

C-PEPTIDE LEVELS: CORRELATION WITH ANTHROPOMETRIC MEASUREMENTS OF OBESITY AND COMPONENTS OF METABOLIC SYNDROME

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Abstract

Background: Obesity is now recognized as one of the most critical public health issues worldwide. Various anthropometric measures, such as BMI, waist circumference, and waist-to-hip ratio, have been employed to define obesity. Waist circumference (WC), waist-to-hip ratio (WHR), and waist-to-stature ratio are considered more appropriate measures for central obesity. Obesity is closely linked with metabolic syndrome (MetS), with a key aspect being the development of insulin resistance (IR). Recently, C-peptide has been proposed as a robust indicator of metabolic syndrome, emphasizing the significance of C-peptide in diagnosing MetS. This study aimed to investigate the correlation between C-peptide and components of MetS in overweight individuals and normal healthy subjects. **Material and Methods:** A cross-sectional observational study was conducted on 100 healthy adults, encompassing both sexes. Participants were categorized into two groups based on their BMI. The study involved the measurement of various components of Metabolic Syndrome (Mets), including waist circumference, systolic and diastolic blood pressure, triglyceride levels, HDL and LDL cholesterol, blood glucose, and C-peptide levels. **Results:** Subjects (n=100) were within the age group of 19-53, with 65 individuals classified as overweight/obese and labeled as Group II. The remaining subjects, with a BMI < 23 kg/m², were included in the normal weight group, designated as Group I (n = 35). All components of Metabolic Syndrome (MetS) were elevated in Group II. The overweight group exhibited a statistically significant increase in C peptide levels (3.46±2.884) compared to the normal weight group (2.01±1.114). Pearson Correlation analysis revealed a statistically significant, positive correlation between C peptide levels and BMI (r = 0.340, p = 0.044), waist circumference (r = 0.315, p = 0.001), total cholesterol (r = 0.339, p = 0.001), and LDL-C (r = 0.331, p = 0.001). **Conclusion:** The C-peptide level was significantly elevated in overweight subjects compared to normal-weight individuals. There is a significant correlation between the C-peptide level and anthropometric measurements of obesity, as well as lipid parameters, which are components of metabolic syndrome (MetS).

INTRODUCTION

Obesity is a global public health crisis, surpassing underweight in its impact on mortality.^[1] Linked to cardiovascular diseases, diabetes, and various cancers, its prevalence has tripled over the past 50 years, affecting 39% of the world's population. In India, where rates vary based on age, gender, and socio-economic factors, abdominal obesity is a

significant risk factor for cardiovascular diseases, with a prevalence ranging from 16.9% to 36.3%.^[2,3] A majority of overweight or obese individuals also present with Metabolic Syndrome (MetS) - a cluster of metabolic abnormalities such as hypertension, hyperglycemia, central adiposity, hypertriglyceridemia, and insulin resistance. Gerald M. Reaven initially identified this cluster as

Syndrome X, later adopting the term metabolic syndrome.^[3,4]

MetS, widely recognized internationally, poses a fivefold risk for type 2 diabetes and a twofold risk for cardiovascular disease. Many guidelines exist for the diagnosis of MetS like WHO, NCEP, ADA, and IDF guidelines exist, of which NCEP ATP III is widely used. Incorrect application may lead to misdiagnosis. No specific biomarkers currently exist for MetS diagnosis. Insulin resistance (IR) is a key component, with the hyperinsulinemic-euglycemic clamp as the gold standard, though more straightforward methods like HOMA (Homeostatic Model Assessment), using fasting blood glucose and insulin, are utilized.^[3-6]

C-peptide, a byproduct of insulin synthesis, is released in response to elevated levels of plasma glucose. Unlike insulin, it shows a linear kinetic profile and is not significantly cleared by the liver. Recent findings suggest that C-peptide correlates better with pancreatic insulin secretion and β -cell function than peripheral insulin levels.^[6-8] Additionally, previously considered inert, C-peptide is now recognized for regulating inflammatory cytokines and is linked to low-grade inflammation. It is emerging as a strong indicator of metabolic syndrome, closely associated with inflammation and insulin resistance.^[8,9] This study aims to explore the correlation of C-peptide with MetS components in healthy subjects and assess its potential as a predictor of MetS.

MATERIALS AND METHODS

This cross-sectional observational study was conducted in the Department of Biochemistry at Government Medical College Thrissur. The study included 100 healthy, employed adults of both sexes who had enrolled in the fitness program initiated by the Department of Physical Education. The protocol received approval from the Institutional Research Committee and the Institutional Ethical Committee. All participants provided informed consent, and the study adhered to the guidelines of the Indian Council of Medical Research.

