*Original Article*

# Study of Circulatory Level of Omentin-1 in Type2 Diabetes Mellitus and Association with Carotid Artery Atherosclerosis

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***ABSTRACT:***

***Background:*** *Diabetes mellitus is associated with severe cardiovascular complications, including vascular calcification and accelerated atherosclerosis. The omentin gene is located in the 1q22-q23 chromosomal region, which has been linked to type 2 diabetes in several populations, suggesting that omentin may be a candidate gene for type 2 diabetes susceptibility in humans.*

***Objective:*** *The aim of the study was to study the relationships between serum omentin-1 and carotid atherosclerosis in type2 diabetic patients.*

***Subjective:*** *This cross-sectional study was conducted on 90 subjects divided into two groups.*

***Results:*** *The results of this study showed a highly significant decrease of omentin1 level in diabetic patients, also, the ankle brachial index show a significant decrease in diabetic group less than the control group. There was a negative significant correlation between Omentin-1 level with carotid intimal thickness in diabetic patients, also it was found that there was a negative correlation between Omentin-1 level and BMI, waist circumference, duration of DM.*

***Conclusion:*** *we conclude that there was a* ***significantly*** *decreased omentin-1 level in type 2 DM patients as compared with controls, with a larger decrease among patients with increased CIMT*

**INTRODUCTION:**

Diabetes mellitus is associated with severe cardiovascular complications, including vascular calcification and accelerated atherosclerosis, leading to increased morbidity and mortality in diabetic patients.[1,2]

The plasma level of omentin is produced by fat tissue that surrounds our internal organ. This enhances the effect of insulin in regulation of sugar which is associated with different conditions such as insulin resistance, diabetes mellitus, obesity, endothelial dysfunction and atherosclerosis. It is one of the novel adipokines synthesized mainly in the visceral adipose tissue.[3,4] Omentin is a novel fat depot-specific adipokine that was identified in 2003 from a visceral omental adipose tissue cDNA library.[4]

The omentin gene is located in the 1q22-q23 chromosomal region, which has been linked to type 2 diabetes in several populations,[5,6] suggesting that omentin may be a candidate gene for type 2 diabetes susceptibility in humans.[7] The recombinant omentin-1 enhances insulin-stimulated glucose uptake . Several clinical studies have shown that the serum omentin-1 level is significantly decreased in diabetic patients obese patients or patients with polycystic ovary syndrome.[8,9] In addition, circulating omentin-1 levels are negatively correlated with metabolic risk factors, including body mass index, waist circumference, and insulin resistance.[9,10]

The circulating level of omentin-1 in an Egyptian population with type 2 diabetes, with and without ischemic heart disease. Although they did not detect clear differences in serum omentin-1 levels between type 2 diabetes patient with and without ischemic heart disease, multiple regression analysis showed that IL-6 level was an independent risk factor influencing serum omentin-1 level.[11,12] This suggests that omentin-1 is regulated by inflammation. Inflammation is the most important factor linking type 2 diabetes to the progression of cardiovascular complication.[13] Serum omentin-1 levels were lower in patients with acute coronary syndrome or stable angina pectoris compared to controls.[14]

Circulating omentin-1 had a negative correlation with atherosclerotic parameters. However, no previous studies have clarified the relationship of serum omentin-1 with atherosclerosis in subjects with type 2 diabetes. Carotid intima-media thickness (IMT) and arterial stiffness are useful surrogate markers for subclinical atherosclerosis and are significantly correlated with various metabolic risk factors.[15,16]

In prospective studies, both arterial stiffness and carotid IMT have proven to be consistent and independent predictors for cardiovascular events.[17]

## AIM OF THE WORK

The aim of the study was to study the relationships between serum omentin-1 and carotid atherosclerosis in type 2 diabetic patients.

## PATIENTS & METHOD

### Patients:

This cross-sectional study was conducted on 90 subjects divided into two groups.

**Group I:** 60 type 2 diabetic patients. **Group II:** 30 non- diabetic healthy control group.

All participates was give written informed consent after explaining the nature and the aim of the study. The healthy control group was including those without any chronic cardiovascular or metabolic disease and not receiving any long-term medication for both conditions.

