Association of Serum C-Peptide with the Components of Metabolic Syndrome among Non Diabetic Obese

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Abstract

Background : Obesity is a major health concern and is associated with metabolic syndrome that increases the risk for cardiovascular disease and diabetes mellitus. C-peptide or connecting peptide, is a short polypeptide that connects A-chain of insulin to its B-chain in the proinsulin molecule. In different studies it was found that C-peptide level are associated with Metabolic Syndrome and its complication. C-peptide is also reported to be more reliable than insulin as a measure of endogenous insulin secretion, insulin resistance and pancreatic beta cell function. The aim of the study is to observe the association of C-peptide levels with the components of metabolic syndrome in non diabetic obese subjects.

Materials and methods : This was a hospital based cross-sectional study comprising hundred non diabetic apparently healthy obese subjects age between 30-70 years. This study was carried out at the Department of Biochemistry and Outpatient Department of endocrinology, Chittagong Medical College Hospital. Samples were collected by non-probability convenient sampling.

Results : Serum C-peptide was significantly higher in Metabolic Syndrome positive subjects (4.29±0.28 ng/ml) than non-Metabolic Syndrome (1.72± 0.12ng/ml). There was significant association between Metabolic Syndrome and increased serum C-peptide concentration. Serum C-peptide levels were significantly associated and positively correlated with serum triglyceride, blood pressure, fasting plasma glucose and negatively correlated with HDL-C in the cases.

Conclusion : However, this study did not find any significant association between WC (Waist Circumference) or HDL and Serum C-peptide concentration. Higher C-peptide level was associated with the components of Metabolic Syndrome and BMI (obesity) was the most important factor affecting the C-peptide concentration to develop Metabolic Syndrome.

Key words: BMI; BP; C-peptide; FPG; Lipid Profile; Metabolic syndrome.

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Introduction

Metabolic Syndrome (MetS) is a cluster of health problems that include abdominal fat, high blood pressure, high triglycerides, elevated blood sugar and low HDL cholesterol. The underlying causes of metabolic syndrome include overweight and obesity, insulin resistance, an unhealthy dietary pattern, physical inactivity, genetic factors and aging.[1]

The National Health and Nutritional Examination Survey estimates that ~30% of overweight and ~60% of obese men and women meet the criteria for a diagnosis of MetS.[2] Each component of the MetS is an independent risk factor for cardiovascular disease, together producing a wide spectrum of vascular and cardiac diseases.[3-6]

The Asia-Pacific region is facing a significant epidemic of MetS. In most countries nearly 1/5th of the adult population or more were affected by MetS with a secular increase in prevalence.[7] Bangladesh, a developing country with fast economic growth, has been experiencing rapid urbanization since the past several decades.[8,9] This development and urbanization raises the concern that the chronic disease burden may show an increasing trend in future, especially due to altering food habit including increased access to and popularity of processed food, irregular meal times, less physical activity, etc.[10] The proportion of adults categorized as overweight and have increased obese, particularly amongst the wealthiest, most educated, living in urban areas of Bangladesh due to absence of effective treatment and is likely to get worse overtime.[11] A recent meta-analysis

demonstrated that, the observed overall pooled prevalence of metabolic syndrome in Bangladesh (30%) was slightly higher than the prevalence estimated around the world (between 20% and 25%).[1,12] A key component of MetS is the development of insulin resistance or impaired glucose tolerance. Simpler, cheaper surrogate indices to detect insulin resistance require knowing the fasting plasma glucose, insulin concentration and the C-peptide concentration.[13] C-peptide is secreted in equimolar amounts with insulin from pancreatic beta cells and is reported to be a more useful laboratory parameter than insulin in evaluating endogenous insulin reserve.[14,15]

Recently, C-peptide, which was believed to be an inert biomolecule, was discovered to be a part of the immune response by regulating inflammatory cytokines.[16] Within the past two decades, the biological importance of C-peptide has emerged as a regulator of low-grade inflammation.[17] Since MetS is influenced by a chronic low-grade inflammation, this would insinuate that C-peptide concentrations might correlate with components of MetS. In a study of young Arab females, C-peptide was shown to moderately correlate with diastolic blood pressure, waist circumference, as well as high-density lipoprotein.[18] However, this study did not examine the correlation of C-peptide with other components of MetS.[18] Later on, Gonzalez-Mejia et al reported from their study that, insulin and C-peptide correlated with all components of MetS, but C-peptide better correlated with waist circumference, waist to-hip ratio, fasting plasma glucose, and HbA1c.[13] Recently, a study from Bangladesh observed that, in type-2 diabetes mellitus subjects, C-peptide showed significant positive correlations with body mass index, fasting plasma glucose, post parandial glucose, and HbA1c.[19] The study found higher levels of fasting C-peptide in newly diagnosed type-2 diabetes mellitus in comparison to non diabetic controls. [19]

There is scarcity of studies that have comprehensively studied the relationship of C-peptide with Metabolic Syndrome in overweight/obese non diabetic population especially in Bangladesh. Therefore, this study was designed to explore and analyze this association in a group of non diabetic obese Bangladeshi population.

