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Original Research Article

C Peptide to Total Cholesterol Ratio as a Marker of Pancreatic Beta Cell Function in Patient with Type 2 Diabetes Mellitus

Tamboli Dhruvin[1], Jadav Helly Pareshbhai[2], Sanghani Nandita[3], Sanghani Dhairya[4], Shah Praachi[5], Chandwani Kavya[6]

[1]Assistant Professor, Department of Biochemistry, Sal Institute of Medical Sciences, Opp. Science City , Sola Bhadaj Road, Ahmedabad, Gujarat, India

[2]2nd Year MBBS Student, Sal Institute of Medical Sciences, Opp. Science City, Sola Bhadaj Road, Ahmedabad, Gujarat, India

[3]Associate Professor, Sardar Patel Medical College and Research Center, Near 108 Emergency Centre, Nava Naroda, Ahmedabad, Gujarat, India

[4]3rd Year MBBS Student, Sal Institute of Medical Sciences, Opp. Science City, Sola Bhadaj Road , Ahmedabad, Gujarat, India

[5]2nd Year MBBS Student, Dr. M.K. Shah Medical College and Research Center , Near Tapovan Circle , Visat – Gandhinagar Highway, Chandkheda, Ahmedabad, India

[6]2nd Year MBBS Student, Dr. M.K. Shah Medical College and Research Center, Near Tapovan Circle , Visat – Gandhinagar Highway, Chandkheda, Ahmedabad, India

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Corresponding author: Dr. Dhruvin Tamboli

Conflict of interest: Nil

Abstract

Background: Type 2 Diabetes Mellitus (T2DM) is identified by insulin resistance, progressive pancreatic β-cell dysfunction, and irregularities in lipid metabolism. Serum C-peptide is a dependable indicator of endogenous insulin secretion and β-cell function, while elevated total cholesterol indicates dyslipidemia and heightened cardiovascular risk. The C-peptide to Total Cholesterol (C-peptide/TC) ratio has recently garnered attention as a potential combined marker for assessing pancreatic β-cell function and metabolic status in individuals with T2DM.

Aim: To examine the association between serum C-peptide and total cholesterol levels and to evaluate the effectiveness of the C-peptide to Total Cholesterol ratio as an indicator of pancreatic β-cell function in patients with Type 2 Diabetes Mellitus.

Materials and Methods: A case-control study was carried out at GCS Medical College, Ahmedabad, involving 60 participants (30 T2DM patients and 30 age- and gender-matched healthy individuals) aged 25–65 years. Serum total cholesterol was assessed using the enzymatic CHOD-POD technique, while serum C-peptide levels were determined using standard laboratory procedures. The C-peptide/Total Cholesterol ratio was computed and compared between the cases and controls. Statistical significance was considered at $p < 0.05$.

Results: Individuals with Type 2 Diabetes Mellitus exhibited notably higher average total cholesterol levels than the healthy controls (220.5 ± 32.6 mg/dL vs. 183.7 ± 20.41 mg/dL; $p = 0.00014$). The average C-peptide/Total Cholesterol ratio was significantly lower in diabetic patients (0.0100 ± 0.007318) in comparison to controls (0.01571 ± 0.01102; $p = 0.0219$). These results suggest that a decline in β-cell function coincides with deteriorating lipid irregularities in T2DM.

Conclusion: The C-peptide to Total Cholesterol ratio is notably decreased in individuals with Type 2 Diabetes Mellitus and could function as a straightforward, cost-efficient indicator of pancreatic β-cell function and metabolic dysfunction. This ratio could also aid in identifying patients at heightened risk of dyslipidemia and cardiovascular issues. It is advisable to conduct larger prospective studies to confirm its clinical usefulness as a regular biomarker in diabetes care.

Keywords: Diabetes Mellitus, Total Cholesterol, Lipid Profile, Insulin Resistance, Hyperlipidemia, Hypercholesterolemia, Glucose Metabolism, Lipid Metabolism.

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Introduction

Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which leads over time to serious damage to the heart, blood vessels, eyes, kidneys and nerves. The most common is type 2 diabetes, usually in adults, which occurs when the body becomes resistant to insulin or doesn't make enough insulin [1]. Obesity is a recognized risk factor for the onset of Type 2 Diabetes Mellitus and is crucial in the development of insulin resistance. Excess fat, especially in the abdominal region, leads to disrupted insulin signaling and modified glucose metabolism.