## METHODS

- After giving their signed informed written consent; all the participants were subjected to the following:

- **Full history taking**
- **Complete physical examination including:**
  - Body weight and height was measured with the subject wearing light clothes and without shoes in order to calculate body mass index (BMI).[18]
  - Waist circumference.
  - Vital signs (heart rate and arterial blood pressure).
  - Neurological examination for detection of diabetic peripheral neuropathy.
- **Laboratory investigations:**

Blood drawn for metabolic, biochemical and hematological parameters after a 10-12 hours overnight fasting and estimate the following:

- Fasting serum glucose.[19]
- Homeostasis Model Assessment 2 (HOMA2)
- Glycated haemoglobin (HbA1C).[19]
- Serum uric acid.
- Lipid profile
- **Serum Omentin-1 level by using ELISA.[20]**

- Color Doppler examination:
- The carotid artery atherosclerosis was characterized using color Doppler ultrasonic evaluation.[21]

**Assessment of ankle brachial index (ABI) using hand-held Doppler:**

**Doppler Carotid Artery to determine the carotid intima media thickness. [22]**

## RESULTS:

Regarding the demographic data, the sex, 60.0% were males in diabetic group ,while females was 40.0%, in the control group, 53.3% were males and 46.7% females, no significant difference was found between

the two groups regarding sex. The mean age in diabetic group was 57.11±11.47 years, and in control group 53.8±11.90 years, there was no significant difference between the two groups regarding age.

The anthropometric measurements in the two groups show a significant increase in both BMI and waist circumference in the diabetic group more than the control group.

Fourteen patients of diabetic groups (14/60, 23.3%) had family history of CAD while only four (4/30, 13.3%) of control group with no statistical significance between both groups regarding family history of CAD. Twenty three patients of diabetic groups (23/60, 38.3%) had history of hypertension while none (0/30, 0.0%) of control group had history of hypertension with statistical significance between both groups regarding history of hypertension.

Twenty nine patients of diabetic groups (29/60, 48.3%) had dyslipidemia while none (0/30, 0.0%) of control group had dyslipidemia with statistical significance between both groups regarding the presence of dyslipidemia.

Twenty seven patients of diabetic groups (27/60, 45%) were smokers while only three (3/30, 10%) of control group were smokers. Also, five of the diabetic group (5/60, 8.3%) were just ex-smoker while eight (8/30, 26.7%) of the control group were just Ex-smoker in addition to 28 of the diabetic group were non-smokers (46.7%) and in control group 19 (63.3%) with statistical significance increase in the smokers in diabetic group while there was significant increase in non-smoker and Ex-smokers in control group than diabetic group.

Regarding the clinical and laboratory examination of the two studied groups, it was found the systolic and diastolic blood pressure was significantly higher in diabetic patients more than the control, the glycemic parameters including FBS, HbA1c, Fasting serum insulin and HOMA IR show a highly significant increase in diabetic patients more than the control group. The kidney function test which includes creatinine and GFR show a significant abnormality in diabetic patients more than the control group. Omentin-1 level show significant decrease in diabetic patients less than the control group. Also the carotid intimal thickness show a significant increase in diabetic patients more than the control group, ankle brachial index was significantly lower in diabetic patients less than the control group. Finally the lipid profile show a significant increase in diabetic patients more than the control group as shown in table (I).

**Table I: Comparison between the studied groups according to clinical and laboratory data.**

| Blood pressure (mmHg) | Diabetic patients (n = 60) | Control (n = 30) | Test of Sig. | p |
|---|---|---|---|---|
| Systolic | 138.5±16.64 | 115.7±9.97 | 3.414* | 0.001* |
| Diastolic | 85.92±9.63 | 79.17±6.71 | 3.868* | <0.001* |
| Fasting blood glucose | 232.0±47.67 | 89.03±7.72 | 22.638* | <0.001* |
| HbA1C | 10.0±1.72 | 5.13±0.5 | 18.432* | <0.001* |
| Fasting serum insulin | 11.17±2.02 | 4.73±1.10 | 19.565* | <0.001* |
| HOMA IR | 1.90±0.20 | 1.50±0.22 | 8.636* | <0.001* |
| Creatinine (mg/dL) | 1.32±0.38 | 0.92±0.19 | 6.838* | <0.001* |
| GFR (ml/min) | 57.58±27.84 | 100.3±30.54 | 341.50* | <0.001* |
| Omentin-1 level (ng/L) | 797.2±39.35 | 986.3±24.21 | 28.083* | <0.001* |
| Carotid intimal thickness (mm) | 0.83±0.06 | 0.58±0.04 | 22.028* | <0.001* |
| Ankle Brachial index | 0.75±0.14 | 1.01±0.08 | 12.830* | <0.001* |
| Total cholesterol | 178.2±56.44 | 130.4±24.44 | 5.595* | <0.001* |
| Triglycerides | 192.1±89.07 | 117.4±16.66 | 543.0* | 0.002* |
| HDL | 38.68±9.53 | 45.13±7.24 | 3.573* | 0.001* |
| LDL | 134.3±28.04 | 108.0±16.63 | 5.549* | <0.001* |