Materials and methods

The study was a cross sectional study, was carried out at the Department of Biochemistry and Endocrinology, Chittagong Medical College Hospital between July 2020 to June 2021.Non diabetic obese individuals age between 30 and 70 years were enrolled by non-probability convenient sampling as per fulfillment of inclusion criteria. Diabetes mellitus, Acute infection, Active liver and renal disease, Cardio vascular disease, Malignant disease, Endocrine disease, Subject who were taking anti hypertensive, lipid lowering drugs, corticosteroids were excluded. Informed consent was taken from the participants. A predesigned case record form was used to record relevant clinical, medical, demographic socio-economic data. The study was approved by Ethical Review Committee, CMC. Serum C-peptide was measured by Nephelometry in BN ProSpec analyzer. Microsoft Excel and IBM-SPSS v.20 for Windows were used for data processing and analysis. Statistical inference was based on 95% confidence interval and p value < 0.05 was considered statistically significant.Variables were expressed as mean ± Standard Errors of Mean (SEM). Student 't' test and chi (χ^2) square test were used to see associations.

Results

A total number of 100 subjects age ranging from 30 to 70 years were included as per fulfillment of inclusion and exclusion criteria.

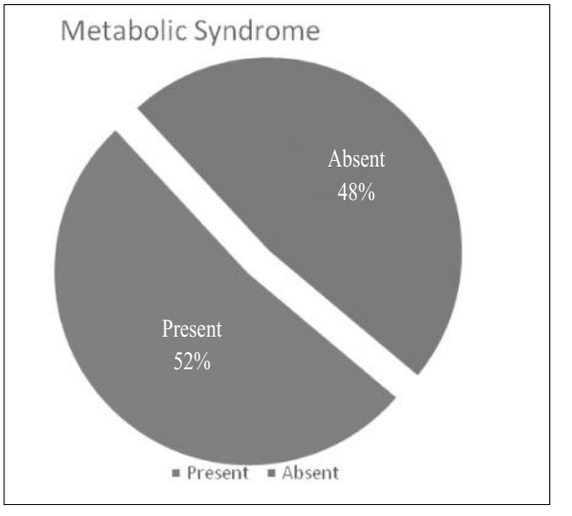

Figure 1 Pie Chart showing Distribution of metabolic syndrome among the study subjects

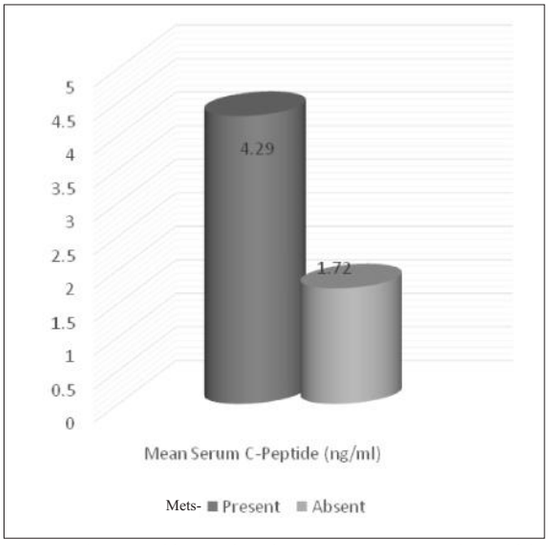

Figure 2 Bar Chart showing Mean serum C-peptide according to metabolic syndrome among the study subjects

Table I Association between serum C-peptide and metabolic syndrome among the study subjects (With Chi-square (χ^2) test significance) (n = 100)

Serum C-peptide Status	Metabolic Syndrome Present (n = 52)	Absent (n = 48)	p Value*
Increased (n = 41)	37 (71.2)	4 (8.3)	p < 0.001
Normal (n = 59)	15 (28.8)	44 (91.7)	Highly Significant

● *Figures within parentheses indicate percentages.*

Table shows that 71.2% subjects with metabolic syndrome had increased serum C-peptide whereas 28.8% subjects with metabolic syndrome had normal serum C-peptide (Table I).

