Relationship Between Serum Zinc Level and Microvascular Complications in Patients with Type 2 Diabetes

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Abstract

Background: Previous studies suggested that zinc level was related to a certain diabetic microvascular complication. However, the relationship between zinc level and all the microvascular complications in type 2 diabetic patients remains unknown. The purpose of this study was to analyze the relationship between zinc level and each diabetic microvascular complication and identify the features related to low serum zinc level.

Methods: We included the hospitalized patients with type 2 diabetes (T2D) at our department from May 30, 2013 to March 31, 2014. We initially compared the serum zinc levels between patients with specific microvascular complications and those without. We then analyzed the association between zinc level and each microvascular complication. Furthermore, we identified the unique features of patients with high and low serum zinc levels and analyzed the risk factors related to low zinc level.

Results: The 412 patients included 271 with microvascular complications and 141 without any microvascular complications. Serum zinc level was significantly lower in patients with diabetic retinopathy (P < 0.001), diabetic nephropathy (DN, P < 0.001), or diabetic peripheral neuropathy (P = 0.002) compared with patients without that specific complication. Lower zinc level was an independent risk factor for DN (odds ratio = 0.869, 95% confidence interval = 0.765–0.987, P < 0.05). The subjects with lower serum zinc level had manifested a longer duration of diabetes, higher level of hemoglobin A1c, higher prevalence of hypertension and microvascular complications, and lower fasting and 2-h C-peptide levels.

Conclusions: Lower serum zinc level in T2D patients was related to higher prevalence of diabetic microvascular complications, and represented as an independent risk factor for DN. Patients with lower zinc level were more likely to have a longer duration of diabetes, poorer glucose control, and worse β-cell function.

Key words: Diabetic Nephropathy; Diabetic Peripheral Neuropathy; Diabetic Retinopathy; Type 2 Diabetes; Zinc

Introduction

Diabetes is a life-threatening chronic disease, with microvascular complications including diabetic retinopathy (DR), diabetic nephropathy (DN), and diabetic peripheral neuropathy (DPN), often bring about a huge burden to patients, their families, and the society.

Zinc plays a major role in the development of both type 1 and type 2 diabetes (T2D). Previous studies suggested that serum zinc level is associated with T2D, and loss-of-function mutations in zinc transporter-8 gene protect against T2D.[1,2] In type 1 diabetic patients, zinc transporter 8 autoantibody represents a key immunodiagnostic marker.[3]

Oxidative stress plays an important role in the development of diabetic microvascular complications. Zinc not only has an antioxidative effect, but also constitutes a key component of many antioxidases. It inhibits the damage associated with lipid peroxidation and induces the clearance of free radicals.

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Patients were not prone to ketoacidosis. Patients retained with only mild symptoms or without the typical symptoms. Disease. Patients were more likely to be overweight or obese, middle-age or older onset of diabetes, with a progressive diabetes. The key diagnostic feature of T2D included a fulfilling either of the above criteria were diagnosed with repeat the plasma glucose test on the other day. Individuals test ≥11.1 mmol/L. People without typical symptoms should mmol/L; or (3) 2-h glucose level in oral glucose tolerance 1999 criteria: (1) typical symptoms with random plasma Diabetes was defined using the World Health Organization All the participants were from the endocrine department. We included all the hospitalized T2D patients in our participants were from the endocrine department. Medical history was obtained including details of height, weight, and waist circumference in all the patients. We also obtained the results of hemoglobin A1c (HbA1c), fasting C-peptide, 2-h C-peptide, lipid profile (total cholesterol [TC], triglyceride [TG], high-density lipoprotein cholesterol [HDL-C], low-density lipoprotein cholesterol [LDL-C]), and serum zinc levels. Urinary ACR was calculated using the average of three sets of ACR results during hospitalization. Estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease formula: eGFR (ml·min⁻¹·1.73 m²) = 186 × serum creatinine (Scr, mg/dl)⁻¹.′⁵⁴ × age (years)⁻⁰.′²⁰³ × (0.742, for female). Zinc level was assayed by nephelometry using the HITACHI LABOSPECT 008 (Hitachi, Japan); HbA1c was assayed by high-performance liquid chromatography method using Premier Hb9210 (PRIMUS, USA); C-peptide was assayed by electrochemiluminescence method using Cobas e411 (Roche, Switzerland); Scr was assayed by enzymic method using Beckman Coulter AU5800 (Beckman Coulter, USA); TC and TG were assayed by enzymic method using Beckman Coulter AU5800 (Beckman Coulter, USA); HDL-C and LDL-C were all assayed by direct method using Beckman Coulter AU5800 (Beckman Coulter); urine ACR was assayed by picric acid method using Cobas c311 (Roche).

