Original article

C-peptide and its correlation to parameters of insulin resistance and obesity in Type 2 diabetes

Dr. Suchanda Gadre[1], Dr. Ashish Bajaj[1], Dr. Sujay Patil[1], Dr. Sangita Sukumaran[2]

[1]Postgraduate student, Dept of Pharmacology, DY Patil University School of Medicine, Navi Mumbai,[2]Professor and Head of Department of Pharmacology, Terna Medical College, Navi Mumbai

Corresponding author : Dr. Suchanda Gadre

Abstract

Type 2 Diabetes Mellitus is well associated with insulin resistance. Many research findings indicate that c-peptide has an important biological activity in relation to diabetes mellitus and as a marker of pancreatic β-cell function. This study thus aims to prove the importance of c-peptide in diagnosis of type 2 Diabetes Mellitus

Materials and Methods: This is a Prospective study held at D.Y.Patil University School of Medicine Nerul, Navi Mumbai. Institutional Ethics Committee approval was taken before the start of the study. Detailed history, Physical parameters and BMI were noted in well piloted case record form. Mean ± SD and Pearson's correlation coefficient with p value <0.05 significant was done for association between c-peptide and laboratory parameters. Chi-square test was used to evaluate data between BMI and c-peptide.

Key words- C-peptide, HOMA IR, Type 2 Diabetes Mellitus

Introduction

The progress of metabolic syndrome continues with the onset of Type 2 diabetes mellitus which is now becoming a major concern all over the world with the rise of its increasing incidences. Type 2 diabetes mellitus is well associated with insulin resistance which is not only the major predictor of future development but also it is a therapeutic target.[1] Along with insulin, C-peptide was initially thought to be just a by-product of insulin production and biologically inert; however, research findings indicate that it does have important biological activity, especially in relation to diabetes mellitus.[3,4] C-peptide measurements have also been used to classify diabetes mellitus and as a marker of pancreatic β-cell function[1].C-peptide is produced by a series of enzymatic cleavages of the precursor molecules preproinsulin and proinsulin. Proinsulin is the precursor of insulin and C-peptide [5,6]. Thus C-peptide measurements represent a better alternative index of insulin secretion and residual β-cell function. Historically Insulin resistance was measured with an invasive test called euglycemic clamp test.(7) A much simpler way to estimate insulin sensitivity is called Homeostasis Model Assessment (HOMA) [7].It is simple mathematical model which can estimate individual's insulin sensitivity HOMA%S and beta cell function HOMA %B from simultaneous measurements of fasting insulin, plasma glucose or c-peptide. Thus HOMA proves to be a useful measure for insulin sensitivity and resistance and is a useful parameter for correlation between insulin resistance, c-peptide and fasting blood glucose levels with other pathological parameters. This study aims to prove the importance of c-peptide measurements in Type 2 diabetes mellitus and their correlation to parameters of insulin resistance and obesity.

Aims and Objectives

1.C-peptide and its correlation to insulin resistance.2.C-peptide and its correlation to BMI.3.C-peptide and its correlation to lipid profile

Materials and Method

This is a prospective study held at D.Y.Patil University School of Medicine Nerul, Navi Mumbai. Subjects were randomly screened from Medicine OPD of the hospital and those fulfilling the eligibility criteria were selected after signing written informed consent form. Subjects were invited into the study after detailed explanation about the study. From among the 200 patients screened, 81 were diabetic and 81 were non diabetic.Institutional Ethics Committee approval was taken before the start of the study. Detailed history of the patient was taken to note the duration of diabetes, whether the subject is on any antidiabetic medication, or any other medication like antidepressants, antipsychotics, antihistaminic, beta blockers that cause weight gain. Detailed family history, history of smoking, alcohol, physical exercise, and diet was taken. Also history of any other serious co-morbidity was noted. Physical parameters like waist circumference and hip circumference, weight and height of subjects was also measured. Weight was recorded to nearest 0.5 Kg and Height was recorded to nearest 0.5 cm. According to weight and height of subject BMI was calculated using the formula weight in kgs/height (m^2). [8]10 ml blood sample was taken from each subject after a period of overnight fasting of 12 hours and the following tests were assessed

