

Serum c-peptide level in newly diagnosed Bangladeshi adults with type 2 diabetes mellitus

A K M Saber Ahmed¹, A B M Kamrul-Hasan², Mohammed Ruhul-Kabir³, Habibur Rahman⁴, Mohammad Shofiullah³, A F M Nazmul-Islam³

¹Department of Biochemistry, Sylhet M A G Osmani Medical College, Sylhet, Bangladesh

²Department of Endocrinology, Mymensingh Medical College Hospital, Mymensingh, Bangladesh

³Department of Medicine, Sylhet M A G Osmani Medical College, Sylhet, Bangladesh

⁴Department of Endocrinology, Sylhet M A G Osmani Medical College, Sylhet, Bangladesh

Copyright: This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited (CC BY 4.0)

Abstract

C-peptide is produced in equimolar amounts to insulin and is the best measure of endogenous insulin secretion. This cross-sectional study was conducted in a tertiary hospital of Bangladesh from January 2016 to December 2017 to assess fasting serum c-peptide as a marker of the endogenous insulin secretory capacity in newly diagnosed subjects with type 2 diabetes mellitus (T2DM). 60 newly diagnosed T2DM subjects were investigated along with 30 age-sex matched healthy controls. Fasting c-peptide was significantly higher in T2DM subjects than controls (8.97 ± 5.96 vs. 1.69 ± 0.66 ng/ml). None of the T2DM subjects had subnormal c-peptide, 19 (32%) had normal c-peptide, and 41 (68%) of them had elevated c-peptide levels. Higher fasting plasma glucose (FPG), plasma glucose 2-hours after 75gm oral glucose tolerance test (PG 2H-OGTT) and HbA1c levels were observed in T2DM subjects with elevated c-peptide in comparison to T2DM subjects having normal c-peptide. In T2DM subjects, c-peptide showed significant positive correlations with body mass index (BMI), FPG, PG 2H-OGTT, and HbA1c. This study found higher levels of fasting c-peptide in newly diagnosed T2DM in comparison to nondiabetic controls. None of the T2DM subjects had a subnormal c-peptide level.

Keywords: type 2 diabetes, endogenous insulin, c-peptide, insulin secretion

 <https://orcid.org/0000-0002-5681-6522>

Correspondence: e-mail < rangassmc@gmail.com >.

Introduction

Diabetes mellitus (DM) is a group of metabolic disorders characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. More than 90% of subjects with DM worldwide have type 2 diabetes (T2DM) ⁽¹⁾. Though insulin resistance in the liver & muscle and β -cell failure represent the core pathophysiological defects in T2DM, it now is recognized that the β -cell failure occurs much earlier and is more severe than previously thought ⁽²⁾. In Asia, the T2DM phenotype appears to be somewhat different from that in the western countries with a younger age of onset and with lower BMI while associated with greater visceral adiposity and reduced insulin secretory capacity ⁽³⁾.

Many studies have evaluated serum c-peptide as a marker of insulin secretion in T2DM subjects (4,5,6,7,8). Data regarding the β -cell secretory state in newly detected Bangladeshi T2DM patients are scarce. The current study was undertaken to address the deficit.

Methods

This cross-sectional study was conducted in the Department of Medicine of M.A.G. Osmani Medical College Hospital, Sylhet, Bangladesh from January 2016 to December 2017, with the permission of the institutional review board of the hospital. All newly diagnosed patients with T2DM attending the Medicine Outpatient Department of the hospital during the study period were considered as the study population. 60 newly diagnosed non-pregnant adult patients with T2DM, age 35 to 65 years, before initiation of any lifestyle modification or pharmacological treatment for DM, were selected by non-probability convenient sampling technique. 30 age and sex-matched otherwise healthy volunteers selected from the patients' attendants and health care professionals were included in the control group. Subjects with any acute illness, any acute or advanced chronic complications of DM were excluded. Informed written consent was taken from each study subject before enrollment; relevant history was taken, physical examinations including anthropometric measurements were done; collected data were recorded in a pre-specified data collection sheet. Obesity status was determined by body mass index (BMI) categories applicable to the Asian Indians and waist circumference ≥ 90 cm in male and ≥ 80 cm in

female were used to define abdominal obesity (9,10). All of the participants were asked to attend the OPD on another convenient day with overnight fasting for at least 8 hours and all attending patients underwent standard oral glucose tolerance test (OGTT) according to the procedure described by World Health Organization ⁽¹¹⁾. Diabetes mellitus was diagnosed according to the American Diabetes Association (ADA) criteria ⁽¹⁾. The fasting blood sample was also used for estimation of HbA1c, serum c-peptide, serum creatinine, and lipid profile.