We initially compared the serum zinc levels among patients with various numbers of microvascular complications. We also compared the features of patients with and without specific microvascular complication. A logistic regression analysis was further conducted to analyze the role of serum zinc as an independent risk factor for each microvascular complication. Finally, we compared the characteristics among patients with different serum zinc levels and performed logistic regression to determine the risk factors contributing to lower serum zinc levels.

Statistical methods
SPSS 19.0 (IBM, USA) was used to analyze the data. Normally distributed data were expressed as mean ± standard deviation (SD). Student’s t-test was used to compare the parameters between two groups. Single-factor analysis of
variance (ANOVA) was used to compare the parameters among multiple groups. Data with abnormal distribution were expressed as median (range). Mann-Whitney $U$ nonparameter test was used to compare the parameters between two groups and the Kruskal-Wallis nonparametric test was used to compare the parameters among multiple groups. The chi-square test was used to compare the ratio among groups. A bivariate regression model was used to analyze the correlation between serum zinc level and each microvascular complication. Multiple regression analysis was used to determine the risk factors for low serum zinc level.

**Results**

The 412 T2D patients included 233 (56.6%) males and 179 (43.4%) females. The mean age of the participants was 56 ± 14 years, and the median duration of diabetes was 10 years. Seventy-eight patients (18.9%) had DR; 91 (22.1%) had DN and 234 (56.8%) had DPN. Sixty patients (14.6%) manifested two different microvascular complications and 36 patients (8.7%) exhibited all the three complications.

**Association between zinc level and diabetic microvascular complications**

We divided all the participants into four groups according to the number of diabetic complications. Among the 412 patients, 141 had none, 175 had one, 60 had two, and 36 had three microvascular complications. The results showed significantly lower zinc level in patients with microvascular complications [Figure 1].

**Comparison of patients with and without specific diabetic microvascular complications**

Among the 412 patients, 78 had DR. Sex, age, duration of diabetes, HbA1c, fasting C-peptide, 2-h C-peptide, LDL-C, eGFR, and zinc levels were significantly different between the two groups with and without DR. Zinc level in DR patients was significantly lower than in patients without retinopathy ($P < 0.001$). Patients with DR had a significantly longer duration of diabetes, higher HbA1c, lower C-peptide level, higher LDL-C level, and lower eGFR [Table 1].

Among the 412 patients, 234 had DPN while 178 did not. Age, duration of diabetes, the prevalence of hypertension, eGFR and zinc level were significantly different between the two groups. Zinc level in patients with DPN was significantly lower than in those without ($P < 0.01$). Patients with DPN had a significantly longer duration of diabetes, higher prevalence of hypertension and lower eGFR [Table 2].

Among the 412 patients, 91 had DN while 321 had no DN. The results showed that age, duration of diabetes, prevalence of hypertension, HbA1c, HDL-C, eGFR, and zinc level were significantly different between the two groups. Zinc level in DN patients was significantly lower than in patients without retinopathy ($P < 0.01$). Patients with DN had a significantly longer duration of diabetes, higher prevalence of hypertension, higher HbA1c, lower HDL-C level, and lower eGFR [Table 3].

We further divided the DN patients according to their urinary ACR into three groups: (1) normal group with ACR <30 mg/g ($n = 321$), (2) microalbuminuria group with $30 \leq$ ACR <300 mg/g ($n = 67$), and (3) macroalbuminuria group with ACR ≥300 mg/g ($n = 24$). A significantly lower zinc level was observed in patients with higher ACR level ($P < 0.01$, Figure 2).

