

Original Research Article

Emerging role of C-peptide as an early biomarker of metabolic syndrome

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ABSTRACT

Background: Metabolic syndrome is a health issue of rising concern as it has a correlation with the occurrence of cardiovascular events. Early identification of this syndrome by evaluating levels of biomarkers such as C peptide can help medical professionals prevent the occurrence of life-threatening cardiovascular diseases.

Methods: This cross-sectional study was carried out in 89 subjects who were diagnosed to have metabolic syndrome. General Physical examination was done and fasting C peptide and insulin levels were quantified, followed by statistical analysis and their correlation. The prevalence of defining parameters of Metabolic Syndrome as per IDF 2005 was studied.

Results: Out of 89 (100%) subjects, 80 (89.8%) subjects (Mean±SD=6.14±3.47) had C- peptide level >1.89 ng/ml which was statistically highly significant (p<0.001). Also, out of 89 (100%) subjects, 67 (24.71%) subjects had insulin level <25 mIU/L which was statistically significant (p<0.001).

Conclusions: It was thereby concluded that serum C peptide levels were raised in patients of Metabolic syndrome and it is superior to serum Insulin levels as an early biomarker of the same.

Keywords: Metabolic syndrome, Microvascular, Biomarker, Proinsulin

INTRODUCTION

The prevalence of lifestyle disorders is increasing in Indian population. Metabolic syndrome is a common life style disorder and it has become one of the major health issue of this century.¹ The world wide prevalence of Metabolic syndrome is estimated to be 25%.² Metabolic syndrome is a cluster of physical conditions and metabolic abnormalities commonly associated with increased risk of developing Type 2 Diabetes Mellitus and myocardial ischemia.³ Morbidity and mortality

associated with these conditions also increase the financial burden on the affected patients and their families.

Metabolic syndrome has been defined most recently by International Diabetes Federation in 2005. According to IDF, metabolic syndrome is defined when a person has central obesity plus any two of the following: increased triglycerides; reduced HDL cholesterol; increased blood pressure; or increased fasting plasma glucose.^{4,5}

Recent studies using Indian specific criteria for overweight (BMI >23), obesity (BMI >25), and abdominal obesity (WC >90 cm in men and >80 cm in women) have found that the prevalence rates among Asian Indians exceeding those in the US population.⁶ Recent trends in Indian population indicate a rise in obesity both in children as well as adults. Cameron et al have concluded that the differences in genetic background, diet, levels of physical activity, smoking, family history of diabetes, and education all influence the prevalence of metabolic syndrome and its components.⁷

In the backdrop of rising trend of metabolic syndrome, which is an important risk factor for life threatening cardiovascular ischemic events, it is worthwhile to investigate for early biomarkers of Metabolic syndrome. C-peptide is a peptide composed of 31 amino acids. It is released from the pancreatic beta-cells during cleavage of insulin from proinsulin. During the course of insulin synthesis, C-peptide is cleaved from proinsulin and eventually released into the bloodstream in amounts equimolar with those of insulin.⁸ Hence C-peptide levels correlate with insulin production and secretion into blood stream.

Our study investigates the levels of C-peptide and serum insulin levels in 89 patients of metabolic syndrome and evaluates the validity of C-peptide level as early biomarker of metabolic syndrome.

METHODS

The present study was conducted in the department of Biochemistry, Subharti Medical College, Meerut and associated metabolic OPD of Chhatrapati Shivaji Suharti Hospital during the month of March, 2015. Before the start of the study, permission was granted from the Ethical Review Committee, of Institute and informed consent was obtained from all participants. Patients attending the Metabolic OPD of Chhatrapati Shivaji Subharti hospital associated with Subharti Medical College, Meerut were screened for Metabolic syndrome and enrolled for the present study.

Informed consent was taken, and detailed history including presenting complaints, past history, family history, history of medicine intake, history of previous illness and other relevant information was taken from each individual patient and recorded. All the patients were subjected to complete general and systemic examination and findings were noted. Waist circumference was also recorded in all of them.

Routine investigation like haemoglobin (Hb), total leucocytes count (TLC), differential leucocytes count (DLC), erythrocyte sedimentation rate (ESR), liver function test (LFT), kidney function test (KFT), and the special investigations like, lipid profile (TG, TC, HDL-C, LDL-C, VLDL-C), fasting blood glucose (FBG), fasting C-peptide and fasting Insulin were estimated in all

the patient blood samples and findings recorded at the Central Biochemistry Laboratory.

Inclusion criteria

Patients who fulfill the criteria of metabolic syndrome proposed by IDF 2005 within the age group of 16 to 65 years and give informed consent for the study.

