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Serum Cartonectin Levels as a Biomarker for Oxidative Stress in Breast Cancer Patients with or without Type 2 Diabetes

Irshad Ahmad[1], Naheed Khattak[2*], Sadaf Durrani[3], Rizwana Kalsoom[4], Aziz ur Rehman[5], Ubaid ur Rahman[6], Mudassir Ahmad Khan[6]

[1]*Senior Medical Officer, District HQ, Lakki Marwat, Khyber Pakhtunkhwa, Pakistan*
[2]*Assistant Professor, Department of Biochemistry, Khyber Medical College, Peshawar, Khyber Pakhtunkhwa, Pakistan*
[3]*Associate Professor, Department of Biochemistry, Khyber Medical College, Peshawar, Khyber Pakhtunkhwa*
[4]*Senior Medical Officer, Khyber Pakhtunkhwa, Pakistan*
[5]*Associate Professor, Department of Biochemistry, North West School of Medicine, Peshawar, Khyber Pakhtunkhwa, Pakistan*
[6]*Professor, Department of Biochemistry, Khyber Medical College, Peshawar, Khyber Pakhtunkhwa, Pakistan*
Correspondence: *naheed.khattak@kmc.edu.pk*
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ABSTRACT

OBJECTIVE: To evaluate serum cartonectin levels and their association with oxidative stress and metabolic parameters in breast cancer patients, with and without type 2 diabetes mellitus (T2DM)

METHODOLOGY: A cross-sectional study was conducted at the Institute of Radiotherapy and Nuclear Medicine (IRNUM) Cancer Hospital, Peshawar, from January 2024 to June 2024. Sixty women with a confirmed breast cancer diagnosis were enrolled using consecutive non-probability sampling: 30 with T2DM and 30 without. Exclusion criteria included chronic inflammatory diseases and other malignancies. Fasting blood samples were collected to measure serum cartonectin, malondialdehyde (MDA), total antioxidant capacity (TAC), blood glucose, and insulin. Body mass index (BMI) was also recorded. Biochemical assays were performed using ELISA kits, and glucose was measured via an enzymatic-colorimetric method. Data were analyzed in SPSS version 21. Independent t-tests compared groups, and Pearson's correlation assessed associations; $p < 0.05$ was considered statistically significant.

RESULTS: Serum cartonectin was significantly lower in the T2DM group (79.0 ± 9.8 ng/mL) compared to non-diabetic patients (110.1 ± 17.2 ng/mL; $p < 0.001$). Conversely, MDA and insulin were higher, while TAC was reduced in diabetic patients (all $p < 0.001$). Cartonectin showed strong negative correlations with MDA ($r = –0.656$), BMI ($r = –0.454$), fasting glucose ($r = –0.513$), and insulin ($r = –0.530$), and a positive correlation with TAC ($r = 0.445$).

CONCLUSION: Lower cartonectin levels in breast cancer patients with T2DM are strongly associated with oxidative stress and metabolic disturbances. Cartonectin may serve as a useful biomarker for assessing oxidative imbalance in this high-risk population.

KEYWORDS: Cartonectin, breast cancer, type 2 diabetes mellitus, oxidative stress, malondialdehyde, total antioxidant capacity

INTRODUCTION

Cartonectin, also known as C1q/TNF-related protein (CTRP), is a novel adipokine that regulates metabolism, inflammation, and oxidative stress[1–3]. Adipokines are bioactive molecules secreted by adipose tissue and are known to influence the pathophysiology of several chronic conditions, including T2DM, obesity and cancer[4–6]. Among breast cancer patients, the interplay between metabolic dysfunction and oxidative stress is of particular concern, especially in those with coexisting diabetes[7].