**Logistic regression analysis of zinc levels and diabetic microvascular complications**

Table 4 summarizes the association between serum zinc level and each diabetic microvascular complication. A negative correlation is shown between zinc level and DN. After adjustment for age, duration of diabetes, prevalence of hypertension, body mass index (BMI), HbA1c and eGFR, there was a significant negative correlation between zinc level and DN (odds ratio: 0.869; 95% confidence interval: 0.765–0.987; $P < 0.05$). Whereas no significant correlations were found between zinc level and either DR or DPN.

![Figure 1: Zinc levels of patients with various number of diabetic microvascular complications.](image1)

![Figure 2: Comparison of zinc levels in patients with different urinary albumin/creatinine ratio. ACR: Albumin/creatinine ratio.](image2)
Table 1: Clinical characteristics of patients with and without diabetic retinopathy

| Items                      | Without DR | With DR | Statistic values | P   |
|----------------------------|------------|---------|------------------|-----|
| N                          | 334        | 78      | –                | –   |
| Male, n (%)                | 198 (59)   | 35 (45) | 5.344*           | 0.023† |
| Age (years), mean ± SD     | 55 ± 14    | 60 ± 11 | –3.479†          | 0.001† |
| Waist (cm), mean ± SD      | 96 ± 11    | 95 ± 12 | 0.731†           | 0.465 |
| BMI (kg/m²), median (range)| 26.0 (17.7–43.2) | 25.2 (17.9–38.9) | –1.349‡          | 0.177 |
| Duration (years), median (range)| 9 (0–42) | 16 (2–37) | –6.691†          | <0.001† |
| Prevalence of hypertension, n (%) | 183 (54.8) | 52 (66.7) | 3.640*          | 0.058 |
| HbA1c (%), median (range)  | 8.5 (5.6–14.7) | 9.1 (5.8–13.9) | –2.822‡         | 0.005‡ |
| C-P (ng/ml), median (range)| 1.97 (0.22–17.78) | 1.40 (0.06–6.65) | –3.731†         | <0.001† |
| 2-h C-P (ng/ml), median (range)| 4.74 (0.26–19.98) | 2.83 (0.11–11.86) | –5.149†         | <0.001† |
| TC (mmol/L), median (range)| 4.4 (2.0–12.0) | 4.7 (2.2–10.0) | 1.413†          | 0.158 |
| TG (mmol/L), median (range)| 1.6 (0.5–18.3) | 1.6 (0.5–10.6) | –1.100†        | 0.271 |
| HDL-C (mmol/L), median (range)| 0.9 (0.4–1.9) | 1.0 (0.4–1.7) | 1.284†        | 0.199 |
| LDL-C (mmol/L), mean ± SD  | 2.6 ± 0.8  | 2.8 ± 0.9 | –2.007†       | 0.045‡ |
| eGFR (ml/min⁻¹·1.73 m⁻²), mean ± SD | 117 ± 34 | 103 ± 33 | 3.337†      | 0.001† |
| Zn (µmol/L), median (range)| 13.69 (8.68–27.90) | 12.80 (7.63–21.40) | –3.947†      | <0.001‡ |

*µ values; †t values; ‡Z values; ††Statistical significance. DR: Diabetic retinopathy; SD: Standard deviation; BMI: Body mass index; HbA1c: Hemoglobin A1c; C-P: C-peptide; TC: Total cholesterol; TG: Triglyceride; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; eGFR: Estimated glomerular filtration rate.

Table 2: Clinical characteristics of patients with and without diabetic peripheral neuropathy

