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ORIGINAL ARTICLE

Evaluation of the relationship between cataracts and serum adiponectin levels: A cross-sectional study

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Abstract

Purpose: Adiponectin is an adipocytokine, which plays an important role in preventing oxidative stress. In this study, we evaluated serum adiponectin levels in diabetes mellitus (DM) patients and the association of serum adiponectin levels with cataractogenesis.

Methods: This was a prospective case–control study performed in the department of endocrinology and metabolism and department of ophthalmology. In total, 47 individuals with type 2 DM and 21 controls were included in the study. Patients with type 1 diabetes, heart failure, hepatic failure, and renal failure, as well as those younger than 18 years or older than 90 years, were excluded from the study.

Results: Although the DM group had a higher frequency of cataracts, the finding was not statistically significant (p=0.067). The serum adiponectin level was lower in the DM group (p<0.001). Glucose, body mass index, and waist circumference values were higher in the DM group (p<0.001, p=0.008, and p<0.001, respectively). In addition, serum adiponectin levels were lower in the DM group with cataracts (DM group with cataracts vs. controls; p=0.008; and DM group without cataracts vs. controls: p=0.738).

Conclusion: Lower serum adiponectin levels were detected in DM patients with cataracts. To the best of our knowledge, this is the first study to demonstrate an association between lower adiponectin levels and the presence of cataracts. We hypothesize that adiponectin may play an important role in the pathogenesis of cataracts.

Keywords: Adiponectin; cataract; diabetes mellitus.

Cataracts are a major cause of blindness worldwide and therefore a significant cause of disability due to visual impairment.[1] Cataracts are particularly common in the developing world.[2] They are also common in individuals with diabetes mellitus (DM). Cataractogenesis is a multifactorial process, which takes several years. The etiologies of cataractogenesis include ultraviolet radiation, medications (e.g., glucocorticoids), trauma, aging, and hypergly-

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cemia. Hyperglycemia may give rise to cataract formation through changes in membrane permeability, osmotic swelling, oxidative stress generated by the polyol pathway, and extensive glycation. Chronic hyperglycemia affects the lens by activation of the polyol pathway, protein kinase C, mitochondrial dysfunction, and post-translational modification of enzymes.[3] Xanthine oxidoreductase enzymes play a role in cataract formation under hyperglycemic conditions. According to the previous research, xanthine oxidase activity may contribute to hyperglycemic lens oxidative injury.[4]

Adiponectin is an adipocyte-derived cytokine, which is downregulated in insulin-resistant obesity. Adiponectin exerts both antidiabetic and anti-atherosclerotic effects by suppressing oxidative stress and inflammation.[5] Adiponectin is an essential adipocytokine, which helps to prevent oxidative and nitrative stress. Increases in reactive oxygen species and insulin resistance are associated with a reduction in serum adiponectin levels.[6]

At present, the only available treatment for cataracts is surgery. However, surgical treatment is not an option for many patients. As a result, alternatives to surgery, including interventions and preventive methods to maintain lens transparency, are of interest. In this study, we evaluated serum adiponectin levels in DM patients and the association of serum adiponectin levels with cataractogenesis.

Materials and Methods

Patients

This was a prospective case–control study performed in the department of endocrinology and metabolism and department of ophthalmology. Forty-seven patients with type 2 DM (23 males and 24 females) and 21 control subjects (11 males and ten females) were included in this study. Type 2 DM was diagnosed according to the criteria of the American Diabetic Association, as follows: A fasting glucose concentration of 126 mg/dL and a postprandial plasma glucose concentration of 200 mg/dL or over after 2 h.

The exclusion criteria included the presence of type 1 diabetes, heart failure, hepatic failure, renal failure, and younger than 18 years or older than 90 years. None of the controls were receiving medication or dietary supplements, and none had a history of diabetes.

The study was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committee (Recep Tayyip Erdoğan University Faculty of Medicine, decision no: 2017/08, date: 10/03/2017). The written informed consent was obtained from the patients and controls before their participation in this study.