As insulin resistance worsens, pancreatic β-cells respond by enhancing insulin secretion to preserve glucose homeostasis. Nevertheless, chronic metabolic stress can ultimately result in β-cell dysfunction and worsening glycemic control. [2,3] C-peptide is a peptide molecule that is released in equal amounts alongside endogenous insulin during the cleavage of proinsulin. Once regarded as a biologically inactive by-product of insulin synthesis, C peptide is now known as a significant marker for assessing pancreatic β-cell function and endogenous insulin secretion. The measurement of serum C-peptide provides important insights into insulin production and can aid in evaluating the metabolic status of individuals with Type 2 Diabetes Mellitus. Recent research has pointed that increased levels of C-peptide may correlate with insulin resistance, obesity, and negative metabolic consequences. [4,5] Dyslipidemia represents a significant metabolic disorder commonly seen in individuals with Type 2 Diabetes Mellitus. Increased levels of total cholesterol, coupled with decreased HDL-cholesterol, enhance cardiovascular risk and advance disease progression. Insulin resistance is closely connected to lipid metabolism irregularities so evaluating the association between serum C peptide and lipid profile may provide additional insights into the metabolic disturbance associated with obesity and diabetes. [6]

Aims and Objective

To examine the association between serum C-peptide and total cholesterol levels and to evaluate the effectiveness of the C-peptide to Total Cholesterol ratio as an indicator of pancreatic β-cell function in patients with Type 2 Diabetes Mellitus.

Material and Methods

Type of study: A hospital based study.

Study design: Case control study.

Sample size: Study population compromised of 60 subjects with age 25-65 years of age who sought health care at Medicine department in GCS Medical College, Ahmedabad. Approval & Consent: This study was conducted after the approval from the institutional Ethics Committee and with written informed consent from each patient after explaining the study procedure to them in their own language.

Sample collection procedure: 30 patients of type 2 DM were randomly selected for the study who had fulfilled the inclusion criteria and 30 age and sex matched healthy individuals as control group.

Inclusion Criteria:

1. Patients attending the outpatient department and inpatient department of Medicine department GCS Medical College, Hospital and Research Centre. Clinically and laboratory diagnosed cases of Type 2 DM [Age between 25 to 65 years] were included in this study.
2. Age and sex matched healthy subjects without any disease were used as control group.

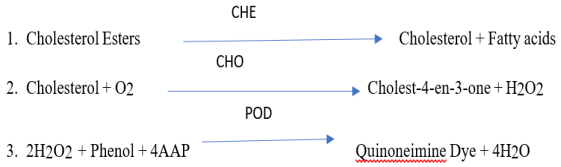
Exclusion Criteria:

1. Clinically and laboratory diagnosed cases of Type 2 DM whose age is less than 25 and more than 65 years were excluded in this study.
2. Clinically and laboratory diagnosed cases of Type 1 DM.

Estimation of Cholesterol:

Principle of Procedure:

1. Cholesterol esters are enzymatically hydrolysed by cholesterol esterase to cholesterol and free fatty acids.
2. Free cholesterol, including that originally present, then oxidized by cholesterol oxidase to cholest-4-en-3-one and hydrogen peroxide.
3. The hydrogen peroxide combines with 4-aminoantipyrine to form a chromophore (quinoneimine dye) which may be quantitated at 505 nm. This reagent is based on the formulation of Allain et al and the modification of Roeschlau with further improvements to render the reagent stable in solution.



Reagent Composition

- Good's Buffer 50 mmol/l Phenol 5 mmol/l
- 4-aminoantipyrine 0.3 mmol/l
- Cholesterol esterase ≥ 200 U/l
- Cholesterol oxidase ≥ 50 U/l

- Peroxidase ≥ 3 kU/l

Reagent Preparation: Reagent is liquid and ready to use.

Reagent Storage:

- The unopened reagents are stable till the expiry date stated on the bottle and kit label when stored at 2–8°C.
- On board stability: min. 30 days if refrigerated (2–10°C) and not contaminated

Calibration: Calibration with calibrator XL MULTICAL, Cat. No. XSYS0034 is recommended.

Calibration frequency: it is recommended to do a calibration

- after reagent lot change
- as required by internal quality control procedures

Measuring range: 4.2 - 695 mg/dl

Specimen Required: No Anticoagulant Human Serum

Results

Serum Total Cholesterol level:

