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Original Research Article

Comparing C-peptide and HbA1c levels in obese patients with and without type 2 diabetes

N. Sridevi*, N. Chowdeswari, A. Navaneeta Lakshmi, P. Madhusudhan, N. Kirmani, Rakesh Anil, Shyam Sunder Kumar

Government Medical College, Vijaywada, Andhra Pradesh, India

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***Correspondence:**
Dr. N. Sridevi,
E-mail: nutakkisridevi74@gmai.com

ABSTRACT

Background: Diabetes mellitus (DM) is a chronic metabolic disorder characterized by either insufficient insulin production by the pancreas or the body's inability to utilize it. HbA1c level of 6.5% was recommended for diagnosing diabetes. C-peptide is a byproduct of insulin synthesis has been widely studied as a diagnostic biomarker for DM. Obesity is a major risk factor for the development of type 2 DM (T2DM) and is associated with insulin resistance. With the increasing global burden of obesity and diabetes, our study investigates the relationship between HbA1c and C-peptide levels in obese individuals with and without diabetes. Objectives were to assess and compare HbA1c and C-peptide levels among obese individuals with diabetes and without diabetes and to evaluate the correlation between these parameters within each group.
Methods: This study was included 30 obese diabetic and 30 obese non-diabetic participants recruited over 3 months. Blood samples were collected for estimating HbA1c and C-peptide. Ethical approval was obtained prior to the study. Data were analyzed using Jamovi software.
Results: HbA1c and C-peptide levels were significantly higher in obese individuals with diabetes compared to non-diabetic obese controls ($p<0.001$). A strong positive correlation was observed between HbA1c and C-peptide levels in both groups, with a stronger association in diabetics ($r=0.94$) compared to non-diabetics ($r=0.88$); both correlations were statistically significant.
Conclusions: Higher levels and strong positive correlation between HbA1c and C-peptide-especially in diabetics-suggests increased insulin secretion in response to poor glycemic control and insulin resistance.

Keywords: Obesity, HbA1c, C-Peptide, Diabetics, Non-diabetics, Insulin resistance

INTRODUCTION

Diabetes is a chronic metabolic disorder characterized by either insufficient insulin production by the pancreas or the body's inability to effectively utilize the insulin it produces. Insulin is a key hormone responsible for regulating blood glucose levels. A common feature of uncontrolled diabetes is hyperglycemia-elevated blood glucose-which, over time, can cause significant damage to various organ systems, particularly the nerves and blood vessels.[1]

The global burden of diabetes has increased dramatically, with the number of people living with the condition rising from 200 million in 1990 to 830 million by 2022. This surge has been especially rapid in low- and middle-income countries compared to high-income nations. In 2021, diabetes was directly responsible for approximately 1.6 million deaths, with nearly 47% of these occurring before the age of 70. Additionally, diabetes contributed to 530,000 deaths from kidney disease, and elevated blood glucose levels were implicated in around 11% of cardiovascular-related deaths.[2]

T2DM affects the body's ability to effectively utilize insulin, leading to elevated blood glucose levels if not managed appropriately. Over time, persistent hyperglycemia can result in serious complications, particularly involving the nerves and blood vessels. T2DM is often preventable, with major risk factors including excess body weight, physical inactivity, and genetic predisposition. Early diagnosis is essential to reduce the risk of long-term complications. Regular medical check-ups and blood tests are vital for timely detection and effective management of the disease.

A World Health Organization (WHO) expert consultation held from 28 to 30 March 2009 reviewed the use of HbA1c as a diagnostic tool for DM. Based on a systematic review of available evidence, the consultation concluded that HbA1c can be used as a reliable diagnostic test. An HbA1c threshold of 6.5% was recommended as the cut-off point for diagnosing diabetes. However, values below 6.5% do not rule out diabetes if glucose-based diagnostic criteria are met.[3]

HbA1c reflects the average plasma glucose concentration over the preceding 8 to 12 weeks.[4] It can be measured at any time of the day and does not require specific preparation, such as fasting. These practical advantages have established HbA1c as the preferred test for monitoring glycaemic control in individuals with diabetes. More recently, there has been growing interest in its use not only as a diagnostic tool for diabetes but also as a screening test for individuals at high risk of developing the disease.[5]

