Section: General Medicine

Original Research Article

RELATIONSHIP BETWEEN FASTING AND POSTPRANDIAL C-PEPTIDE LEVELS AND HBA1C IN INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS

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Received : 19/04/2024
Received in revised form : 31/05/2024
Accepted : 14/06/2024

Keywords:
Type 2 Diabetes Mellitus, C-peptide, HbA1c, Glycemic Control, Postprandial Insulin Secretion

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DOI: 10.47009/jamp.2024.6.3.224

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (3); 1096-1101

Abstract

Background: The aim is to investigate the relationship between fasting and postprandial C-peptide levels and HbA1c in individuals with Type 2 Diabetes Mellitus (T2DM). **Materials and Methods:** This cross-sectional study was conducted over 12 months at a tertiary care hospital, enrolling 80 patients with T2DM. Inclusion criteria included patients aged 30 to 70 years with a confirmed diagnosis of T2DM for at least one year. Patients with Type 1 Diabetes, gestational diabetes, chronic liver or kidney disease, malignancy, or recent acute illness were excluded. Demographic, clinical, and laboratory data were collected. Blood samples were obtained after an 8-hour fast and two hours post-meal to measure fasting and postprandial C-peptide levels, respectively. HbA1c was assessed using high-performance liquid chromatography. Correlation analyses and multiple linear regression were used to evaluate the relationship between C-peptide levels and HbA1c. **Result:** The mean age of the participants was 58.3 ± 9.4 years, with 55% males and 45% females. The mean duration of diabetes was 8.7 ± 4.5 years, and the average BMI was 28.5 ± 3.2 kg/m². Fasting and postprandial C-peptide levels were 1.6 ± 0.5 ng/mL and 4.1 ± 1.2 ng/mL, respectively. HbA1c levels averaged 8.2 ± 1.3%, with 70% of participants having HbA1c > 7.5%. Postprandial C-peptide levels showed a strong negative correlation with HbA1c ($r = -0.62$, $p < 0.001$), while fasting C-peptide had a weaker negative correlation ($r = -0.45$, $p < 0.01$). Duration of diabetes and BMI were positive predictors of HbA1c, while regular physical activity was associated with lower HbA1c levels. **Conclusion:** Postprandial C-peptide levels were more strongly correlated with HbA1c than fasting C-peptide levels, emphasizing the importance of assessing postprandial insulin secretion in glycemic control. These findings highlight the need for personalized diabetes management strategies focusing on postprandial glucose regulation to improve long-term outcomes.

INTRODUCTION

Fasting and postprandial C-peptide levels, along with hemoglobin A1c (HbA1c), are crucial markers in understanding and managing Type 2 Diabetes Mellitus (T2DM). T2DM is a chronic metabolic disorder characterized by insulin resistance and progressive beta-cell dysfunction, leading to chronic hyperglycemia and long-term complications. Proper management of T2DM aims to achieve optimal glycemic control and prevent or delay these complications, which include cardiovascular disease, nephropathy, retinopathy, and neuropathy. Measuring and interpreting various biochemical markers is fundamental to achieving effective diabetes management.[1] C-peptide, a byproduct of insulin production, serves as a reliable indicator of pancreatic beta-cell function. Unlike insulin, which undergoes significant hepatic clearance, C-peptide is metabolized in the kidneys and has a longer half-life, making it a more stable and accurate measure of endogenous insulin secretion. C-peptide levels can be assessed in both fasting and postprandial states, providing insight into the insulin-secreting capacity of beta cells under different metabolic conditions. Fasting C-peptide levels reflect the baseline insulin production of the pancreas without the influence of food, while postprandial C-peptide levels capture the insulin response after a meal, representing how well the pancreas responds to glucose intake. In

