Original Research Article

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Evaluation of serum c-peptide levels in type 2 diabetics in Punjabi population

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ABSTRACT

Background: Diabetes mellitus is a chronic metabolic and endocrine disorder characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both. It is a major cause of mortality and morbidity worldwide. Human insulin and cpeptide are synthesized as a single polypeptide chain known as Proinsulin in the pancreatic beta cells. Serum insulin measurement gives a wrong value of insulin secretion, because insulin after its secretion into the portal vein, passes through the liver where approximately 50% of the delivered insulin is extracted. The measurement of C-peptide, thus provides a better index of endogenous insulin production and pancreatic beta cell function than insulin measurements. **Methods:** The present study was conducted on 100 adult patients of type 2 diabetes mellitus presenting in OPD and emergency or admitted in Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar. Type 1 diabetic patients, pregnant females with diabetes, patients presenting with acute infections, septicaemia, patients with acute or chronic pancreatitis, patients with pancreatic carcinoma were excluded from the study. In this study C-Peptide levels were estimated by DRG C-peptide ELISA method.

Results: In our study, 38% patients had adequate insulin reserve (Normal C-peptide levels). Only 2% patients had poor insulin reserve (C-peptide levels below normal). 60% patients had c peptide levels more than normal, indicating insulin resistance. Increase in fasting c-peptide levels were associated with increased fasting plasma glucose (due to insulin resistance). A positive correlation exists in our study with r value of 0.523.

Conclusions: As majority of patients with elevated FBS and fasting c-peptide were obese, our study infers that obese are more insulin resistant than non-obese. Since c-peptide levels assess the endogenous insulin reserve, it will also be helpful to alter the treatment modality based on it. So, routine c-peptide testing should be done in patients with poor glycaemic control to modify treatment modality accordingly.

Keywords: C-peptide, Type 2 diabetes mellitus

INTRODUCTION

Diabetes mellitus is a chronic metabolic and endocrine disorder characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both. It is a major cause of mortality and morbidity worldwide. The incidence of this disorder is increasing worldwide. Human insulin and c-peptide are synthesized

as a single polypeptide chain known as proinsulin in the pancreatic islet by the beta cells. Proinsulin is cleaved proteolytically to form equimolar amounts of mature insulin and C-peptide and both are released in the portal vein. C peptide is a single peptide chain of 31 amino acids with molecular weight of 30200 g/mol. It is called as C-peptide because it connects the A and B chains of insulin in Proinsulin.²

The great interest in C-peptide is due to the limitations of the use of serum insulin as a measure of insulin secretion because insulin after its secretion into the portal vein, passes through the liver where approximately 50% of the delivered insulin is extracted.³ Within the physiologic range of insulin concentrations, there is variable fraction of hormone extracted by liver. Peripheral insulin concentration therefore is the post hepatic insulin delivery rather than the actually secreted insulin by the pancreatic beta cells.³

Before the development of C-peptide assays, evaluation of beta cell function in insulin treated patients was impossible as the insulin assay was unable to discriminate between secreted and injected insulin. Further, insulin measurements were disturbed more than C-peptide measurements because of the presence of insulin binding antibodies.⁴ The measurement of C-peptide, which is co-secreted with insulin from beta cells of pancreas, thus provides a better index of endogenous insulin production and pancreatic beta cell function than insulin measurements.⁴

With the advent of newer drugs to overcome insulin resistance it has become all the more important to know about the pathophysiology of diabetes, whether endogenous insulin secretion is normal and to know about insulin resistance. Keeping this perspective in mind, this study was conducted to assess the endogenous insulin secretory function in a randomized sample of patients with type 2 diabetes.

METHODS

The present study was conducted on 100 adult patients of Type 2 Diabetes Mellitus presenting in OPD and emergency or admitted in Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar. Informed consent was taken from all the subjects included in the study and the approval from hospital ethical committee was taken. Type 1 diabetic patients, pregnant females with diabetes, patients presenting with acute infections, septicemia, patients with acute or chronic pancreatitis, patients with pancreatic carcinoma were excluded from the study. Patients were assigned a diagnosis of diabetes mellitus (according to ADA criteria), if:

- HBA1C>6.5% or,
- fasting plasma glucose greater than 126 mg/dl (7.0mmol/l) or,
- 2-hr plasma glucose >=200mg/dL (11.1mmol/l) during an OGTT (75gm oral glucose) or,
- In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a plasma glucose >=200mg/dl (11.1mmol/l).

After taking informed consent of the patient, detailed history was taken. Complete general physical examination was done with due emphasis on anthropometry. BMI was calculated by dividing the

weight in Kg and the square of the height in meters. Patients having BMI 30 or more were taken as obese according to WHO criteria.