| Items                      | Without DPN | With DPN | Statistic values | P   |
|----------------------------|------------|---------|------------------|-----|
| N                          | 178        | 234     | –                | –   |
| Male, n (%)                | 107 (60)   | 126 (54) | 1.616*           | 0.229 |
| Age (years), mean ± SD     | 53 ± 16    | 59 ± 11 | –4.815†          | <0.001† |
| Waist (cm), mean ± SD      | 96 ± 12    | 96 ± 11 | –0.079†          | 0.937 |
| BMI (kg/m²), median (range)| 25.6 (17.7–43.2) | 25.9 (17.9–38.9) | –0.203†         | 0.839 |
| Duration (years), median (range)| 7 (0–31) | 11 (0–42) | –5.945†         | <0.001† |
| Prevalence of hypertension, n (%) | 90 (50.6) | 145 (62.0) | 5.365*       | 0.021* |
| HbA1c (%), median (range)  | 8.7 (5.6–14.7) | 8.7 (5.8–13.9) | –0.018§         | 0.986 |
| C-P (ng/ml), median (range)| 1.99 (0.22–7.11) | 1.79 (0.06–17.78) | –1.870‡        | 0.061 |
| TC (mmol/L), median (range)| 4.67 (0.26–19.98) | 4.26 (0.11–15) | –1.726§        | 0.084 |
| TG (mmol/L), median (range)| 4.5 (2.0–12.0) | 4.4 (2.2–10.0) | –1.05‡        | 0.294 |
| HDL-C (mmol/L), median (range)| 1.6 (0.6–18.3) | 1.6 (0.5–15.3) | –0.39§        | 0.696 |
| LDL-C (mmol/L), mean ± SD  | 1.0 (0.4–1.8) | 1.0 (0.4–1.9) | –0.57§       | 0.569 |
| eGFR (ml/min⁻¹·1.73 m⁻²), mean ± SD | 119 ± 34 | 111 ± 34 | 2.442*       | 0.015* |
| Zn (µmol/L), median (range)| 13.99 (8.14–23.55) | 13.23 (7.63–27.90) | –3.159§      | 0.002‡ |

*µ values; †t values; ‡Z values; ††Statistical significance. DPN: Diabetic peripheral neuropathy; SD: Standard deviation; BMI: Body mass index; HbA1c: Hemoglobin A1c; C-P: C-peptide; TC: Total cholesterol; TG: Triglyceride; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; eGFR: Estimated glomerular filtration rate.

Patient profile under different levels of serum zinc and risk factors for lower serum zinc level

We divided all the patients into three groups according to their zinc levels. Zinc levels in upper tertile group ranged from 14.53 to 27.90 µmol/L. The middle tertile range of zinc level was 12.74–14.53 µmol/L and the lower tertile was 7.63–12.74 µmol/L. Patients with low zinc level showed a higher prevalence of all the three diabetic microvascular complications. Compared with the patients with zinc levels within the middle and upper tertiles, those with zinc level within the lower tertile were older and had a longer duration of diabetes, higher HbA1c, lower C-peptide, TC, TG and eGFR levels [Table 5].

The logistic regression analysis revealed that serum zinc level was negatively correlated with age, diabetes duration, HbA1c level, and the prevalence of DN, and was positively correlated with TG level [Table 6].

**Discussion**

Our study showed that the increased incidence of diabetic microvascular complications was accompanied by decreased serum zinc level in patients with T2D. However, evidence
Our study also showed that the zinc level was significantly lower in patients with elevated urinary ACR, patients with an ACR over 300 mg/g were associated with the lowest zinc levels in serum. Our study also suggested that serum zinc level was an independent risk factor for DN. A previous animal study had shown that zinc supplementation raises the zinc levels in renal tubular epithelial cells, up-regulates the expression of metallothionein in the renal tubular cells, and inhibits the renal oxidative damage, inflammation and expression of connective tissue growth factor via its antioxidative effect. Since zinc may exhibit a protective effect in DN, patients with low zinc level were more likely to show an elevated ACR. Brun et al. showed much higher urinary zinc excretion in diabetic rats with albuminuria, concluding that incipient nephropathy in terms of microalbuminuria was associated with a highly significant increase in zinc excretion.

Our study also showed that zinc levels were significantly lower in patients with elevated urinary ACR, patients with an ACR over 300 mg/g were associated with the lowest zinc levels in serum. Our study also suggested that serum zinc level was an independent risk factor for DN. A previous animal study had shown that zinc supplementation raises the zinc levels in renal tubular epithelial cells, up-regulates the expression of metallothionein in the renal tubular cells, and inhibits the renal oxidative damage, inflammation and expression of connective tissue growth factor via its antioxidative effect.