**Correlation results:**

There was a negative correlation between Omentin-1 level and carotid intimal thickness. it was found that there was a negative correlation between Omentin-1 level and BMI (r=-0.33, p 0.01), waist circumference (r=0.294, p 0.22), duration of DM (r=-0.361, p 0.005), while no significant correlation with age in diabetic patients. there was a negative Correlation between Omentin-1 level and fasting blood sugar (r=-0.549, p <0.001), HbA1c (r=-0.438, p <0.001), HOMA IR (r=-0.38, p0.027), there was no significant correlation between omentin-1 and, fasting serum insulin. there was a negative Correlation between Omentin-1 level and carotid intimal thickness (r=-0.32, p 0.013), there was positive correlation between omentin-1 and ABI (r=0.320, p 0.012). there was a negative Correlation between Omentin-1 level and total cholesterol (r=-0.702, p <0.001), LDL (-0.319, p 0.013), triglyceride (r=-0.426, p 0.001) and positive correlation between omentin-1 and HDL (r=0.349, p 0.006) as shown in the following figures.

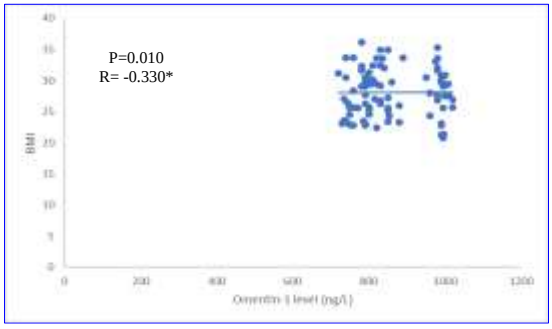


Figure 1: Correlation between omentin -1 level and BMI.

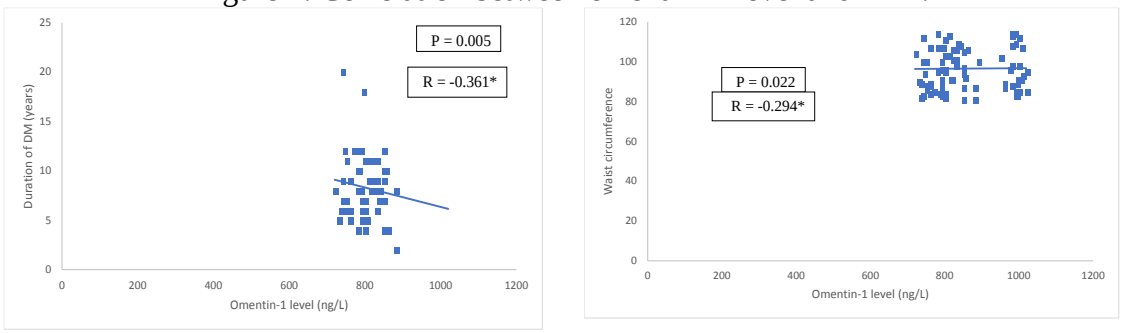


Figure 2: Correlation between Omentin-1 level and duration of DM and waist circumference.

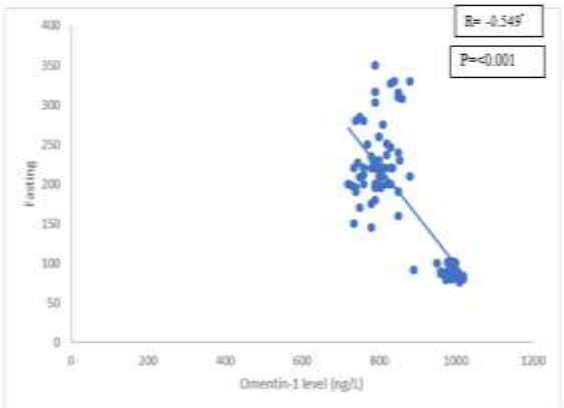


Figure 3: Correlation between omentin-1 level and fasting blood glucose level.

