A Study on Evaluation of Correlation between C-peptide, HbA1c and BMI in Type -2 Diabetes Mellitus Patients

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Abstract

Background: Type 2 diabetes mellitus is a significant health issue throughout the world particularly in South-East Asia due to its complications, such as those related to metabolism and the cardiovascular system. Type 2 DM is characterized by insulin resistance and a relative insulin deficiency. A measure of the pancreas' ability to secrete endogenous insulin is the serum C-peptide concentration. Patients with Type 2 DM and elevated BMI have higher levels of HbA1c and C-peptide. The aim of the study was to evaluate the correlation between C-peptide, HbA1c and BMI in T2 DM patients.

Materials and methods: This cross sectional comparative study was conducted in the Department of Biochemistry and the Department of Endocrinology, Chattogram medical college hospital from 1st July 2018 to 30th June 2019. A total of 150 study populations were enrolled, of which 50 healthy control subjects (Group B) and 100 T2 DM patients (Group A) that met the enrollment criteria. Data were collected by using a pre tested structured questionnaire containing all the variables of interest. The variables studied included age, sex, height, weight, BMI, plasma glucose, C-peptide, HbA1c.

Results: The average BMI of the cases in this study was 26.75 kg/m^2, which was higher than the mean BMI of the controls (23.42 kg/m^2). The mean HbA1c of group A (7.80%) was significantly raised than group B (5.17%). The mean C-peptide levels in group A was significantly higher than those in group B, 1.67 mmol/l and 0.55 mmol/l, respectively. About 97% of the participants in Group A exhibited elevated serum C-peptide levels, compared to 30% of the subjects in Group B.

Conclusion: In contrast to glycemic state, C-peptide appears to be a better indicator of endogenous insulin production and/or insulin resistance. These findings provide support to the notion that raising serum C-peptide and HbA1c levels can aid in the detection and management of diabetes mellitus, particularly when combined with oral hypoglycemic medications.

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Introduction

Type-2 diabetes mellitus is a disorder of metabolism characterized by chronic hyperglycemia and hyperlipidemia and other complications. It may be due to deficiency or defect of functions of insulin. The incidence of DM is increasing in the last few years in this subcontinent including Bangladesh which is about 12.5% and prevalence is 2.4% in rural and 11.6% in urban population.[1] Data showed that in 2018, an estimated 422 million adults are living with diabetes in the world. About 1.5 million deaths was occurred in 2016 due to DM. Although not suffered from DM higher than optimal blood glucose caused an additional 2.2 million death, due to increase the risks of cardiovascular and others diseases.[2]

The main pathology of Type 2 DM isinsulin resistance with relative insulin deficiency.[3,4] Proinsulin split into C-peptide (Connecting peptide) and insulin before it releasing from pancreatic beta cell. C-peptide can be estimated in place of insulin to measure the endogenous insulin secreting capacity of pancreatic β–cells. Insulin is secreted as proinsulin which has A chain and B chain and connected by connecting peptide or C-peptide, is a short amino acid polypeptide. It is produced in equimolar amounts to endogenous insulin but is excreted at a more constant rate over a- longer time.[5,6] C-peptide is a widely used to measure of B cells functions. There are some limitations of the use of serum insulin as measure of insulin secretion, so the great interest in C-peptide measurement. Insulin after secretion into the portal vein, pass through the liver where approximately 50% of the secreted insulin are under goes first pass metabolism. So peripheral insulin concentrations are less than the actually secreted insulin by the pancreatic beta cells.[7,8] It is unable to discriminate between secreted and injected insulin as they are structurally same. So evaluation of beta cells function in insulin treated

patients is not possible with insulin assay. But C-peptide is not altered by liver and its estimation can determine the actual endogenous insulin secretion accurately and discriminate injected insulin.[9,10]

HbA1c or glycated hemoglobin is produced in patients with persistence hyperglycemia by nonenzymatic glycosylation of hemoglobin. HbA1c represent the integrated value of glucose over the preceding 6-8 weeks and providing additional criterion for assessing glucose control. In health it is about 4-6%.[11]