1) Fasting blood glucose

2) Fasting C-peptide

3) Fasting Insulin levels

4) Lipid profile i.e. Total cholesterol, Triglycerides HDL, LDL, VLDL

Fasting blood glucose and lipid profile was tested in the pathology laboratory of D Y Patil University School of Medicine and fasting c-peptide and insulin level were assayed using the Elisa kit. The correlation between Insulin and c-peptide and fasting blood glucose level was assessed using HOMA IR (HOMA IR= FPI * FBG/22.5;

FPI=fasting Plasma Insulin, FBG = Fasting Blood Glucose)

Study eligibility criteria

Inclusion criteria

1) Subjects of either gender greater than 20 years of age.

2) Newly diagnosed cases of type 2 diabetes mellitus and not on any antidiabetic drugs.

3) Subjects willing to sign a written informed consent.

Exclusion Criteria

1) Subjects of Type 1 diabetes

2) Subjects on drugs causing weight gain like antipsychotics, antidepressants, beta blockers, antihistaminic, lithium, oral contraceptives 4) Subjects with renal impairment, hepatic impairment or any other serious co-morbidity.

5) Subject not willing to sign the written informed consent form.

Study duration- 1year

Sample size- 162 patients

Statistical analysis

Descriptive data were analysed using Mean ± SD. Association between c-peptide and laboratory parameters was done using Pearsons correlation coefficient and p value <0.05 was taken as significant.

Observations & Results

Out of 200 subjects screened, those who fulfilled the eligibility criteria were invited for the study and fasting blood glucose level, c-peptide level, fasting Insulin level, lipid profile was assessed in the pathology laboratory of D Y Patil University School of Medicine after an overnight fast of 12 hours. Following results were obtained which were then statistically analysed with Pearson's correlation coefficient

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

Table 1: Demographic data & Biochemical parameters

Parameters	Diabetics(81) Mean ± SD	Non Diabetics (81) Mean ± SD
AGE(years)	54.90 ± 11.59	43.49 ±16.17
MALES	40	37
FEMALES	41	44
BMI	26 ± 5	24 ± 4.48
W:H	0.93±0.05	0.91 ±0.05
FBS(mg/dl)	159.30 ± 67.84	93.71 ± 13.07
Total Cholesterol(mg/dl)	194.49 ± 53.50	171.44 ± 36.04
Triglycerides mg/dl	164.22 ±99.11	113.16 ± 71.87
HDL mg/dl	40.71 ±11.58	39.57 ± 10.20
LDL mg/dl	119.08 ± 47.78	106.20 ± 29.62
VLDL mg/dl	32.32 ± 19.96	2.59 ±14.37
INSULIN µIU/ml	11.05 ±9.90	10.25 ± 9.18
C-PEPTIDE(ng/ml)	1.87± 1.55	1.72 ± 2.28

Table 1 show the diabetic group had higher BMI, Fasting Blood Sugar and lipid profile compared to Non-diabetic group.

Table 2 Correlation of C-peptide and Insulin with lipid profile and fasting Blood Glucose levels in Diabetics

parameters	C-Peptide		Insulin	
	r	p	r	p
FBS	0.034	0.755(ns)	-0.090	0.409(ns)
Cholesterol	0.102	0.350(ns)	-0.020	0.854(ns)
TG	0.208	0.546(ns)	-0.032	0.769(ns)
HDL	0.052	0.634(ns)	0.093	0.394(ns)
LDL	-0.001	0.992(ns)	-0.073	0.504(ns)
VLDL	0.207	0.055(ns)	0.041	0.707(ns)
r= pearsons correlation coefficient p<0.0.5 significant, p=ns(not significant)				

No significant correlation was established between insulin and c- peptide with any of the parameters as the p value was <0.05. (Table 2)