Table II Correlation between serum C-peptide and numerical variables among the study subjects (n = 100)

Correlation Between	Pearson's Correlation Coefficient (r)	p Value *
Serum C-peptide and BMI	+ 0.075	p > 0.05 Not Significant
Serum C-peptide and WC	+ 0.242	p < 0.05 Significant
Serum C-peptide and SBP	+ 0198	p < 0.05 Significant
Serum C-peptide and DBP	+ 0.149	p > 0.05 Not Significant
Serum C-peptide and FPG	+ 0.533	p < 0.001 Highly Significant
Serum C-peptide and STG	+ 0.641	p < 0.001 Highly Significant
Serum C-peptide and SHDL	- 0.212	p < 0.05 Significant

This table demonstrates that there were positive and significant correlation of Serum C-peptide with WC, SBP, FPG, STG. There were positive correlation but not significant between Serum C-peptide with BMI and DBP. In this study there were negative but significant correlation between Serum C-peptide and HDL (Table II).

Table III Association between serum C-peptide status and components of metabolic syndrome among the non diabeticobese (With Chi-square (χ^2) test significance) (n = 100)

Components of Metabolic Syndrome		Serum C-peptide Status Increased (n = 41)	Normal (n = 59)	p Value
Waist Circumference Status	Central Obese (n = 100)	41 (100.0)	59 (100.0)	p > 0.05 Not Significant
	Normal (n = 0)	0 (0.0)	0 (0.0)	
BP Status	Elevated (n = 25)	16 (39.0)	9 (15.3)	p < 0.01 Highly Significant
	Normal (n = 75)	25 (61.0)	50 (84.7)	
Fasting Serum TG Status	Increased (n = 50)	36 (87.8)	14 (23.7)	p < 0.001 Highly Significant
	Normal (n = 50)	5 (12.2)	45 (76.3)	
Fasting Serum HDL Status	Decreased (n = 46)	23 (56.1)	23 (39.0)	p > 0.05 Not Significant
	Normal (n = 54)	18 (43.9)	36 (61.0)	
Fasting Plasma Glucose Status	Pre-diabetic (n = 42)	28 (68.3)	14 (23.7)	p < 0.001 Highly Significant
	Normal (n = 58)	13 (31.7)	45 (76.3)	

● *Figures within parentheses indicate percentages.*

Table demonstrates that there were highly significant association between Serum C-peptide and Blood Pressure, fasting serum triglyceride, Fasting plasma glucose among the study population. The association of serum C-peptide level between WC and HDL was not statistically significant (Table III).

Table IV Distribution of components of metabolic syndrome according to serum C-peptide status among the non diabetic obese (With independent samples t- test significance) (n = 100)

	Serum C-peptide Status	n	Mean	± SEM	Median	Sign.*
Waist Circumference (cm)	Increased	41	107.00	1.33	106.00	p < 0.01 Highly Significant
	Normal	59	102.98	0.81	101.00	
	TOTAL	100	104.63	0.75	104.00	
Systolic BP (mmHg)	Increased	41	128.29	2.34	130.00	p < 0.001 Highly Significant
	Normal	59	117.78	1.81	120.00	
	TOTAL	100	122.09	1.52	120.00	
Diastolic BP (mmHg)	Increased	41	84.27	1.45	85.00	p < 0.01 Highly Significant
	Normal	59	79.07	1.17	80.00	
	TOTAL	100	81.20	0.94	80.00	
Fasting Serum Triglyceride (mg/dl)	Increased	41	219.85	10.30	210.00	p < 0.001 Highly Significant
	Normal	59	141.80	4.04	134.00	
	TOTAL	100	173.80	6.17	149.50	
Fasting Serum HDL (mg/dl)	Increased	41	39.98	0.48	40.00	p < 0.05 Significant
	Normal	59	41.39	0.32	41.00	
	TOTAL	100	40.81	0.28	41.00	
Fasting Blood Glucose (mg/dl)	Increased	41	111.20	3.25	110.00	p < 0.001 Highly Significant
	Normal	59	90.56	2.09	90.00	
	TOTAL	100	99.02	2.07	97.00	

Table shows that mean difference of SBP, DBP, FPG, STG, WC among the Serum C-peptide increased and normal cases respectively is statistically highly significant whereas fasting HDL was found statistically just significant (Table IV).

Discussion

The study was designed to evaluate the association of serum C-peptide with the components of Metabolic Syndrome among non diabetic obese. The number of the non diabetic obese were hundred (n=100). Out of them 52% cases were positive for metabolic syndrome whereas 48% were negative. (Fig=1). In a previous study 37% Bangladeshi population, 54.8% Mexican and 49.4% Korean obese population were positive for metabolic syndrome.[12,13,20] This study revealed that there was significant ($p<0.001$) association of serum C-peptide with Metabolic Syndrome (Table=I).