Exclusion criteria

Patients with following medical conditions were excluded from the study, insulinoma, patients on exogenous insulin, corticosteroids, levodopa, and oral contraceptives, history of fructose or galactose intolerance, deranged kidney functions, uncontrolled hypertension, diabetic ketoacidosis, congestive heart failure, pregnancy, acromegaly, cushing's syndrome as well as acute anxiety, psychological stress and severe exercise.

Waist circumference

Waist circumference was measured at the plane between anterior superior iliac spines and lower costal margin at the narrowest part of the waistline while the patient was standing and at the end of normal expiration.¹²

Reference range

According to IDF definition waist circumference in adult men ≥ 90 cm (≥ 36 inch) and in adult women ≥ 80 cm (≥ 32 inch) is considered as a component of metabolic syndrome

Sample collection

After 12 to 14 hours of fasting, venous blood sample was collected under all aseptic conditions, 2 ml in EDTA vacutainer for routine investigations and 4 ml in plain vacutainer for special investigation and 2 ml in Sodium fluoride vacutainer for fasting blood glucose. Plain and Sodium fluoride vacutainers were allowed to clot for 30-60 minutes. Serum was separated by centrifugation for 5 minute at 1500 rpm. Thyroid profile, LFT, KFT tested in serum from plain vacutainer and Hemoglobin, TLC, DLC, ESR tested from EDTA vacutainer. Serum C-peptide was estimated by ELISA method by DRG® C-Peptide ELISA KIT. The DRG C-Peptide ELISA Kit works on the principle of enzyme-linked immunosorbent assay (ELISA). Serum insulin was estimated by quantitative ELISA method by DRG® INSULIN ELISA KIT. Insulin is the principal hormone responsible for the control of glucose metabolism. Insulin ELISA also works on solid phase enzyme-linked immunosorbent assay.

Statistical analysis

The data collected was compiled, results and observations drawn and statistically analyzed using Excel 2007, R2.8.0

Statistical package for the social sciences (SPSS) for windows version 16.0 (SPSS Inc; Chicago, IL, USA). We performed unpaired student t test to study the association of c-peptide and insulin with the metabolic syndrome and its components. A p<0.05 was considered as statistically significant.

RESULTS

The present study included 89 diagnosed cases of Metabolic syndrome. In our study total number of subjects were 89 (100%), out of which number of subjects in the age group <25 years were 21 (23.6%), in the age group 26-35 years were 29 (32.6%), in the age group 36-45 years were 27 (30.3%), and in the age group of 46-55 years and >55 years were 6 (6.7%) each.

The maximum no of subjects were in the age group 26-35 years. Number of males were slightly greater than female.

As shown in Table 1, it was found that out of total number of subjects, waist circumference of 48 (53.9%)

males was ≥90 cm and waist circumference of 41 (46.9%) females was ≥80 cm. Fasting Blood sugar of 56 (62.9%) subjects was ≥100 mg/dl, and of 33 (37.1%) was <100 mg/dl. The HDL-C of 36 (40.4%) subjects was ≥40 (in males) and ≥50 (in females) and of 53 (59.6%) subjects was <40 (in males) and <50 (in females).The Fasting Triglyceride of 36 (40.4%) subjects was ≥150 mg/dl and of 53 (59.6%) subjects was <150 mg/dl.

Distribution of subjects according to C-peptide and Insulin levels was done as shown in Table 2. The C-peptide and Insulin values were analyzed statistically by unpaired students t test. It was found that out of 89 (100%) subjects, 80 (89.8%)subjects (Mean±SD = 6.14±3.47) had C- peptide level>1.89 ng/ml which was statistically highly significant (p<0.001), 5 (5.6%) subjects (mean± SD = 0.49 ±0.24) had C-peptide level <0.78 ng/ml and 4 (4.49%) subjects (Mean±SD =1.35±0.45) had C-peptide level ≥0.78 but≤1.89 ng/ml which is the normal range of C-peptide.

Table 1: Distribution of subjects according to parameters of metabolic syndrome.

Parameters of metabolic syndrome	Levels of parameters(as per cut off values)	Subjects	
		N	%
Waist circumference (cm)	Male ≥ 90	48	53.9
	Female ≥80	41	46.9
Blood sugar (mg/dl)	<100	33	37.1
	≥100	56	62.9
Hdl_c (mg/dl)	Male <40 and female <50	53	59.6
	Male ≥40 and female ≥50	36	40.4
Triglyceride (mg/dl)	<150	36	40.4
	≥150	53	59.6

(subject: 89) (%:100). All samples are fasting

Table 2: Distribution of insulin and C-peptide levels as per different age groups.