The patient's pupils were first dilated, followed by retro-illumination lens imaging (EAS-1000; Nidek, Tokyo, Japan) and digital slit-lamp imaging (model DC-1; Topcon, Tokyo, Japan) using an FD-21 flash attachment. Cataractogenesis was determined by trained masked graders using the Wisconsin Cataract Grading System.[7]

Measurements

The weight, height, systolic blood pressure, and diastolic blood pressure values of the subjects were measured. The body mass index (BMI) was calculated as weight in kilograms divided by height-squared in meters (kg/m^2). After 12 h of fasting, 5 ml of blood was drawn into vacuum plain tubes. The blood tubes were centrifuged at 1.500 g for 10 min. The serum samples were then stored at −80°C until analysis.

Serum triglycerides, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, fasting plasma glucose, and HbA1c levels were measured using the photometric method and a chemistry autoanalyzer (Roche Cobas C 311; Roche Diagnostics Ltd., Rotkreuz, Switzerland). Serum insulin levels were determined using the electrochemiluminescence method and a Roche Cobas e 411 immunoanalyzer (Roche Diagnostics Ltd., Rotkreuz, Switzerland). Serum adiponectin levels were measured by an enzyme-linked immunosorbent assay (ELISA) using human adiponectin platinum ELISA reagents (Affymetrix-eBioscience, Vienna, Austria), CombiWash (Human Diagnostics Worldwide, Germany), and an AccuReader (Metertech Inc., Taiwan).

Statistical Analysis

The data were displayed as the mean ± standard deviation. Data normality was analyzed using the Shapiro–Wilk and Kolmogorov–Smirnov tests. The categorical data were analyzed using the Chi-square test. To analyze statistical differences in nonparametric and parametric variables in the control and DM groups, the Mann–Whitney U-test and a t-test, respectively, were used. Kruskal–Wallis test was used for evaluation of three groups (DM with cataracts, DM without cataracts, and controls). Post hoc analysis of Kruskal–Wallis test with Tamhane's T2 was performed for serum adiponectin levels between paired groups. The relationship among clinical and laboratory variables was analyzed using nonparametric methods (Spearman's r correlations). $P<0.05$ was considered statistically significant. All statistical analyses were carried out using SPSS 21.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

The demographics and clinical characteristics of the DM patients and controls are summarized in Table 1. There were no between-group differences in the age and sex of the participants. The frequency of cataracts in the DM group was higher than control group, but the finding was not statistically significant (p=0.067). The clinical and laboratory parameters of the controls, DM patients without cataracts, and DM patients with cataracts are displayed in Table 2. Serum adiponectin level was lower in the DM group (p<0.001). Glucose, BMI, and waist circumference values were higher in the DM group (p<0.001, p=0.008, and p<0.001, respectively). In addition, serum adiponectin levels were lower in the DM group with cataracts (DM group with cataracts vs. controls; p=0.008; DM group without cataracts vs. controls: p=0.738) (Table 3). Figure 1 shows the serum adiponectin levels in the three groups. Serum adiponectin levels were significantly higher in the control group compared to those

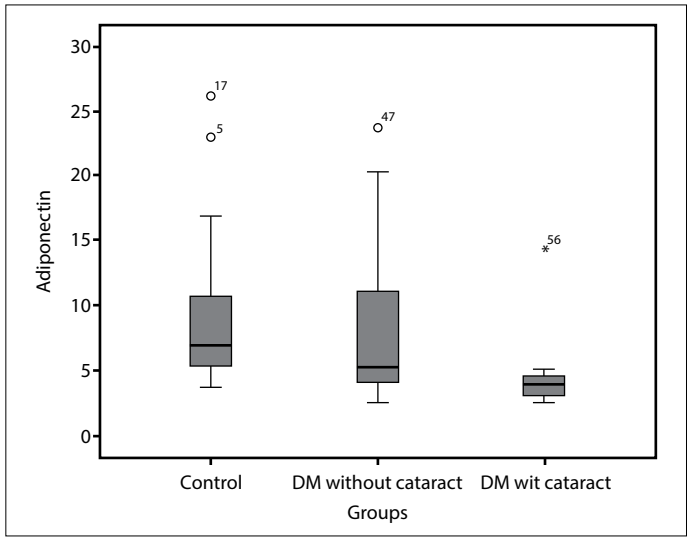

Fig. 1. Serum adiponectin concentrations in three groups. DM: Diabetes mellitus.