Following investigations were performed in each patient

- A. Hemogram (hemoglobin, total leukocyte count, differential leukocyte count, platelet count).
- B. Fasting blood sugar estimation by GOD-POD method (Trinder).⁶
- C. C-peptide levels by DRG C-peptide ELISA.⁷
- D. Glycosylated hemoglobin (HbA1c) estimation by Nyocard Reader (Jeppsson).⁸
- E. Fasting lipid profile
- Serum total cholesterol was estimated by enzymatic method as described by Allain.⁹
- Serum Triglyceride was estimated by GPO-trinder method as described by Trinder.¹⁰
- Serum high density lipoprotein (HDL) was estimated by Phosphotungstic Acid method as described by Brustein et al.¹¹
- Serum low density lipoprotein (LDL) was estimated by Friedwald equation given by Friedwald.¹²
- Serum very low density lipoprotein (VLDL) was estimated by Friedwald- equation given by Friedwald.¹²
- Dyslipidemia was diagnosed by The third report of the expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III, or ATP III) by National Cholesterol Education Program's (NCEP's) guidelines.

In this study, c peptide levels of less than 0.5 ng/ml were considered less than normal, between 0.5 and 3.2 ng/ml as normal and more than 3.2 ng/ml as more than normal.

After completion of the study, the data was analysed, compared and evaluated statistically. Chi square test for non-parametric data and student's t test for parametric data were applied. p value of less than 0.05 was considered significant and less than 0.001 as highly significant.

RESULTS

This study was conducted on 100 patients, 27-82 years old with mean age of 54 years, having sex distribution with 43 males and 57 females. Mean height, weight and BMI of the patients were 160.8cm, 71.03 kg and 27.74 kg/m² respectively. 46% patients were obese and remaining 54% were non-obese (Table 1).

Mean fasting blood sugar (FBS) of all patients in our study was 213.21 mg/dl. Mean HbA1c of all patients in our study was 10.17%. Mean C peptide levels in our study was 7.9 ng/ml. Dyslipidemia was present in 51% of all patients (Table 2).

Table 1: Demographic data of subjects in study.

Parameter	Value
Mean age	54 years
Sex distribution	Male: female $= 43:57$
Mean height	160.8 cm
Mean weight	71.03 kg
Mean BMI	27.74 kg/m^2
Obesity	46%

Table 2: Investigations of subjects in study.

Parameter	Value
Mean FBS	213.21 mg/dl
Mean HbA1c	10.17%
Mean C-peptide levels	7.9 ng/ml
Dyslipidemia (Number of patients)	51%

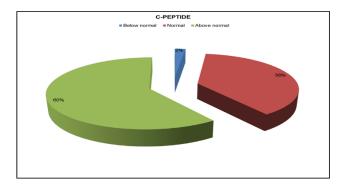


Figure 1: C-peptide levels in the study group.

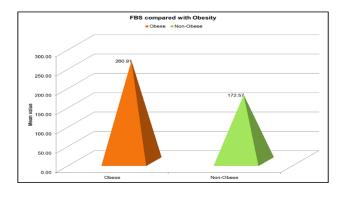


Figure 2: Mean fasting blood sugar levels in obese and non-obese patients.

C peptide levels were below normal (< 0.5 ng/ml) in 2%, normal (0.5 - 3.2 ng/ml) in 38% and above normal (> 3.2 ng/ml) in 60 % patients (Figure 1).

Mean fasting blood sugar (FBS) levels were much higher in obese patients (260.91±60.82 mg/dl) as compared to non-obese patients (172.57±47.29 mg/dl). This indirectly indicates that the insulin resistance plays an important role in causing elevated FBS level despite elevated c peptide levels in the obese patients (Figure 2).

Mean C peptide levels were much higher in obese (13.53±8.48) than non-obese patients (3.12±3.15). The increased levels of C- peptide along with increased FBS in obese patients indicate insulin resistance (Figure 3).

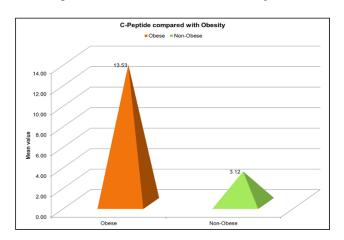


Figure 3: Mean C-peptide levels compared in obese and non-obese patients.

Mean fasting blood sugar (FBS±SD) were 143.50±2.12 mg/dl in below normal C-Peptide (< 0.5 ng/ml), 169.32±43.18 mg/dl in normal C-peptide (0.5 - 3.2 ng/ml) and 243.33±67.96 mg/dl in above normal C-peptide (>3.2 ng/ml) patients. Thus, mean FBS levels were higher in patients with higher than normal C-peptide levels which is highly significant statistically (p<0.001). This shows that increase in fasting c-peptide levels were associated with increased fasting plasma glucose due to insulin resistance. A positive correlation exists in our study with r value of 0.523 (Table 3).