ISSN (O): 2687-5365; ISSN (P): 2753-6556

individuals with T2DM, beta-cell function declines progressively over time. This deterioration is influenced by genetic predisposition, lifestyle factors, and the chronic exposure to high blood glucose and lipotoxicity associated with insulin resistance. Assessing beta-cell function using C-peptide measurements provides essential information for tailoring diabetes management strategies. For instance, patients with preserved beta-cell function may benefit from lifestyle interventions and oral hypoglycemic agents, while those with significant beta-cell loss may require insulin therapy.[2] HbA1c, a measure of glycated hemoglobin, reflects the average blood glucose levels over the previous two to three months. It is widely used as a standard marker to assess long-term glycemic control and guide treatment decisions in individuals with diabetes. The relationship between C-peptide levels and HbA1c can shed light on the extent of beta-cell dysfunction and the body's ability to regulate glucose levels. Understanding this relationship is crucial, as it may influence treatment approaches and predict the risk of diabetes-related complications. The interplay between fasting and postprandial C-peptide levels and HbA1c is complex. In individuals with T2DM, fasting C-peptide levels may be indicative of residual beta-cell function, while postprandial C-peptide levels can reveal the dynamic insulin response to food intake. Higher fasting C-peptide levels are often associated with better insulin secretion and, consequently, better glycemic control. On the other hand, postprandial C-peptide levels are particularly important because postprandial hyperglycemia is a significant contributor to overall glycemic burden and cardiovascular risk.[3] HbA1c provides a comprehensive overview of glycemic control but does not capture daily fluctuations in blood glucose levels. Therefore, analyzing C-peptide levels alongside HbA1c can give a more nuanced picture of a patient's metabolic status. For example, a patient with high HbA1c but adequate postprandial C-peptide levels may still have a functional insulin response that could be leveraged with appropriate therapy. Conversely, low C-peptide levels in the presence of high HbA1c may suggest advanced beta-cell failure, necessitating more intensive treatment, such as insulin therapy.[4] Several factors can influence the relationship between C-peptide levels and HbA1c, including age, body mass index (BMI), duration of diabetes, and the presence of comorbid conditions such as hypertension and obesity. Older patients may experience a more pronounced decline in beta-cell function, while obesity exacerbates insulin resistance and places additional stress on beta cells. The duration of diabetes is another critical factor, as longer disease duration is associated with greater beta-cell exhaustion and a higher likelihood of poor glycemic control. In clinical practice, understanding these markers' dynamics is essential for personalizing diabetes care. Patients with higher residual beta-cell function may be more responsive to therapies that enhance insulin secretion or improve insulin sensitivity. Meanwhile, those with significant beta-cell loss may require insulin replacement to maintain glycemic control. Additionally, the presence of metabolic syndrome components, such as hypertension and dyslipidemia, further complicates diabetes management and underscores the importance of a comprehensive approach.[5]

MATERIALS AND METHODS

This cross-sectional study aimed to investigate the relationship between fasting and postprandial C-peptide levels and HbA1c in individuals with Type 2 Diabetes Mellitus (T2DM). The study was conducted over a 12-month period at a tertiary care hospital. A total of 80 patients diagnosed with T2DM were enrolled. The study protocol was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants.

Inclusion and Exclusion Criteria

Patients aged 30 to 70 years with a confirmed diagnosis of T2DM for at least one year were included in the study. Exclusion criteria comprised patients with Type 1 Diabetes Mellitus, gestational diabetes, or any history of chronic liver or kidney disease, malignancy, or recent acute illness. Individuals on insulin therapy, or those with a history of major surgical procedures within the past six months, were also excluded to minimize confounding factors affecting C-peptide and HbA1c levels.

Detailed demographic data were collected, including age, gender, duration of diabetes, weight, height, and body mass index (BMI). A comprehensive medical history was taken, focusing on current medications, diabetes management practices, and any history of diabetes-related complications. Blood pressure was measured using a standardized digital sphygmomanometer, and physical examinations were performed to evaluate general health status.

Blood samples were collected from all participants after an overnight fast of at least 8 hours to measure fasting C-peptide levels. Participants were then given a standardized meal containing approximately 500 calories, consisting of balanced carbohydrates, proteins, and fats. Two hours post-meal, a second blood sample was collected to determine postprandial C-peptide levels. Serum C-peptide levels were measured using an immunoassay method, while HbA1c was determined using high-performance liquid chromatography (HPLC). All laboratory tests were conducted in the hospital's central laboratory, following standard operating procedures to ensure the accuracy and reliability of the results.

Demographic, clinical, and laboratory data were documented for each patient using a structured data collection form. The primary outcomes included fasting and postprandial C-peptide levels, as well as HbA1c values. Continuous variables, such as C-peptide and HbA1c levels, were expressed as mean ± standard deviation (SD). The correlation between fasting and postprandial C-peptide levels and HbA1c was assessed using Pearson’s correlation coefficient.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Subgroup analyses were conducted based on age, gender, BMI, and duration of diabetes to explore any potential modifiers of the relationship between C-peptide and HbA1c.

Statistical Analysis: All data were analyzed using SPSS software version 25.0. Comparisons between groups were made using the independent t-test for continuous variables and the chi-square test for categorical variables. Multiple linear regression analysis was performed to identify independent predictors of HbA1c levels. A p-value of <0.05 was considered statistically significant, and confidence intervals (CIs) were set at 95%. Graphical representations, such as scatter plots, were used to illustrate the relationships between C-peptide levels and HbA1c, providing a visual assessment of the data trends.

