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Original Research Article

A Study of Serum C-Peptide Level in Obese and Non-Obese Type 2 Diabetes Mellitus Patients at SMS Hospital, Jaipur

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Abstract

Background: Diabetes mellitus (DM) 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. Obesity is associated with an increased risk of developing insulin resistance, which is a risk factor for Type 2 Diabetes Mellitus. C-peptide has recently been shown to be a biologically active peptide which corrects vascular, neural and renal dysfunction in patients with DM. So we evaluated the serum C-peptide level in obese and Non-Obese Type 2 Diabetes Mellitus Patients in tertiary centre .at SMS Hospital, Jaipur.

Materials & Methods: After taking necessary permissions, a cross sectional study was conducted at Department of Biochemistry and Department of Endocrinology / Medicine, SMS Hospital, Jaipur. This study includes 100 obese patients suffering from type 2 diabetes aged 30-80 years compared with 100 non obese cases. Samples were analyzed for the measurement of serum glucose by Colorimetric method, C-peptide by chemiluminescence assay method and HbA1C measured by latex turbidimetric method.

Results: Results were analyzed statistically by Student's t-test and Pearson correlation coefficient test. C-peptide in Non-Obese patients was 3.62 ± 1.63 ng/ml and in obese patients was 8.71 ± 1.59 ng/ml. C-peptide levels were significantly high in obese patients. There was statistically highly significant positive correlation between serum c peptide levels with Fasting blood sugar and HbA1c in diabetic patients.

Conclusion: Measurement of C-peptide is a better index of endogenous insulin production and pancreatic beta cell function than insulin measurements; it will also be helpful to alter the treatment modality based on it. 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.

Keywords: Diabetes Mellitus (DM), Glycated haemoglobin(Hba1c), C Peptide.

Introduction

Diabetes mellitus(DM) is a chronic metabolic and endocrine disorder characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action or both. The incidence of this disorder is increasing worldwide. [1]

Diabetes Mellitus represents a significant global health problem. According to WHO August 2011, 346 million people worldwide have diabetes. [2] The incidence of Diabetes Mellitus is also increasing with the increase in unhealthy dietary habits, physical inactivity and sedentary lifestyle. [3]

The two broad categories of Diabetes Mellitus are designated Type1 Diabetes Mellitus(T1DM) and Type2 Diabetes Mellitus(T2DM). Type1 Diabetes Mellitus is the result of complete or near total insulin deficiency whereas Type2 Diabetes Mellitus is a heterogeneous group of disorders characterized by a variable degree of insulin resistance, impaired insulin secretion and increased glucose production. [4] Type 2 Diabetes Mellitus is a major health problem worldwide. India has the highest number of patients with known diabetes worldwide. [5]

60% - 80% of patients with Type 2 Diabetes Mellitus are obese. [6] Obesity is associated with an increased risk of developing insulin resistance, which is a risk factor for Type 2 Diabetes Mellitus. [7] Insulin resistance is characterized by decreased ability of insulin to act on peripheral tissues. Hence, insulin concentration is rather higher than that in those with normal glucose tolerance indicating that insulin resistance rather than insulin deficiency is the fundamental defect in obesity and Type 2 Diabetes Mellitus. Obesity itself can accelerate the progressive decline in beta cell function in patients with Type 2Diabetes Mellitus. [8]

Insulin level in blood may be assayed to monitor the amount of insulin secreted by the beta cells and to check for insulin resistance. [9] Assay of serum insulin as a measure of insulin secretion has several limitations. Recent evidence proves that C-peptide, a cleavage product released into the circulation during insulin synthesis can be used as an indicator of insulin secretion. C-peptide is a 31 amino-acid peptide that links the A chain and B chain in the proinsulin molecule. The physiology of C-peptide makes it appropriate for assessing insulin secretion. It is less susceptible to hepatic degradation with a half-life 2 - 5 times longer than that of insulin, is free from interference with insulin antibodies and allows discrimination of endogenous and exogenous sources of Insulin. [10]

C-peptide has recently been shown to be a biologically active peptide which corrects vascular, neural and renal dysfunction in patients with Type 1 Diabetes Mellitus (T1DM). A comparative study of basal serum C-peptide levels between obese and non-obese patients with Type2 Diabetes Mellitus helps us to compare the insulin secretion in the obese and non-obese patients as one C-peptide molecule is released into the circulation with the secretion of each insulin molecule. A high C-peptide level denotes insulin resistance and a low level denotes beta cell dysfunction

Similar studies in Type 2 Diabetes Mellitus(T2DM) patients are limited. So we evaluated the serum C-peptide level in obese and Non-Obese Type 2 Diabetes Mellitus Patients in tertiary centre at SMS Hospital, Jaipur to study the correlation between obesity and Type 2 DM.