C-peptide is a byproduct of insulin synthesis, cleaved from proinsulin in equimolar amounts with insulin, and serves as a proxy for endogenous insulin production.[6] Beyond its diagnostic utility, C-peptide is now recognized as a biologically active molecule and has been widely studied as a diagnostic biomarker for diabetes.[7-10] More recently, it has emerged as a potential indicator of metabolic syndrome, underscoring its diagnostic significance in metabolic disorders.[11] Given that both metabolic syndrome and insulin resistance (IR) are strongly linked to an increased risk of developing T2DM, evaluating the biomarker potential of C-peptide in identifying IR-prone individuals-such as those with prediabetes or early-stage diabetes-may offer valuable insights for early screening and intervention.

Obesity is a medical condition characterized by excessive accumulation of body fat that may impair health. According to the National Institutes of Health, obesity is defined using the body mass index (BMI), calculated as weight in kilograms divided by the square of height in meters; a BMI greater than 30 is classified as obese.[12] The expansion of fat mass in obesity occurs through both an increase in adipocyte size (hypertrophy) and number (hyperplasia).[13] This excess fat accumulation typically results from an imbalance between caloric intake and energy expenditure. Obesity is a major risk factor for the development of T2DM and is strongly associated with insulin resistance.[14]

With the increasing global burden of obesity and diabetes driven by globalization, urbanization, sedentary lifestyles, and changing dietary habits, there is a growing need to understand metabolic alterations associated with these trends. This study investigates the relationship between HbA1c and C-peptide levels in obese individuals with and without diabetes to evaluate insulin dynamics across different glycemic states. Given the limited research in this area, particularly within the context of globalization and lifestyle transitions, our findings aim to offer valuable insights into early metabolic changes and potential risk stratification in obesity-related diabetes.

Aims and objectives

Aim and objectives were to assess HbA1c levels and C-peptide levels among obese individuals with diabetes (Group 2) and without diabetes (Group 1), to compare HbA1c levels and C-peptide levels between the two groups and to find the correlation between HbA1c and C-peptide within the two groups.

METHODS

This cross-sectional case control study was carried out at Government General Hospital, Vijayawada. 30 cases of obese with diabetes and 30 cases of obese without diabetes were recruited consecutively for a period of 3 months from patients attending the daily O.P. services. A sample size of 29 per group was calculated based on a correlation coefficient (r) of 0.5 with 80% power and a 5% significance. This was rounded to 30 participants per group. A similar size was used in some previous studies.[15,16]

The study included both male and female participants aged above 30 years who gave consent and who met the required criteria through purposive sampling. Caution was taken to include participants in both the groups with BMI above 30 so that study to be conducted only on obese persons.[12]

Only diabetics with HbA1c>6.5, diagnosed recently within 2 years and on oral hypoglycemic drugs were included as the cases. And non diabetics with HbA1c<5.7, devoid of any systemic illnesses including PCOS were included as controls (to avoid those on metformin).

This study excluded male and female individuals aged below 30yrs and who are not willing to give informed consent. Also, non-obese individuals and obese individuals with any systemic disorders which influence the insulin levels were excluded from the study.

Venous blood samples were collected under aseptic conditions. Two ml mixed with EDTA for estimation of HbA1c. HbA1c was done by fully automatic analyzer (by

turbidimetric method) to assess the glycemic status of the subjects. C-Peptide was analyzed by ELISA. Normal range was 0.78-1.89 ng/ml.

Ethical and institutional permissions are taken before commencing the study.

Data were entered in Microsoft excel**,** and statistical analysis was performed using Jamovi (a free, open-source statistical software). Independent sample t test (Welch's) was performed. Pearsons's correlation coefficient used.

RESULTS

Table 1 shows that BMI is similar across both groups, which is ideal, it helps isolate the effect of diabetes. HbA1c and C-peptide levels are significantly higher in diabetic obese individuals.

Table 1: Descriptives.