Biochemical Analysis:

Plasma glucose, serum creatinine, and fasting lipid profile was estimated by a semi-auto analyzer (Screen Master 3000 manufacturer: Biochemical System International, Italy), HbA1c was assayed by immunofluorescence assay on NGSP certified quantitative immunoassay analyzer Getein 1100 (Getein Biotech, Inc, China), serum c-peptide was assayed by quantitative ELISA method (DRG C-Peptide) with ELISA reader plate (DAS srl, Italy). All the biochemical analyses were done in the Department of Biochemistry of the hospital.

Statistical analysis:

Statistical analysis was done using Statistical Packages for Social Sciences (SPSS) software version 23.0 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0, Armonk, NY: IBM Corp.). The categorical variables were represented as percentages and measurable variables as mean \pm standard deviation (SD). Student's t-test and Chi-square test were performed as applicable for comparing the variables between different groups. Pearson's correlation test was used to observe the correlation of c-peptide level with other variables. p-value ≤ 0.05 was considered to be statistically significant.

Results

Demographic, clinical and biochemical characteristics of the study population are shown in table 1. The T2DM group and control group subjects did not differ in respect of age, sex, and serum creatinine levels. T2DM subjects had a higher frequency of first-degree relatives with T2DM; BMI and waist-to-hip ratio was higher in the T2DM group than the control group. The c-peptide level was also higher in T2DM subjects than controls.

Table 1. Demographic, clinical and biochemical characteristics of the study participants

Variables	T2DM (n=60) Mean ± SD or %	Control (n=30) Mean ± SD or %	p
Age (years)	45.0 ± 6.5	42.6 ± 3.9	0.070a
Gender			
Male	75%	80%	0.597b
Female	25%	20%	
Have family H/O T2DM	65%	40%	0.024b
BMI (Kg/M2)	25.79 ± 2.27	24.64 ± 1.40	0.012a
Waist:Hip Ratio	0.95 ± 0.02	0.94 ± 0.01	0.034a
Fasting Plasma Glucose (mg/dL)	155.53 ± 65.69	94.13 ± 9.05	<0.001a
Pl. Glucose 2 hour after OGTT (mg/dL)	277.98 ± 91.29	117.47 ± 17.26	<0.001a
HbA1c (%)	8.72 ± 2.17	5.65 ± 0.35	<0.001a
S. Creatinine (mg/dL)	1.02 ± 0.17	1.09 ± 0.16	0.071a
Total Cholesterol (mg/dL)	188.19 ± 30.99	Not done	
Triglyceride (mg/dL)	190.90 ± 68.68	Not done	
LDL-Cholesterol (mg/dL)	112.03 ± 22.34	Not done	
HDL-Cholesterol (mg/dL)	37.42 ± 2.88	Not done	
C-peptide (ng/mL)	8.97 ± 5.96	1.69 ± 0.66	<0.001a

BMI = Body mass index; ^aby Student's t-test; ^bby Chi-square Test

Table 2. Comparison of BMI, fasting plasma glucose, plasma glucose 2hrs after OGTT, and HbA1c between T2DM subjects with normal and high c-peptide

Variables	Normal C-Peptide (0.5-3.2 ng/ml) (n=19) Mean ± SD	High C-Peptide (>3.2 ng/ml) (n=41) Mean ± SD	p
BMI (Kg/M2)	25.77 ± 2.14	25.90 ± 2.33	0.838
Fasting Plasma Glucose (mg/dL)	124.21 ± 35.34	170.05 ± 71.55	0.011
Pl. Glucose 2 hour after OGTT (mg/dL)	234.95 ± 74.65	297.93 ± 92.17	0.012
HbA1c (%)	7.53 ± 1.90	9.26 ± 2.07	0.003

BMI = Body mass index; p-value by Student's t-test

Table 3. Correlations of c-peptide with other variables in T2DM subjects

Variables	r value	p value
Age (years)	0.068	0.607
BMI (Kg/M2)	0.337	0.008
Waist-to-Hip ratio	0.179	0.170
Serum creatinine (mg/dL)	-0.013	0.919
Fasting Plasma Glucose (mg/dl)	0.436	0.001
Pl. Glucose 2 hour after OGTT (mg/dL)	0.402	0.001
HbA1c (%)	0.367	0.004

by Pearson correlation

Table 2 shows the metabolic parameters of the T2DM subjects with normal and high c-peptide levels.

