



Original Article

Omentin-1 and diabetic retinopathy in type 2 diabetic patients

Mohamed Abdelraouf Korany^{a,*}, Ahmed Sonbol^b, Sameh Mohamed Elgouhary^c^a Internal Medicine Department, Faculty of Medicine, Menoufia University, Egypt^b Clinical Pathology Department, Faculty of Medicine, Menoufia University, Egypt^c Ophthalmology Department, Faculty of Medicine, Menoufia University, Egypt

ARTICLE INFO

Article history:

Received 31 January 2018

Revised 25 March 2018

Accepted 12 April 2018

Available online 3 May 2018

Keywords:

Omentin-1

Diabetic retinopathy

ABSTRACT

Background: Diabetic retinopathy (DR) is one of the most common and serious micro vascular complication affecting type 2 diabetic patients.

The literature on adipokines as a possible mechanism in the pathogenesis of DR is contradictory.

We are in need for more explanation about the pathogenesis of DR and also in need for reliable biomarker for early diagnosis of such complication.

The aim of this work was to study the serum level of omentin-1 and its relation to diabetic retinopathy in type 2 diabetes mellitus (type 2 DM).

Patients and methods: This study was conducted on 75 type 2 DM patients; 20 healthy subjects served as a control group. All participants were classified into 4 groups:

- **Group1:** Included 25 type 2 diabetics without retinopathy.
- **Group2:** Included 25 type 2 diabetics with non proliferative diabetic retinopathy (NPDR).
- **Group 3:** Included 25 type 2 diabetics with proliferative diabetic retinopathy (PDR).
- **Group 4:** Included 20 healthy subjects as a control group.

Thorough history taking and physical examination with calculation of body mass index (BMI), investigations were done including serum creatinine, lipid profile, glycosylated haemoglobin (HbA1c), C-reactive protein (CRP), urine albumin creatinine ratio (UACR) and serum omentin-1. Fundus examination was carried out by an expert ophthalmologist.

Results: Serum omentin-1 level was significantly lower in diabetic patients compared with the control, and in DR compared with diabetics without DR and in PDR compared with NPDR.

There was a negative significant correlation between serum omentin-1 level and BMI, HbA1c, CRP, total cholesterol, low density lipoprotein (LDL) and Serum triglycerides (TG) and positive significant correlation with high density lipoprotein (HDL).

Conclusions: From this study we can conclude that serum omentin-1 is significantly lower in patients with DR compared with diabetics without retinopathy and in PDR patients compared with NPDR patients.

Also, there is a negative significant correlation between serum omentin-1 and HbA1c, BMI, CRP and some lipid parameters.

© 2018 Alexandria University Faculty of Medicine. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Diabetic retinopathy is a leading cause of visual loss in working-age individuals worldwide, as the prevalence of diabetes mellitus increases, the development of DR as a micro vascular complication of diabetes¹ mellitus also rises. Furthermore, previous studies

demonstrated that DR has also been associated with cardiovascular and all-cause mortality in patients with type 2DM, which adds value to investigate the risk^{2,3} factors and early diagnosis for DR.

There are several proposed pathological mechanisms by which diabetes mellitus may lead to development of retinopathy such as aldose reductase enzyme, advanced glycated end products, oxidative stress and vascular endothelial growth factor [VEGF].^{4,5}

Omentin-1 is identified adipokine that is preferentially generated by visceral adipose tissue.⁶ Omentin-1 plays an anti-inflammatory role through inhibition of tumor necrosis

Peer review under responsibility of Alexandria University Faculty of Medicine.

* Corresponding author at: 90 Fawzi Moaz Street, Smoha, Alexandria, Egypt.

E-mail address: mohammedelsayed29@icloud.com (M. Abdelraouf Korany).

<https://doi.org/10.1016/j.ajme.2018.04.003>

2090-5068/© 2018 Alexandria University Faculty of Medicine. Production and hosting by Elsevier B.V.

