Content available at: https://www.ipinnovative.com/open-access-journals

International Journal of Clinical Biochemistry and Research

Journal homepage: https://www.ijcbr.in/

Original Research Article

Role of circulating C-peptide in the Indian population with Type 2 diabetics with nephropathy: A triangular relationship between C-peptide, HbA1C and microalbuminuria

Balaji Vijayam[1,*], Taarika Balaji[1], Madhuri S Balaji[1], Seshiah Veerasamy[1], Vinothkumar Ganesan[2,*]

[1]*Dept. of Diabetology, Dr. V Balaji Diabetes Care and Research Institute, Chennai, Tamil Nadu, India*
[2]*Dept. of Medical Research, Dr. V Balaji Diabetes Care and Research Institute, Chennai, Tamil Nadu, India*

ARTICLE INFO

Article history:
Received 18-01-2023
Accepted 11-02-2023
Available online 05-04-2023

Keywords:
C- peptide
Diabetes mellitus
HbA1C
Insulin resistance
Nephropathy

ABSTRACT

Background: C-peptide levels can initially be normal or increased in type 2 diabetes mellitus (T2DM), which is connected to insulin resistance; however, as the condition progresses, these levels may fall. According to studies, kidney failure has diabetes as its primary cause, accounting for 44% of all new cases. In addition, it's critical to strictly regulate blood sugar levels and lower protein intake. Along with insulin, the pancreas produces a molecule called C-peptide. The hormone insulin regulates the body's glucose levels.

Materials and Methods: A total of 300 subjects divided into 150 CKD progression diabetic nephropathy and 150 non-progressions diabetic nephropathy based on clinical parameter assessment. All patients had their body weight and body mass index (BMI) assessed. Fasting serum C peptide, HbA1C, serum creatinine, blood urea nitrogen, urine albumin, and creatinine were among the laboratory tests performed. Using the MDRD algorithm, creatinine clearance was determined from serum creatinine value. The parameters were statistically compared with respective subjects.

Results: The small case-control study found a no relationship between serum C-peptide levels and both microalbuminuria and HbA1C.

Conclusion: Risk of microalbuminuria may be higher in patients with low serum C peptide levels. In patients with T2DM, replacing C-peptide and administering insulin may be useful. The possibility that C-peptide may play a part in the prevention and treatment of diabetic nephropathy will need to be investigated in studies including longer-term C-peptide administration.

1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycaemia. There is always Beta-cell malfunction in diabetes mellitus, regardless of the kind. The hallmark of type 1 diabetes mellitus (T1DM) is the autoimmune-driven destruction of beta cells, which typically results in absolute insulin deficiency[1] and eventually decreases insulin secretion and a corresponding decline in C-peptide levels, a marker of endogenous insulin secretion and beta cell function. Initially having normal or high C-peptide levels, type 2 diabetes mellitus is linked to insulin resistance and can become less severe as the condition progresses.[2] Diabetes mellitus patients have hypertension two to three times more frequently than people without the condition, which increases the risk of cardiovascular disease and renal damage.[3] According to studies, kidney failure is mostly

* *Corresponding authors.*
E-mail address: balajivijayam@gmail.com (B. Vijayam).

https://doi.org/10.18231/j.ijcbr.2023.010

caused by diabetes, which accounts for 44% of all new cases. According to recent studies, controlling high blood pressure is a crucial element in reducing this condition. Blood sugar levels must be tightly controlled, and protein consumption must be decreased. Before kidney damage occurs, treatment for preventing diabetic renal disease should start.

Along with insulin, the pancreas also produces a molecule called c-peptide. The hormone insulin regulates the body's glucose (blood sugar) levels. The body uses glucose as its primary energy source. If the body isn't producing enough insulin, diabetes may be present. There are studies that support the biological activity of C-peptide,[4] which contrasts with the clinical significance of C-peptide as a measure of endogenous insulin production. Importantly, certain investigations have revealed that C-peptide possesses renoprotective qualities. Higher C-peptide levels have been linked in observational studies of people with diabetes mellitus type 1 or type 2 to lower prevalence of microvascular sequelae, including diabetic nephropathy,[5–8] summarized in.[9] Additionally, after receiving a pancreas transplant, which replenishes both C-peptide and insulin from transplanted beta cells,[10,11] individuals with type 1 diabetes have demonstrated better renal function. Finally, limited studies in which type 1 diabetic experimental individuals received C-peptide have demonstrated that C-peptide may enhance renal function in these patients regardless of any potential impact on glucose management.[12,13] However, further research is needed to fully understand C- peptide therapeutic potential for people with diabetic kidney disease. Whether the potential advantage of C-peptide is exclusive to people with diabetes or is applicable to a larger population of patients is unknown at this time. The purpose of the study is to ascertain how T2DM affects nephropathy, circulating levels of C-peptide, HbA1C, and microalbuminuria.