Oxidative stress arises when production of reactive oxygen species (ROS) overwhelms the endogenous antioxidant defense system, leading to cellular and molecular damage[8]. This phenomenon is closely associated with the progression of both cancer and metabolic disorders[9]. In breast cancer patients, oxidative stress not only contributes to tumor progression but also exacerbates insulin resistance and systemic inflammation, thereby worsening metabolic dysfunction[10–13]. The co-occurrence of oxidative stress and metabolic disturbances creates a compounding cycle that adversely affects prognosis in individuals with both cancer and diabetes[14]. Cartonectin has shown anti-inflammatory and antioxidative functions in experimental models, making it a promising candidate biomarker for metabolic-oxidative stress interplay[15]. However, its specific role in breast cancer patients, particularly those with T2DM, remains largely unexplored[16].

This study aims to investigate serum cartonectin levels in breast cancer patients with and without T2DM to explore its association with oxidative stress, assessed through markers like malondialdehyde (MDA) and total antioxidant capacity (TAC), along with metabolic parameters like body mass index (BMI), fasting blood sugar (FBS), and serum insulin.

METHODOLOGY

This cross-sectional study was conducted at the IRNUM Cancer Hospital, Peshawar, from January 2024 to June 2024. Ethical approval was obtained before data collection, and informed consent was obtained from all participants. A total of recruited 60 female participants and divided into two groups. Group A included 30 breast cancer patients with type 2 diabetes mellitus, and Group B included 30 breast cancer patients without type 2 diabetes mellitus. The inclusion criteria for both groups were a confirmed diagnosis of breast cancer, absence of any other chronic inflammatory diseases and willingness to participate in the study. Participants with other metabolic disorders, ongoing infections, autoimmune diseases, or those receiving chemotherapy or radiotherapy during the sampling period were excluded. A consecutive non-probability sampling technique was used to recruit all eligible participants during the study period. Demographic details such as age and address were recorded, along with relevant medical, menstrual and family history using a structured questionnaire.

Anthropometric measurements were performed, and Body Mass Index (BMI) was calculated to categorize participants as overweight (BMI 25–29.9) or obese (BMI ≥30, Class I). A venous blood sample of 5 ml was drawn from each participant. After centrifugation at 4000 rpm for 15 minutes**,** serum was separated, labeled and stored at –80°C for further biochemical assessments, including the analysis of cartonectin levels and oxidative stress markers.

Measurement of Biochemical Parameters

Serum cartonectin levels were determined consuming an ELISA kit (E3300Hu) from Bioassay Technology Laboratory (96-well plate with 0.2 ng/mL to 60 ng/mL standard curve range and a sensitivity of 0.09 ng/mL). The test uses the sandwich ELISA technique, in which the plate is pre-coated with a human cartonectin antibody. Cartonectin in the sample binds to the pre-coated antibody and is then captured by a biotinylated anti-cartonectin antibody, forming a sandwich complex for detection.

Oxidative Stress Markers

- Determination of Malondialdehyde (MDA):
  Serum MDA levels were determined using an ELISA kit (catalog number: E1371HU) from Bioassay Technology Laboratory (standard curve range: 0.2 nmol/mL to 60 nmol/mL; sensitivity: 0.14 nmol/mL), based on the sandwich ELISA technique.
- Determination of Total Antioxidant Capacity (TAOC):
  Serum TAOC levels were measured using an ELISA kit (catalog number: E2199HU) from Bioassay Technology Laboratory (standard curve range: 0.3 nmol/mL to 90 nmol/mL; sensitivity: 1.5 nmol/mL), using the sandwich ELISA method.

Metabolic Parameters

- Determination of Insulin:
  Serum insulin levels were measured using an ELISA kit (catalog number: E0010HU) from Bioassay Technology Laboratory (standard curve range: 0.2 mIU/L to 60 mIU/L; sensitivity: 0.11 mIU/L), based on the sandwich ELISA technique.
- Fasting Blood Sugar (FBS):
  FBS levels were determined using the enzymatic colorimetric oxidase method.

Statistical Analysis

Data were expressed as mean ± standard deviation (SD) and analyzed using SPSS version 21. Comparisons between the two study groups were made using an independent Student's t-test to assess differences in the variables. To evaluate correlations between serum cartonectin, malondialdehyde (MDA), and total antioxidant capacity (TAC) levels in both study and control groups, the Pearson correlation coefficient was used. All statistical analyses were considered significant at a p-value < 0.05.