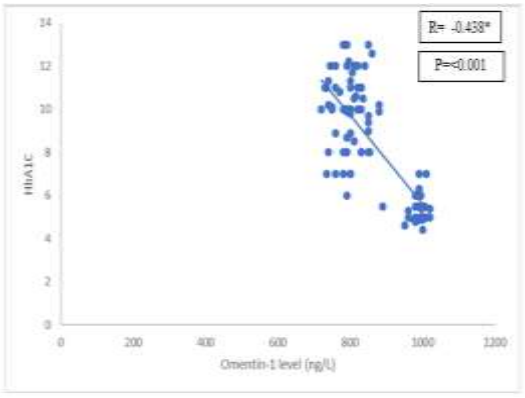


Figure 4: Correlation between omentin-1 level and HbA1c.

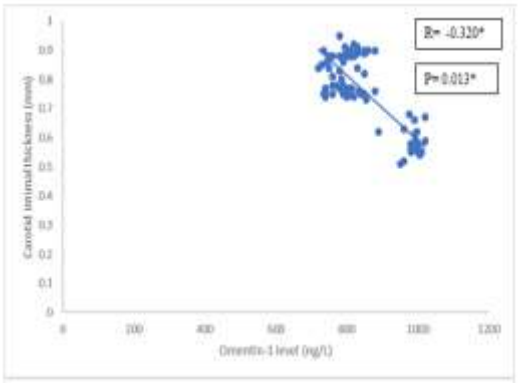


Figure 5: Correlation between Omentin-1 level and Carotid intimal thickness.

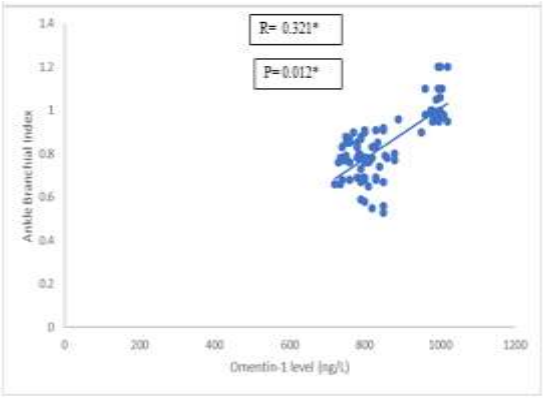


Figure 6: Correlation between Omentin-1 level and Ankle Brachial index.

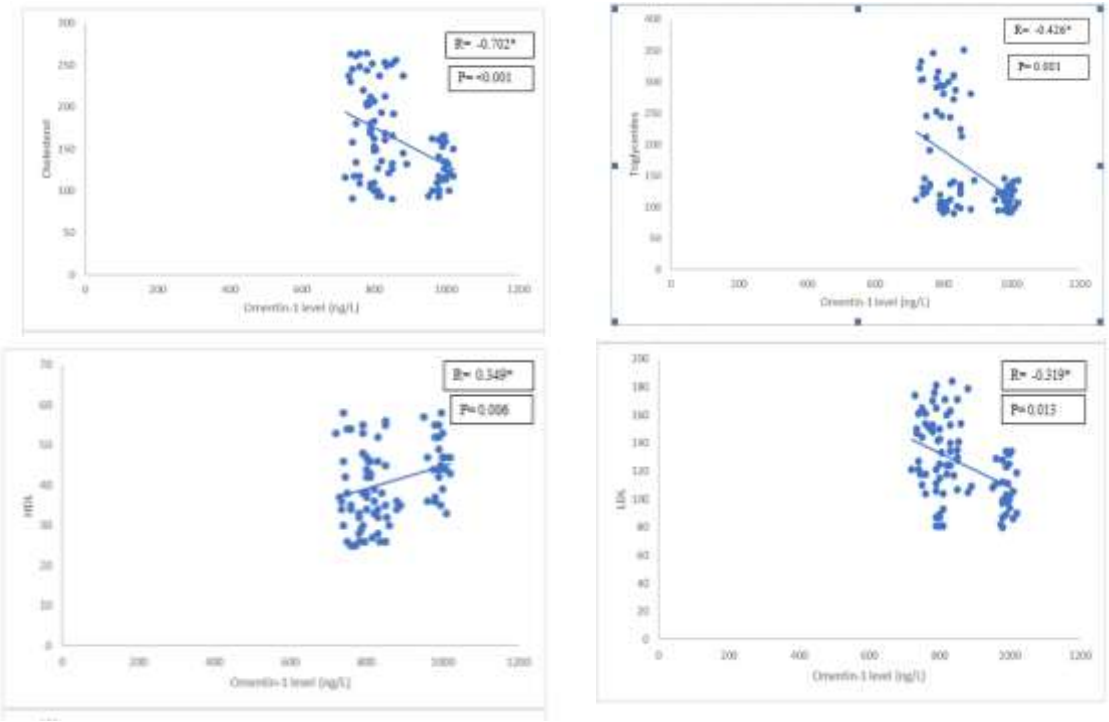


Figure 7: Correlation between Omentin-1 level and Lipid profile.