2. Materials and Methods

This is a small case-control investigation. We assessed the baseline clinical and laboratory profiles of patients with type 2 diabetes mellitus, including newly diagnosed cases. Patients who had undergone screening for type 2 diabetes clinical studies provided the data. Each patient who was screened provided their informed consent, and the Institutional Ethics Committee had already authorised each trial. Males and females over the age of 18 were both included in the study. A thorough history was gathered, including information on the disease's duration. Each patient had a careful physical check-up. We also gathered information on concurrent illnesses and anti-diabetic medication. All patients had their body weight and body mass index (BMI) assessed. Biochemical blood tests included serum C peptide was measured using on DiaSorin, Italy and HbA1C, urea, creatinine, blood urea nitrogen, urine albumin were measured using dedicated reagent on Cobas c501 (Roche diagnostic, Germany). Using the MDRD algorithm, creatinine clearance was determined from serum creatinine value.

2.1. Inclusion criteria

T2DM with nephropathy patients (Age 30–70) will diagnose and selected for this study by the clinician and either the patient or his relatives who had given informed consent for the study.

2.2. Exclusion criteria

T1DM, obesity, chronic kidney disease, hepatic failure, cerebrovascular accident, pregnancy or are breast feeding and chronic illness patients will be excluded from this study.

2.3. Statistical analysis

To compare the values across patients in various categories, data were examined using a student "t" test. Using Pearson correlation, correlation analysis was performed. P values of 0.05 were deemed significant.

3. Results

Age, Body mass index (BMI), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), mm Hg, Fating Blood Sugar (mg/dl), Postprandial Blood Sugar (mg/dl), Glycated Hemoglobin A1c (HbA1c), Urea (mg/dl), Creatinine (mg/dl), Uric Acid (mg/dl), Hemoglobin (g/dl), Microalbuminuria (mg/dl) and C-peptide (ng/ml) Values are expressed as Mean + SD.

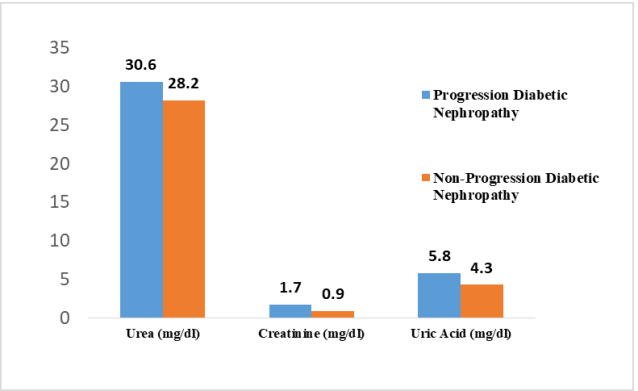

Fig. 1: Diabetic profile

4. Discussions

Numerous early investigations looked into the potential physiological impacts of C-peptide following the identification of the mode of insulin manufacturing. For glucose loading, it was sought after but not discovered

Table 1: Clinical characteristics of progression diabetic nephropathy and non-progression diabetic nephropathy (n=300)