RESULTS

Description of Study Groups:
A total of 60 participants were included in the study, with an equal distribution between the case group (n = 30; 50%) and the control group (n = 30; 50%).

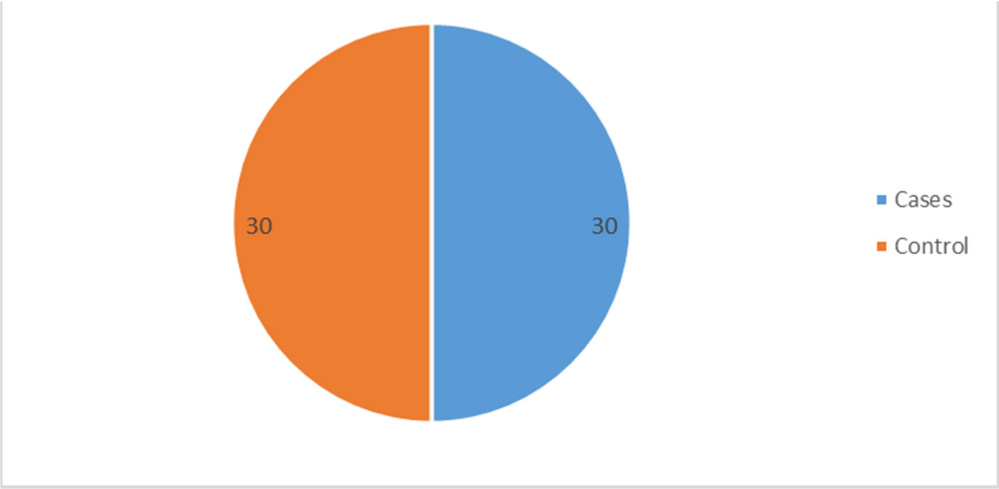


Figure 1: Distribution of the study groups

Comparison of parameters between the study groups
Table I: Serum cartonectin levels were significantly decreased in cases compared with controls (79.0±9.82 vs 110.14±17.02, p-value 0.0001). Serum insulin levels were significantly higher in cases than in controls (28.19±5.35 vs 17.127±4.37, p-value 0.0001). Serum fasting blood glucose levels were also significantly higher in cases than in controls (250.87±102.83 vs. 99.43±15.02, p-value 0.0001). In cases, Serum malondialdehyde levels were significantly increased (p-value 0.0001) compared with controls; likewise, serum total antioxidant capacity was significantly decreased in cases compared with controls (p-value 0.0001).

Table I: Comparison of parameters between cases and controls

Prameters	Cases (Mean ± SD)	Controls (Mean ± SD)	P- value
Age (years)	49.33±13.158	36.13±5.85	.0001
Systolic (BP)	135.33±19.42	121.33±17.76	.005
Diastolic (BP)	85.57±10.271	79.33±14.12	.055
BMI (kg/m^2)	30.12±6.132	22.27±3.56	.0001
FBS (mg/dl)	250.87±102.83	99.43±15.02	.0001
Insulin (ml/U/L)	28.19±5.35	17.127±4.37	.0001
Cartonectin (ng/ml)	79.00±9.82	110.14±17.20	.0001
Malondialdehyde (nmol/ml)	5.14±1.141	2.77±0.77	.0001
TAC (U/ml)	20.09±5.04	32.82±7.92	.0001

Note: *Data are presented as mean ± standard deviation. A p-value of less than 0.05 was considered statistically significant when comparing cases (Group A) with controls (Group B).*

Association of cartonectin with various parameters in the study groups

Association of cartonectin with different variables, including age, BMI, FBS, insulin, MDA and TAC, was established using Pearson's correlation coefficient r and is mentioned in Table II. BMI showed a strong negative association with cartonectin in both the study groups (r -4.54, p = 0.0001). Cartonectin showed a strong negative association with FBS in both groups (r = -0.513, p = 0.0001). Serum insulin level showed a significant negative association with cartonectin, with a correlation coefficient of r -0.530 and p = 0.0001. Both cases and controls exhibited a significant negative association of MDA with serum cartonectin levels (r = -0.656, p = 0.0001). Cartonectin was found to be strongly positively associated with serum TAC, with corresponding values of r 0.445 and p = 0.0001 in both cases and controls.