Table 3: Correlation of C-peptide and Insulin with lipid profile and Fasting Blood Glucose levels Non-Diabetics

parameters	C-Peptide		Insulin	
	R	p	R	p
FBS	0.186	0.094(ns)	0.109	0.329(ns)
Cholesterol	0.070	0.532(ns)	0.008	0.943(ns)
TG	0.138	0.216(ns)	-0.028	0.802(ns)
HDL	0.293	0.007*	0.115	0.303(ns)
LDL	-0.083	0.458(ns)	0.009	0.936(ns)
VLDL	0.13	0.244(ns)	-0.028	0.802(ns)
*p <.05 significant, P=NS(Not significant) r=pearsons correlation coefficient				

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

No significant correlation was found between c-peptide and insulin levels with biochemical parameters but a positive correlation was established between c-peptide and HDL level in the non-diabetic group(p value= 0.007)

Table 4: Correlation of Insulin, c-peptide and lipid profile with HOMA IR

Parameters	Diabetics(81)		Non Diabetics(81)	
	HOMA IR			
	R	p	R	p
W:h	-0.0236	0.833	0.074	0.503
FBS	0.174	0.109	0.364	0.00005
Cholesterol	-0.005	0.963	-0.0026	0.0985
TG	0.038	0.728	0.119	0.280
HDL	0.102	0.350	0.215	0.049
LDL	-0.049	0.654	-0.413	0.194
VLDL	0.045	0.680	0.115	0.297
Insulin	0.922	<0.00001*	0.974	<0.00001*
C-peptide	0.197	0.069	0.481	<0.00001*

- *P <0.05 significant, r= pearsons correlation coefficient

Table 4 shows correlation of insulin, c-peptide and lipid profile with HOMA-IR.A significant positive correlation was found in diabetic and non-diabetic group between HOMA IR and fasting insulin levels (p< 0.00001). There was no significant correlation between HOMA IR and c-peptide levels (p value= 0.069) in the diabetic group. A positive correlation was established between HOMA IR and c-peptide (p value <0.00001) in the non diabetic group.

Table 5: Distribution according to the BMI

BMI	DIABETICS(n=81)	NON DIABETICS(n=81)
<25	42	47
>25	39	33

Table 5 shows that out of 81 subjects of either group 39 (48.14%) were obese (BMI >25) in the diabetic group and 42(55.55%) were non obese. In the non diabetic group 47 (58.02%) were non obese and 33(40.74%) were obese. Thus it shows that in diabetes the number of obese subjects were more in number than in non diabetic.

Table 6: Distribution according to c-peptide

Fasting C-peptide	Diabetics	Non Diabetics
0.1-0.5	09 (11.1%)	12 (14.81%)
0.6-0.9	12 (14.81%)	20 (24.69%)
1-2.9	48 (59.25%)	43 (53.08%)
3-6	11 (13.5%)	03 (3.70%)
>6	01 (1.2%)	03 (3.70%)

Table 6 shows the distribution of c-peptide levels among diabetics and non diabetics. Here it can be seen that c-peptide levels between 1-2.9 ng/ml was found in 53.08% of non diabetics and 59.25% of diabetics. C-peptide level of more than 6ng/ml was found in three subjects (3.70%) in non diabetic group and in one subject(1.2%) in diabetic group.

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

Table 7 BMI and Fasting C-Peptide Distribution in Diabetics

BMI	Fasting C-Peptide					Total
	0.1-0.5	0.6-0.9	1-2.9	3-6	>6	
<25	04	09	26	05	0	44
>25	04	04	22	06	01	37

P= 0.00

Table 7 shows that out of 81 diabetics 44 were non obese with BMI <25 and 37 were obese with BMI >25. Table also shows the significance of increasing BMI with increasing c-peptide levels.

In obese category six (16.21%) patients were having c-peptide level 3-6 ng/ml as compared to 5(11.36%) in non obese group.Same number of patients was seen with c-peptide level 0.1-0.5 ng/ml in both the group. C-peptide level of 1-2.9 ng/ml was observed in 26 (59.09%) non obese and 22(59.45%) in obese group Table 7 shows that the BMI values and the levels of fasting c-peptide (p=0.000) were highly associated. The correlation was found to be moderately positive (r=0.403) (p=0.000), indicating that as the BMI increases the fasting c-peptide levels increases.