Clinical Characteristics	Progression Diabetic Nephropathy (n=150)	Non-Progression Diabetic Nephropathy (n=150)	P values
Age (Years)	35.5 ± 11.6	32.4 ± 10.6	0.01
Gender			
No. of males	80	94	
No. of female	70	56	
Body mass index (BMI)	27.1 ± 0.54	20.23 ± 2.5	< 0.0001
SBP, mm Hg	160.9 ± 8.2	127 ± 5.6	< 0.0001
DBP, mm Hg	92.54 ± 1.3	71.4 ± 1.2	< 0.0001
Diabetic Profile			
Fasting Blood Sugar (mg/dl)	156 ± 8.5	124 ± 2.6	< 0.0001
Postprandial Blood Sugar (mg/dl)	320 ± 10.2	237 ± 2.8	< 0.0001
Glycated Haemoglobin (HbA1c)	8.0 ± 1.7	7.7 ± 1.5	0.1
Renal Function Test			
Urea (mg/dl)	30.6 ± 21.1	28.2 ± 21.4	0.3
Creatinine (mg/dl)	1.7 ± 2.4	0.9 ± 0.4	0.0001
Uric Acid (mg/dl)	5.8 ± 5.0	4.3 ± 1.52	0.0005
Hemoglobin (g/dl)	7.2 ± 2.8	12.1 ± 1.2	< 0.0001
Microalbuminuria (mg/dl)	68.8 ± 171.2	63.4 ± 152.4	0.7
Fasting C-peptide (ng/ml)	2.7 ± 1.3	3.14 ± 1.6	0.009
Postprandial C-peptide (ng/ml)	6.0 ± 3.4	6.52 ± 3.3	0.1

Table 2: Clinical correlation between fasting C-peptide, HbA1C, and microalbuminuria in progression diabetic nephropathy and non-progression diabetic nephropathy

Subjects		Fasting C-peptide			
		HbA1C		Microalbuminuria	
		Pearson	Spearman	Pearson	Spearman
Progression Diabetic	r	-0.140	-0.12	-0.045	0.08
Nephropathy	p	0.08	0.11	0.5	0.3
Non- Progression Diabetic	r	0.097	0.03	0.013	0.05
Nephropathy	p	0.23	0.62	0.87	0.4

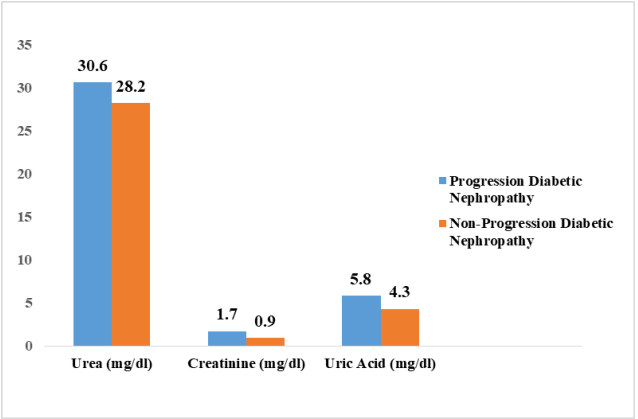

Fig. 2: Renal function test

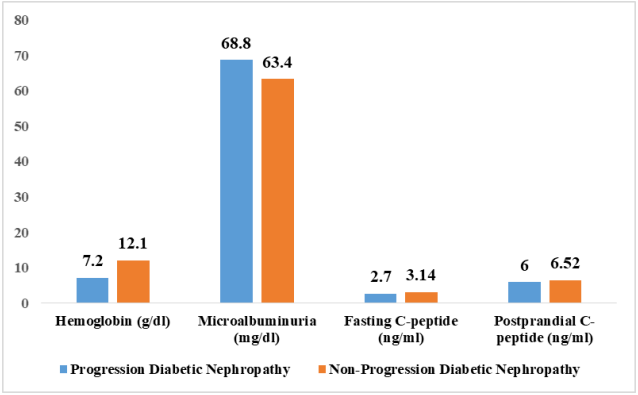

Fig. 3: Clinical parameters

to have any insulin-like effects on blood glucose levels and glucose disposal.[14,15] Recent research has shown that the C-peptide binds to cell surfaces specifically, indicating the presence of G protein-coupled membrane receptors. In those with type 1 diabetes who lack C-peptide, this may promote particular intracellular mechanisms that

