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Fasting c-peptide level and its correlation with body mass index and duration of diabetes in type 2 diabetes

Anand Sonwane[1], L. Romesh Sharma[2], Santa Naorem[3], Lallan Prasad[4], Salam Ranabir[5]

[1]Senior Resident,[2]Assistant Professor,[3]Professor, [4]Professor, [5]Associate Professor, Department of Medicine, Regional Institute of Medical Sciences, Imphal, Manipur, India
Corresponding author: Anand Sonwane

Abstract:- *Background: The determination of c-peptide provides an assessment of endogenous secretory reserves in patients with diabetes mellitus and is considered a more reliable indicator of insulin secretion than insulin itself. . The present study was undertaken to assess relationship between serum c-peptide level with patient characteristics and chronic complication of diabetes. Methods : Cross sectional observational study conducted in the Department of Medicine for 2 years. Inclusion criteria: Patients diagnosed with T2DM according to American Diabetes Association criteria or those already on glucose lowering agents. Exclusion criteria: Patients having renal failure (defined as serum creatinine > 1.5 mg/dl in males and 1.4mg/dl in females) and pregnancy. The sample size for the study was 100. Fasting c-peptide level was determined by a two site sandwich immunoassay using direct chemiluminescent technology. Plasma glucose (fasting and PP), serum creatinine and lipid profile was estimated. Statistical analysis: Analysis of variance (ANOVA) was used to find the significance of study parameters between 3 or more groups of patients. Chi – square / Fisher exact test was used to find the significance of study parameters on categorical scale between 2 or more groups. Results: In the present of 100 type 2 diabetics, the mean age of the patients was 58.04±12.5 years. The mean BMI was 22.58±3.38 kg/m2. The mean waist circumference was 88.82±6.78cm. As the duration of diabetes increases the fasting c-peptide levels goes down and with increase in body mass index there is corresponding increase in fasting c-peptide level. There was no association between fasting c-peptide levels and chronic complications of diabetes. Conclusion: Decline in c-peptide levels with longer duration of diabetes and lower BMI indicates these patients may require insulin therapy for better glycemic control. And the residual functioning beta cell mass can be assesed with c-peptide levels.*

Keywords: *Body mass index, C peptide, Duration of diabetes, Diabetes Mellitus*

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I. Introduction

The determination of c-peptide provides an assessment of endogenous secretory reserves in patients with diabetes mellitus and is considered a more reliable indicator of insulin secretion than insulin itself.[1] As it gives an idea about the functional beta cell mass, it may help to decide the nature of treatment, like OHA or insulin, in T2DM.[2] Some studies have shown correlation between c-peptide levels with chronic complications of diabetes.[3] Patients with low c-peptide levels receiving insulin had better clinical outcomes. Those with normal to high levels and receiving insulin had worse clinical outcomes suggesting that phenotype targeted insulin therapy may be important.[4] There are very few studies done on c-peptide in Indian type 2 diabetics.[1,5] The present study was undertaken to assess relationship between serum c-peptide level with patient characteristics and chronic complication of diabetes.

II. Methods

This was a cross sectional observational study conducted in the Department of Medicine in a teaching institute. The study duration was 2 years from October 2013 to septmber 2015, and it was conducted in patients attending Endocrine Clinic and patients admitted in medicine wards.

Inclusion criteria: Patients diagnosed with T2DM according to American Diabetes Association criteria[6,7] or those already on glucose lowering agents (oral or injectables)

Exclusion criteria: Patients having renal failure (defined as serum creatinine > 1.5 mg/dl in males and 1.4mg/dl in females) and pregnancy.

The sample size for the study was 100.

The fasting c-peptide level was determined by using the ADVIA Centaur XP Immunoassay Systems, Siemens Medical Solutions, USA, Inc. The assay is a two site sandwich immunoassay using direct chemiluminescent

technology which uses constant amount of two antibodies. The normal cut-off level of the assay was 0.81-3.85ngm/ml.

Plasma glucose was estimated using glucose oxidase method using GLUC-PAP manufactured by Randox Laboratories Limited, 55 Diamond Road, Crumlin, County Antrim, BT29 4QY, United Kingdom.