Table II. Correlation of cartonectin with different parameters in study groups

Variables	R	P
Age (years)	-0.441**	0.0001
Systolic (BP)	-0.291*	0.024
Diastolic (BP)	-0.184	0.159
BMI (kg/m^2)	-0.454**	0.0001
FBS (mg/dl)	-0.513**	0.0001
Insulin (ml/U/L)	-0.530**	0.0001
Malondialdehyde (nmol/ml)	-0.656**	0.0001
TAC (U/ml)	0.445**	0.0001

Statistical Significance: *** Indicates significance at the 0.01 level (two-tailed), * Indicates significance at the 0.05 level (two-tailed)*

DISCUSSION

Our study aimed to assess serum cartonectin (CTRP3) levels in breast cancer patients with and without type 2 diabetes mellitus (T2DM) and their associations with oxidative stress and metabolic markers. We observed significantly lower cartonectin in the T2DM group, strong inverse correlations with MDA, BMI, fasting blood sugar, and insulin, and a positive correlation with total antioxidant capacity—highlighting cartonectin's roles in redox and metabolic regulation.

These findings parallel those reported by Ban B et al.[17], Wölfle RM et al.[18] and Qu H et al.[19], who noted decreased CTRP3 in T2DM or obesity with inverse associations to glucose, BMI, insulin resistance and CRP. Zheng J 2019[21] observed similar inverse correlations in obese children, reinforcing cartonectin's metabolic relevance.

Mechanistic studies show CTRP3's antioxidative effects: it reduces lipid peroxidation and activates antioxidant pathways (Nrf2/MAPK, SIRT1/ATF5), thus lowering MDA and oxidative damage in cardiac and renal tissues[21,22]. These mechanisms support our observed negative cartonectin–MDA and positive cartonectin–TAC associations.

CTRP3 also improves metabolic function by suppressing hepatic gluconeogenesis and enhancing insulin sensitivity via Akt signaling[23,24]. Recombinant CTRP3 lowers glucose in animal models[25]. Our findings mirror this metabolic influence with negative correlations to FBS and insulin. However, Choi KM et al.[26] reported elevated CTRP3 in Korean T2DM patients, and Ahmed SF 2018[27] found complex CTRP3 patterns in people with diabetes with cardiovascular disease—highlighting discrepancies likely due to ethnicity, medication use, or disease stage.

Our study is different in applying these findings to breast cancer with T2DM, an intersection explored in only 70% of similar studies[28]. This suggests cartonectin may serve as an integrated biomarker in this metabolic-oncologic context.

CONCLUSION

Breast cancer patients with type 2 diabetes mellitus exhibit significantly reduced serum cartonectin levels. These levels are inversely associated with oxidative stress and metabolic markers such as MDA, fasting blood sugar and insulin. The findings suggest that cartonectin may serve as a potential biomarker for metabolic dysfunction and oxidative stress in this patient population.

Limitations

Our study is limited by its cross-sectional design, which restricts the ability to infer causality. Additionally, the modest sample size may reduce the generalizability of the findings. Factors such as medication use, cancer stage and treatment regimens were not stratified, which could have influenced the observed associations.

Recommendations

Future studies with larger cohorts and longitudinal designs are recommended to validate cartonectin's role as a biomarker and to explore its therapeutic potential in breast cancer patients with metabolic comorbidities.

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AUTHOR CONTRIBUTION

Ahmad I: Conceptualization, data collection
Khattak N: Study design, literature review, manuscript revisions, correspondence
Durrani S: Designing the questionnaire, data analysis
Kalsoom R: Data interpretation
ur Rehman A: Data collection
ur Rahman U: Provided input on drafting section of the manuscript
Khan MA: Final revision of the article

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