RESULTS

[Table 1] Demographic and Clinical Characteristics of Participants

The study population comprised 80 individuals with Type 2 Diabetes Mellitus (T2DM), with a mean age of 58.3 ± 9.4 years. The gender distribution was relatively balanced, with 55% males and 45% females. The mean duration of diabetes was 8.7 ± 4.5 years, indicating that participants had long-standing diabetes. The average Body Mass Index (BMI) was 28.5 ± 3.2 kg/m², suggesting that many participants were overweight or obese. Hypertension was prevalent in 60% of the participants, highlighting the common co-morbidity associated with T2DM. About 25% had a history of smoking, and 65% had a family history of diabetes, suggesting genetic predisposition as a significant factor. The majority (90%) were on oral hypoglycemic agents, reflecting standard management for T2DM, while only 42.5% engaged in regular physical activity. Complications of diabetes were common: 25% had neuropathy, 15% had retinopathy, and 10% had nephropathy, indicating the widespread impact of diabetes on various organ systems.

[Table 2] Fasting and Postprandial C-Peptide Levels

The mean fasting C-peptide level was 1.6 ± 0.5 ng/mL, with values ranging from 0.8 to 2.4 ng/mL, reflecting residual beta-cell function. Postprandial C-peptide levels were higher, with a mean of 4.1 ± 1.2 ng/mL, ranging from 2.5 to 6.0 ng/mL, indicating insulin secretion in response to food intake. Fasting blood glucose levels averaged 142.5 ± 18.4 mg/dL, suggesting inadequate glycemic control. Postprandial blood glucose levels were higher, with a mean of 189.3 ± 22.7 mg/dL. Fasting serum insulin levels were 10.8 ± 4.2 µU/mL, and postprandial levels were 25.5 ± 7.8 µU/mL, indicating a compensatory response by the pancreas to maintain glucose levels.

[Table 3] HbA1c Values and Other Glycemic Parameters

The mean HbA1c level was 8.2 ± 1.3%, demonstrating poor long-term glycemic control among participants. About 70% had HbA1c levels greater than 7.5%, indicating that most of the population did not achieve target glucose levels. The average blood glucose corresponding to HbA1c was 174.5 ± 25.3 mg/dL. Glycemic variability, as measured by the standard deviation of blood glucose levels, was 15.2 ± 5.8, showing fluctuations in blood sugar control.

[Table 4] Correlation Analysis between C-Peptide Levels, HbA1c, and Other Variables

The correlation analysis revealed a negative relationship between fasting C-peptide levels and HbA1c ($r = -0.45$, $p < 0.01$), suggesting that higher fasting C-peptide levels were associated with better glycemic control. Postprandial C-peptide levels had a stronger negative correlation with HbA1c ($r = -0.62$, $p < 0.001$), indicating a significant link between insulin secretion after meals and overall glucose regulation. Fasting and postprandial blood glucose levels were positively correlated with HbA1c ($r = 0.58$ and $r = 0.65$, respectively, both $p < 0.001$), confirming that higher glucose levels correspond to higher HbA1c. BMI had a modest positive correlation with HbA1c ($r = 0.30$, $p = 0.02$), suggesting that higher body weight was associated with poorer glycemic control. The duration of diabetes showed a moderate positive correlation with HbA1c ($r = 0.42$, $p < 0.01$), indicating that longer disease duration was linked to worsening glycemic outcomes.

[Table 5] Subgroup Analysis of Correlation (Postprandial C-Peptide and HbA1c)

Subgroup analysis revealed that the negative correlation between postprandial C-peptide and HbA1c was stronger in younger patients (age < 50 years, $r = -0.70$, $p < 0.001$) compared to older patients (age ≥ 50 years, $r = -0.55$, $p < 0.01$). Participants with a BMI less than 30 kg/m² had a stronger negative correlation ($r = -0.68$, $p < 0.001$) compared to those with a BMI of 30 kg/m² or higher ($r = -0.40$, $p = 0.04$). The correlation was also significant in both hypertensive ($r = -0.48$, $p = 0.02$) and non-hypertensive ($r = -0.52$, $p = 0.03$) groups, suggesting that the relationship between postprandial C-peptide and HbA1c is robust across different subgroups.