affect renal and nervous system function.[15] A recent study discovered a weak correlation between serum C peptide, renal indices, and diabetes duration. The levels of serum C peptide, urine albumin excretion, and urine albumin creatinine ratio all had negative correlations with each other. Early on in the course of type 1 diabetes, glomerular hyperfiltration is a common complication.[16] This condition is not resolved by adequate insulin therapy.[17] However, type 2 diabetics who have insulin and C-peptide levels that are within or above the normal range do not exhibit glomerular hyperfiltration or hypertrophy.[18,19] C-peptide has a positive impact on renal function in diabetics, although the exact mechanism by which it does so is unknown. However, as demonstrated by investigations of renal function in animals with experimental diabetes, it is likely that C-peptide may have had a direct impact on the glomerular processing of albumin. In streptozotocin-diabetic rats, the effect of C-peptide on glomerular hyper filtration and protein leakage from the kidneys has been studied.[20] Comparatively to diabetic control rats, the administration of C-peptide for 90 minutes was associated by decreased glomerular hyper filtration and a notable reduction in protein leakage. Both renal Na1-K1-ATPase and eNOS (endothelial nitric oxide synthase) can be stimulated by C-peptide. Particularly in renal and nerve tissue, both of these enzyme systems have been shown to exhibit reduced activity in type 1 diabetes.[21,22] Regional blood flow in the kidney as well as glomerular membrane permeability and transport can be affected by C-peptide. There is now proof that replacing C-peptide in type 1 diabetes leads to improved renal function, as shown by correction of glomerular hyper filtration and decreased urine albumin excretion, as well as amelioration of nerve dysfunction.[23]

According to the results of the current investigation, there is a bad link between disease duration and serum C peptide levels, which may signal growing beta cell failure. Additionally, there was a negative connection between HbA1C and serum C peptide level, which suggests that patients with low serum C peptide levels had poor glycaemic control and require insulin therapy. Even in mature-onset diabetes mellitus, C peptide is a more reliable indicator of insulin secretion than insulin, and measuring it is crucial for determining if a person is dependent on insulin. While not statistically significant, our study also found a negative connection between urine albumin levels and C peptide values. Protein leakage is reduced by C peptide's diminution of glomerular hyper filtration. There may not have been a significant link between C peptide level and urine albumin excretion rate since there were not many individuals in our study with below normal C peptide levels. Our study's limitations warrant discussion. A valid conclusion on the relationship between serum C peptide level and renal parameters cannot be drawn from the small number of patients with low serum C peptide levels.

5. Conclusion

There is no connection between serum C peptide levels, microalbuminuria, and HbA1c was discovered by the study. Low serum C peptide levels are possible in patients at risk for microalbuminuria. Combining insulin delivery and C-peptide replacement may be beneficial for T2DM patients. Longer-term C-peptide administration trials will be required to determine whether C-peptide may help in the prevention and treatment of diabetic nephropathy.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare no conflict of interest.

References

1. WHO Expert committee on the diagnosis and classification of Diabetes mellitus: Report in the diagnosis and classification of diabetes mellitus. *Diabetes case*. 1997;20:1183–97.
2. Kim CS, Nam JH, Nam JS, Park JS, Kang ES, Ahn CW, et al. Clinical and biochemical characteristics of non-obese type 2 diabetic patients with glutamic acid decarboxylase antibody in Korea. *Metabolism*. 2007;55(8):1107–12.
3. Kaplan NM, Rosenstock J, Raskin PA. Differing view of treatment of hypertension in patients with diabetes mellitus. *Arch Intern Med*. 1987;147:1160–2.
4. Wahren J, Ekberg K, Jornvall H. C-peptide is a bioactive peptide. *Diabetologia*. 2007;50(3):503–9.
5. Bo S, Gentile L, Castiglione A, Prandi V, Canil S, Ghigo E, et al. C-peptide and the risk for incident complications and mortality in type 2 diabetic patients: a retrospective cohort study after a 14-year follow-up. *Eur J Endocrinol*. 2012;167(2):173–80.
6. Panero F, Novelli G, Zucco C, Fornengo P, Perotto M, Segre O, et al. Fasting plasma C-peptide and micro- and macrovascular complications in a large clinic based cohort of type 1 diabetic patients. *Diabetes Care*. 2009;32(2):301–5.
7. Kim BY, Jung CH, Mok JO, Kang SK, Kim CH. Association between serum C-peptide levels and chronic microvascular complications in Korean type 2 diabetic patients. *Acta Diabetol*. 2012;49(1):9–15.
8. Zheng WC, Chen L. Factor analysis of diabetic nephropathy in Chinese patients. *Diabetes Metab Syndr*. 2011;5(3):130–6.
9. Luppi P, Kallas A, Wahren J. Can C-peptide mediated anti-inflammatory effects retard the development of microvascular complications of type 1 diabetes? *Diabetes Metab Res Rev*. 2013;29(5):357–62.
10. Boggi U, Vistoli F, Amorese G, Giannarelli R, Coppelli A, Mariotti R, et al. Results of pancreas transplantation alone with special attention to native kidney function and proteinuria in type 1 diabetes patients. *Rev Diabet Stud*. 2011;8(2):259–67.
11. Cantarovich D, Perrone V. Pancreas transplant as treatment to arrest renal function decline in patients with type 1 diabetes and proteinuria. *Semin Nephrol*. 2012;32(5):432–6.
12. Johansson B, Kernell A, Sjoberg S, Wahren J. Influence of combined C-peptide and insulin administration on renal function and metabolic control in diabetes type 1. *J Clin Endocrinol Metab*. 1993;77(4):976–81.
13. Johansson BL, Borg K, Fernqvist-Forbes E, Kernell A, Odergren T, Wahren J. Beneficial effects of C-peptide on incipient nephropathy and neuropathy in patients with Type 1 diabetes mellitus. *Diabet Med*. 2000;17(3):181–9.