Table 3: FBS compared with c-peptide levels.

C peptide levels	FBS (mg/dl) Mean±SD	P Value	r value	
C peptide below normal (< 0.5 ng/ml)	143.50±2.12			
C peptide normal (0.5 - 3.2 ng/ml)	169.32±43.18	0.000^{**}	0.523	
C peptide above normal (> 3.2 ng/ml)	243.33±67.96			
**II: -1-1 C:: f: (< 0.001)				

^{**}Highly Significant (p < 0.001)

Mean HbA1c was higher (11.18±2.37) in patients with c peptide above normal (> 3.2 ng/ml) and was statistically

highly significant (p<0.001). This study shows poor glycemic control in patients having insulin resistance

(high c peptide levels). This shows that increase in fasting c-peptide levels were associated with increased HbA1C levels due to insulin resistance. A positive correlation exists in our study with r value of 0.440 (Figure 4).

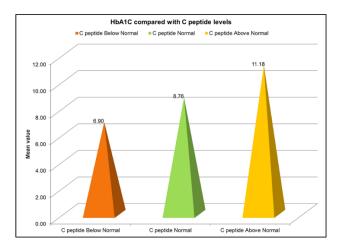


Figure 4: Mean Hba1c levels compared with c-peptide levels

Dyslipidemia (according to NCEP ATP III guidelines) was seen in 48% patients also having above normal c peptide levels (>3.2ng/ml) and was statistically highly significant (p<0.001) (Figure 5).

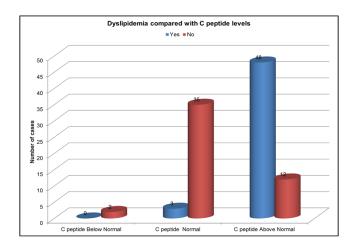


Figure 5: Dyslipidemia compared with c-peptide levels.

DISCUSSION

Diabetes Mellitus is the commonest endocrine disorder in the population. The clinical syndrome is due to either absolute or relative deficiency of insulin. It is a major cause of mortality and morbidity worldwide. Type 1 DM is caused by auto immune destruction of the beta cells of the pancreas, rendering it unable to synthesize and secrete insulin. Type 2 DM is a result of combination of insulin resistance and inadequate secretion of insulin.¹³

The great interest in C-peptide is due to the limitations of the use of serum insulin as a measure of insulin secretion because insulin after its secretion into the portal vein, passes through the liver where approximately 50% of the delivered insulin is extracted. Before the development of C-peptide assays, evaluation of beta cell function in insulin treated patients was impossible as the insulin assay was unable to discriminate between secreted and injected insulin. Further, insulin measurements were disturbed more than C-peptide measurements because of the presence of insulin binding antibodies. The measurement of C-peptide, which is co-secreted with insulin from beta cells of pancreas, thus provides a better index of endogenous insulin production and pancreatic beta cell function than insulin measurements.¹⁴

With the advent of newer drugs to overcome insulin resistance it has become all the more important to know about the pathophysiology of diabetes, whether endogenous insulin secretion is normal and to know about insulin resistance. Keeping this perspective in mind, this study was conducted to assess the endogenous insulin secretory function in a randomized sample of patients with type 2 diabetes.

In this study, the fasting c-peptide levels in the obese patients were increased compared to the non-obese individuals. The fasting plasma glucose levels were also elevated despite elevated c-peptide levels in the obese patients, proving the role of insulin resistance.

As majority of patients with elevated FBS and fasting c-peptide were obese, our study infers that obese are more insulin resistant than non-obese. Dyslipidemia was also more in patients having high c peptide levels.

Since c-peptide levels assess the endogenous insulin reserve, it will also be helpful to alter the treatment modality based on it. Those patients with adequate insulin reserve, will only require diet and exercise modalities of treatment to improve insulin sensitivity in addition to oral hypoglycemic insulin sensitizing drugs. And those patients with poor insulin reserve in the form of low c-peptide levels will require insulin therapy.

CONCLUSION

Since, measurement of C-peptide is a better index of endogenous insulin production and pancreatic beta cell function than insulin measurements, this study suggests routine c-peptide testing in patients with poor glycaemic control so that treatment modality can be modified based on c-peptide levels (endogenous insulin reserve).

Moreover, in clinical practice, emphasis should be given to educating patients about lifestyle modifications and to prevent obesity.

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Ethical approval: The study was approved by the

institutional ethics committee

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