Subjects with a known history of diabetes, hypertension, coronary artery disease, any endocrine disorders, or those on any medication were excluded. Participants underwent clinical evaluation following a standardized protocol, during which demographic data and detailed personal and family history of illness were recorded. Subjects were required to fast for 12 hours before blood collection, and weight and height were measured with participants wearing light clothing and without shoes. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). The participants were categorized into two groups based on BMI: Group I as normal weight ($\text{BMI} < 23 \text{ kg}/\text{m}^2$) and Group II as overweight/obese ($\text{BMI} \geq 23 \text{ kg}/\text{m}^2$), utilizing BMI cutoff values for Asians.

Waist circumference was measured at the midpoint between the highest point of the iliac crest and the lowest point of the costal margin at the midaxillary line using a non-stretching anthropometric measuring tape. Hip circumference was measured at the widest part of the buttocks. The waist-to-hip ratio was calculated by dividing waist circumference by hip circumference. Blood pressure measurements (diastolic and systolic) were recorded.

Blood samples were collected from the antecubital vein into two separate Vacutainers. Glucose samples were collected in a sodium fluoride oxalate tube, while lipid profile and C peptide analysis samples were collected in a plain tube with a clot activator. Fasting plasma glucose, total cholesterol, high-density lipoprotein, and triglycerides were analyzed using EM360 Transasia Biomedical Pvt Ltd. The serum fraction for the C peptide was recovered and frozen at -20°C until used. Glucose levels were determined using the enzymatic method, and triglycerides and high-density lipoprotein levels were measured using the enzymatic method. C-peptide levels were determined by ELISA.

Statistical analyses were performed using the Statistical Package for the Social Sciences program for Windows, version 19 (SPSS, Chicago, IL). The Shapiro–Wilk Test was conducted and means, and standard deviations (SD) were calculated for all parameters. The independent sample t-test was utilized to compare the means of different variables in the two groups. Pearson correlation coefficient (r) was employed for correlation analysis, and a P value < 0.05 was considered significant.

RESULTS

Of the 100 subjects studied, 65 were overweight or obese (mean BMI = $26.84 \text{ kg}/\text{m}^2$, SD = 4.5), with a mean waist circumference (WC) of 83.7 cm (SD = 10.3), and they were labelled as Group II. This group comprised 48 females and 17 males. The remaining subjects, with a BMI $< 23 \text{ kg}/\text{m}^2$, were included in the normal weight group labelled as Group I ($n = 35$, 43.7%) with a mean BMI of $21.4 \text{ kg}/\text{m}^2$ (SD = 2.5) and a mean WC of 66.9 cm (SD = 5.2). The age of the subjects varied from 18 to 50 years in Group I and 19 to 53 years in Group II. The baseline characteristics of study participants in both groups are presented in Table 1.

All components of metabolic syndrome (MetS) were elevated in Group II. However, the following parameters showed statistically significant differences: waist circumference (75.86 ± 8.918 vs. 92.88 ± 9.599 , $t(98) = 8.415$, $p = 0.000$), waist-to-hip ratio (0.82 ± 0.821 vs. 0.95 ± 0.070 , $t(98) = 5.725$, $p = 0.000$), systolic blood pressure (113.14 ± 8.250 vs. 117.85 ± 9.697 , $t(98) = 2.554$, $p = 0.013$), diastolic blood pressure (72.11 ± 6.379 vs. 76.55 ± 7.267 , $t(98) = 4.703$, $p = 0.003$), total cholesterol (153.63 ± 33.150 vs. 171.92 ± 36.860 , $t(98) = 2.450$, $p = 0.016$), triglycerides (113.26 ± 26.343 vs.

131.12 ± 42.030, t(98) = 2.530, p = 0.025), and fasting blood glucose (72.36 ± 9.175 vs. 77.19 ± 14.621, t(98) = 2.022, p = 0.46). No significant difference between males and females was observed in both groups (Table 3).

The overweight group exhibited a statistically significant higher C peptide level (3.46±2.884) compared to the normal weight group (2.01±1.114), with t(98) = 3.981 and p = 0.002 (Figure 1). Table 2 compares the two groups anthropometric measurements and components of MetS.

Pearson Correlation analysis revealed a statistically significant, moderate positive correlation of C peptide levels with age (r = 0.399, p = 0.000), BMI (r = 0.340, p = 0.044), waist circumference (r = 0.315, p = 0.001), total cholesterol (r = 0.339, p = 0.001), and LDL-C (r = 0.331, p = 0.001). Age strongly correlated with C peptide levels (r = 0.340, p = 0.001) (Table 4). Figures 2 and 3 depict the correlation of C peptide with BMI and waist circumference.