Age group	Insulin levels			C-peptide levels		
	<2	2-25	≥25	<0.78	≥0.78 -≤1.89	>1.89
<25	0	17	4	1	1	19
26-35	0	21	8	3	1	25
36-45	0	19	8	0	1	26
46-55	0	6	0	0	1	5
>55	1	3	2	1	0	5
Total	1	66	22	5	4	80

Similarly, out of 89 (100%) subjects, 67 (24.71%) subjects had insulin level<25 mIU/L which was statistically significant (p<0.001). Out of 67 subjects, only 1 subject (Mean±SD = 1.8±0.0) had Insulin level<2 mIU/L and 66 subjects (Mean±SD = 13.05±26.58) had Insulin level in the normal range i.e.≥2 but<25 mIU/L. Remaining 22 subjects (24.7%) had Insulin level ≥25 mIU/L (Mean±SD = 43.1±16.85). Only 22 subjects were found with abnormally higher Insulin levels≥25 mUI/L in comparison with 80 subjects (89.8%) with abnormally

higher C-peptide levels≥1.89 ng/ml which was statistically highly significant (p<0.001).

With reference to age groups too, it is worthwhile to note that in the all the age groups, abnormally higher C-peptide is present in patients of normal insulin levels with a significantly high correlation.

DISCUSSION

Metabolic syndrome remains a major health problem.¹ Various researchers have tried to identify its disease burden in India. Comparison of different studies conducted at various cities across India showed prevalence ranging from 22.1% to 41% across urban south India.⁹⁻¹¹ Increasing evidence has recently emerged from several laboratories that C-peptide has great potential relevance to the pathophysiology and treatment of diabetes, possibly acting as a peptide hormone beneficially affecting renal, nervous and microvascular functions in diabetic animals.^{12,13} Several studies have found a strong correlation between C-peptide levels and components of metabolic syndrome. These studies have concluded that an elevated fasting serum C-peptide levels can constitute a clinically important early biomarker of the Metabolic Syndrome.^{14,15} We have tried to explore the levels of C-peptide and insulin levels in metabolic syndrome patients of Chattrapati Shivaji Subharti Hospital, Meerut in order to evaluate potential of C-peptide as early biomarker of Metabolic syndrome. We have included 89 patients of Metabolic syndrome as per our inclusion and exclusion criteria and studied their C-peptide and insulin levels. We found that in almost all age groups, number of patients with abnormally higher C-peptide levels is significantly higher than those with abnormally higher insulin levels. Most of the patients displayed abnormal C-peptide levels while most of the patients displayed normal insulin levels, despite affected by Metabolic syndrome. So C-peptide levels are rising above normal baseline very early in the patients of Metabolic syndrome. This can be attributed to the fact that C-peptide levels correlate directly with insulin secretion as insulin and C-peptide are secreted in equimolar amount. But the insulin is regularly uptaken by liver for its metabolic need and hence the fasting serum insulin levels don't correlate with insulin secretion. In the case of Metabolic syndrome, liver might increase uptake of insulin to compensate the pathological disturbances of Metabolic syndrome and therefore normal serum fasting insulin levels despite increased production and secretion of insulin can be seen. In a Russian study done by Beliakin et al also, same findings were reported and C-peptide was estimated to be better marker than insulin to predict cardiovascular risk in the patients of Metabolic syndrome.¹⁶

C-peptide levels must be interpreted with caution in renal failure. Approximately half of C-peptide produced is removed by the kidneys, the majority of which is degraded via peritubular uptake with approximately 5% of total C-peptide produced excreted unchanged in the urine.^{17,18} Therefore, blood levels of C-peptide can be falsely elevated where there is renal impairment.¹⁹ Currently models of renal function adjusted C-peptide levels as a predictor of cardiovascular risk are in nascent stage but C-peptide in combination with various cardiovascular risk factors can enable us to predict the chances of cardiovascular ischemia.

Limitations

The number of patients included is small and further confirmation needs extensive research on larger group of population.

CONCLUSION

It can be deduced from this study that serum C-peptide levels are abnormally high in most of the patients of metabolic syndrome while serum insulin levels are high only in a few of them, which shows the superiority of estimation of C-peptide levels over Insulin levels. C-peptide level measurement can be a sensitive marker for metabolic syndrome, which is the precursor of life-threatening Cardio-vascular diseases. In addition to this C-peptide level estimation can also be deployed as a predictor of cardio-vascular disease risk along with other risk factors.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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