Plasma CTRP-3 concentration in newly diagnosed Type II diabetes mellitus patients; A cross-sectional study

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ABSTRACT

Objective

To assess the levels of serum cartonectin, fasting blood glucose, in type 2 diabetic patients and to compare these levels with matched non-diabetic control people.

Methodology

This study was conducted according to a cross-sectional design in an out-patient department and questionnaire was used to collect the data and a biochemical automated analyzer was used to perform glucose, cholesterol (Chol), HDL, LDL1, VLDL, and triglycerides (TG) assays, descriptive analysis was performed using SPSS.

Results

Overall, our findings revealed that the mean concentration of serum cartonectin in recently diagnosed diabetes patients was considerably lower than in control groups. However, when it came to gender, male patients (0.43 ± 0.87) had a greater serum cartonectin content than female patients (0.24± 0.53), while control participants (2.34 ± 1.66 and 2.45 ± 1.68, respectively) had the opposite results. In patient participants, the mean serum cartonectin concentration was strongly related to their age groups. In patients, serum cartonectin concentrations rise with age and are unaffected by standard therapies. Furthermore, overweight patients had the lowest cartonectin concentration (0.247 ± 0.50) compared to normal and obese BMI (0.30 ± 0.75 and 0.78 ±1.136). FBS levels in patients were significantly higher than in controls (p=0.001). Furthermore, there were no significant variations in age, BMI, cholesterol, TG, HDL, LDL1, and VHDL across the examined groups. In comparison, patients' FBS, GTT1, GTT2, GTT3, and cartonectin characteristics showed a significant difference.

Conclusion

When compared to controls, serum cartonectin levels were shown to be lower in T2DM patients. The sub-factor study revealed that sex, BMI, age, FBS, and GTT all have a substantial impact on this relationship. Cartonectin emerges as a promising potential diagnostic for the prognosis and early recognition of T2DM patients, based on our findings.

Key words: Diabetic patients, Myocardial infarction, Cartonectin, Fasting Blood Glucose, Glucose Tolerance Test

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a group of metabolic disorders characterized by an aberrant insulin response. No doubt insulin is a crucial hormone in maintaining the body's natural balance. Currently, the prevalence of this kind of diabetes is rising, which is most likely connected to sedentary lifestyles and obesity epidemics.[1, 2] Obesity is widely recognized as a public health issue with a complex etiology and pathogenesis and detrimental effects on glucose metabolism regulation. Adipose tissue has traditionally been thought of as a storage organ. It is currently recognized as the primary endocrine organ, releasing adipocytokines[3], which are a class of regulatory substances. These molecules are regarded to constitute a "link" between adipose tissue and hormonal disorders including obesity causes insulin sensitivity to be altered and metabolic irregularities because increasing fat tissue has a variable

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secretion pattern depending on current metabolism.[4, 5] C1q TNF-related protein-3 (also referred as cartducin or cartonectin) is a crucial component of the newly identified regulatory peptides produced spontaneously by adipose tissue and peripheral organs, which play a key role in the pathophysiology of metabolic abnormalities in type 2 diabetes patients.[4, 6] Cartonectin (CTR3) is a peptide hormone produced primarily by adipocytes.[6] CTRP3 is a member of the C1q/TNF protein family, which shares several structural similarities with adiponectin (ADPN). The other is the most well-known member of the family of CTRP, which regulates insulin levels in tissues and is a commonly used biomarker for measuring medication efficacy in obese people with diabetes problems.[6, 7] Insulin resistance and the onset of type 2 diabetes are linked to a drop in this adipocytokine's plasma levels.[6] In line with the studies conducted by Wang et al. (2017), Peterson et al. (2016) and Ban et al. (2014) about the CTRP3 functions in inflammatory processes and has anti-inflammatory capabilities by inhibiting the concentration of pro-inflammatory cytokines as well as IL-6 and TNF, according to previous studies.[7-9] The quantity of leptin in the blood is inversely related to the level of CTRP3 in the blood.[6] Cartonectin inhibits both glucogenesis and adipogenesis. Cartonectin may also aid in the reduction of lipotoxicity caused by adipose tissue fat buildup that is abnormal[10] CTRP3 acts as a moderate vasodilator and increases endothelial cellular proliferation during angiogenesis.[11] CTRP3 contains anti-inflammatory and cardioprotective properties, comparable to adiponectin.[11, 12] Previous investigations on the levels of CTRP3 in diabetic individuals are similarly inconsistent. In Choi et al.[13] study, CTRP3 levels in patients increased. Other studies found a decrease in the specified adipocytokine in people with type 2 diabetes and/or obesity; however, other research reported a decline in the described adipocytokine in patients with type 2 diabetes and/or obesity.[8, 11, 14-16] Other diseases linked to obesity, like T2DM, overweight hypertension, and polycystic ovarian syndrome, have reduced blood CTRP3 levels than healthy people, according to several clinical studies.[8] CTRP3 indicates that they might be useful in detecting metabolic abnormalities in type 2 diabetes patients commencing insulin treatment. Additionally, the medication caused a different sort of change in anti-inflammatory adipocytokines plasma level.[10]