**DISCUSSION:**

The results in this study showed the demographic data in both studied groups (diabetic and control) was matched regarding basic data including age and sex, this results eliminate the effect of both age and sex on the net results. While the anthropometric measurements show significant increase in diabetic patients more than the control group, the BMI and waist circumference was significantly higher in diabetic more than control. This results was agreement with national surveys carried out by Bays et al., (2007)[23], they study The relationship of body mass index to diabetes mellitus, this study carried out on random sample of 200,000 subjects, this study confirms the converse – that the majority of patients with these metabolic diseases are either overweight or obese. These results provide nationally representative data regarding the important relationship between BMI and these metabolic diseases. [23]

In current study, family history of hypertension and dyslipidemia was significantly higher in diabetic group more than the control group. In agreement with our stud, Ranasinghe et al., 2015[24], study the influence of family history of Hypertension on disease prevalence and associated metabolic

risk factors, in this study they found that the risk associated with family history in the current population appeared to be independent of other known risk factors, including age, anthropometric parameters (BMI) and lifestyle factors (physical activity).[24]

The blood pressure in the diabetic patients in our study showed a highly significant increase more than the control group, type 2 diabetes mellitus and hypertension overlap in the population. We analyzed the pattern of blood pressure (BP) changes during the development of hypertension in patients with or without diabetes mellitus**.**[25]

In study carried out by Tsimihodimos et al., 2018[26], on Hypertension and Diabetes Mellitus, the first main finding of this study is that not only does the presence of hypertension predict future diabetes mellitus, in agreement with earlier epidemiological observations, but also the incidence of hypertension increases significantly in the presence of diabetes mellitus.[26]

The glycemic profile of the diabetic patients in our study showed a significant increase in fasting blood glucose, HbA1c, and HOMA IR, more than the control group, these results obey the inclusion criteria of diabetic patients group.

The renal function test including creatinine and GFR in current study showed a highly significant increase in creatinine and significantly decrease in GFR, our results was agreement with study carried out by Bamanikar et al., (2016)[27], they Study of Serum urea and Creatinine in Diabetic and nondiabetic patients. This study shows that poorly controlled blood sugar levels would cause increase in the serum urea and creatinine levels and thus increase the chances of the patient suffering from diabetic nephropathy. This corroborates with the findings of other studies which reported that hyperglycemia is one of the major causes of progressive renal damage.[27]

An increase in urea and creatinine level is seen when there is damage to the kidney. Increase in blood urea and creatinine level in the presence of high blood sugar level in diabetic patient indicates damage to the kidney. Studies conducted by Shrestha et al[28] had found that increase urea and serum creatinine in diabetic rats indicates progressive renal damage.[28]

In the current study, Serum omentin-1 level in diabetic group ranged between 720-880 μg/L with a mean value of 797.2±39.35 μg/L while in the control group it ranged between 890-1020 μg/L with a mean of 986.3±24.21 μg/L and the statistical analysis revealed significant decrease in omentine-1 in diabetic group than the control group (P = 0.001).

In agreement with our study, Tawfeek et al., (2014)[29], study the Relationship between omentin-1 and carotid intima thickness in type 2 diabetes mellitus, this study showed a significant decrease in serum omentin-1 levels among diabetic patients in comparison with the normal group. [29]

Greulich *et al.*[30] found that omentin-1 was highly expressed and secreted by epicardial adipose tissue, had reduced expression among type 2 DM patients compared with controls, and was positively correlated with diastolic function. These data suggest that omentin may not only serve as a biomarker for metabolic disorders but also as a cardio protective adipokine, and that a decrease in its level could contribute to the induction of cardiovascular dysfunction in DM patients. [30]

