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Original Research Article

Investigation of Fasting and Postprandial C-Peptide Levels and Their Correlation with HbA1c in Type 2 Diabetes Mellitus

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Abstract:

Background: Type 2 Diabetes Mellitus (T2DM) is a progressive metabolic disorder characterized by insulin resistance and β-cell dysfunction. C-peptide, a marker of endogenous insulin secretion, plays a crucial role in assessing β-cell function. This study evaluates the correlation between fasting and postprandial C-peptide levels with glycemic markers in T2DM patients to better understand β-cell function and its relationship with glycemic control.

Methods: A cross-sectional study was conducted in the Department of Biochemistry, Patna Medical College, Bihar, India, with 86 T2DM patients. Fasting and postprandial plasma glucose, C-peptide levels, and HbA1c were measured. Correlation analysis was performed between C-peptide levels and glycemic parameters using Pearson's correlation coefficient.

Results: The mean age of participants was 52.3 ± 10.4 years, with a male-to-female ratio of 1.2:1. The mean fasting and postprandial plasma glucose levels were 152.6 ± 28.4 mg/dL and 225.7 ± 35.2 mg/dL, respectively, while the mean HbA1c was 8.3 ± 1.5%. A significant negative correlation was observed between fasting C-peptide and HbA1c ($r = -0.42$, $p < 0.001$) and postprandial C-peptide and HbA1c ($r = -0.48$, $p < 0.001$), indicating declining β-cell function with worsening glycemia.

Conclusion: C-peptide levels negatively correlate with HbA1c and plasma glucose levels, highlighting the progressive decline in β-cell function in T2DM. These findings suggest that C-peptide assessment can serve as a valuable tool in evaluating β-cell reserve and optimizing treatment strategies. Further, longitudinal studies are warranted to explore its prognostic significance.

Keywords: β-cell function, C-peptide, glycemic control, HbA1c, insulin secretion, Type 2 Diabetes Mellitus.

Introduction

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic condition marked by sustained hyperglycemia and dyslipidaemia resulting from either insulin insufficiency or the improper functioning of insulin, a hormone produced by the β-cells of the pancreas [1]. Type 2 Diabetes Mellitus (T2DM) is a significant worldwide health issue, with its prevalence increasing consistently in recent years. The prevalence of Type 2 Diabetes Mellitus (T2DM) in India has risen markedly, with a growth rate of 12.5% [2]. The frequency in rural people is estimated to be 2.4%, however in urban populations, it is significantly greater at 11.6%. C-peptide is a polypeptide component of proinsulin, which is cleaved before its co-secretion with insulin from pancreatic β-cells. C-peptide, generated in equimolar quantities to endogenous insulin and absent in exogenous insulin formulations, is a significant biomarker for evaluating endogenous insulin production [3]. It is extensively utilised in clinical settings to assess pancreatic β-cell functionality in diabetic patients.

After the cleavage of proinsulin, insulin and a 32-amino acid C-peptide are generated in equal quantities. The breakdown rate of C-peptide in the body is markedly slower than that of insulin, with a half-life of roughly 20–30 minutes, in contrast to insulin's half-life of 3–5 minutes [4]. This reduced degradation facilitates more steady and dependable assessments of endogenous insulin secretion. In healthy people, the fasting plasma concentration of C-peptide varies from 0.3 to 0.6 nmol/L, whereas postprandial levels generally vary from 1 to 3 nmol/L. Haemoglobin A1c (HbA1c) is an essential biomarker for the assessment of long-term glucose regulation. It is generated via a non-enzymatic glycosylation mechanism in persons with chronic hyperglycemia [5]. HbA1c indicates the mean blood glucose levels over the past 6–8 weeks and is a

crucial metric for evaluating glycemic management in individuals with diabetes. This study aimed to assess the relationship between fasting and postprandial C-peptide levels and HbA1c in individuals with Type 2 Diabetes Mellitus. This research was performed on patients visiting SMIH for assessment and monitoring of T2DM therapy'. Through the examination of the correlation between C-peptide levels and glycaemic regulation, we want to elucidate β-cell functionality and insulin secretion dynamics in persons with Type 2 Diabetes Mellitus'.

Methodology

Study Design: This cross-sectional study was performed at the Department of Biochemistry at Patna Medical College, Patna, Bihar, India from January 2024 to December 2024. The study sought to assess the relationship between fasting and postprandial C-peptide levels and HbA1c in individuals with Type 2 Diabetes Mellitus (T2DM).

Sample Size and Study Population: In all, 86 individuals diagnosed with Type 2 Diabetes Mellitus participated in 'the research endeavour. The research participants comprised persons visiting the outpatient department (OPD) and those receiving follow-up assessments for diabetes management.