Although circulating CTRP-3 has been linked to T2DM, obesity, and other conditions in previous research, little is known about its connections to newly discovered T2DM. Therefore, biomarker studies deserve additional research. As a result, serum cartonectin concentrations were compared in newly diagnosed T2DM patients (who had not yet started treatment) to age, and BMI matched control subjects, as well as other significant biochemical characteristics.

METHODOLOGY

Study design and setting

This study was conducted in Out Patient Department (OPD) District Head Quarter (DHQ), Mufti Mehmood Memorial Teaching Hospital (MMH) and Zanana Hospital of Dera Ismail Khan After receiving the ethical approval (DIR/KMU-AS&RB/SC/00/1375) from AS&RB KMU. The duration of the study was six months conducted between April 2021 to October 2021 according to a cross-sectional study.

Data collection

After being properly informed about the study, all participants give signed informed consent. Demographic data (age and race), complete medical and family history were all recorded on a well-documented questionnaire.

Biochemical analysis

The researchers used a Hitachi 7600 biochemical automated analyzer to perform glucose, cholesterol (Chol), HDL, LDL1, VLDL, and triglycerides (TG) assays [8]. A commercially available ELISA kit (Aviscera, Santa Clara, USA) was used to determine the quantity of cartonectin in serum with an intra-assay coefficient of variation of less than 6%, according to the manufacturer's methodology [8].

Data analysis

The data from all of the participants were analyzed using descriptive statistical analysis as means and standard deviation (SD) in SPSS (Statistical Package for Social Sciences) version 21, with a significance level of $P<0.05$.

RESULTS

Correlation of cartonectin concentration (ng/ml) with covariates

According to a Spearman Rank analysis, serum cartonectin was significantly inversely associated with glucose, GTT1-3, Chol, TG, HDL, LDL1, and VHDL, while age and BMI were shown to be strongly positively associated (Table 1) in the case of the patient group. In the control group BMI, GTT2, Chol, HDL, LDL1 non-significantly negatively correlated with serum cartonectin and positively non significantly correlated with age, FBS, GTT1,3, TG and VDHL ($p>0.05$).

Parameters	Patients		Control	
	R	*p.value*	*R*	*p.value*
Age	0.312**	0.004	0.057	.606
BMI	0.062	0.575	-0.052	.634
FBS	-0.369**	0.001	0.074	.504
GTT1	-0.319**	0.003	0.049	.655
GTT2	-0.342**	0.001	-0.043	.693
GTT3	-0.289**	0.007	0.096	.380
Chol	-0.083	0.451	-0.106	.335
TG	-0.068	0.533	0.141	.198
HDL	-0.061	0.578	-0.214*	.049
LDL1	-0.047	0.667	-0.051	.644
VHDL	-0.040	0.714	0.008	.940

Table 1: Correlation of different variables associated with Cortonectin. FBS (Fasting blood glucose) (mg/dL), GTT (Glucose tolerance test) mg/dL, Chol (Cholesterol) (mg/dL), TG (Triglycerides) (mg/dL), HDL (High-density lipoproteins) (mg/dL), HDL (Low-density lipoproteins) (mg/dL), VHDL (Very-density lipoproteins) (mg/dL).

Biochemical analysis

According to Table 2, FBS was found to be 164.43 ± 55.41 and 102.02 ± 4.35 (p=0.000) for the patient and control group, GTT (1-3) was 216.76 ± 52.46, 227.96 ± 55.71, 220.85 ± 54.79 and 150.34 ± 21.53, 164.58 ± 110.56, 157.18 ±28.18 (p=0.000) for patient and control group, respectively. Cholesterol levels were 185.39 ± 36.679, 182.33 ± 36.19 (p=0.58) for the patient and control groups, respectively. TG, HDL, LDL1, and VHDL levels were 169.98±45.33, 159.79 ± 41.32 and 38.56 ± 17.82, 39.45 ± 19.27 and 112.82 ± 28.08, 111.63 ± 29.06 and 36.16 ± 21.18, 32.68 ± 9.22 for patient and control group, respectively and p>0.05 was deemed to be non-significant.