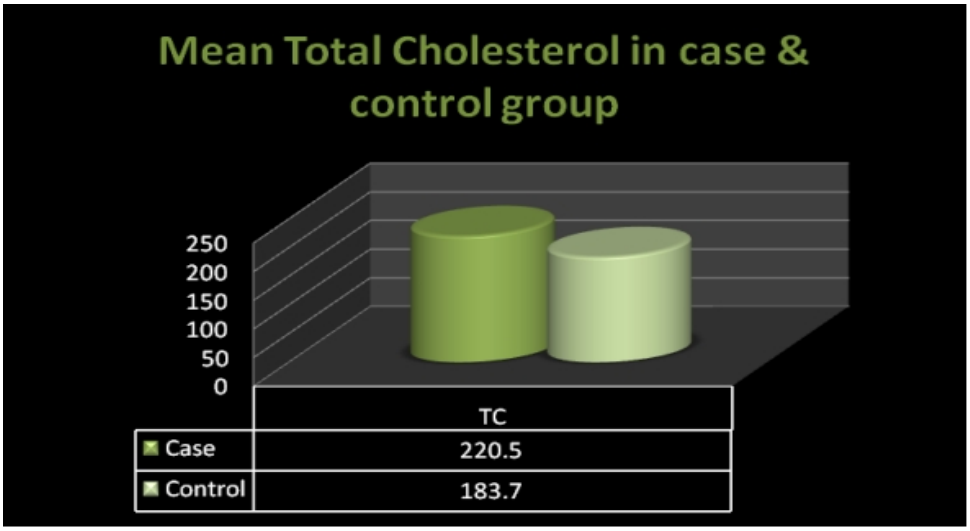


Figure 1: Mean Total Cholesterol in case & control group

Table 1:

	Case	Control	P Value
TC	220.5 ± 32.6	183.7 ± 20.41	0.00014

From the above diagram, it was seen that mean TC level in the cases have slightly higher than in the controls & it is also statistically significant ($p<0.05$).

C-Peptide to TC Correlation between Cases & Controls:

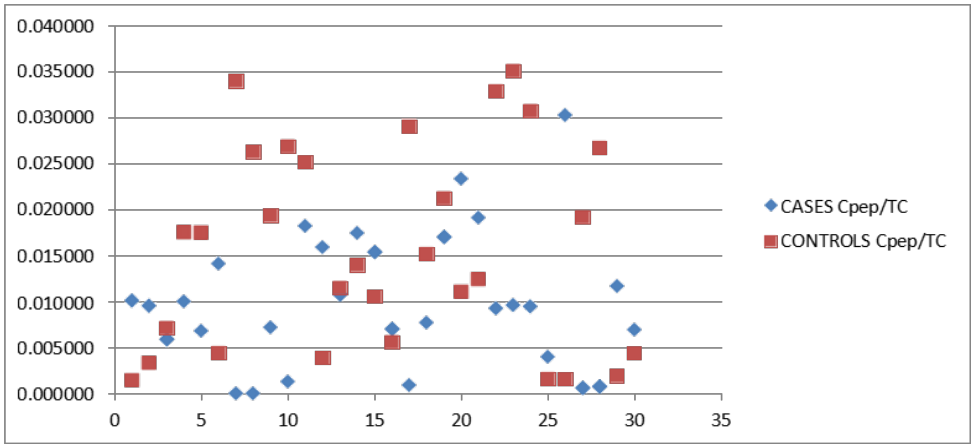


Figure 2:

Table 2:

	Case	Control	P Value
C-peptide/TC	0.0100±0.007318	0.01571±0.01102	0.0219

From the above graph, it was seen that mean C-peptide/TC level in the controls have slightly higher than in the cases & it is also statistically significant ($p<0.05$).

Individuals with Type 2 Diabetes Mellitus exhibited notably higher average total cholesterol levels than the healthy controls (220.5 ± 32.6 mg/dL vs. 183.7 ± 20.41 mg/dL; $p = 0.00014$). The average C-peptide/Total Cholesterol ratio was significantly lower in diabetic patients (0.0100 ± 0.007318) in comparison to controls (0.01571 ± 0.01102; $p = 0.0219$). These results suggest that a decline in β-cell function coincides with deteriorating lipid irregularities in T2DM

Discussion

C-peptide had a positive correlation between with BMI in T2DM patients. Serum C-peptide showed a significant positive correlation with total cholesterol. The findings of this study highlighted that elevated C-peptide levels may be associated with an adverse metabolic profile. Insulin resistance can alter lipid metabolism, resulting in increased cholesterol levels and reduced HDL-cholesterol. Similar observations have been reported in previous studies where higher C-peptide levels were associated with metabolic abnormalities and increased cardiometabolic risk. [5,6,7] Finding reveals that total cholesterol (T-CH) levels tend to rise with age ($R = 0.3$, $p = 0.001$) which focusing on important monitoring significance of controlling cholesterol levels, particularly in older adults while HDL Levels surprisingly shows no discernible relationship with age ($p = NS$).