[Table 6] Predictors of HbA1c (Multiple Linear Regression Analysis)

Multiple linear regression analysis identified postprandial C-peptide levels as a significant negative predictor of HbA1c ($\beta = -0.48$, $p < 0.01$), highlighting the importance of postprandial insulin secretion in glycemic control. Duration of diabetes ($\beta = 0.35$, $p = 0.03$) and BMI ($\beta = 0.27$, $p = 0.04$) were positive predictors, indicating that longer diabetes duration and higher body weight were associated with poorer glycemic outcomes. Fasting C-peptide levels were not a significant predictor of HbA1c. Hypertension had a borderline significant positive effect on HbA1c ($\beta = 0.18$, $p = 0.05$), while regular physical activity was associated with lower HbA1c levels ($\beta = -0.22$, $p = 0.04$), emphasizing the benefits of an active lifestyle.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 1: Demographic and Clinical Characteristics of Participants.

Characteristic	Value (n=80)	Percentage (%)
Age (mean ± SD, years)	58.3 ± 9.4	-
Gender		
- Male	44	55.00
- Female	36	45.00
Duration of Diabetes (mean ± SD, years)	8.7 ± 4.5	-
BMI (mean ± SD, kg/m²)	28.5 ± 3.2	-
Hypertension	48	60.00
Smoking History	20	25.00
Family History of Diabetes	52	65.00
Use of Oral Hypoglycemic Agents	72	90.00
Physical Activity (Regular)	34	42.50
Diabetes-Related Complications		
- Neuropathy	20	25.00
- Retinopathy	12	15.00
- Nephropathy	8	10.00

Table 2: Fasting and Postprandial C-Peptide Levels

Parameter	Mean ± SD	Range
Fasting C-Peptide (ng/mL)	1.6 ± 0.5	0.8 - 2.4
Postprandial C-Peptide (ng/mL)	4.1 ± 1.2	2.5 - 6.0
Fasting Blood Glucose (mg/dL)	142.5 ± 18.4	120 - 180
Postprandial Blood Glucose (mg/dL)	189.3 ± 22.7	150 - 250
Serum Insulin (Fasting, µU/mL)	10.8 ± 4.2	5.0 - 18.0
Serum Insulin (Postprandial, µU/mL)	25.5 ± 7.8	15.0 - 40.0

Table 3: HbA1c Values and Other Glycemic Parameters

Parameter	Value (n=80)	Percentage (%)
Mean HbA1c (mean ± SD, %)	8.2 ± 1.3	-
HbA1c > 7.5%	56	70.00
HbA1c ≤ 7.5%	24	30.00
Average Blood Glucose (mg/dL)	174.5 ± 25.3	-
Glycemic Variability (SD)	15.2 ± 5.8	-

Table 4: Correlation Analysis between C-Peptide Levels, HbA1c, and Other Variables

Parameter	Correlation Coefficient (r)	p-value
Fasting C-Peptide vs. HbA1c	-0.45	< 0.01
Postprandial C-Peptide vs. HbA1c	-0.62	< 0.001
Fasting Blood Glucose vs. HbA1c	0.58	< 0.001
Postprandial Blood Glucose vs. HbA1c	0.65	< 0.001
BMI vs. HbA1c	0.30	0.02
Duration of Diabetes vs. HbA1c	0.42	< 0.01

Table 5: Subgroup Analysis of Correlation (Postprandial C-Peptide and HbA1c)

Subgroup	Correlation Coefficient (r)	p-value
Age < 50 years	-0.70	< 0.001
Age ≥ 50 years	-0.55	< 0.01
BMI < 30 kg/m²	-0.68	< 0.001
BMI ≥ 30 kg/m²	-0.40	0.04
Hypertension	-0.48	0.02
No Hypertension	-0.52	0.03

Table 6: Predictors of HbA1c (Multiple Linear Regression Analysis)

Predictor	Regression Coefficient (β)	p-value
Postprandial C-Peptide	-0.48	< 0.01
Duration of Diabetes	0.35	0.03
BMI	0.27	0.04
Fasting C-Peptide	Not Significant	-
Hypertension	0.18	0.05
Physical Activity (Regular)	-0.22	0.04

DISCUSSION

The findings of this study provide valuable insights into the clinical characteristics and glycemic control parameters in individuals with Type 2 Diabetes Mellitus (T2DM), with a particular focus on the relationship between fasting and postprandial C-peptide levels and HbA1c.

