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Evaluation of the Relationship between Serum Copeptin Level and Diabetic Retinopathy in Patients with Type 2 Diabetes

Diabetic retinopathy (DR) is a major cause of blindness worldwide. Copeptin (CP) is an inactive analog of arginine vasopressin (AVP), which is secreted in equal amounts to AVP. Due to its longer half-life and more stable structure than AVP, CP is considered a reliable biomarker that can determine AVP function [1]. Studies have shown that plasma CP levels are increased in patients suffering from type 2 diabetes (T2D), and are associated with disease progression and complications [2]. CP may be directly involved in the DR process by regulating the function of the retinal vascular endothelial cells [3]. Considering the unknown role of CP in DR and recommendations to conduct further studies [3, 4], this study aimed to assess the association between serum CP levels and DR in patients with T2D.

This case-control study included 30 T2D patients with retinopathy (15 patients with proliferative retinopathy and 15 patients with non-proliferative retinopathy). Thirty other matched T2D cases without retinopathy were included as controls. Serum levels of copeptin as well as other biochemical parameters including fasting serum glucose, HbA1c, and levels of total cholesterol, triglycerides, low-density lipoprotein-cholesterol, high-density lipoprotein-cholesterol, urea, creatinine, alanine aminotransferase and aspartate aminotransferase were measured in all patients and compared between the groups. The study protocol was approved by the Research Ethics Committee of the Birjand University of Medical Sciences, Birjand, Iran (IR.BUMS.REC.1397.200).

There was no significant difference between the two groups regarding clinical and laboratory characteristics, except for diastolic blood pressure ($p = 0.03$). The groups were also comparable in terms of gender, age, duration of diabetes and comorbidities ($p > 0.05$); however, a significant difference was noted between the two groups regarding the type of used medications ($p = 0.04$). The results demonstrated higher serum CP levels in patients with T2D and retinopathy (proliferative and non-proliferative) compared with cases without retinopathy; however, this difference was not significant ($p = 0.10$) (Tab. 1). In patients with retinopathy, mean serum CP levels were 3.27 ± 1.47 and 3.80 ± 3.75 pmol/L in the proliferative and non-proliferative patients, respectively, which were not significantly different from patients without retinopathy ($p = 0.20$). In either of the groups with and without retinopathy, serum CP levels did not differ between subgroups with HbA1c levels below and above 7% ($p > 0.05$). No significant correlation was observed between CP and

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Table 1. Comparison of Clinical and Laboratory Characteristics in Patients without Retinopathy and with Retinopathy

Variables	With retinopathy (n = 30) Mean ± SD	Without retinopathy (n = 30) Mean ± SD	P
Age [years]	57.50 ± 7.05	55.37 ± 7.25	0.19*
Duration of diabetes [years]	9.80 ± 5.68	8.23 ± 4.23	0.26*
Weight [kg]	73.28 ± 11.35	70.72 ± 10.06	0.35**
Height [cm]	158.53 ± 8.89	156.00 ± 9.50	0.29**
BMI [kg/m^2]	28.63 ± 2.59	29.10 ± 3.38	0.82**
Fasting serum glucose [mg/dL]	156.57 ± 57.09	165.70 ± 59.56	0.68*
HbA1c [%]	8.38 ± 1.62	8.08 ± 1.84	0.25*
Serum AST [U/L]	16.20 ± 3.32	17.60 ± 5.89	0.57*
Serum ALT [U/L]	18.13 ± 6.63	23.89 ± 23.72	0.44*
Systolic blood pressure [mmHg]	127.67 ± 13.57	129.67 ± 16.02	0.89*
Diastolic blood pressure [mmHg]	76.17 ± 6.65	80.43 ± 8.91	0.03*
Serum TG [mmol/L]	104.80 ± 31.48	120.67 ± 55.68	0.26*
Serum cholesterol [mmol/L]	156.60 ± 31.12	172.20 ± 35.28	0.06*
Serum LDL-C [mmol/L]	87.63 ± 28.61	89.50 ± 29.30	0.80**
Serum HDL-C [mmol/L]	41.23 ± 4.30	45.63 ± 11.43	0.15*
Serum Cr [mg/dL]	0.96 ± 0.16	0.95 ± 0.17	0.48*
Serum urea [mg/dL]	28.33 ± 8.85	27.20 ± 9.95	0.64**
Serum copeptin [pmol/L]	3.54 ± 2.81	2.44 ±0.87	0.10*

*Mann-Whitney U, ** Independent t-test
ALT — alanine aminotransferase; AST — aspartate aminotransferase; BMI — body mass index; Cr — creatinine; HbA1c — glycated hemoglobin; HDL-C — high-density lipoprotein cholesterol; LDL-C — low-density lipoprotein cholesterol; SD — standard deviation; TG — triglycerides

biochemical parameters including serum lipids in either of the diabetic groups with and without retinopathy ($p > 0.05$).

In several previous studies performed by Zhao et al. [4], Halawa et al. [5], Zhu et al. [6], and Li et al. [7], the mean serum CP levels in diabetic patients with retinopathy were significantly higher than those in cases without retinopathy. In our study, which is the first of its kind in an Iranian population, patients with retinopathy had higher serum CP levels compared with patients without retinopathy, though the difference did not reach statistical significance. This lack of significance might be due the small sample size of this study (n = 60). Moreover, the possibility of divergent findings in different ethnic groups cannot be excluded as most of the previous evidence has been derived from the Chinese population [4, 6, 7].

Based on the findings of the present study, mean serum CP levels in diabetic patients with retinopathy (non-proliferative and proliferative) were not significantly different from those in patients without retinopathy; however, this lack of difference might be due to the small population size of the present study. It is recommended that future studies with larger population sizes and longitudinal designs explore the association between CP levels with diabetic retinopathy and its subtypes.

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Conflict of interests

None declared.

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