Variables	Group	N	Mean	Median	SD	SE
BMI	**Non-diabetics**	30	30.92	31.00	0.492	0.0898
	Diabetics	30	30.84	30.65	0.722	0.132
HbA1c	**Non-diabetics**	30	5.03	5.30	0.635	0.1160
	Diabetics	30	9.08	9.00	1.488	0.272
C-peptide	**Non-diabetics**	30	1.19	1.23	0.360	0.0657
	Diabetics	30	5.29	4.79	1.992	0.364

Table 2: Independent samples t test.

Variables		Statistic	Df	P	Mean difference	SE difference	Effect size
BMI	**Welch's t**	0.522	51.1	0.604	0.0833	0.160	0.135
HbA1c	**Welch's t**	-13.711	39.2	<0.001	-4.0500	0.295	-3.540
C-peptide	**Welch's t**	-11.101	30.9	<0.001	-4.1027	0.370	-2.866

*Note. H_a $\mu_{Non\text{-}Diabetics} \neq \mu_{Diabetics}$

Table 2 shows that HbA1c and C-peptide levels are statistically significantly higher in diabetic obese individuals. HbA1c (d=-3.540) and C-peptide (d=-2.866) show very large effect sizes (Cohen's d>0.8), indicating strong, meaningful differences between diabetic and non-diabetic obese groups.

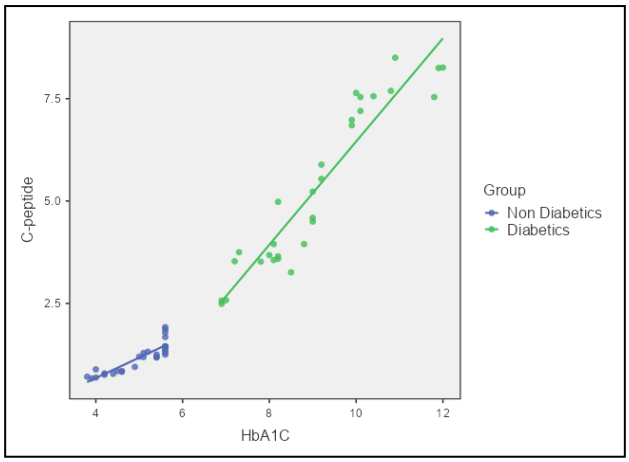

Figure 1: Correlation between HbA1c and C-peptide among obese.

Table 3: Correlation.

Group	Pearson's r	P value
Diabetics	0.94	<0.00001
Non-diabetics	0.88	<0.00001

There is a strong positive correlation between HbA1c and C-peptide in both diabetic and non-diabetic obese individuals (Figure 1). The association is stronger in diabetics (r=0.94) than in non-diabetics (r=0.88), both statistically significant (Table 3). This suggests that as glycemic levels (HbA1c) increase, C-peptide levels also increase-likely reflecting increased insulin secretion or resistance. Regression lines are shown for each group (Figure 1).

DISCUSSION

In the present study, both groups exhibited comparable BMI values (30.92 in non-diabetics and 30.84 in diabetics), indicating no substantial difference in body weight status between them. The low standard deviation (SD) and standard error (SE) in both groups suggest a consistent distribution of BMI.

The mean HbA1c level in non-diabetics was 5.03%, which falls within the normal range (≤5.6%), whereas diabetics had a markedly elevated mean HbA1c of 9.08%, exceeding the diagnostic threshold for diabetes (>6.5%). This pronounced difference indicates poor glycemic control in the diabetic group and suggests that HbA1c serves as a strong indicator of diabetes status.

The mean difference in HbA1c between the two groups was 4.05%, with a highly significant p value and a very large effect size (Cohen's d=-3.540). These findings confirm that HbA1c levels are substantially higher in

diabetics, reflecting a clear and statistically significant group difference.

Non-diabetics exhibited a mean C-peptide level of 1.19 ng/mL, which falls within the normal reference range (0.78-1.89 ng/mL), reflecting normal insulin production. In contrast, diabetics demonstrated a substantially higher mean C-peptide level of 5.29 ng/mL, suggesting increased insulin secretion-likely a compensatory response to insulin resistance, commonly observed in T2DM. The higher standard deviation in diabetics (SD=1.992) indicates considerable variability in C-peptide levels within this group.

The mean C-peptide level was 4.10 ng/mL lower in non-diabetics. This difference was statistically significant ($p<0.001$) and accompanied by a very large effect size (Cohen's $d=-2.866$), confirming that diabetics have significantly higher C-peptide levels compared to non-diabetics.