This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

factor- α [TNF- α] induced superoxide production in vascular smooth cells.⁵

Angiogenesis is thought to be one of the underlying mechanisms of diabetic microvascular complications such as diabetic nephropathy and DR. It was found that omentin-1 decreases in vitro migration and angiogenesis in human endothelial cells induced by sera, C-reactive protein and VEGF. Thus omentin-1 appear to be a protective adipokine that it induces vasodilation and inhibit endothelial cell migration, vascular inflammation and angiogenesis as well as reducing endothelial dysfunction.^{7,8}

The literature on adipokines as a possible mechanism in the pathogenesis of DR is contradictory.^{9,10}

The aim of this work is to compare serum levels of omentin-1 in type 2 diabetes mellitus with and without retinopathy and to investigate the relationship between serum omentin-1 level and diabetic retinopathy.

2. Patients and methods

A total of 75 T2DM and 20 healthy subjects as a control group were enrolled in this study, they were classified into 4 groups:

- **Group 1:** Included 25 T2DM without micro vascular complications aged 56.5 ± 7.2 years. 12 of them were males and 13 were females.
- **Group 2:** Included 25 T2DM had nonproliferative diabetic retinopathy (NPDR) aged 55.9 ± 6.4 years 12 of them were males and 13 were females.
- **Group 3:** Included 25 T2DM had proliferative diabetic retinopathy (PDR) aged 55.9 ± 8.1 years. 14 of them were males and 11 were females.
- **Group 4:** included 20 healthy subjects serving as a control group aged 55.8 ± 6.1 years. 10 of them were males and 10 were females.

The patients selected from the inpatient department and out patient clinics of the Internal Medicine department in Menoufia University. The selected patients gave consent for participation in the study before they were exposed to examination and investigations. The study was conducted from June 2017 to January 2018. The protocol of the study was approved by the ethical committee of faculty of medicine.

Exclusion criteria

Type I DM, diabetic nephropathy (UACR ≥ 30 mg/g creatinine), diabetic neuropathy, malignancy, acute infection, chronic inflam-

matory diseases, collagen disorders and uncontrolled hypertension.

All participants were subjected to thorough history with special emphasis on age, sex and duration of diabetes mellitus. Complete physical examination performed to all subject with estimation of weight and height to calculate body mass index. Investigations included fasting blood glucose, glycosylated hemoglobin, lipid profile, urine analysis, serum creatinine, urine albumin creatinine ratio, C-reactive protein and serum omentin-1 level was measured using an enzyme-linked immune sorbent assay.¹¹

Patients under went detailed eye examinations using the early treatment of diabetic retinopathy study protocol of seven-standard- field stereoscopic fundus photographs and graded according to clinical early treatment of diabetic retinopathy study criteria [no retinopathy, NPDR and PDR].¹² **Statistical methodology**

Data were analyses using statistical package for the social science (SPSS) software computer program, versions. Quantitative data were presented as mean and SD.

Qualitative data were presented as frequency and percentage. To compare between groups we used χ^2 test, analysis of variance test, and least significant difference. Correlation between two parameters was made using correlation coefficient. Significance level value was p equal to or less than 0.05.

3. Results

There was no significant difference as regard age and sex between the studied groups. BMI was significantly higher in diabetic groups compared to control group. HbA1c, CRP were significantly higher in PDR and NPDR groups compared with diabetic group without DR and control group.

Serum omentin-1 was significantly lower in diabetic patients with PDR compared with the other groups, and in NPDR compared with diabetics without DR and controls (Table 1).

There was a negative significant correlation between serum omentin-1 concentrations and duration of diabetes, BMI, HbA1c, CRP, total cholesterol, LDL, TG, and a negative significant correlation with HDL (Table 2).