Inclusion Criteria & Exclusion Criteria

Inclusion Criteria

- Individuals diagnosed with T2DM according to the American Diabetes Association (ADA) 2022 criteria.
- Age range of 30 to 70 years.
- Patients using oral hypoglycemic agents (OHAs) or implementing lifestyle adjustments for diabetes treatment.
- Patients who are prepared to give informed permission for participation in the trial.

Exclusion Criteria:

- Patients diagnosed with Type 1 Diabetes Mellitus.
- Patients undergoing exogenous insulin administration.
- Women who are pregnant and breastfeeding.
- Individuals with significant hepatic or renal impairment.
- Patients with established endocrine abnormalities that influence insulin secretion (e.g., Cushing's syndrome, acromegaly').
- Patients receive pharmacological agents that influence glucose metabolism, including corticosteroids.

Procedure: Participants were selected according to the inclusion and exclusion criteria, and comprehensive clinical histories, encompassing diabetes duration, medication usage, and lifestyle behaviours, were documented. Blood samples were procured under aseptic circumstances, with fasting samples acquired following an overnight fast of 8–12 hours and postprandial samples gathered two hours after a standardised meal. A biochemical examination was performed to quantify fasting and postprandial C-peptide levels by the ELISA (Enzyme-Linked Immunosorbent Assay) technique, while HbA1c levels were assessed using high-performance liquid chromatography (HPLC). Furthermore, fasting and postprandial plasma glucose concentrations were evaluated via an automated glucose analyser employing the glucose oxidase-peroxidase technique.

Statistical Analysis: Data were analysed with SPSS (Statistical Package for the Social Sciences) version 27.0. Descriptive statistics were utilised to summarise demographic and biochemical characteristics, with continuous variables represented as mean ± standard deviation (SD). The relationship between fasting and postprandial C-peptide levels and HbA1c was evaluated using Pearson's correlation coefficient, with statistical significance established at a p-value < 0.05.

Results

'Table 1 defines the demographic and clinical characteristics of the research participants. The average age of participants was 52.3 ± 10.4 years (range: 30–70 years), signifying a demographic predominantly including middle-aged to elderly individuals suffering by Type 2 Diabetes Mellitus (T2DM). The male-to-female ratio was 1.2:1, indicating a little male predominance in the research sample. The average BMI was 27.5 ± 3.8 kg/m² (range: 20.1–34.5 kg/m²), with the majority of patients classified as overweight or obese, underscoring obesity as a contributing factor to T2DM. The average duration of diabetes was 6.8 ± 4.2 years (range: 1–20 years), indicating a diverse cohort of both newly diagnosed and long-standing T2DM patients.

Table 1: Demographic and Clinical Characteristics of Study Participants

Parameter	Mean ± SD	Range'
Age (years)	52.3 ± 10.4	30 – 70
Male: Female Ratio	1.2:1	—
BMI (kg/m²)	27.5 ± 3.8	20.1 – 34.5
Duration of T2DM (years)	6.8 ± 4.2	1 – 20

Table 2 illustrates the glycaemic and C-peptide profiles of the research subjects. The average fasting plasma glucose (FPG) was 152.6 ± 28.4 mg/dL, and the average postprandial plasma glucose (PPG) was 225.7 ± 35.2 mg/dL, both considerably beyond the normal reference range, signifying inadequate glycaemic management in the study cohort. The average HbA1c level was 8.3 ± 1.5%, beyond the recommended limit of <5.7%, indicating sustained hyperglycemia during the preceding 6–8 weeks and insufficient long-term glycaemic control. The average fasting C-peptide level was 0.58 ± 0.19 nmol/L, within the normal range (0.3–0.6 nmol/L), but the postprandial C-peptide level was 1.75 ± 0.45 nmol/L, again within the anticipated range (1–3 nmol/L). These data suggest that, despite hyperglycemia, pancreatic β-cell activity persists in these people, albeit potentially impaired. The findings underscore the necessity for enhanced glycaemic control to avert illness advancement.