In our study, we found lower zinc levels in DR patients than in those without DR, consistent with previous studies, suggesting that zinc might play an important role in the development of DR. Zinc is a retinal protective factor, by stabilizing the membrane structure, activating metallothionein, clearing free radicals and inhibiting lipid peroxidation, it may reduce the expression of vascular endothelial growth factor, and inhibit the neovascularization and exudation. Our results suggest that in T2D patients with a relatively low zinc level, the protective effect of the anti-oxidative zinc may be reduced, and the risk of DR may be elevated. Our study failed to reveal any independent relationship between zinc level and DR, perhaps due to the limited sample size. Furthermore, we failed to adjust the zinc intake from the food, leading to possible impact on the serum zinc level. Finally, we did not collected the detailed information of DR, which may be helpful for us to further analyze the association between zinc level and different stage of DR.

Table 3: Clinical characteristics of patients with and without diabetic nephropathy

| Items                              | Without DN | With DN | Statistical values | P  |
|------------------------------------|------------|---------|--------------------|----|
| N                                  | 321        | 91      |                    |    |
| Male, n (%)                        | 186 (58)   | 47 (52) | 1.144*             | 0.338 |
| Age (years), mean ± SD             | 55 ± 14    | 60 ± 14 | −2.727*            | 0.007† |
| Waist (cm), mean ± SD              | 95 ± 11    | 97 ± 13 | −0.993             | 0.322 |
| BMI (kg/m²), median (range)        | 25.8 (17.7–40.8) | 25.6 (17.9–43.2) | −0.086† | 0.932 |
| Duration (years), median (range)   | 10 (0–42)  | 13 (0–37)| −3.325†            | 0.001† |
| Prevalence of hypertension, n (%)  | 163 (50.8) | 72 (79.1)| 23.242*            | <0.001† |
| HbA1c (%), median (range)          | 8.5 (5.6–14.7) | 9.1 (5.8–13.2)| −2.279* | 0.023† |
| C-P (ng/ml), median (range)        | 1.89 (0.06–8.58) | 1.86 (0.11–17.78) | −0.296| 0.767 |
| 2-h C-P (ng/ml), median (range)    | 4.41 (0.11–18.09) | 3.90 (0.60–19.98) | −1.654 | 0.098 |
| TC (mmol/L), median (range)        | 4.5 (2.0–10.8) | 4.5 (2.2–12.0) | −0.513† | 0.608 |
| TG (mmol/L), median (range)        | 1.6 (0.5–15.3) | 1.6 (0.5–18.3) | −0.25† | 0.803 |
| HDL-C (mmol/L), median (range)     | 1.0 (0.4–1.9) | 0.9 (0.4–1.7) | −2.063† | 0.039‡ |
| LDL-C (mmol/L), mean ± SD          | 2.7 ± 0.8  | 2.6 ± 0.9 | 0.115† | 0.908 |
| eGFR (ml/min⁻¹·1.73 m⁻²), mean ± SD | 118 ± 33  | 101 ± 34 | 4.354* | <0.001† |
| Zn (μmol/L), median (range)        | 13.80 (8.68–27.9) | 12.65 (7.63–22.80) | −4.29* | <0.001† |

*P values, †t values, ‡Z values, §Statistical significance. DN: Diabetic nephropathy; SD: Standard deviation; BMI: Body mass index; HbA1c: Hemoglobin A1c; C-P: C-peptide; TC: Total cholesterol; TG: Triglyceride; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; eGFR: Estimated glomerular filtration rate.