Materials and Methods

After taking Necessary permission from the institute ethical committee, Research review Board and Department of endocrinology, the study was conducted at Central Lab, Department of Biochemistry and endocrinology OPD SMS Medical

College and hospital, Jaipur. This study was a hospital based comparative Cross sectional study and sampling for the study was done from period of August 2019 to November 2020. An informed written consent was obtained from the cases and controls. 100 obese patients aged 30-80 years were suffering from type 2 diabetes were taken as cases. Age Matched non obese Type 2 DM patients willing to participate in the study giving written consent were taken as controls.

Patients with the following condition: Type 1 DM, Gestational diabetes, Pancreatic carcinoma, Acute pancreatitis, Chronic pancreatitis and Septicemia were excluded.

Selection of subject was based on inclusion and exclusion criteria; matched controls and cases were included in the present study after obtaining informed consent. A proforma was used to record relevant information and patient's data. 5 mL of venous blood was collected in plain vacutainer, serum glucose was analyzed by Colorimetric method, C-peptide was analyzed by Chemiluminescence assay and 2 mL into EDTA containing vacutainer for Hba1c Assay by turbidimetry. Quantitative data analyzed in the form of mean with standard deviation, as & when required suitable test of significance used to infer data. Levels of statistical significance set at a P value<0.05.

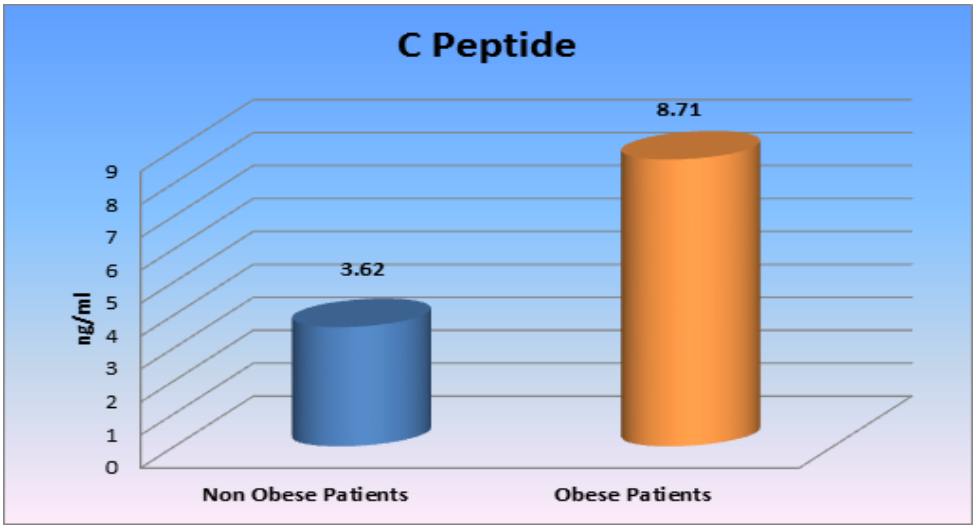
Results

The characteristics of the studied population, including age, the mean levels of blood sugar and HBA1c are shown in Table 1.

Table 1: Statistical Indices of the study

Test/ Parameters	Non-Obese Cases (n=50)	Obese Cases (n= 50)	P value
Age (years)	52.4 ± 13.66	54.5 ± 13.67	0.22(NS)
Fasting Blood Glucose (mg/dl)	183.90 ± 20.34	228.7 ± 33.36	<0.01 (S)
HBA1C (%)	7.80 ± 0.83	10.5 ± 1.70	<0.01 (S)
BMI (kg/m^2)	22.29 ± 1.50	30.58 ± 2.55	<0.01 (S)
C-peptide (ng/ml)	3.62 ± 1.63	8.71 ± 1.59	<0.01 (S)

Serum C peptide: C-peptide in Non-Obese patients was 3.62 ± 1.63 ng/ml and in obese patients was 8.71 ± 1.59 ng/ml. This difference has been found as statistically highly significant (p <0.001) as shown in Table 1 and Graph 1.