The most important variable of the study, C-peptide was significantly higher in case of Metabolic Syndrome positive subjects (4.29+ 0.28 ng/ml) than Non Metabolic Syndrome (1.72+ 0.12ng/ml) ($p<0.001$). (Fig=2). The distribution of serum C-peptide status among the study groups showed high association (Chi-square (χ^2) $p<0.001$) between Metabolic Syndrome positive and increased serum C-peptide concentration where Seventy one (71.2%) of Metabolic Syndrome positive subjects demonstrated increased C-peptide concentration as opposed to Eight (8.3%) of Non Metabolic Syndrome subjects. (Table I). M Elba Gonzela- Mejia et al, Sophia Boudoulas Meis et al showed that C-peptide and insulin were significantly higher in Mets subjects ($p<0.05$).[13,22] A. Abdullah, H. Hasan, V Raigangar and W. Bani-Issa showed significant positive correlation between C-peptide and WC, HDL-C.[18] M. Elba Gonzalez-Mejia et al showed that there was a strong positive correlation between C-peptide and waist circumference, BMI, fasting plasma glucose, and a moderate correlation with waist-to-hip ratio, diastolic and systolic blood pressures, triglyceride, and high-density lipoprotein.[13] Abdullah et al. and Mariyam et al. also observed positive correlation between C-peptide level and FPG.[23,24] In this study there were significant positive correlation between serum C-peptide and WC, SBP,FPG, STG. Whereas significant negative correlation between Serum C-peptide and SHDL (Table II) The same observation was cited by a study of Shaheena Banu, Nasimudeen R. Jabir et al.[25]

RECHARD W. BERGSTROM LAURA L et al showed that there were significant correlation between intra abdominal fat and C-peptide level in non diabetic men.[26] In this study, Pearson correlation between serum C-peptide and waist circumference was found significant (Table II).

A positive correlation between BMI and basal serum C-peptide levels was also observed by Park S W et al Shaheena Banu, Nasimudeen R. Jabir et al A.B.M. Kamrul Hasan, Mohammed Ruhul-kabir, Md. Habibur Rahman et al.[27,25,19] This study also reveled positive correlation between BMI and basal serum C-peptide levels. (Table-II). N.Clear, Jones O et al in their study observed that basal insulin and C-peptide concentration are higher in obese than non-obese patients.[28] The increased level of C-peptide in overweight and obese patients indicate insulin resistance.

Elevated blood pressure or Hypertension, Serum Triglyceride were significantly associated with increased C-peptide level in obese subjects in this study (Table-III). The same observation was cited by a study of Jin-young Min PhD, Kyoung-bok Min MD PhD.[29]

Serum C-peptide as a risk factor for CVD was significantly and negatively associated with serum HDL-C level in the individual without diabetes observed by them.[30] But in our study there was no association between serum C-peptide and HDL-C level (Table-III).

Significant differences were also found in levels of C-peptide, WC, SBP, DBP, STG, SHDL, FPG. (Table-IV).This observation was similar to the study done by them.[18]

Limitations

The present study had certain limitations. The purposive method of sampling and relatively small sample size can be mentioned as examples. Besides, cross-sectional study is observational and does not indicate any causal relationships between C-peptide and Metabolic Syndrome. Further studies are required to determine the effect of C-peptide has on the components of Metabolic Syndrome.

Conclusion

In conclusion, this study revealed significant association between Metabolic Syndrome and Serum C-peptide concentration. Among the obese subjects, C-peptide levels were significantly higher in Metabolic Syndrome positive subjects compared to Non Metabolic Syndrome. Increased C-peptide level in cases was significantly associated with and positively correlated to Blood pressure, Triglyceride and Fasting plasma glucose.

Recommendations

- The sample size could be increased substantially so that a generalized conclusion could be made among the Bangladeshi population.
- Cohort study should be done for more practical information.
- Serum C-peptide related attention should be raised and its determination as a routine test may minimize the insulin resistance complications.
- Community based interventions should be aimed to convey awareness to follow a healthy lifestyle, promote healthy food alternatives and increase in physical activity.

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Contribution of authors

SA- Conception, design, acquisition of data, drafting and final approval.

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

MH- Design, critical revision and final approval.

NT- Acquisition of data, critical revision and final approval.

HH- Data analysis, critical revision and final approval.

MTA- Data analysis, critical revision and final approval.

Disclosure

All the authors declared no competing interests.

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