Correlations of serum c-peptide level with other variables in T2DM subjects are given in table 3. Serum c-peptide showed significant positive correlations with BMI, fasting plasma glucose, plasma glucose 2 hours after OGTT, and HbA1c.

Discussion

T2DM is one of the leading causes of morbidity and mortality globally. While all ethnic groups are affected, the prevalence of T2DM in South Asians is extremely high and is continuing to rise rapidly. Though the South Asians share the basic pathophysiological defects of T2DM observed in other ethnic groups, there is strong evidence to suggest that South Asians are more insulin resistant than Caucasians with the onset of diabetes at younger ages and with comparatively lower BMI. In addition to an increased propensity for insulin resistance, South Asians may also experience early declines in β -cell function compared with other ethnic groups and an early impairment in β -cell function could also be a key pathophysiological mechanism in T2DM development in South Asians⁽¹²⁾

There are different methods to measure β -cell secretory function. Acute insulin response (AIR) or AIRmax is the gold standard for assessment of β -cell function but difficult to perform in a clinical setting⁽¹³⁾. Assay of serum insulin as a measure of insulin secretion has several limitations as insulin has a half-life of 3-5 minutes and almost half of all insulin secreted by the pancreas is degraded by hepatic first-pass metabolism. So, peripheral insulin concentration reflects post-hepatic

insulin delivery rather than the actual secretory rates of insulin. C-peptide secreted in the equimolar amount of insulin has negligible extraction by the liver and constant peripheral clearance making its half-life longer than insulin. For these reasons, it is commonly used in preference to insulin measurement when assessing β -cell function in clinical practice⁽¹⁴⁾.

The current study assessed the endogenous insulin secretory capacity of the participants by measuring fasting serum c-peptide. None of the newly diagnosed T2DM subjects had a c-peptide level below the normal range. C-peptide was higher in new T2DM subjects in comparison to the non-diabetic otherwise healthy controls (8.97 ± 5.96 vs. 1.69 ± 0.66 ng/ml, $p < 0.001$). This indicates that the study subjects had no absolute reductions in insulin secretion; there was a compensatory increase in insulin secretion in many to overcome the insulin resistance which was not measured in this study. Only a few studies have evaluated c-peptide status in T2DM, particularly in newly diagnosed T2DM. Neha et al., in their study, found new T2DM subjects to have higher c-peptide levels than healthy controls⁽⁴⁾.

In this study, 41 (68%) of the T2DM subjects had elevated (>3.2 ng/ml) fasting c-peptide level and the rest 19 (32%) had normal level (0.5-3.2 ng/ml) of c-peptide. Higher level c-peptide indicates the potential good response to insulin sensitizers and other oral anti-diabetic drugs⁽¹⁴⁾. The mean HbA1c of the studied T2DM subjects was 8.72% (± 2.17). Kamrul-Hasan et al. found higher HbA1c ($10.69\% \pm 2.64$) in newly diagnosed Bangladeshi T2DM subjects in another study⁽¹⁵⁾. The HbA1c level of this study subjects indicates that their diabetes can be controlled by metformin plus another second line oral anti-diabetes drug without insulin use⁽¹⁴⁾. The high c-peptide group of the T2DM subjects had significantly higher levels of FPG, plasma

glucose 2 hours after OGTT, and HbA1c than the normal c-peptide group. In the initial stage of T2DM, when blood glucose rises there is a compensatory rise of insulin secretion in a proportionate manner to keep the blood glucose within the normal range. If exaggerated insulin secretion cannot overcome the insulin resistance, hyperglycemia occurs (2). Higher glycemic indices in high c-peptide T2DM subjects match the pathophysiology of T2DM. The c-peptide level was found to have significant positive correlations with FPG, plasma glucose 2 hours after OGTT, and HbA1c in T2DM subjects. Higher mean FPG and HbA1c in patients with a higher c-peptide level and positive correlations of c-peptide with FPG and HbA1c were also observed by Deep et al.(5). Abdullah et al. and Mariyam et al. also observed positive correlations between c-peptide level and FPG (6, 7).