Serum creatinine ….(Manufatured by RANDOX laboratories UK).

Lipid profile was estimated by enzymatic method using Vitros chemistry, Ortholand Diagnostics Inc, Rochester, NY, USA.

Statistical analysis: Descriptive and inferential statistical analysis is carried out in the present study. Results on the continuous measurements are presented on mean±SD and results on categorical measurements are presented in numbers (%). Significance is assessed at 5% level. Analysis of variance (ANOVA) was used to find the significance of study parameters between 3 or more groups of patients. Chi – square / Fisher exact test was used to find the significance of study parameters on categorical scale between 2 or more groups.

III. Results

In the present of 100 type 2 diabetics, the mean age of the patients was 58.04±12.5 years. The mean BMI was 22.58±3.38 kg/m2. The maximum numbers of patients were having BMI 18-23 kg/m2. The mean waist circumference was 88.82±6.78cm.

Table 1: Association of duration of diabetes mellitus with fasting C-peptide levels

Duration of diabetes	Fasting C-peptide levels			Total
	<0.81 ngm/ml	0.81 to 3.85 ngm/ml	>3.85 ngm/ml	
0	6(8.6%)	2(7.1%)	0(0%)	8(8%)
1-2	12(17.1%)	2(7.1%)	2(100%)	16(16%)
3-5	10(14.3%)	16(57.1%)	0(0%)	26(26%)
6-10	34(48.6%)	6(21.4%)	0(0%)	40(40%)
11-15	2(2.9%)	2(7.1%)	0(0%)	4(4%)
16-20	2(2.9%)	0(0%)	0(0%)	2(2%)
>20	4(5.7%)	0(0%)	0(0%)	4(4%)
Total	70(100%)	28(100%)	2(100%)	100(100%)

P=0.001**

Analysis done using Fisher Exact test

Table 2: Association of BMI with fasting C-peptide levels

BMI (kg/m^2)	Fasting C-peptide levels			Total
	<0.81 ngm/ml	0.81 to 3.85 ngm/ml	>3.85 ngm/ml	
<18	6(8.6%)	0(0%)	0(0%)	6(6%)
18-23	44(62.9%)	12(42.9%)	2(100%)	58(58%)
23.1-28	16(22.9%)	12(42.9%)	0(0%)	28(28%)
28.1-33	2(2.9%)	4(14.3%)	0(0%)	6(6%)
>33.1	2(2.9%)	0(0%)	0(0%)	2(2%)
Total	70(100%)	28(100%)	2(100%)	100(100%)

P=0.062. Analysis done using Fisher Exact test

Table 3: Association of plasma glucose with fasting C-peptide levels

Variables	Fasting C-peptide levels			Total (n=100)	P value
	<0.81 ngm/ml (n=70)	0.81 to 3.85 ngm/ml (n=28)	>3.85 ngm/ml (n=2)		
Fasting BG (mg/dl)					
• <100	0(0%)	0(0%)	0(0%)	0(0%)	
• 100-126	8(11.4%)	2(7.1%)	0(0%)	10(10%)	0.773
• >126	62(88.6%)	26(92.9%)	2(100%)	90(90%)	
Post-prandial BG (mg/dl)					
• <140	0(0%)	0(0%)	0(0%)	0(0%)	
• 140-200	22(31.4%)	12(42.9%)	0(0%)	34(34%)	0.375
• >200	48(68.6%)	16(57.1%)	2(100%)	66(66%)	

BG- plasma glucose. Analysis done by using ANOVA method.

The above figure shows variations of HbA1c levels with respect to fasting c-peptide levels.

In the above figure we've shown the correlation of fasting c-peptide levels and plasma triglyceride levels.