Table 1. The demographics and clinical characteristics

	Control	DM	p-value
Age (Year)	53.86±13.82	55.19±8.99	0.572*
Gender (Female/Male, n)	10/11	24/23	0.793†
Smoking (Yes/No, n)	5/16	7/40	0.493†
Cataract (Present/Absent, n)	3/18	17/30	0.067†

Parameters were presented as mean±standard deviation. *Mann–Whitney U-test, †Chi-square test. DM: diabetes mellitus.

Table 3. Post hoc analysis of Kruskal–Wallis test for serum adiponectin levels between groups

	p-value
Control vs. DM with cataract	0.008*
Control vs. DM without cataract	0.738
DM with cataract vs. DM without cataract	0.026

*P≤0.05/6 accepted as statistically significant. DM: Diabetes mellitus, vs.: versus.

Table 4. Simple regression analysis between serum adiponectin levels and various parameters

Parameters	r	p-value
Age (year)	−0.113	0.359
Waist (cm)	−0.131	0.285
BMI	0.187	0.127
Glucose (mg/dL)	−0.372**	0.002
Insulin (µU/mL)	−0.049	0.880
TC (mg/dL)	0.068	0.582
TG (mg/dL)	−0.126	0.304
LDL-C (mg/dL)	0.084	0.494
HDL-C (mg/dL)	0.263*	0.030

Spearman's Correlation analysis of laboratory parameters. *Correlation is significant at the 0.01 level (two-tailed). **Correlation is significant at the 0.05 level (two-tailed). BMI: Body mass index; TC: Total cholesterol; TG: Triglyceride; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol.

Table 2. Laboratory parameters and clinical features

	Control	DM without cataract	DM with cataract	p-value
Age (year)	53.86±1.82	51.83±8.07	61.12±7.48	0.008*
Waist (cm)	96.43±7.20	107.60±9.24	108.94±11.47	<0.001*
BMI	27.82±3.011	32.18±5.00	30.51±4.92	0.008*
Glucose (mg/dL)	99.62±13.89	163.77±61.77	154.47±40.15	<0.001*
TC (mg/dL)	187.52±48.00	194.80±46.95	192.76±42.98	0.725
TG (mg/dL)	141.38±80.59	165.27±68.82	178.00±120.57	0.330
HDL-C (mg/dL)	68.57±89.456	47.73±12.26	48.65±12.06	0.711
LDL-C (mg/dL)	113.05±42.64	114.03±40.32	110.65±31.33	0.947
Insulin (µU/mL)	8.58±3.26	10.76±6.22	12.79±5.83	0.687
Adiponectin (ng/mL)	9.24±6.02	7.71±5.48	4.41±2.70	<0.001*

Parameters were presented as mean±standard deviation. *P<0.05 accepted as statistically significant, Kruskal–Wallis test. DM: Diabetes mellitus; BMI: Body mass index; TC: Total cholesterol; TG: Triglyceride, HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol.

in the DM group without cataracts and the DM group with cataracts. Spearman's correlation analysis showed that serum adiponectin levels in the type 2 DM patients were negatively correlated with glucose levels (r=–0.372, p<0.002) and positively correlated with high-density lipoprotein levels (r=0.263, p<0.030) (Table 4).

Discussion

In this study, we found lower adiponectin levels in DM patients with cataracts. DM is a well-known risk factor for cataractogenesis.[8] To the best of our knowledge, this is the first study to demonstrate that adiponectin levels are associated with the presence of cataracts. Many previous studies showed that serum adiponectin levels were lower in patients with DM.[9] According to one study, low adiponectin levels were likely to be related to the development of complications, such as retinopathy.[10] In this study, although serum levels of adiponectin were lower in diabetic patients, the finding was statistically significant only in the DM patients with cataracts.