In diabetics, a Pearson's correlation coefficient of $r=0.94$ with $p<0.00001$ indicates a very strong and statistically significant positive correlation between HbA1c and C-peptide. This suggests that as HbA1c increases, C-peptide levels also rise, reflecting elevated insulin production in response to worsening glycemic control.

Similarly, in non-diabetics, $r=0.88$ with $p<0.00001$ also denotes a very strong positive and significant correlation, although slightly weaker than in diabetics. This indicates that even among individuals without diabetes, C-peptide levels tend to increase with rising HbA1c, though within a narrower physiological range.

Overall, diabetics exhibit higher and more variable levels of both HbA1c and C-peptide, consistent with the presence of insulin resistance and impaired glucose regulation. In contrast, the non-diabetic group shows tightly clustered values, reflecting more stable physiological control. The linear nature of these relationships supports the use of Pearson's correlation and regression models in this analysis.

A study by Shajith et al reported that mean levels of HbA1c, C-peptide, and three additional markers of insulin resistance were significantly higher in non-lean, non-obese Asian Indian patients with T2DM diagnosed within one year and on metformin monotherapy, compared to non-lean, non-obese, non-diabetic Asian Indian controls.[17] Similarly, our study demonstrates higher HbA1c and C-peptide levels in obese individuals with diabetes compared to their non-diabetic obese counterparts in an Indian population.

In contrast to our findings, a study by Chowta et al observed a negative correlation between serum C-peptide and HbA1c ($r=-0.207$, $p>0.05$), as well as with the duration of diabetes, suggesting a different trend in insulin secretory response over time.[18]

A study by Sasho et al observed that obese patients with T2DM experience a more rapid decline in insulin secretion, as indicated by decreasing C-peptide levels, which contributes to poorer glycemic control reflected by elevated HbA1c.[19]

Similarly, Ismail et al reported significant inverse correlations between HbA1c and both early and late C-peptide responses. Their findings suggest that patients with a stronger or more delayed insulin secretory response tend to have lower HbA1c levels.[20]

Miya et al further supported this association, noting that reduced β-cell function-indicated by a high proinsulin-to-C-peptide (PI:C) ratio or low C-peptide levels-is linked with sustained hyperglycemia and higher HbA1c, even in the absence of changes in glucose variability.[21]

In contrast, a study by Banu et al which investigated the relationship between C-peptide and insulin resistance in individuals with metabolic syndrome, found no significant correlation between C-peptide and HbA1c.[22]

Supporting our findings, Aruna observed a positive correlation between HbA1c and C-peptide levels in her study, indicating that as glycemic control worsens, insulin secretion also tends to increase. Notably, this positive association was more pronounced in individuals with poor glycemic control (HbA1C>9%), suggesting a compensatory response to heightened insulin resistance. This pattern is characteristic of early to mid-stage type 2 diabetes, where pancreatic β-cells are still capable of increasing insulin output before significant functional decline or exhaustion occurs.[23]

CONCLUSION

HbA1c and C-peptide levels are significantly higher in obese individuals with diabetes, with strong effect sizes. A strong positive correlation between HbA1c and C-peptide-especially in diabetics-suggests increased insulin secretion in response to poor glycemic control and insulin resistance. These findings highlight the value of C-peptide in evaluating metabolic status in obesity.

Recommendations

Incorporating C-peptide measurements alongside HbA1c in routine screening for obese individuals-especially those at risk for or diagnosed with diabetes-can provide a more comprehensive assessment of insulin dynamics and metabolic status. Since elevated C-peptide levels may reflect compensatory hyperinsulinemia due to insulin resistance, early monitoring can help identify prediabetic or high-risk individuals, enabling earlier intervention.

Obesity clinics and metabolic care centers should consider incorporating C-peptide testing into their risk stratification protocols to facilitate more individualized treatment planning. This can support targeted lifestyle interventions

aimed at improving insulin sensitivity and preventing disease progression.

Future research should follow obese individuals longitudinally to evaluate how changes in HbA1c and C-peptide predict the progression of insulin resistance and diabetes development.

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