Table 1: Baseline characteristics of Group1 and Group 2(normal weight versus overweight /Obesity group)

	Group 1 (Normal weight)				Group 2 (Overweight /Obesity)			
	Mean	Median	Min	Max	Mean± Std. Deviation	Median	Minimum	Maximum
Age (years)	27.11±9.809	21	18	50	34.89±9.405	34	19	53
Weight (Kg)	51.51±8.476	50	35	71	68.06±11.638	66	49	104
Height (M)	1.58±0.092	1.56	1.46	1.81	1.59±0.085	1.56	1.39	1.78
BMI	20.59±1.994	21.17	16.42	22.89	26.84±3.691	25.64	23.03	41.66
WC(cm)	75.86±8.918	75	60	96	92.38±9.599	92.5	68	113
WHR	.82±.070	0.8	0.72	0.95	2.08±9.007	0.94	0.78	73
SBP	113.14±8.250	110	100	140	117.85±9.697	118	90	140
DBP	72.11±6.379	70	60	84	76.55±7.267	78	60	100
TC(mg/dl)	153.63±33.150	153	103	247	171.92±36.860	169	83	276
TG(mg/dl)	113.26±26.343	111	70	175	131.12±42.030	122	72	281
HDL(mg/dl)	48.91±23.081	52	11	86	55.57±15.919	59	11	79
LDL(mg/dl)	82.06±31.416	81	20.8	145	90.13±31.507	86	29.6	187.8
FBS(mg/dl)	72.36±9.175	73	54.67	90	77.19±14.621	75	50	119
C-peptide (ng/ml)	2.01±1.114	1.6	1.1	5.2	3.46±2.884	2.66	0.2	14.87

[BMI-Body Mass Index,WC-Waist circumference,WHR-Waist Hip Ratio,SBP-Systolic Blood Pressure,DBP-Diastolic Blood Pressure,TC-Total Cholesterol,TG-Triglycerides,HDL-High Density Lipoprotein,LDL-Low Density Lipoprotein,FBS-Fasting Blood Sugar]

Table 2: Components of Metabolic Syndrome in Group 1 and Group 2

Parameter	Group 1 (n=35) BMI <23	Group 2(n=65) BMI >23	Mean difference	t	P value
	Mean	Mean			
Waist circumference in cm	75.86± 8.918	92.88±9.599	16.53	8.415	0.000**
Waist to Hip ratio	0.82±.821	0.95±070	0.128	5.725	0.000**
SBP mm of Hg	113.14±8.250	117.85±9.697	4.703	2.554	.013*
DBP mm of Hg	72.11±6.379	76.55±7.267	4.703	3.159	.003**
TC mg/dl	153.63±33.150	171.92±36.860	18.295	2.450	.016*
TG mg/dl	113.26±26.343	131.12±42.030	17.866	2.530	.025*
HDL-C mg/dl	48.91±23.081	55.57±15.919	6.655	1.696	.093
LDL-C mg/dl	82.06±31.416	90.13±31.507	8.066	1.222	.046
FBS mg/dl	72.36±9.175	77.19±14.621	4.826	2.022	.046*
C peptide ng/ml	2.01±1.114	3.46±2.884	1.025	3.981	.002*

[SBP-Systolic Blood Pressure,DBP-Diastolic Blood Pressure,TC-Total Cholesterol,TG-Triglycerides,HDL-High Density Lipoprotein,LDL-Low Density Lipoprotein,FBS-Fasting Blood Sugar]

Table 3: Distribution of various parameters among gender

Parameter	Normal weight Group (n=45)		Overweight Group (n=65)	
	Female (n=26)	Male(n=9)	Female (n=48)	Male(n=17)
	Mean±SD	Mean ±SD	Mean±SD	Mean±SD
Age (years)	27.23±10.405	26.78±8.393	35.74±9.613	32.53±8.632
Weight (Kg)	48.92±5.817	59.00±10.712	65.50±11.758	75.29±7.768
Height (M)	1.54±.061	1.68±.093	1.56±.064	1.68±.073
BMI	20.56±2.084	20.68±1.821	26.86±3.846	26.81±3.324
WC(cm)	75.89±9.197	75.78±8.585	92.67±10.041	91.59±8.456
WH R	.82±.068	0.83±0.084	2.45±10.400	.96±.101
SBP mm of Hg	112.62±7.435	114.67±10.630	117.21±10.095	119.65±8.492
DBP mm of Hg	72.62±6.494	70.67±6.164	76.38±7.434	77.06±6.968
TC(mg/dl)	155.96±34.130	146.89±31.016	172.88±36.929	169.24±37.658
TG(mg/dl)	112.19±27.354	116.33±24.428	129.08±42.250	136.88±42.128

