Levels among Study Participants

Fasting C-Peptide (ng/mL)	Frequency	Percentage (%)
<1.0	22	18.3
1.0 – 2.0	64	53.3
>2.0	34	28.4

Table 7: Distribution of Postprandial C-Peptide Levels

Postprandial C-Peptide (ng/mL)	Frequency	Percentage (%)
<2.5	18	15.0
2.5 – 4.0	76	63.3
>4.0	26	21.7

Table 8: Distribution of HbA1c Values in Study Population

HbA1c (%)	Frequency	Percentage (%)
6.5 – 7.5	24	20.0
7.6 – 9.0	54	45.0
>9.0	42	35.0

Table 9: Correlation Between Fasting C-Peptide and HbA1c

Parameter	Correlation Coefficient (r)	p-value
Fasting C-Peptide vs HbA1c	-0.412	<0.001

Table 10: Correlation Between Postprandial C-Peptide and HbA1c

Parameter	Correlation Coefficient (r)	p-value
Postprandial C-Peptide vs HbA1c	-0.468	<0.001

Table 1 showed that the majority of the study participants were in the 51–60 years age group, indicating a higher prevalence of Type 2 Diabetes Mellitus in middle-aged adults. Table 2 reflected a slight male predominance in the study population. Table 3 revealed that most patients were either overweight or obese, emphasizing the strong association between increased BMI and insulin resistance. Table 4 indicated that nearly half of the subjects had a diabetes duration of 5–10 years, representing a mid-stage chronic diabetic profile. Table 5 demonstrated that oral hypoglycemic agents (OHAs) were the most common treatment modality, with a smaller proportion receiving insulin in combination. Table 6 showed that the fasting C-peptide levels were predominantly in the intermediate range (1.0–2.0 ng/mL), indicating partial preservation of basal β-cell function. Table 7 revealed that postprandial C-peptide levels were generally higher than fasting values, with the majority in the 2.5–4.0 ng/mL range, suggesting responsive but limited β-cell reserve. Table 8 illustrated that more than 80% of patients had HbA1c values above 7.5%, reflecting poor long-term glycemic control. Table 9 showed a statistically significant inverse correlation between fasting C-peptide and HbA1c levels, and Table 10 confirmed a similar negative correlation between postprandial C-peptide and HbA1c, indicating that lower endogenous insulin secretion is associated with worsening glycemic control.

Discussion

Type 2 Diabetes Mellitus (T2DM) is characterized by progressive β-cell dysfunction alongside peripheral insulin resistance, ultimately resulting in poor glycemic control and metabolic derangements [11]. Assessing the residual β-cell functional reserve in diabetic patients offers valuable insight into disease staging, therapeutic planning, and prognosis. In this context, C-peptide serves as a clinically reliable surrogate marker of endogenous insulin secretion due to its metabolic stability and longer plasma half-life compared to insulin [12].

This study aimed to evaluate both fasting and postprandial C-peptide levels in adult T2DM patients and correlate them with HbA1c to understand the association between endogenous insulin production and long-term glycemic control. The findings demonstrated a clear inverse relationship between C-peptide levels and HbA1c, reinforcing the hypothesis that reduced β-cell function is associated with worsening glycemic status in patients with T2DM [13,14].

The mean fasting and postprandial C-peptide values in our study suggest that while a majority of patients retained partial β-cell responsiveness, a significant subset exhibited low C-peptide levels, consistent with late-stage T2DM or progressive β-cell exhaustion. These findings are in line with the observations made by Saisho et al., who emphasized that declining C-peptide levels over time reflect the natural course of β-cell depletion in poorly controlled diabetes [15].

Our correlation analysis showed a statistically significant negative correlation between both fasting and postprandial C-peptide with HbA1c. This is concordant with studies conducted by Bonser et al. and Yoon et al., where patients with lower C-peptide levels tended to have higher HbA1c values, indicating reduced insulin secretory capacity and inadequate glycemic regulation. These results underscore the importance of considering β-cell functional markers like C-peptide in evaluating the pathophysiology and clinical behavior of T2DM beyond mere blood glucose or HbA1c readings. [16]

Interestingly, the relatively stronger correlation observed with postprandial C-peptide as compared to fasting levels may be attributed to the dynamic response of β-cells to glucose stimulus, reflecting

the true physiologic adaptability of the pancreas. This aligns with findings reported by Yamada et al., who suggested that postprandial or stimulated C-peptide levels are superior in assessing residual β-cell functionality than fasting levels alone [17].

The study also highlighted those overweight and obese patients constituted the majority, reinforcing the well-documented role of adiposity in the pathogenesis of insulin resistance and β-cell dysfunction. Moreover, most patients were on oral hypoglycemic agents, with a smaller fraction requiring insulin, which corresponds with the observed intermediate C-peptide levels in this population, suggesting partial but declining endogenous insulin secretion [18].

From a practical standpoint, incorporating C-peptide testing, especially postprandial measurements, into routine evaluation protocols may help clinicians classify diabetic patients more accurately, tailor pharmacologic strategies, and decide on insulin initiation when warranted. In resource-limited settings like India, where cost-effective strategies are essential, C-peptide offers a feasible and informative tool for guiding diabetic care, especially in distinguishing between insulin-requiring and non-insulin-dependent patients [19,20].

However, it is also important to interpret C-peptide values in the context of confounding factors like renal function, body composition, and medication use, which may affect secretion or clearance. Though such variables were addressed through exclusion criteria in our study, further prospective investigations with larger sample sizes and longitudinal follow-up are warranted to substantiate these findings.

In summary, this study reaffirms that C-peptide is a meaningful biochemical indicator of β-cell health and an important adjunct to HbA1c in understanding glycemic control in T2DM patients. It bridges the gap between glucose-centric evaluation and insulin secretory dynamics, offering a more personalized approach to diabetes management.

Conclusion

The present study concludes that both fasting and postprandial C-peptide levels show a statistically significant inverse correlation with HbA1c in patients with Type 2 Diabetes Mellitus. This indicates that declining endogenous insulin secretion, as reflected by lower C-peptide levels, is associated with poorer glycemic control. Postprandial C-peptide demonstrated a slightly stronger correlation with HbA1c, highlighting its value in assessing β-cell responsiveness to glucose load.

These findings emphasize the clinical relevance of incorporating C-peptide measurement into the routine assessment of diabetic patients, not only to evaluate residual β-cell function but also to assist in individualizing treatment strategies. C-peptide testing, particularly postprandial, can aid in identifying patients who are likely to benefit from insulin therapy or require closer metabolic monitoring. Ultimately, the combined assessment of C-peptide and HbA1c provides a more comprehensive view of the pathophysiological status of T2DM and supports a more informed, patient-centric approach to disease management.

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