HbA1c act as indicator for estimation of the mean blood glucose level and also predicts the risk of complication of DM patients. It may be suggested for diagnostic criteria for to detect more diabetic and pre diabetic cases than fasting blood glucose or OGTT.[12]

Accumulation of excess adipose tissue is known as obesity. However, in the presence of nutritional abundance and sedentary life style and importantly influenced by genetic factors and this system increase adipose energy store and adverse health effects. Insulin resistance or DM, coronary heart diseases and hyperlipidemia are the major adverse effects of obesity.[13] The most widely used tools to gauge the obesity is body mass index (BMI), which is measured by weight in kg and height in meter square (kg/ m^2).[14]

Estimation of C- peptide has more advantage over insulin. The fasting C-peptide levels are useful intype 2 diabetic patients with poor glycemic controlto assess the endogenous insulin reserve. So, routine C-peptide testing might be done in patients with poor glycemic control treated with oral hypoglycemic agents to modify treatment modality accordingly. The aim of the study was to evaluate the correlation between C-peptide, HbA1c and BMI in T2 DM patients.

Materials and methods

This cross sectional comparative study was conducted in the Department of Biochemistry and the Department of Endocrinology Chittagong Medical College Hospital (CMCH) from 1st July 2018 to 30th June 2019. A total of 150 study populations were enrolled, of which 50 healthy control subjects (Group B) and 100 Type 2 DM patients (Group A) met the inclusion and exclusion requirements. Diabetes patients with oral hypoglycemic agents & ages 30 to 70 years were included. Patients with insulin-dependent diabetes, patients with GDM, acute and chronic pancreatitis, and acute infections were excluded. Permission for the study was taken from the concerned departments and Ethical Review Committee of Chittagong Medical College, Chattogram. All the patients included in this study was informed and explained properly about the nature and purpose of the study.

Data were collected by using a pre tested structured questionnaire containing all the variables of interest. The variables were studied age, sex, height, weight, BMI,plasma glucose, C-peptide, HbA1c. Serum C- peptide was measured by Chemiluminescence assay, HbA1c by HPLC and plasma glucose by enzymatic colorimetric test, GOD-POD method.

The data was analyzed by computer based software IBM-SPSS V 20.0. All the data were presented by mean ± SD and percentage. Confident level was fixed at 95% and p value of 0.05% or less was considered significant. Student's t-test for quantitative or continuous variable, chi-square test for categorical variables was done where applicable.

Results

The study was conducted to evaluate the correlation between C-peptide, HbA1c and BMI with T2DM patient.

Table I Distribution of age among the study groups- (With t-test significance)

	Study Group	n	Mean	SD	Significance
Age (Years)	Group A (Cases)	100	38.23	13.22	p= 0.001
	Group B (Control)	50	31.66	4.62	Highly significant

Table shows that the mean age (38 years) is significantly higher in cases than that of control.

Table II Distribution of BMI status among the study groups (With Chi square significance)

BMI status	Group A		Group B		
	n	%	n	%	
Normal (18.5-22.9 kg/m2)	42	42	39	78	
Obese (>25.0 kg/m2)	58	58	11	22	χ^2 value = 17.39, p < 0.001. Highly significant

Table III Distribution of serum HbA1c in study groups (With t- test significance)

	Study group	Mean	SD	Sign.
HbA1c (Normal-<5.7%)	Group A	7.80	2.14	p < 0.001
	Group B	5.17	0.27	Highly significance

Table shows that mean HbA1c was significantly higher in cases (7.80 %) than that of control (5.17%).

Table IV Distribution of serum HA1c status among the study groups (With Chi- square χ^2 significance), (With number and present distribution)

HbA1c status	Group A		Group B	
	n	%	n	%
Normal (< 5.7%)	18	18	49	98
Increased (5.7- 10%)	70	70	1	2
Increased (> 10%)	12	12	0	0
	χ^2 value=86.325		p< 0.001(highly sign)	

Table shows that about 82% cases had increased HbA1c than that of control, 2%, which is statically significance.