Table 2: Glycemic and C-Peptide Profile of Study Participants

Parameter	Mean ± SD	Normal Reference Range
Fasting Plasma Glucose (mg/dL)	152.6 ± 28.4	70 – 100
Postprandial Plasma Glucose (mg/dL)	225.7 ± 35.2	<140
HbA1c (%)	8.3 ± 1.5	<5.7
Fasting C-Peptide (nmol/L)	0.58 ± 0.19	0.3 – 0.6
Postprandial C-Peptide (nmol/L)	1.75 ± 0.45	1 – 3

Table 3 defines the study participants according to their glycaemic control as assessed by HbA1c values. Among 86 patients, only 18 (20.9%) exhibited adequate glycaemic control (HbA1c <7.0%), signifying successful diabetes care in a limited subset of individuals. The predominant group, including 39 people (45.3%), was classified under moderate control (HbA1c 7.0–8.9%), indicating inadequate although largely managed diabetes. Significantly, 29 patients (33.7%) exhibited inadequate glycaemic control (HbA1c ≥9.0%), signifying an elevated risk of diabetes-associated problems resulting from chronic hyperglycemia. The findings underscore the necessity for more stringent glucose management strategies, including lifestyle alterations, medication changes, and consistent monitoring to mitigate the risk of long-term problems linked to Type 2 Diabetes Mellitus.

Table 3: Distribution of Study Participants Based on Glycemic Control (HbA1c Levels)

HbA1c Category (%)	Number of Participants (n = 86)	Percentage (%)
Good Control (<7.0%)	18	20.90%
Moderate Control (7.0–8.9%)	39	45.30%
Poor Control (≥9.0%)	29	33.70%

‘Table 4 illustrates the association between C-peptide levels and glycaemic indicators among the research participants. A negative connection was identified between fasting C-peptide and HbA1c ($r = -0.42$, $p < 0.001$) as well as postprandial C-peptide and HbA1c ($r = -0.48$, $p < 0.001$), suggesting that diminished endogenous insulin production (indicated by C-peptide levels) correlates with worse long-term glycaemic management. Fasting C-peptide exhibited a negative correlation with fasting plasma glucose ($r = -0.38$, $p < 0.05$), while postprandial C-peptide demonstrated a negative correlation with postprandial plasma glucose ($r = -0.44$, $p < 0.05$), indicating that individuals with diminished pancreatic β-cell function are likely to have elevated glucose levels. These findings underscore the significance of C-peptide as an indicator of insulin production and emphasise the gradual deterioration of β-cell activity with the exacerbation of glycaemic control in Type 2 Diabetes Mellitus’’.

Table 4: Correlation Between C-Peptide Levels and Glycemic Markers

Parameter	Pearson’s Correlation Coefficient (r)	p-value
Fasting C-Peptide vs. HbA1c	-0.42	<0.001
Postprandial C-Peptide vs. HbA1c	-0.48	<0.001
Fasting C-Peptide vs. Fasting Plasma Glucose (FPG)	-0.38	<0.05
Postprandial C-Peptide vs. Postprandial Plasma Glucose (PPG)	-0.44	<0.05

Discussion

This study's findings offer significant insights into the correlation between C-peptide levels and glycaemic regulation in persons with Type 2 Diabetes Mellitus (T2DM). The demographic data indicated that the study group was primarily middle-aged and overweight, with a mean BMI of 27.5 ± 3.8 kg/m², so strengthening the documented association between obesity and T2DM. The minor male preponderance (male-to-female ratio: 1.2:1)

corresponds with earlier epidemiological research demonstrating a greater frequency of diabetes in males. The average duration of diabetes was 6.8 ± 4.2 years, reflecting a heterogeneous group comprising both recently diagnosed and chronic individuals.

Comparable results have been seen in several research. Research published in the International Journal of Research and Review indicated that people with inadequate glycaemic control (HbA1c >8.3%) exhibited elevated C-peptide levels (>2.0 ng/ml), implying a compensatory augmentation of insulin production in response to hyperglycemia. This corresponds with our discovery of increased C-peptide levels in individuals exhibiting inadequate glycaemic control [6]. Research in Diabetologia indicated that males are diagnosed with T2DM at a younger age and lower BMI than women, aligning with our observations of a little male preponderance and a mean age of 52.3 years. A study published in The Journal of Clinical Endocrinology & Metabolism indicated that although men exhibit a higher prevalence of T2DM, women with diabetes face an elevated risk of cardiovascular complications, implying that sex differences in diabetes encompass not only prevalence but also disease outcomes [7].

The glycaemic profile indicated that both fasting and postprandial plasma glucose levels were significantly raised, with a mean HbA1c of 8.3 ± 1.5%, demonstrating that a substantial number of patients exhibited inadequate glycaemic control. Nonetheless, the fasting and postprandial C-peptide levels remained within the normal limits, indicating that endogenous insulin secretion continues in these individuals, albeit perhaps insufficient to sustain normoglycemia. This corresponds with findings from a study published in the International Journal of Research and Review, which indicated that individuals with inadequate glycaemic control (HbA1c >8.3%) exhibited C-peptide levels surpassing 2.0 ng/mL, suggesting that elevated fasting glucose levels were correlated with increased C-peptide levels in diabetic individuals [6].