4. Discussion

There are many factors incriminated in the pathogenesis of DR, such as dysglycemia, insulin resistance, inflammation and angiogenesis. So, to determine the relation of DR and omentin-1, we also

Table 1
Comparison between the studied groups as regard demographic and laboratory parameters.

	Group 1	Group 2	Group 3	Group 4	F-test	p	LSD
Age (years)	56.5 \pm 7.2	55.9 \pm 6.4	55.9 \pm 8.1	55.8 \pm 6.1	0.050	0.985	–
Duration of diabetes (years)	8.6 \pm 1.19	9.3 \pm 2.4	10.2 \pm 2.5	–	3.594	0.033*	2,3,vs1
Glycosylated hemoglobin (%)	6.8 \pm 1.9	7.8 \pm 0.8	9.1 \pm 0.9	5.1 \pm 0.4	46.370	<0.001 [†]	2,3,vs,1
Body mass index (kg/m ²)	26.6 \pm 2.9	28.5 \pm 2.8	29.0 \pm 3.5	22.3 \pm 2.6	22.371	<0.001 [†]	1,2,3v4, 2,3v1
Total cholesterol (mg/dl)	190.3 \pm 28.1	192.4 \pm 28.6	189.8 \pm 31.4	179.4 \pm 30.2	0.823	0.484	
LDL (mg/dl)	112.8 \pm 33.6	122.9 \pm 18.8	124.8 \pm 16.8	120.6 \pm 21.4	1.551	0.207	
HDL (mg/dl)	36.8 \pm 7.7	34.5 \pm 6.7	33.4 \pm 6.9	38.8 \pm 7.8	2.469	0.067	
Triglyceride (mg/dl)	154.6 \pm 33.6	170 \pm 30.7	180.6 \pm 32.8	144.2 \pm 33.7	5.558	0.002 [†]	2,3vs1,4, 3vs1,2
C-reactive protein (mg/l)	6.7 \pm 1.2	8.4 \pm 1.6	10.2 \pm 1.4	4.1 \pm 1.2	80.045	<0.001 [†]	2,3vs1,4, 3vs1,2, 2vs1,4
Serum omentin-1 (ng/L)	1332.40 \pm 66.24	1115.30 \pm 29.45	888.73 \pm 21.42	2060 \pm 1326.07	13.021	<0.001 [†]	3vs1,2,4, 2vs1,4
Sex					X ²		
Male (n%)	12 (48%)	12 (48%)	14 (56%)	10 (50%)	0.430	0.934	–
Female	13 (52%)	13 (52%)	11 (44%)	10 (50%)			

LDL: Low density lipoprotein.

HDL: High density lipoprotein.

Anova test, LSD: Least significant difference.

Table 2

Correlation between serum omentin-1 and other studied parameters in the diabetic patients.

	r	p
Age	0.248	0.291
Sex	0.195	0.410
Duration of diabetes	-0.450	0.004*
Body mass index	-0.467	0.038*
HbA1c	-0.877	<0.001*
Total cholesterol	-0.560	0.010*
LDL	-0.590	0.006*
HDL	0.568	0.009*
Triglyceride	-0.576	0.008*
CRP	-0.789	<0.001*

HbA1c: Glycosylated hemoglobin.

LDL: Low density lipoprotein.

HDL: High density lipoprotein.

CRP: C-reactive protein.

r: Correlation coefficient.

study its relation to HbA1c, BMI, CRP (as inflammatory marker) and lipids profile.

In our study serum omentin-1 levels were significantly decreased in diabetic groups compared with the control group, and in diabetics with retinopathy compared with diabetics without retinopathy, also there was a negative significant correlation between serum omentin-1 and HbA1c.

Our data in agreement with that of Tan et al.⁸ who found that: omentin-1 levels were decreased in subjects with impaired glucose tolerance, type 1 and type 2 DM, suggesting that omentin-1 is important for glucose metabolism-in vitro, omentin-1 increases insulin signal transduction by activating the protein kinase B and enhances insulin-mediated glucose transport in adipocytes.