Table V Distribution of serum C-peptide among the study groups (With t- test significance)

	Study Group	Mean	SD	Significance
Serum C-peptide (0.3-0.6nmol/L)	Group A	1.67	0.69	p<0.001
	Group B	0.55	0.17	Very highly significance

Table shows that mean C-peptide was significantly higher in cases (1.67 ± 0.69) than that of control (0.55± 0.17)

Table VI Distribution of serum C-peptide according to BMI among the cases (Group A)-(With t- test significance)

	BMI Group	n	Mean	SD	Sign.
Serum C-peptide (nmol/L)	Normal	42	1.2	0.32	p < 0.0001
	Increased	58	2.00	0.69	Very highly significance

Table shows that mean serum C-peptide was significantly higher in diabetic cases (2.00 nmol/l) with increased BMI than in those with normal BMI (1.2 nmol/L).

Discussion

This study was conducted in the Department of Biochemistry and Department of Endocrinology in Chittagong Medical College. A total of 150 volunteers were included in the study; 50 healthy individuals were included in the control group (Group B), while 100 T2DM patients receiving oral hypoglycemic medication were in the case group. In this study mean age in group A (38 years) was higher than group B (34 years).

The mean BMI of the cases in this study was 26.75 kg/m^2, which was higher than the mean BMI of the controls (23.42 kg/m^2) and this was statistically significant (p = 0.001). Additionally, it was also observed that percentage of high BMI were more in group A (58%) than group B (22%).

Regarding HbA1c, mean HbA1c was significantly higher in group A (7.80%) than in group B (5.17%). It was also observed that Hb A1c was increased in approximately 82% subject in group A, whereas in group B ,it was only 2%, which was similar to others study.[14,15,16]

Mean C-peptide, the most significant variable in this investigation, was substantially higher in group A than in group B, 1.67 mmol/l and 0.55 mmol/l, respectively. About 97% of the participants in Group A had elevated serum C-peptide levels, compared to 30% of the subjects in Group B, which was statistically significant, p<0.001. This results was consistent with the similar study, Deep HS et al and Bilal BA et al.[17, 18]

When compared to T2 DM participants with increased BMI than that of T2 DM with normal BMI, the mean serum C-peptide levels were significantly higher, 2.00 nmol/L and 1.21 nmol/L, respectively, with a p value of < 0.0001.A similar result was observed by the study done by Bilal et al.[18]

In present study Pearson's correlation coefficient (r) showed that there was a positive correlation between BMI and C-peptide inT2 DM group, r = +0.71, p = 0.001. A similar result was observed in other study was done by Park SW et al. The increased level of serum C-peptide in T2 DM subjects with raised BMI indicate insulin resistance.[19]

In this study a weak positive correlation was observed between serum C-peptide and HbA1c in T2 DM subjects (r = +0.17), however it was not statistically significant, p > 0.05.

In addition, a significant positive correlation between HbA1c and BMI was revealed (r = +0.61, p = 0.001) and a similar result was observed in a study done by Jhone's O et.al. Obesity plays a central role in the pathophysiology of both T2 DM and its macrovascular complication.[20]

Limitation

- Small sample size and a purposive sampling method.
- Causality cannot be derived from a cross-sectional study because it is an observational study.

Conclusion

This study demonstrated a significant association between T2 DM and HbA1c levels. The mean C-peptide was significantly higher in the group of diabetes individuals with elevated BMI compared to those with normal BMI. There was a positive correlation between C-peptide and BMI. HbA1c and BMI had a positive correlation as well. C-peptide seems to be more of an indicator of endogenous insulin secretion and or insulin resistance rather than glycemic status. In T2DM with increased BMI, the mean HbA1c was higher, which is a sign of poor glycemic control in DM patients who are obese. These observations support the agreement that increasing serum C-peptide and HbA1c can be useful in diagnosis and treatment of the diabetes mellitus.

Recommendation

- Studies with large sample size are required in this field to further validate these findings and ascertain whether controlling serum C-peptide concentration affects prognosis.
- Informing the general public on the value of exercise and weight management can help to prevent insulin resistance and, ultimately, the onset of type 2 diabetes mellitus.

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Contribution of authors

MKH- Conception, design, acquisition of data, manuscript writing and final approval.

MMU- Conception, design, acquisition of data, manuscript writing and final approval.

MHI- Interpretation of data, critical revision and final approval.

Disclosure

All the authors declared no conflict of interest.

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