This implies that within this specific study population, "good" cholesterol levels may stay pretty consistent as people age! LDL Levels: LDL cholesterol levels was increase in with age ($R = 0.3$, $p = 0.001$), that increase risk of cardiovascular disease. These relationships are very important to decreasing cardiovascular risk and maintaining the health of old aged T2DM patients. Individuals diagnosed with type 2 diabetes may have varying total cholesterol levels; the median values were somewhat higher in the T2DM group (201 mg/dl versus 170 mg/dl, respectively) and showed statistically significant differences. (P-value = 0.001)(8) The role of population dietary cholesterol intake in the development of the T2DM and gestational diabetes mellitus (GDM) has garnered increasing attention in recent years with the potential association between cholesterol dysmetabolism and T2DM becoming increasingly clear in basic medical research. A meta-analysis of cohort studies involving 355,230 participants found that high dietary cholesterol intake was associated with a 15% increased risk of T2DM (RR: 1.15; 95% CI 1.03–1.28; $I^2 = 58.6\%$). Dose–response analysis revealed that each 100 mg/day increase in cholesterol intake corresponded to 5% increase in T2DM risk (RR: 1.05; 95% CI 1.04–1.07) [12]. Huang et al. showed that TC and LDL-C levels were significantly higher in T2DM patients in the low C-peptide group than in the control group. They also found that low C-peptide caused an increased incidence of various complications including diabetic nephropathy, retinopathy, and coronary heart disease. [9] a meta-analysis of observational studies involving 30,123 participants demonstrated that elevated dietary cholesterol intake significantly increased the risk of GDM (RR: 1.49; 95% CI 1.18–1.88; $I^2 = 50.5\%$) with each 100 mg/day increment in cholesterol intake linked to a 32% higher risk of GDM (RR: 1.32; 95% CI 1.20–1.45) [10]. These breakthroughs have provided critical insights into the mechanisms underlying cholesterol metabolism and opened new avenues for screening metabolic diseases and developing therapeutic interventions targeting cholesterol homeostasis. Concurrently, the role of cholesterol metabolism in the pathogenesis of T2DM has gained significant attention. Cholesterol may contribute to T2DM by modulating β-cell function and insulin secretion. In this review, we examine recent progress in understanding the mechanisms by which dysregulated cholesterol metabolism drives T2DM, including disruptions in Ca^{2+} homeostasis, PERK-eIF2α signaling, Golgi stress, inflammation, and oxidative stress. We also explore cholesterol-induced alterations in BAs metabolism, gut microbiota composition, and the LAAMP pathway. However, due to the complex interplay of cholesterol metabolism in vivo, the precise mechanisms linking cholesterol dysregulation to T2DM remain unclear. Thus, further mechanistic studies are needed to elucidate these pathways and offer new therapeutic possibilities for T2DM. Additionally, exploring the new functions of cholesterol and sterol intermediates in the mevalonate pathway represents an important direction for future research aimed at preventing chronic diseases [11]. The findings from large, longitudinal cohort studies that have revealed a significant association between cholesterol levels and the incidence of T2DM, including studies conducted in 28,476 individuals with coronary heart disease in China [13], 120,613 participants in Japan [14], and 8,485,539 participants in Korean [15].

Conclusion

The study shows that individuals with Type 2 Diabetes Mellitus have notably higher levels of total cholesterol in their blood and a lower ratio of C-peptide to Total Cholesterol compared to healthy people. These results suggest a close link between declining pancreatic β-cell function, lipid metabolism issues, and the onset of insulin resistance. While C-peptide levels reflect natural insulin production, their interpretation can be affected by insulin resistance levels. Combining C-peptide with total cholesterol in the C-peptide/Total Cholesterol ratio offers a more thorough evaluation of pancreatic β-cell function and metabolic health. The reduced ratio in diabetic patients indicates compromised β-cell reserves and worsening dyslipidemia, both contributing to disease progression and heightened cardiovascular risk. The high cholesterol levels in diabetic patients underscore the importance of routine lipid monitoring, as dyslipidemia significantly contributes to serious vascular complications like coronary artery disease and stroke. Therefore, assessing the C-peptide/Total Cholesterol ratio can help healthcare providers detect declining β-cell function early on, enabling prompt intervention and better metabolic management. The study's strengths lie in its use of controls matched for age and sex and in exploring a new biochemical ratio combining endocrine and lipid markers. Yet, the relatively small sample size and single-center study design may restrict the findings' applicability. Additionally, the lack of long-term monitoring prevents determining the ratio's predictive value for diabetic complications. To conclude, the C-peptide to Total Cholesterol ratio shows promise as a cost-effective, straightforward, and valuable marker for evaluating pancreatic β-cell function in Type 2 Diabetes Mellitus patients. It offers insights beyond standard biochemical parameters and could aid in assessing disease severity and cardiometabolic risks. Future studies involving multiple centers, larger cohorts, and extended follow-ups are necessary to establish reference values and confirm its utility in clinical settings.

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