A clinical study of patients suffering from diabetes mellitus, reported that serum and vitreous omentin levels were related to¹³ the severity of DR, and experimental investigations have shown that omentin has a potent vasodilatory effect in isolated vessels mediated by endothelium derived nitric oxide, a strong vasodilator of the retinal arterioles.⁸

In our study there was a negative correlation of serum omentin-1 with total cholesterol, LDL, TG and a positive correlation with HDL which concurs with¹⁴ other studies. Omentin-1 can activate^{15,16} S'-AMP protein kinase which works as powerful endogenous cholesterol synthesis inhibitor, and thus we can speculate that omentin-1 could contribute to regulation of cholesterol synthesis, via this pathway. Although relationship between omentin-1 and HDL cholesterol is unclear, dysregulation of omentin might affect the insulin signal, resulting in altered HDL production.¹⁷

In the current study, there was a negative significant correlation between serum omentin-1 and BMI. Some studies have also shown that omentin-1 serum levels were generally lower in obese groups with or without type 2 DM.¹⁸ In a study performed by de Souza Batista et al.¹⁹ plasma levels of omentin were measured in lean, overweight, and obese, otherwise healthy subjects. The authors found that plasma omentin levels were highest among the lean subjects and these levels were inversely correlated with BMI, waist circumference and insulin resistance.

Also we noticed in our study, a negative significant correlation between serum omentin-1 and CRP. This finding came in consistency with Tan et al. study.⁸ A study performed to evaluate the effects of metformin treatment on omentin-1 levels in polycystic ovary syndrome subjects and effects of omentin-1 levels on vitro angiogenesis. They concluded that changes in CRP were significantly negatively correlated with changes in serum omentin-1.

Also Yilmaz et al.²⁰ performed a study to assay the circulating levels of omentin-1 chemerin and adiponin and examined their association with clinical, biochemical and histological phenol types

in patients with non-alcoholic fatty liver disease. They found during their study that serum omentin-1 levels were significantly associated with CRP. Some researchers have pointed out²¹ that inflammatory factor may have a role in the pathogenesis of microangiopathy.

CRP is a marker of inflammation and widely used in clinic for monitoring inflammation.

The role of CRP in diabetic micro angiopathy may be related to induction of insulin resistance, suppression of nitric oxide synthase and complement activation.²²

In the current study, serum omentin-1 is significantly lower in PDR compared with NPDR which may indicate the role of omentin-1 in the inhibition of angiogenesis. It was found that omentin-1 decreases in vitro migration, and angiogenesis in human endothelial cells induced by sera, C-reactive protein and VEGF.⁵

5. Conclusion

Serum omentin-1 is significantly lower in diabetic retinopathy compared to diabetic without retinopathy and in PDR compared with NPDR. There is a negative correlation between serum omentin-1 levels and duration of diabetes. BMI, HbA1c, CRP and some lipid parameters. So, decreased level of omentin-1 may play an important role in the pathogenesis and development of DR but we are still in need for further studies to prove whether serum omentin-1 level could be used as a biomarker for early diagnosis of DR and whether offer a new therapeutic opportunity for DR.

Source of support

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

None.