Though no difference was observed in BMI between T2DM subjects with high c-peptide level and normal c-peptide level, a significant positive association was found between c-peptide and BMI in the studied T2DM subjects. Obesity is associated with insulin resistance and more insulin secretion is needed to overcome the

higher level of insulin resistance in obese subjects. Mariyam et al. had similar observations (7).

Conclusion

Insulin secretion estimated by measurement of fasting c-peptide was either normal or high in newly diagnosed T2DM subjects in the current study indicating a predominant role of insulin resistance in the etiology of T2DM in Bangladeshi subjects. Further research can explore the exact contribution of insulin resistance and insulin secretory defects in this area.

Limitations of the study:

Our sample size was small and randomization of sampling was not done. This was a single tertiary level hospital-centered study so the result may not reflect the whole community. Insulin resistance was not measured so the relative insulin deficiency could not be demonstrated.

Conflicts of interest:

None

References

- (1) American Diabetes Association. 2. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes-2019. *Diabetes Care*. 2019;42(Suppl. 1):S13–S28
- (2) DeFronzo RA. From the Triumvirate to the Ominous Octet: A New Paradigm for the Treatment of Type 2 Diabetes Mellitus. *Diabetes*. 2009;58(4):773-95.
- (3) Saisho Y. β -cell dysfunction: Its critical role in prevention and management of type 2 diabetes. *World Journal of Diabetes*. 2015;6(1):109-24.
- (4) Neha, Sharma A, Kaur J, Uppal V, Singh I. Correlation of Serum C-Peptide and Serum uric acid Levels with Glycated Hemoglobin in Patients of Type 2 Diabetes Mellitus. *International Journal of Clinical Biochemistry and Research*. 2016;3(3):330-4.
- (5) Deep HS, Singh BP, Singh SP. Evaluation of serum C-Peptide levels in type 2 diabetics in Punjabi population. *International Journal of Advances in Medicine*. 2017;4(4):1026-30.
- (6) Abdullah BB, Patil BS, Thaseen A. Significance of C Peptide on T2DM-A Study in the north karnataka population in india. *Al Ameen J Med Sci*. 2010;3(1):65-78.
- (7) Mariyam SB, Muthubevi SB, Vasantha SC. Serum C-Peptide level in obese and non-obese patients with type 2 diabetes mellitus. *J Evolution Med Dent Sci*. 2017;6(5):350-3.
- (8) Tajiri Y, Kimura M, Mimura K, Umeda F. Variation of fasting serum C-Peptide level after admission in Japanese patients with type 2 diabetes mellitus. *Diabetes Technology & Therapeutics*. 2009;11(9):593-9.
- (9) WHO expert consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *The Lancet*. 2004;363(9403):157-63.
- (10) The IDF consensus worldwide definition of metabolic syndrome. Guideline for definition of the metabolic syndrome. International Diabetes Federation. 2006.
- (11) World Health Organization: Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: Report of a WHO/IDF consultation. Geneva, Switzerland: World Health Organization. 2006.
- (12) Gujral UP, Pradeepa R, Weber MB, Narayan KM, Mohan V. Type 2 diabetes in South Asians: similarities and differences with white Caucasian and other populations. *Ann N Y Acad Sci*. 2013;1281(1):51-63.
- (13) Cobelli C, Toffolo GM, Man CD, Campioni M, Denti P, Caumo A, et al. Assessment of β -cell function in humans, simultaneously with insulin sensitivity and hepatic extraction, from intravenous and oral glucose tests. *Am J Physiol Endocrinol Metab*. 2007;293(1):E1-15.
- (14) Leighton E, Sainsbury CAR, Jones GC. A Practical Review of C-Peptide Testing in Diabetes. *Diabetes Ther*. 2017;8(3):475-87.

(15) Kamrul-Hasan ABM, Fariduddin M, Ghosh DK, Moinul-Islam, Atikur-Rahman M, Nusrat-Sultana, et al. Vitamin B12 is Found Sufficient in Newly Diagnosed Type 2 Diabetes in a Hospital Based Study. *Int J Diabetes Metab Disord.* 2016;1(1):1-5.