In agreement with our study, Al-Nimer et al., 2009[31], study the Increased mean carotid intima media thickness in type 2 diabetes mellitus patients, they found that type 2 diabetes mellitus patients with non blood pressure component metabolic syndrome have significant greater mean common carotid IMTs than those who are free from metabolic syndrome.[31]

Chung et al.[32] showed that the most influential factor affecting the validity of ABI was diabetes, with an odds ratio (OR) of 4.36 for the false negative results taken as a primary end point. Indeed, several studies showed that the decrease of the diagnostic efficiency of ABI is related to certain clinical situations related to diabetes such as neuropathy or foot wounds. For instance, the sensitivity of ABI

falls to 53% (specificity 95%) in the presence of peripheral neuropathy.[32]

In patients with an advanced vascular profile, an ABI<0.9 had 54.4% sensitivity in diabetic versus 72.6% in non-diabetic patients when comparing it toDUS.34This decrease in ABI sensitivity can also be explained by arterial stiffness secondary to MAC. This results in poorly compressible vessels and a high ABI. Indeed, high index values (>1.3e1.4) are particularly frequent in diabeticpatients,17,52 more specifically when diabetes is concomitant to kidney disease, neuropathy or foot lesions. In this case, high ABI values and MAC correlate with the duration and severity of diabetes. Therefore, the sensitivity of ABI seems to be limited in case of complicated or long-standing diabetes leading to more MAC.[33]

In our study, the lipid profile in diabetic patients showed a highly significant increase more than the control group, Cholesterol, triglycerides and LDL showed a highly significant increase in diabetic patients group more than the control group, on the other hand the HDL showed a significantly decreased in diabetic patients group less than the control group.

In study agreement with our study, carried out by Elnasri et al., (2008)[34], on Patterns of lipid changes among type 2 diabetes patients, they found that nearly half our diabetic patients had some disorder in their lipid profile. [34]

This result is to some extent lower than that reported in international studies. For example, 70% of the Americans and up to 85% of Finnish diabetic patients were reported to have lipid abnormalities. The Canadian Heart Association reported that up to half the diabetic patients had low HDL-C. The difference in dietary habits and climate are claimed to justify the difference in lipid profile between our study and international studies. The findings of other regional studies are somewhat similar to our study. Nigerian and Kuwaiti studies show an incidence of lipid disorders of around 50% among diabetic patients. In accordance with other studies, the most common recognized abnormality was hypertriglyceridemia (which was reported in nearly half the patients).[35]

In this study, it was found that there was a negative significant correlation between Omentin-1 level and carotid intimal thickness (P <0.05), this results was agreement with study carried out by Nishimura et al., (2019)[36], they study the Plasma omentin levels are inversely associated with atherosclerosis in type 2 diabetes patients with increased plasma adiponectin levels: a cross‐sectional study, they found that there was a significant negative correlation between omentin-1 and carotid intimal thickness.[36]

Our study showed that there was a negative correlation between Omentin-1 level and BMI (r=-0.33, p 0.01), waist circumference (r=0.294, p 0.22), duration of DM. (r=-0.361, p 0.005)

The negative correlation of omentin-1 level with BMI and waist circumference is explained by de souza Batista *et al*.[37], who reported that among various human tissues, visceral adipose tissue produces a large amount of omentin and its gene expression in the visceral fat depot is reduced in obese individuals. [37]

In this study, it was found a negative Correlation between Omentin-1 level and fasting blood sugar (r=-0.549, p <0.001), HbA1c (r=-0.438, p <0.001), HOMA IR (r=-0.38, p0.027), there was no significant correlation between omentin-1 and, fasting serum insulin

This results agrees with the findings of Shibata *et al*[38]., who reported that omentin-1 levels were significantly lower in patients with one or more risk factors of metabolic disorders such as hyperlipidemia. Further, they found a significantly negative correlation between omentin-1 levels and cholesterol, triglyceride, and LDL levels. [38]

In our results, it was found that there was a negative Correlation between Omentin-1 level and carotid intimal thickness and there was positive correlation between omentin-1 and ABI. Recently, in a meta-analysis Agasthi et al[39]. Found that serum omentin level is independently and negatively associated with coronary artery disease.[39]

## CONCLUSION

This study showed a significantly decreased omentin-1 level in type 2 DM patients as compared with controls, with a larger decrease among patients with increased CIMT. There was a negative correlation between omentin-1 level and other risk factors for cardiovascular and metabolic disorders such as lipid profile. Hence, we can consider omentin-1 levels to be predictive of atherosclerosis and early vascular complications of DM.

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