References

- Delcourt C, Massin P, Rosilio M. Epidemiology of diabetic retinopathy: expected vs reported prevalence of cases in the French population. *Diabetes Metab.* 2009;35:431–438.
- Van Hecke MV, Dekker JM, Stehouwer CD, et al.. Diabetic retinopathy is associated with mortality and cardiovascular disease incidence: the EURODIAB prospective complications study. *Diabetes Care.* 2005;28:1383–1389.
- Juutilainen A, Lehto S, Rönnemaa T, Pyörälä K, Laakso M. Retinopathy predicts cardiovascular mortality in type 2 diabetic men and women. *Diabetes Care.* 2007;30:292–299.
- Fong DS, Aiello LP, Ferris FL, Klein R. Diabetic retinopathy. *Diabetes Care.* 2009;27:2540–2553.
- Keenan HA, Costacou T, Sun JK, et al.. Clinical factors associated with resistance to microvascular complications in diabetic patients of extreme disease duration. *Diabetes Care.* 2007;30:1995–1997.
- Kazama K, Usui T, Okada M, Hara Y, Yamawaki H. Omentin plays an anti-inflammatory role through inhibition of TNF- α -induced superoxide production in vascular smooth muscle cells. *Eur J Pharmacol.* 2012;686:116–123.
- Yamawaki H, Tsubaki N, Mukohda M, Okada M, Hara Y. Omentin, a novel adipokine, induces vasodilation in rat isolated blood vessels. *Biochem Biophys Res Commun.* 2010;393(4):668–672.
- Tan BK, Adya R, Randeve S. Omentin: a novel link between inflammation, diabetes, and cardiovascular disease. *Trends Cardiovasc Med.* 2010;20:143–148.
- Jung CH, Kim BY, Mok JO, Kang SK, Kim CH. Association between serum adipocytokine levels and microangiopathies in patients with type 2 diabetes mellitus. *J Diabetes Investig.* 2014;5:333–339.
- Matsuda M, Kawasaki F, Yamada K. Impact of adiposity and plasma adipocytokines on diabetic angiopathies in Japanese Type 2 diabetic subjects. *Diabet Med.* 2004;21:881–888.
- Porstmann T, Kiessig ST. Enzyme immunoassay techniques, an overview. *J Immunol Methods.* 1992;150:5–21.
- Told R, Baratsits M, Garhöfer G, Schmetterer L. Early treatment diabetic retinopathy study (ETDRS) visual acuity. *Ophthalmology.* 2013;110(10):960–965.

13. Wan W, Li Q, Zhang F. Serum and vitreous concentrations of omentin-1 in diabetic retinopathy. *Dis Markers*. 2015;754312.
14. Auguet T, Quintero Y, Riesco D, et al.. New adipokines vaspin and omentin. Circulating levels and gene expression in adipose tissue from morbidly obese women. *BMC Med Genet*. 2011;12:60.
15. Ji-Yin Z, Chan L, Lawrence CH, Shiwen Z. Omentin: linking metabolic syndrome and cardiovascular disease. *Curr Vasc Pharmacol*. 2014;12:136–143.
16. Kataoka Y, Shibata R, Ohashi K, et al.. Omentin prevents myocardial ischemic injury through AMP-activated protein kinase- and Akt-dependent mechanisms. *J Am Coll Cardiol*. 2014;63:2722–2733.
17. Yan P, Liu D, Long M, et al.. Changes of serum omentin levels and relationship between omentin and adiponectin concentrations in type 2 diabetes mellitus. *Exp Clin Endocrinol Diabetes*. 2011;119:257–263.
18. Moreno-Navarrete JM, Catalán V, Ortega F, et al.. Circulating omentin concentration increases after weight loss. *Nutr Metab*. 2010;7:27.
19. de Souza Batista CM, Yang RZ, Lee MJ, et al.. Omentin plasma levels and gene expression are decreased in obesity. *Diabetes*. 2007;56:1655–1661.
20. Yilmaz Y, Yonal O, Kurt R. Serum levels of omentin, chemerin and adiponin in patients with biopsy-proven nonalcoholic fatty liver disease. *Scand J Gastroenterol*. 2011;46:91–97.
21. Amanullah S, Jarai A, Govindan M, Bash MI, Khatheej S. Association of CRP with diabetic and non diabetic individual. *Jordan J Biol Sci*. 2010;3(1):7–12.
22. Chunlian C, Yufang Y, Zhicheng W. Study of the correlation between serum chemerin and c-reactive protein levels of type 2 diabetic patients and insulin resistance and macroangiopathy. *J Chinese General Practice*. 2013;16:2438–2440.