IV. Discussion

In the present study of 100 type 2 diabetic patients evaluating c-peptide, among the patients with fasting c-peptide less than <0.81, there were fewer patients with BMI>23. Possible explanation finding maybe, the obesity is associated with increased insulin resistance so to overcome this insulin resistance there is more insulin secretion leading to increased c-peptide level. Similar findings have also been reported by other studies [1,8-10] Thunander M et al[11] states that c-peptide at diagnosis was increased with increasing BMI level and also with age within each BMI group. A study conducted by Nakayama H et al[12] also states that there is positive correlation between BMI and increment in c-peptide levels (CPR) post-glucagon stimulation. Despite showing this initial high CPR response obese subjects showed a rapid decline in B-cell function. Significant contributors to the decline rate of CPR were the BMI and fasting plasma glucose levels.

Our study also demonstrated that as the duration of diabetes increases the fasting c-peptide level decreases, which is statistically significant ($p<0.001$). As the duration of diabetes increases there is gradual loss of beta cell function which leads to decreased c-peptide levels. The decline in beta-cell dysfunction in type 2 diabetes was most probably caused by progressive loss of beta cell mass. Similar results are reported by other authors.[5,13] Chowta MN et al[1] reported that there is inverse correlation between duration of diabetes and fasting c-peptide levels. Zangeneh et al[14] states that insulin secretion decreases over time in many patients with type 2 diabetes mellitus. Although the decrease in insulin secretion over time is characteristic of type 2 diabetes mellitus, it is not evitable.

Histological studies of the pancreas from subjects with long standing type 2 diabetes had showed disruptions of islet structure and a marked reduction in beta-cell numbers. Regulation of beta cell mass involves a balance between beta-cell replication and apoptosis. However the beta cell loss by apoptosis appears to play a major role in the progression of the disease.[14]

A study conducted by Shim et al[13] also states that fasting c-peptide levels decreases with increase in duration of diabetes and fasting glucose, postprandial glucose and HbA1c levels were increased with the increase in duration of diabetes. Glucotoxicity caused by elevated plasma glucose levels has been 111implicated as a primary cause of beta cell dysfunction. Increased glucose levels activate the hexosamine pathway and contribute to the excess generation of reactive oxygen species, resulting in inhibition of insulin gene transcription and insulin secretion.[15] Lower levels of c-peptide and decreased beta cell function have been linked to greater levels of glucose variability and glucose variability is known tobe associated with increased complications and mortality in patients with diabetes.

Total cholesterol, LDL-C, triglycerides, and Apo- B were significantly higher in patients with high c-peptide levels than in patients with low c-peptide levels.[10]

It has been shown that the accumulated free fatty acids generated by the hydrolysis of TGs in the islets can decrease an elevation in nitric oxide production, inducing B-cell apoptosis.[15]

In our study we found that diabetic retinopathy was seen in 30% of the population and neuropathy in 4% of population. Nakayama et al[12] in their study said that there is inverse correlation between fasting c-peptide level and diabetic retinopathy along with HbA1c. Another study by Santos et al[16] said that diabetic retinopathy is independently associated with duration of diabetes and glycated hemoglobin. In our study we didn't find any significant association with other comorbid illnesses as well as albuminuria.

Study conducted by Chowta et al[1] also states that serum c-peptide levels were negatively correlated with creatinine clearance, urine albumin excretion and urine albumin creatinine ratio. Yoon HJ et al[10] stated that those with higher post glucagon increment c-peptide had a lower prevalence of retinopathy. Low basal and stimulated c-peptide levels were associated with a high prevalence of diabetic retinopathy and nephropathy. Low c-peptide levels were associated with the progression of diabetic microangiopathy such as retinopathy and nephropathy. C-peptide has been shown to be associated with autonomic nerve function in type 2 DM. Basal c-peptide levels was significantly associated with diabetic retinopathy and nephropathy but not with neuropathy [10]

C-peptide may exert direct effect on the glomerular handling of albumin. C-peptide has the capacity to stimulate both renal Na-K ATPase and Enos (endothelial nitric oxide synthase). C-peptide can influence glomerular membrane permeability and transport as well as renal blood flow. Patients with low serum c-peptide level may have increased risk of microalbuminuria.[1]

V. Conclusion

In the study conducted by us, we found that the fasting c-peptide levels increases with increasing body mass index and decreases with increasing duration of diabetes. We found that there is no correlations of fasting c-peptide levels and the complications associated with diabetes.

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