Table 8 BMI and Fasting C-Peptide Distribution in non diabetics

BMI	Fasting C-Peptide					Total
	0.1-0.5	0.6-0.9	1-2.9	3-6	>6	
<25	08	13	22	01	01	45
>25	04	07	19	04	02	36

Table 8 shows out of total 81 non diabetics patients with BMI more than 25 was observed in 36(44.44%) patients. Out of 36 the c-peptide level 3-6ng/ml was observed in 4(11.11%) and c-peptide level more than >6 ng/ml was seen in only 02 patients (5.55%). Adequate c-peptide levels 1-2.9ng/ml was seen in 19 patients (52.77%). Only 4(11.11%) patients had levels less than 0.6ng/ml indicating poor insulin reserve.Table also shows that total 45(55.55%) patients from 81 were non obese i.e. BMI <25 and in them c-peptide was adequate in 22(48.88%), and only 1 patient were observed with c-peptide 3-6ng/ml and >6ng/ml group respectively. In non obese category 8(17.77%) patients had c-peptide level <0.6 ng/ml. The table shows that as the BMI level increases fasting c-peptide level also increases.

Discussion

Metabolic syndrome continues with the progress of Type 2 Diabetes mellitus. Insulin resistance is the major cause of Type 2 DM. Physical factors also contribute to the development of type 2 diabetes like obesity, diet and lack of exercise. In this study it is clearly evident that out of total 81 subjects from the diabetic group 48.14% are obese and the mean ± SD of the diabetic group for all lab parameter is more than the non diabetic group. Insulin resistance is not only the major predictor of the type 2 diabetes mellitus but is also the therapeutic target. Along with insulin, C-peptide is produced in equal amounts and is the best measure for endogenous insulin in patients with diabetes as stated by A.G.Jones et al in a study conducted in UK [15].Normal c-peptide levels between 1-2.9 ng/ml was found in 43(53.08%) in non diabetics and 48 (59.25%) in diabetics group. This study also proves the correlation of endogenous insulin and c-peptide was significant.A strong correlation between BMI and c-peptide can be seen with p value <0.05. This shows that as BMI increases c-peptide also increases. There were similar findings in a study conducted at a Bijapur hospital, North Karnataka [11]. Although no such significance was found in the non diabetic group but a strong

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

correlation was seen between c-peptide and insulin when calculated by HOMA IR in the non diabetic group which is also similar to the study conducted in Bijapur hospital, North Karnataka[11].

Limitation of this study was small sample size. Inclusion of type 1 diabetes in the study would have further helped in studying the correlation between type 1 diabetes and c-peptide. Further limitation of our study includes the case control study design and lack of nutritional status of participants as insulin levels are influenced by dietary factors.

Conclusion

C-peptide measurement in Type 2 diabetes mellitus can be a useful as it is produced in equal amounts with the endogenous insulin secretion. C-peptide levels can also be useful for differentiating between Type 1 and Type 2 diabetes mellitus. C-peptide measurements can be cost effective as compared to insulin measurements thus adding an extra beneficial point for patients who have to undergo wide variety of routine investigations for diagnosis or treatment of type 2 diabetes mellitus. Based on the data obtained from this study c-peptide proves a useful parameter for measurement in Type 2 diabetes mellitus.