Lower adiponectin levels in individuals with cataracts may be related to increased oxidative stress. In DM patients, increased reactive oxygen species production and decreased expression of antioxidant catalyze and superoxide dismutase were associated with decreased production of adipocytokines, such as adiponectin, in adipose tissue.[6] Oxidative stress may have an important function in the pathogenesis of DM and cataractogenesis, as it increases free-radical production and leads to a decline in antioxidant defense.[11,12] In the previous research, adiponectin replacement therapy improved insulin resistance, hyperglycemia, and tissue triglyceride content by increasing fatty acid oxidation and reducing oxidative stress and inflammation.[13]

We demonstrated that glycemic control was poorer in a cataract group compared to that in a non-cataract group. Hyperglycemia resulted in an increase in glucose flux through the polyol pathway, thereby leading to a reduction in the conversion of glucose to sorbitol. The accumulation of sorbitol in the lens tissue resulted in the development of cataracts.[14] Omotosho et al.[15] revealed that sorbitol dehydrogenase was lower in diabetic cataract patients compared to DM patients.

Cataractogenesis may be linked to an accumulation of ceramides in the lens tissue. Ceramides are lipids that play a role in insulin resistance, cell death, inflammation, and atherosclerosis.[16] For reasons not known, the ceramide content of the lens dramatically increases after middle age.[17] Therefore, the ceramide content possibly plays a role in cataractogenesis.[16] Ceramides are presumably formed by hydrolysis of sphingomyelins in the lens. In a previous study, adiponectin administration resulted in a marked reduction in hepatic ceramide content and insulin resistance.[18] We do not know whether the ceramide content was higher in the lenses of patients with the lower adiponectin serum levels. If so, there may be another mechanistic relationship between adiponectin and cataractogenesis.

According to some research, autophagy may play a role in adiponectin-associated protection against cataractogenesis. Activation of autophagy eliminates damaged cell structures, including mitochondria.[19] An adiponectin-autophagy relationship was reported in cardiomyocytes.[20] Sometimes autophagy maintains stress adaptation that prevents cell death by suppressing apoptosis, whereas under other cellular conditions, it establishes an alternative cell-death tract.[21] In research on hepatic cells, adiponectin provided protection against apoptosis of hepatocytes by preventing activation of caspase-8 and Bax expression, thereby inducing an anti-apoptotic effect.[22] The 5'-adenosine monophosphate-activated protein kinase (AMPK) plays a role in the induction of autophagy. Globular adiponectin defended chondrocytes against H_2O_2-induced apoptosis by inducing autophagy, possibly associated with AMPK and mammalian target of rapamycin (mTOR) (AMPK/mTOR) signal-pathway activation.[23] Impairment of autophagy in lens cells culminated in the loss of stress resistance and inhibition of differentiation, which led to cataract formation.[24]

The present study has a number of limitations. These include the small sample size and absence of cataract grading. Another limitation is the absence of information on lifestyle-related factors, such as dietary habits and exercise. The absence of data on adiponectin receptors in lens tissue, which is important to address the relation between adiponectin and cataractogenesis, is another limitation.

Conclusion

Adiponectin plays a crucial role in the pathogenesis of cataractogenesis, and cataractogenesis is known to be associated with hyperglycemia. Before our study, information was lacking on serum adiponectin levels in cataract patients. In our study, serum adiponectin levels were lower in DM patients with cataracts. Lower serum adiponectin levels might play an important role in cataract development.

Ethics Committee Approval: This study was approved by Recep Tayyip Erdoğan University Faculty of Medicine Ethics Committee (10.03.2017 date; number 2017/08).