Graph 1: Comparison of Mean C peptide levels between non obese patients and Obese patients

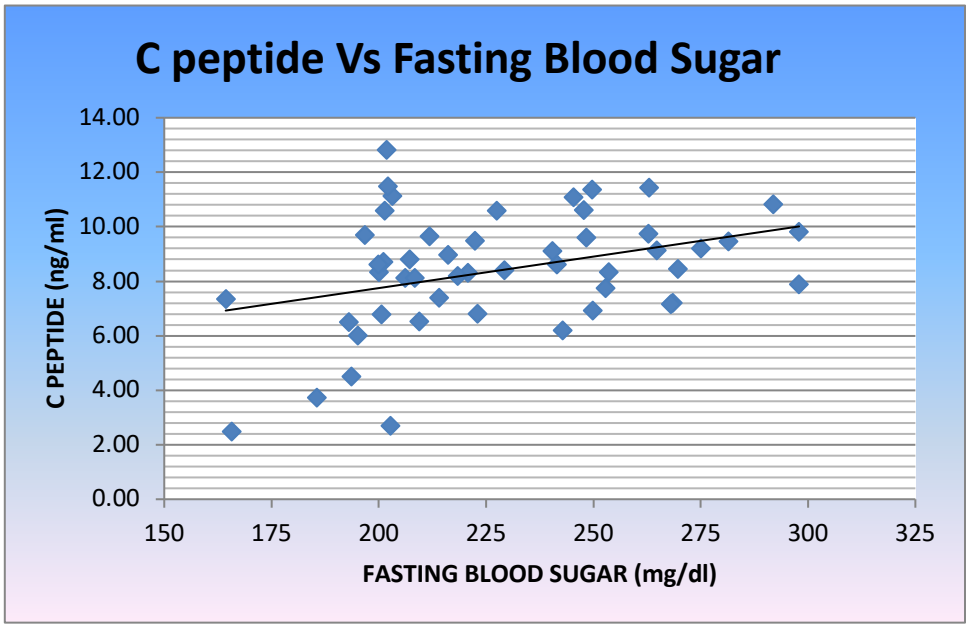
- **Statistical Correlations of C peptide levels with FBS and HbA1c:**

Table 2 : Statistical Correlations of C peptide levels with FBS and HbA1c

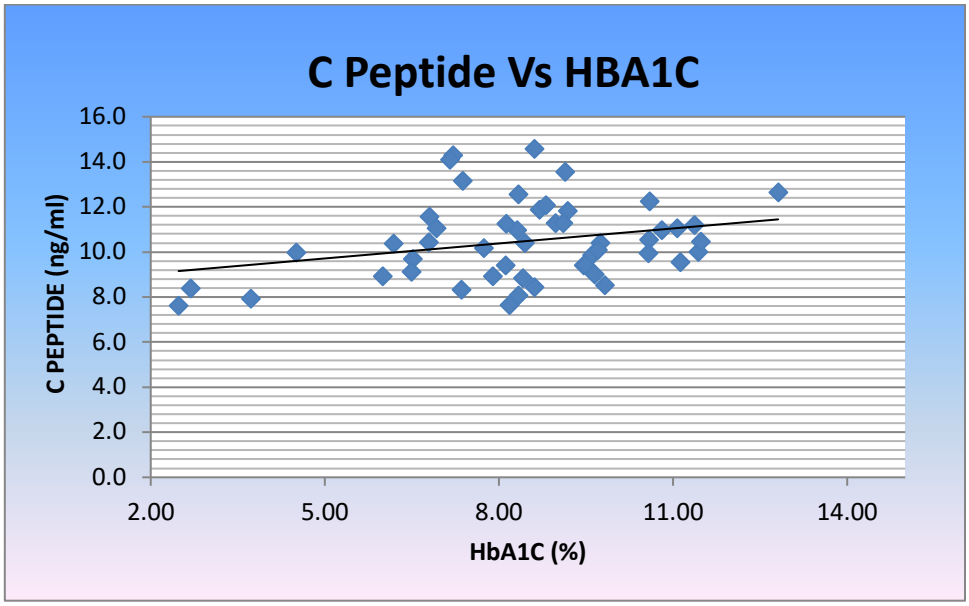
Parameter	P value	R Score	R^2	Significance
C-peptide vs. Fasting Blood Sugar	0.034728	0.2993	0.0896	S
C-peptide vs. HbA1C	0.046921	0.2824	0.0797	S

*Data analysis using Pearson correlation analysis

Above table shows correlation between C-peptide and Fasting blood sugar. It shows positive (r score = 0.2993) and significant (p value <0.05) (Graph 2) correlation between them. It also shows correlation between C-peptide and HbA1C which is positive (r score = 0.2824) and statistically significant (p value <0.05). (Graph 3)



Graph 2: Pearson correlation between C peptide and FBS



Graph 3: Pearson correlation between C peptide and HBA1c

Discussion

With the rising incidence of T2DM in younger patients and development of new therapies aimed at preserving insulin secretion, the measurement of insulin secretion is becoming increasingly relevant. Recent evidence proves that C-peptide, a cleavage product released into the circulation during insulin synthesis can be used as an indicator of insulin secretion.