Biochemical Parameters	Patients	Control	p. value
Age	44.82 ± 10.14	47.80 ±11.10	.070
FBS	164.43 ± 55.41	102.02 ± 4.35	.000
BMI	25.52 ± 4.18	24.87 ± 4.47	.330
GTT1	216.76 ± 52.46	150.34 ± 21.53	.000
GTT2	227.96 ± 55.711	164.58 ± 110.56	.000
GTT3	220.85 ± 54.79	157.18 ± 28.18	.000
Chol	185.39 ± 36.67	182.33 ± 36.19	.585
TG	169.98 ± 45.33	159.79 ± 41.32	.128
HDL	38.56 ± 17.827	39.45 ± 19.27	.757
LDL	112.82 ± 28.08	111.63 ± 29.06	.787
VHDL	36.16 ± 21.185	32.68 ± 9.226	.167
Cartonectin	0.33 ± 0.73	2.41 ± 1.67	.000

Table 2. Biochemical analysis of study subjects (patients and controls). FBS (Fasting blood glucose) (mg/dL), GTT (Glucose tolerance test) mg/dL, Chol (Cholesterol) (mg/dL), TG (Triglycerides) (mg/dL), HDL (High-density lipoproteins) (mg/dL), HDL (Low-density lipoproteins) (mg/dL), VHDL (Very-density lipoproteins) (mg/dL).

This study included 85 participants, all of the participants were newly diagnosed, and at the time their blood samples were taken for this study, they were not on any medications, and 85 participants were non-diabetic control group without any complications. The serum was promptly aliquoted on ice and maintained at 80 °C. Anthropometric measures were taken on all of the patients. All of the participants were weighed on the same machine (Certeza Ps-812 Digital Weighing Scale) throughout the study and their BMI was calculated. Subjects of different age groups were indicated in Table 3.

Demographical and clinical data

In the current study, 42 females and 43 males were patients, while 55 females and 30 males were included as a control. When a comparison was made for cortonectin concentration (ng/ml) in females and males, it was found that 0.24 ± 0.53 and 0.43 ± 0.87, respectively in the case of the patient group, while in the case of the control group, it was 2.45 ± 1.68 and 2.34 ± 1.66, respectively with p=0.000 which indicated there was quite significant different among both groups (Table 4).

Age Group (years)	Patients	Controls
20-30	8 (9.4%)	9 (10.6%)
31-40	31 (36.5%)	17 (20.0%)
41-50	23 (27.1%)	26 (30.6%)
51-60	16 (18.8%)	24 (28.2%)
>60	7 (8.2%)	9 (10.6%)
Total	85 (100.0%)	85 (100.0%)

Table 3. Subject (patient and control) age (years) wise distribution.

Genders	Subjects		p.value
	Patients	Control	
Females	42 (49.4%)	55 (64.7%)	.044*
Males	43 (50.6%)	30 (35.3%)	
Total	85 (100.0%)	85 (100%)	
Comparison of Cartonectin concentration (ng/ml) in male and female			
Females	0.24+0.53	2.45+1.68	0.000*
Males	0.43+0.87	2.34+1.66	

Table 4. Comparison of gender wise Cartonectin concentration (ng/ml) in patients and control groups. *Significance at p≤ 0.05 at 95% confidence interval.

According to Table 5, Cortonectin concentration in 20-30 years of age group patient and control age group, was found to be significant (p=0.016), while the concentration for remaining age group was also found to significant (p<0.05).

Age Group	Patients	Controls	p.value
20-30	0.12 ± 0.10	2.16 ± 2.10	.016*
31-40	0.14 ± 0.37	2.69 ± 1.60	.000*
41-50	0.38 ± 0.91	2.16 ±1.92	.000*
51-60	0.60 ± 0.87	2.52 ± 1.55	.000*
>60	0.64 ± 1.10	2.60 ± 0.85	.001*

Table 5. Concentration of cartonectin (g/ml) in different age (years) wise groups. *Significance at p≤ 0.05 at 95% confidence interval.

BMI was categorized into three major groups (normal, overweight and obese), in the patient group, 47.1%, 41.2%, and 11.8% of

participants were fall into normal, overweight and obese

categories, respectively. While in the control group, 60%, 30.6%, and 9.4% were fall in the normal, overweight and obese. Cortonectin concentration was found lower in the obese group of the patient (0.301 ± 0.75), while in the control group, it was 1.67 ± 1.38 (p>0.05) as shown in Table 6.