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References

1. Pascolini D, Mariotti SP. Global estimates of visual impairment: 2010. Br J Ophthalmol 2012;96:614–8. [CrossRef]
2. Resnikoff S, Pascolini D, Etya'ale D, et al. Global data on visual impairment in the year 2002. Bull World Health Organ 2004;82:844–51.
3. Kyselova Z, Stefek M, Bauer V. Pharmacological prevention of diabetic cataract. J Diabetes Complications 2004;18:129–40.
4. Miric DJ, Kisic BB, Zoric LD, Mitic RV, Miric BM, Dragojevic IM. Xanthine oxidase and lens oxidative stress markers in diabetic and senile cataract patients. J Diabetes Complications 2013;27:171–6. [CrossRef]
5. Yamauchi T, Kadowaki T. Physiological and pathophysiological roles of adiponectin and adiponectin receptors in the integrated regulation of metabolic and cardiovascular diseases. Int J Obes (Lond) 2008;32 Suppl 7:S13–8. [CrossRef]
6. Liu J, Lloyd SG. High-fat, low-carbohydrate diet alters myocardial oxidative stress and impairs recovery of cardiac function after ischemia and reperfusion in obese rats. Nutr Res 2013;33:311–21. [CrossRef]
7. Gali HE, Sella R, Afshari NA. Cataract grading systems: A review of past and present. Curr Opin Ophthalmol 2019;30:13–8.
8. Snow A, Shieh B, Chang KC, et al. Aldose reductase expression as a risk factor for cataract. Chem Biol Interact 2015;234:247–53. [CrossRef]
9. Weyer C, Funahashi T, Tanaka S, et al. Hypoadiponectinemia in obesity and Type 2 diabetes: Close association with insulin resistance and hyperinsulinemia. J Clin Endocrinol Metab 2001;86:1930–5. [CrossRef]
10. Yilmaz MI, Sonmez A, Acikel C, et al. Adiponectin may play a part in the pathogenesis of diabetic retinopathy. Eur J Endocrinol 2004;151:135–40. [CrossRef]
11. Dayanand CD, Kutty AV. Protein carbonyl content as a stable Oxidative stress marker in Type II diabetes. Int J Biol Med Res 2012;3:2362–5.
12. Jensen SJ. Oxidative stress and free radicals. J Mol Structure 2003;666–667:387–92. [CrossRef]
13. Cheng J, Wang M, Ma H, Li H, Ren J, Wang R. Adiponectin inhibits oxidative stress and modulates TGF-b1 and COL-1 expression via the AMPK pathway in HSC-T6 cells. Zhonghua Gan Zang Bing Za Zhi 2015;23:69–72.
14. Srivastava SK, Ramana KV, Bhatnagar A. Role of aldose reductase and oxidative damage in diabetes and the consequent potential for therapeutic options. Endocr Rev 2005;26:380–92. [CrossRef]
15. Omotosho I, Obisesan O, Oluleye O. Sorbitol dehydrogenase activity in diabetes mellitus and cataract patients. J Appl Med Sci 2014;3:61–5.
16. Chaurasia B, Summers SA. Ceramides-lipotoxic inducers of metabolic disorders. Trends Endocrinol Metab 2015;26:538–50. [CrossRef]
17. Deeley JM, Hankin JA, Friedrich MG, et al. Sphingolipid distribution changes with age in the human lens. J Lipid Res 2010;51:2753–60. [CrossRef]
18. Wang ZV, Scherer PE. Adiponectin, the past two decades. J Mol Cell Biol 2016;8:93–100. [CrossRef]
19. Yan S, Huda N, Khambu B, Yin XM. Relevance of autophagy to fatty liver diseases and potential therapeutic applications. Amino Acids 2017;49:1965–79. [CrossRef]
20. Essick EE, Wilson RM, Pimentel DR, et al. Adiponectin modulates oxidative stress-induced autophagy in cardiomyocytes. PLoS One 2013;8:e68697. [CrossRef]
21. Maiuri MC, Zalckvar E, Kimchi A, Kroemer G. Self-eating and self-killing: Crosstalk between autophagy and apoptosis. Nat Rev Mol Cell Biol 2007;8:741–52. [CrossRef]
22. Nepal S, Kim MJ, Lee ES, et al. Modulation of Atg5 expression by globular adiponectin contributes to autophagy flux and suppression of ethanol-induced cell death in liver cells. Food Chem Toxicol 2014;68:11–22. [CrossRef]
23. Hu J, Cui W, Ding W, Gu Y, Wang Z, Fan W. Globular Adiponectin Attenuated H2O2-Induced Apoptosis in Rat Chondrocytes by Inducing Autophagy Through the AMPK/mTOR Pathway. Cell Physiol Biochem 2017;43:367–82. [CrossRef]
24. Chai P, Ni H, Zhang H, Fan X. The evolving functions of autophagy in ocular health: A double-edged sword. Int J Biol Sci 2016;12:1332–40. [CrossRef]