In this study total 100 patients were included and divided into 2 groups obese and non-obese and we compared them according to different parameters. In our study mean age in non-obese and obese patients was 52.4 ± 13.66 years and 54.5 ± 13.67 years respectively. In this study, C-peptide in non-obese patients was 3.62 ± 1.63 ng/ml and in obese patients was 8.71 ± 1.59 ng/ml. it shows C-peptide level was significantly higher (p value <0.01) in obese patients in comparison to non-obese patients.

Similar results were found by Shamha Beegum Mariyam et al [11] in 2017 they observed difference in C-peptide value between obese and non-obese was statistically significant ($p < 0.05$). Mean C-peptide of the obese group was significantly higher than that of the non-obese group ($p < 0.05$).

Another study conducted by Hardeep Singh Deep et al [12] in 2017 found significant difference in mean C-peptide level. Mean C-peptide levels were much higher in obese (13.53±8.48) ng/ml than non-obese patients (3.12±3.15) ng/ml. The increased levels of C- peptide along with increased FBS in obese patients indicate insulin resistance.

Our finding is in accordance with those reported by Sung Tae Kim et al, which showed that basal C-peptide concentration is mainly influenced by BMI. [13] Similar results were reported by Michael H. Shanik et al concludes that obese patients are hyperinsulinaemic. [14]

Assay of fasting and post-glucose load of C-peptide levels in obese subjects by Enzo Bonora et al showed that the high C-peptide level seen in obesity is due to hyperinsulinaemia, which depends on pancreatic hypersecretion of insulin and C-peptide in the fasting state. [15] The findings are in accordance with the observation by Olefsky et al that insulin resistance and hyperinsulinaemia are associated with obesity and both abnormalities improve after weight loss, thus highlighting the importance of lifestyle modifications in the management of T2DM. [16]

When we saw correlation between C-peptide and Fasting blood sugar. It shows positive (r score = 0.2993) and significant (p value <0.05) correlation between them. Correlation between C-peptide and HbA1c showed positive (r score = 0.2824) significant (p value <0.05) relation between them.

A study conducted by Hardeep Singh Deep et al[12] in 2017 found Mean fasting blood sugar 143.50±2.12 mg/dl in below normal C-peptide (< 0.5 ng/ml) and 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, they found mean FBS levels higher in patients with higher-than-normal C-peptide levels which was highly significant (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 their study with r value of 0.523. This study also shows poor glycemic control (high HBA1c) 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 their study with r value of 0.440.

According to another study conducted by Bilal Bin Abdullah et al [17] majority of patients with elevated FBS and fasting C-peptide were obese. Their study infers that obese were more insulin resistant than non-obese. N Clare, Jones O et al [18] in their study observed that basal plasma glucose, insulin and C-peptide concentrations are higher in obese than non-obese patients. Relimpio F et al studied [19] relationship between C-peptide/blood sugar ratios in orally treated well controlled diabetics. In well controlled Non-Insulin Dependent Diabetes Mellitus patients not receiving exogenous insulin, both C-peptide levels and the C-peptide/blood sugar ratio have statistically significant relationships with clinical/biochemical variables presenting a well-known association with insulin resistance.

Possible mechanism of that may be persons who were overweight or obese at diagnosis exhibited slightly more residual beta-cell function. Although the significance was marginal, the proportions of patients with preserved C-peptide levels increased as BMI increased from underweight, to normal, to overweight or obese. In a multivariate-adjusted model, C-peptide preservation was more frequently evident in overweight or obese persons compared with underweight persons at the time of diagnosis of diabetes, consistent with the data of previous studies. [20-21] Although overweight or obese persons had slightly more residual beta-cell function, such patients developed hyperglycemia and diabetes triggered by the glucotoxicity and lipotoxicity associated with insulin resistance. [21,22]

Conclusion

Since, measurement of C-peptide is a better index of endogenous insulin production and pancreatic beta cell function than insulin measurements; 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. 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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