Body Mass Index (BMI)	Patients	Control	p. value
Normal	40 (47.1%)	51 (60.0%)	0.23
Overweight	35 (41.2%)	26 (30.6%)	
Obese	10 (11.8%)	8 (9.4%)	
Cartonectin concentrations(ng/ml)			
Normal	0.301 ± 0.75	2.52 ± 1.64	.000*
Overweight	0.24 ± 0.50	2.44 ± 1.79	.000*
Obese	0.78 ± 1.13	1.67 ± 1.38	0.155

Table 6. BMI and Cartonectin concentrations (ng/ml) in participants (patient and control groups). *Significance at p≤ 0.05 at 95% confidence interval.

DISCUSSION

Given its favorable effect on the process of T2DM development and associated effects, including as insulin resistance, inflammation, and endothelial dysfunction, decreased levels of cartonectin can be a factor that exacerbates pathogenic circumstances in people with T2DM. Diabetes complications, particularly microvascular complications, are exacerbated as a result of this. Cartonectin is a unique adipokine, and has been exposed to perform a variety of physiological functions, comprising regulation of energy metabolism, the excretion of adipokines, inflammation, and cell differentiation and development via an endocrine medium. When ELISA was used to measure serum cartonectin levels in newly diagnosed T2DM patients, we discovered that they were lower than non-diabetic participants. Cartectin appears to have similar qualities, such as insulin sensitization, anti-inflammatory, and cardioprotective effects.[17] There is evidence from preclinical studies that cartonectin levels are lower in obese and newly diagnosed T2DM patients.[8, 16] While according to Choi, et al, [13] the levels of cartonectin were shown to be high. In our study, the lowest (0.247 ± 0.50) cartonectin concentration was noted in overweight patients in comparison with normal and obese BMI (0.30 ± 0.75 and (0.78 ± 1.136) patients and obese patients suffered from a similar struggle. Wolf et al, [16] discovered significantly reduced cartonectin levels in obese patients, but Wagnerm et al,[18] discovered significantly greater cartonectin levels in obese male patients. According to Deng[19], cartonectin levels are decreased in people with obesity and hypertension. Cartonectin levels were found to be greater in type-2 diabetic patients, and also discovered that serum cartonectin, glucose, and CRP levels have a negative connection.[20] There were another study conducted on the Chinese population concluded that cartonectin levels in the blood are substantially lower in Chinese individuals with obesity and type 2 diabetes than in healthy people. It is associated with chronic inflammation, glucose and lipid metabolism, and insulin resistance.[15] We also discovered a negative association between cartonectin levels and glucose as well. However, in the case of gender, serum cartonectin concentration level was higher in male (0.43 ± 0.87) patients as compared to female patients (0.24 ± 0.53); opposite results were observed in control participants who were 2.34 ± 1.66 and 2.45 ± 1.68, respectively. The mean serum cartonectin concentration was significantly associated with different age groups in patient-participants. The serum cartonectin concentrations' values increase with age in patients and normal treatments. Patients with PCOS have decreased levels of adipose tissue cartonectin. In the current study it was found that the amount of FBS in patients was substantially greater than in controls (p=0.001). In addition, Age, BMI, Chol, TG, HDL, LDL1, and VHDL showed that there was no discernible difference between the groups studied.

In comparison, a significant difference was observed in FBS, GTT1, GTT2, GTT3 and cartonectin parameters in subjects, Tan, et al [21] also discovered negative links between glucose, BMI, TG, LDL, and CRP and also discovered that after six months of metformin treatment, the level of serum cartonectin in this patient group increased. Similarly, cartonectin was found to be inversely connected with glucose and LDL levels while positively correlated with BMI in the present study. A negative relationship exists between circulating cartonectin levels and T2DM status, according to the findings of systematic review and meta-analysis. This relationship may be influenced by BMI and gender.[22] Cartonectin was found to be lower in females than in males in the current investigation, while in control, that was the opposite, which is not inconsistent with prior animal and human investigations that discovered a sex-specific pattern for cartonectin expression and blood levels.[11, 18] These findings suggested that hormonal state may influence CTRP3, although more research is needed in this area.

CONCLUSION

Our findings suggest cartonectin as a potential biomarker for T2DM patient prediction and early diagnosis. Additionally, pharmacological drugs that raise circulation cartonectin levels, such as cartonectin and/or cartonectin, may open up a new therapeutic avenue for the treatment of T2DM patients. However, because the current investigation was cross-sectional, we could not draw any conclusions about a causal association between lower cartonectin serum levels and diabetic nephropathy. In this area, more research is needed to back up this theory.

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