References

1. Tricia A Bal MD; C-peptide: Roles in diabetes, insulinoma, and hypoglycaemia; Winter/Spring 2009 · www.siemens.com/diagnostics
2. Palmer JP, Fleming GA, Greenbaum CJ, et al. C-peptide is the appropriate outcome measure for type 1diabetes clinical trials to preserve beta-cell function: report of an ADA workshop, 21-22 October 2001
3. Pramanik, K. Ekberg, Z. Zhong et al., "C-peptide binding to human cell membranes: importance of Glu27," Biochemical and Biophysical Research Communications, vol. 284, no. 1, pp. 94–98, 2001.
4 E. Hills, N. Al-Rasheed, N. Al-Rasheed, G. B. Willars, and N. J. Brunskill, "C-peptide reverses TGF-β1-induced changes in renal proximal tubular cells: implications for treatment of diabetic nephropathy," American Journal of Physiology, vol. 296, no. 3, pp. F614–F621, 2009.
5 Palmer JP, Fleming GA, Greenbaum CJ, et al. C-peptide is the appropriate outcome measure for type 1 diabetes clinical trials to preserve beta-cell function: report of an ADA workshop, 21-22 October 2001. Diabetes mellitus 2004; 53(1):250-64.
6 Marques RG, Fontaine MJ, Rogers J. C-peptide: much more than a by product of insulin biosynthesis. Pancreas 2004; 29(3):231-8.
7 M. K. Garg, M. K. Dutta, and Namita Mahalle; Study of beta-cell function (by HOMA model) in metabolic syndrome; Indian J Endocrinol Metab. 2011 Jul; 15(Suppl1): S44–S49.
8 Vittal B G, Praveen G, Deepak P; A Study Of Body Mass Index In Healthy Individuals And Its Relationship With Fasting Blood Sugar; Journal of clinical and Diagnostic research ; 2010 ; Vol 4; Issue 6; 3421 – 3424
9 McAuley KA, Mann JI, Chase JG, Lotz TF, Shaw GM. Point: HOMA—Satisfactory for the Time Being. Diabetes Care. 2007; 30:2411–3
10 Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: Insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 2005; 28:412

11 Bilal Bin Abdullah *, Basanagouda S Patil and A. Thaseen; Significance of C – Peptide in Type 2 Diabetics - A Study in the North Karnataka Population of India; Al Ame en J Med Sci 2010; 3(1);65-78

12 Gillies CL, Abrams KR, Lambert PC, et al. Pharmacological and lifestyle interventions to prevent

13 Or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and metaanalysis. BMJ 2007; 334: 299.

14 Lyssenko V, Almgren P, Anevski D, et al. Predictors of and longitudinal changes in insulin sensitivity and secretion preceding onset of type 2 diabetes. Diabetes 2005; 54: 166-74.

15 Standl E. Importance of cell management in type 2 diabetes. Int J Clin Pract Suppl 2007 June; (153): 10 19.

16 A G Jones; and A T Hattersley; "The clinical utility of C-peptide measurement in the care of patients with diabetes" Diabet Med. 2013 Jul; 30(7): 803–817.

17 Wahren J, Kallas A, Sima AA. The clinical potential of C-peptide replacement in type 1 diabetes. Diabetes. 2012; 61:761–772. [PMC free article] [Pub Med]

18 Brandenburg D. History and diagnostic significance of C-peptide. Exp Diabetes Res. 2008; 2008:576862. [PMC free article] [Pub Med]

19 Nikolaus, M.; Daniel W. C-Peptide and atherogenesis: C-peptide as a mediator of lesion development in patients with type 2 Diabetes Mellitus.Exp. Diabetes Res., 2008, 2008, 385108

20 Shaheena Banu, Nasimudeen R. Jabir, C N Manjunath1, Shazi Shakil and Mohammad A. Kamal; C-Peptide and its Correlation to Parameters of Insulin Resistance in the Metabolic Syndrome; CNS & Neurological Disorders - Drug Targets, 2011; 10; 921-927

21 Shakti Aggarwal, Atul Goel and Anju Jain; Role of C-peptide in Identification of Patients Suspected of Having Latent Autoimmune diabetes in Adults (LADA) in North Indian Type 2 Diabetes mellitus Population; International Journal of Pharma and Bio Sciences; Vol.1;Issue-3;Jul-Sep.2010

22 Misra A, Misra R, Wijesuriya M, Banerjee D. The metabolic syndrome in South Asians: continuing escalation and possible solutions. Indian J Med Res. 2007; 125:345–54. [Pub Med]