14. Hoogwerf B, Bantle J, Gaenslen H, Greenberg B, Senske B, Francis R, et al. Infusion of synthetic human C-peptide does not affect plasma glucose, serum insulin, or plasma glucagon in healthy subjects. *Metabolism*. 1986;35(2):122–5.
15. Wahren J, Ekberg K, Johansson J, Henriksson M, Pramanik A, Johansson BL, et al. Role of C-peptide in human physiology. *Am J Physiol Endocrinol Metab*. 2000;278(5):59–68.
16. Mogensen CE, Andersen MJ. Increased kidney size and glomerular filtration rate in untreated juvenile diabetes: Normalisation by insulin treatment. *Diabetologia*. 1975;11(3):221–4.
17. Christiansen JS, Frandsen M, Parving HH. The effect of intravenous insulin infusion on kidney function in insulin-dependent diabetes mellitus. *Diabetologia*. 1981;20(3):199–204.
18. Friedman E, Sheih SD, Hirsch S, Boshell B. No supranormal glomerular filtration (GFR) in type II (non-insulin-dependent) diabetes. *Am Soc Nephrol*. 1981;14:102.
19. Schmitz A, Gundersen H, Österby R. Glomerular morphology by light microscopy in non-insulin-dependent diabetes mellitus. *Diabetes*. 1988;37(1):38–43.
20. Sjöquist M, Huang W, Johansson BL. Effects of C-peptide on renal function at the early stage of experimental diabetes. *Kidney Int*. 1998;54(3):758–64.
21. Djemli A, Gallice P, Coste T, Jannot M, Dufayet D, Raccah D, et al. Ex vivo and in vitro effects of insulin and C-peptide on Na/K ATPase activity in red blood cell membranes of type 1 diabetic patients. *Diabetologia*. 1999;42:154.
22. Kunt T, Forst T, Closs E, Wallerath U, Förstermann R, Lehmann R, et al. Activation of endothelial nitric oxide synthase (eNOS) by C-peptide. *Diabetologia*. 1998;41:176.
23. Johansson BL, Borg K, Fernqvist-Forbes E, Kernell A, Odergren T, Wahren J. Beneficial effects of C-peptide on incipient nephropathy and neuropathy in patients with type I diabetes: A three-month study. *Diabet Med*. 2000;17(3):181–9.

Author biography

Balaji Vijayam, Chairman & Managing Director, Senior Consultant

Taarika Balaji, Consultant

Madhuri S Balaji, Senior Consultant

Seshiah Veerasamy, Senior Consultant

Vinothkumar Ganesan, Clinical Research Scientist
https://orcid.org/0000-0003-3673-6717

Cite this article: Vijayam B, Balaji T, Balaji MS, Veerasamy S, Ganesan V. Role of circulating C-peptide in the Indian population with Type 2 diabetics with nephropathy: A triangular relationship between C-peptide, HbA1C and microalbuminuria. *Int J Clin Biochem Res* 2023;10(1):66-70.