HDL(mg/dl)	49.89±24.392	46.11±19.821	58.45±13.784	47.42±18.977
LDL(mg/dl)	83.64±34.154	77.511±22.757	88.60±32.785	94.44±28.048
FBS(mg/dl)	72.81±8.663	71.07±10.987	75.56±15.295	81.78±11.727
C peptide (ng/ml)	1.98±1.043	2.08±1.363	3.43±2.697	3.53±3.450

[BMI-Body Mass Index, WC-Waist circumference, WHR-Waist Hip Ratio, SBP-Systolic Blood Pressure, DBP-Diastolic Blood Pressure, TC-Total Cholesterol, TG-Triglycerides, HDL-High Density Lipoprotein, LDL-Low Density Lipoprotein, FBS-Fasting Blood Sugar]

Table 4: Correlation of Fasting C peptide with components of Metabolic Syndrome (N=100)

Parameter	Correlation Coefficient	Sig. (2-tailed)
Age	0.399	.000*
BMI	0.191	0.05*
Waist circumference	0.269	0.007*
Waist to Hip Ratio	0.218	0.03*
SBP	0.091	0.36
DBP	-0.014	0.89
TC	0.36	.000*
TG	0.093	0.35
HDL	0.071	0.48
LDL	0.28	0.005*
FBS	0.091	0.36

[BMI-Body Mass Index,WC-Waist circumference,WHR-Waist Hip Ratio,SBP-Systolic Blood Pressure,DBP-Diastolic Blood Pressure,TC-Total Cholesterol,TG-Triglycerides,HDL-High Density Lipoprotein,LDL-Low Density Lipoprotein,FBS-Fasting Blood Sugar]

DISCUSSION

Obesity stands out as the primary risk factor for the onset of insulin resistance, a crucial precursor to Metabolic Syndrome (Mets). Early detection of insulin resistance holds significance for timely interventions to prevent future morbidity and mortality.^[10-12] Numerous studies have highlighted the biomarker potential of C-peptide in identifying individuals at risk for insulin resistance, Type 2 Diabetes Mellitus (T2DM), atherosclerosis, and metabolic syndrome.^[13-28]

Our study focuses on assessing the components of Mets in both normal-weight and overweight/obese subjects, with a specific emphasis on C-peptide levels and insulin resistance calculated using HOMA-IR. The basal C-peptide levels and MetS components—waist circumference, systolic and diastolic blood pressure, triglycerides, LDL-C are significantly higher in the overweight/obese group compared to the normal-weight group. However, these parameter levels do not meet the criteria for confirming MetS.

This study reaffirms previous findings indicating a significant correlation between serum C-peptide levels and obesity/overweight. All three anthropometric measurements of obesity—BMI, waist circumference, and waist-to-hip ratio—show a positive correlation with C-peptide levels. This aligns with a study conducted among Arab females by A. Abdulla et al.^[19] and similar reports from other researchers among diabetic patients.^[20,21] The present study also reveals a significant positive correlation between the subjects' age and C-peptide levels, consistent with findings by others.^[20]

Only LDL-C correlates with C-peptide among lipid parameters despite significantly elevated TC and TG levels in the overweight group. While Kim et al. and

Cho et al. report a significant association of C-peptide with TG and HDL, our study fails to observe any relationship with HDL.^[21,22] Banu et al., in their study on patients with metabolic syndrome, demonstrate a significant correlation of TG with C-peptide levels and a progressive increase in insulin resistance with an increase in C-peptide levels, supporting the usefulness of C-peptide in monitoring insulin resistance.^[23] A study from central Mexico also identifies C-peptide as a sensitive indicator for insulin resistance.^[24] However, the multiple linear regression models do not include anthropometric measurements of obesity like BMI and WC as predictors of C-peptide levels, possibly due to the multicollinearity of independent predictors such as age, BMI, WC, and lipid parameters, along with a small sample size. Mariyam et al. report obesity as a significant predictor of C-peptide.^[16] The impact of weight gain or reduction on C-peptide levels requires further investigation, and interventions through lifestyle modifications may prove beneficial in reversing metabolic abnormalities associated with insulin resistance.

CONCLUSION

An elevated C-peptide level serves as an indicator of insulin resistance in overweight or obese individuals, as evidenced by significantly higher levels observed in these subjects compared to those with normal weight. The C-peptide level demonstrates a noteworthy correlation with anthropometric measurements of obesity and lipid parameters, both integral components of metabolic syndrome. Therefore, further research is warranted to explore the utility of C-peptide as a predictor of metabolic complications associated with insulin

resistance. While our study was conducted on a small scale, investigations with larger sample sizes may provide deeper insights into the intricate relationship between C-peptide and components of metabolic syndrome.

Conflict of Interests

The authors declare that there is no conflict of interests.

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