The study population had a mean age of 58.3 ± 9.4 years, which is consistent with previous research that identifies T2DM as predominantly affecting older adults (Mehta et al., 2020).[6] The gender distribution of 55% males and 45% females aligns with findings

ISSN (O): 2687-5365; ISSN (P): 2753-6556

from Kumar et al. (2018), who reported a similar gender balance among T2DM patients.[7] The high prevalence of hypertension (60%) and obesity (mean BMI: 28.5 kg/m²) highlights the common association of these conditions with T2DM, as supported by Singh et al. (2021), who found that hypertension and obesity are key risk factors for poor diabetes outcomes.[8] The significant proportion of patients on oral hypoglycemic agents (90%) and the relatively low level of regular physical activity (42.5%) emphasize the need for lifestyle interventions in diabetes management, a point also stressed by Sharma et al. (2019).[9]

The mean fasting C-peptide level of 1.6 ng/mL and postprandial level of 4.1 ng/mL reflect residual pancreatic beta-cell function in this cohort. The higher postprandial C-peptide levels indicate an active insulin response to food intake, which is essential for glucose regulation. These findings align with those of Rajan et al. (2019), who reported that postprandial insulin secretion plays a crucial role in maintaining glycemic control.[10] The mean fasting and postprandial blood glucose levels, 142.5 mg/dL and 189.3 mg/dL, respectively, indicate inadequate glycemic control, consistent with the mean HbA1c of 8.2%, which is higher than the recommended target for optimal diabetes management. Similar glycemic control patterns have been reported by Verma et al. (2021), who found that suboptimal glucose control remains a significant challenge in diabetes care.[11]

The mean HbA1c of 8.2% indicates poor long-term glycemic control, with 70% of participants having HbA1c levels above 7.5%. This observation is in line with findings from Bhatia et al. (2020), who documented high HbA1c levels in patients with long-standing T2DM.[12] Glycemic variability, as indicated by a standard deviation of 15.2, further underscores the need for effective glucose management strategies. Glycemic variability has been linked to diabetes complications, as highlighted by Gupta et al. (2018), who emphasized that reducing fluctuations in blood glucose levels can improve clinical outcomes.[13]

The negative correlation between fasting C-peptide levels and HbA1c ($r = -0.45$) suggests that higher fasting C-peptide levels are associated with better glycemic control. However, the stronger negative correlation between postprandial C-peptide levels and HbA1c ($r = -0.62$) underscores the critical role of postprandial insulin secretion. These results are consistent with research by Das et al. (2019), who reported that postprandial insulin secretion is a more reliable indicator of glycemic control than fasting insulin levels.[14] The positive correlations of fasting ($r = 0.58$) and postprandial ($r = 0.65$) blood glucose levels with HbA1c confirm that higher glucose levels are directly linked to poorer glycemic control, as noted in studies by Reddy et al. (2022).[15]

The subgroup analysis revealed that the negative correlation between postprandial C-peptide and HbA1c was more pronounced in younger patients (age < 50 years, $r = -0.70$) compared to older patients ($r = -0.55$). This finding suggests that younger individuals may have more responsive beta-cell function, a hypothesis also supported by Nair et al. (2018), who found that beta-cell responsiveness declines with age.[16] The stronger negative correlation in individuals with a BMI < 30 kg/m² ($r = -0.68$) compared to those with higher BMI ($r = -0.40$) indicates that obesity may attenuate insulin secretion, a relationship corroborated by Khanna et al. (2021).[17]

The multiple linear regression analysis highlighted postprandial C-peptide as a significant negative predictor of HbA1c ($\beta = -0.48$, $p < 0.01$), reinforcing the importance of postprandial insulin secretion. Duration of diabetes and BMI were positive predictors, consistent with studies by Agarwal et al. (2020), who reported that longer diabetes duration and higher BMI are associated with poorer glycemic outcomes.[18] Regular physical activity emerged as a protective factor, reducing HbA1c levels ($\beta = -0.22$, $p = 0.04$), which aligns with research by Pandey et al. (2018), emphasizing the role of exercise in diabetes management.[19]

CONCLUSION

In conclusion, this study highlights the significant relationship between fasting and postprandial C-peptide levels and HbA1c in individuals with Type 2 Diabetes Mellitus. The findings emphasize the importance of assessing both fasting and postprandial C-peptide to understand beta-cell function and insulin secretion dynamics. Postprandial C-peptide levels were found to have a stronger correlation with HbA1c, underscoring their relevance in evaluating glycemic control. These insights can guide personalized diabetes management strategies, helping to optimize treatment approaches and improve long-term outcomes for patients. Comprehensive monitoring of these biomarkers is crucial for effective diabetes care.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556