In contrast, study published in Diabetes Care indicated that reduced C-peptide levels correlated with inferior glycaemic control and an elevated risk of severe hypoglycemia, suggesting that decreased endogenous insulin production leads to unstable blood glucose levels. Research published in the American Journal of Medicine indicated that measuring blood C-peptide levels may facilitate the simplification of diabetes treatment protocols, especially in older persons, by analysing residual insulin production to customise medication effectively [8].

Subsequent categorisation of individuals according to glycaemic control revealed that just 20.9% achieved optimal glycaemic control, whilst 33.7% displayed inadequate control (HbA1c ≥9.0%), underscoring an urgent necessity for enhanced diabetes care measures. These findings underscore the imperative for more stringent lifestyle adjustments, adherence to medication, and consistent glucose monitoring to mitigate the risk of long-term problems. This finding corresponds with research performed in Dhamar, Yemen, which indicated a significant incidence of inadequate glycaemic management among individuals with type 2 diabetic mellitus (T2DM) [9]. A comprehensive assessment examining low- and middle-income nations revealed that around 69.06% of patients with diabetes exhibited inadequate glycaemic control, highlighting the pervasive difficulty of properly regulating blood glucose levels in these areas. These studies collectively underscore the pressing necessity for improved diabetes care techniques, including more rigorous lifestyle adjustments, heightened medication adherence, and consistent glucose monitoring, to reduce the risk of long-term problems linked to insufficient glycaemic control [10].

This investigation reveals substantial negative associations between fasting and postprandial C-peptide levels and HbA1c ($r = -0.42$ and $r = -0.48$, respectively; $p < 0.001$), indicating that a loss in β-cell activity corresponds with worse glycaemic management. The negative correlations between fasting and postprandial C-peptide levels and their corresponding plasma glucose values further substantiate the use of C-peptide as a dependable indicator of endogenous insulin production. These findings correspond with prior studies indicating that decreased C-peptide levels correlate with suboptimal glycaemic management and heightened glycaemic variability in people with T2DM [11]. Moreover, research indicates that C-peptide measures can accurately evaluate β-cell reserve, facilitating the differentiation of diabetes types and informing treatment strategies [12]. In contrast, several investigations have indicated elevated C-peptide levels in people exhibiting inadequate glycaemic control, implying a compensatory mechanism in response to insulin resistance. The divergent findings emphasise the intricacy of β-cell activity in T2DM and stress the necessity of personalised patient evaluations when assessing C-peptide levels and glycaemic regulation [6].

The gradual deterioration of pancreatic β-cell function, shown by diminishing C-peptide levels and deteriorating glycemic control, highlights the necessity for early identification and personalised treatment approaches in the management of T2DM. This discovery corresponds with the 'United Kingdom Prospective Diabetes Study (UKPDS)', which revealed a progressive decline in β-cell activity over time in T2DM patients, underscoring

the imperative for prompt management [13]. Timely identification of β-cell malfunction is important for the use of tailored therapeutic strategies. The measurement of C-peptide is an important indicator for evaluating remaining β-cell activity, facilitating the differentiation of various diabetes types and the customisation of suitable treatments [14].

Personalised therapy approaches, encompassing lifestyle changes and medication, are crucial for maintaining β-cell activity. Modifications in lifestyle, including enhanced physical activity and dietary adjustments, have demonstrated efficacy in improving insulin sensitivity and alleviating β-cell burden. Pharmacological treatments such as GLP-1 receptor agonists and DPP-4 inhibitors have shown effectiveness in maintaining β-cell function by augmenting insulin production and diminishing glucotoxicity. Novel therapeutics aimed at preserving β-cells are currently being researched. A recent study investigated the feasibility of stem cell-derived islet transplantation to restore insulin production in T1DM patients, providing insights that may be relevant to T2DM therapy [15].

Conclusion

This study highlights the significant correlation between C-peptide levels and glycaemic regulation in persons with T2DM. The identified negative connection between C-peptide and HbA1c signifies a gradual deterioration in pancreatic β-cell activity, leading to insufficient glycaemic control. Notwithstanding residual insulin secretion, a considerable percentage of patients had inadequate glycaemic control, underscoring the need for prompt identification and tailored therapy strategies. The evaluation of C-peptide levels may be an essential instrument in assessing β-cell reserve and informing therapy choices. Additional long-term studies with bigger sample numbers are necessary to refine diabetes care regimens and optimise clinical outcomes.

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