Table 4: Logistic regression analysis of zinc level and diabetic microvascular complications in patients with type 2 diabetes

| Microvascular complications | OR (95% CI) | P    |
|-----------------------------|-------------|------|
| DR                          | 0.900 (0.782–1.035) | 0.138 |
| DN                          | 0.869 (0.765–0.987) | 0.031* |
| DPN                         | 0.967 (0.882–1.060) | 0.468 |

*Statistical significance. OR: Odds ratio; 95% CI: Confidence interval; DR: Diabetic retinopathy; DN: Diabetic nephropathy; DPN: Diabetic peripheral neuropathy.
Table 5: Clinical characteristics of people with different serum zinc levels

| Items                          | Upper tertile | Middle tertile | Lower tertile | Statistic values | P      |
|-------------------------------|---------------|----------------|---------------|-----------------|--------|
| N                             | 137           | 137            | 138           | –               | –      |
| Male, n (%)                   | 90 (66)       | 77 (56)        | 66 (48)       | 8.943*          | 0.011* |
| Age (years), mean ± SD        | 51 ± 14       | 57 ± 13        | 61 ± 12       | 20.634*         | <0.001*|
| Waist (cm), mean ± SD         | 97 ± 11       | 95 ± 11        | 95 ± 12       | 1.631*          | 0.197  |
| BMI (kg/m²), median (range)   | 26.1 (18.6–43.2) | 25.4 (18.1–35.7) | 25.4 (17.7–40.0) | 5.239* | 0.073  |
| Duration (years), median (range) | 7 (0–26)  | 10 (0–31)      | 13 (0–42)     | 26.665*         | <0.001*|
| Prevalence of hypertension, n (%) | 67 (48.9) | 83 (60.6)      | 85 (61.6)     | 5.57*           | 0.062  |
| HbA1c (%), median (range)     | 8.3 (5.6–14.7) | 8.4 (5.8–13.5) | 9.1 (5.8–14.5) | 6.784*         | 0.034* |
| C-P (ng/mL), median (range)   | 2.14 (0.45–4.79) | 1.87 (0.06–17.78) | 1.69 (0.11–7.11) | 13.984* | 0.001* |
| 2-h C-P (ng/mL), median (range) | 5.10 (0.75–19.98) | 4.29 (0.11–18.09) | 3.84 (0.60–11.11) | 17.565* | <0.001* |
| TC (mmol/L), median (range)   | 4.7 (2.0–12.0) | 4.4 (2.5–10.8) | 4.3 (2.2–10.0) | 6.434*          | 0.040* |
| TG (mmol/L), median (range)   | 1.9 (0.6–18.3) | 1.6 (0.6–14.9) | 1.4 (0.5–10.6) | 24.546*         | <0.001* |
| HDL-C (mmol/L), median (range) | 0.9 (0.4–1.9) | 1.0 (0.6–1.8)  | 1.0 (0.4–1.8) | 5.424*          | 0.066  |
| LDL-C (mmol/L), mean ± SD     | 2.6 ± 0.9     | 2.6 ± 0.8      | 2.7 ± 0.9     | 0.511*          | 0.601  |
| eGFR (ml/min·1.73 m²), mean ± SD | 1216 ± 35 | 114 ± 32       | 109 ± 34      | 4.792*          | 0.009* |
| Prevalence of DR, n (%)       | 14 (10.2)     | 26 (19.0)      | 38 (27.5)     | 13.433*         | 0.001* |
| Prevalence of DN, n (%)       | 18 (13.1)     | 25 (18.2)      | 48 (34.8)     | 20.473*         | <0.001*|
| Prevalence of DPN, n (%)      | 63 (46.0)     | 85 (62.0)      | 86 (62.3)     | 9.778*          | 0.008* |

*P<0.05; †P<0.01; ‡P<0.001

Table 6: Logistic regression analysis of risk factors related to low serum zinc level

| Factors                          | OR (95% CI) | P      |
|----------------------------------|-------------|--------|
| Sex                              | 1.200 (0.674–2.136) | 0.553 |
| Age                              | 0.955 (0.928–0.983) | 0.002*|
| Diabetes duration                | 0.950 (0.905–0.996) | 0.034*|
| HbA1c                            | 0.744 (0.632–0.877) | 0.000*|
| C-P                              | 0.959 (0.707–1.300) | 0.787 |
| 2-h C-P                          | 1.069 (0.930–1.228) | 0.349 |
| TC                               | 0.916 (0.695–1.207) | 0.534 |
| TG                               | 1.503 (1.196–1.888) | 0.000*|
| eGFR                             | 1.200 (0.674–2.136) | 0.553 |
| DR                               | 0.855 (0.367–1.995) | 0.718 |
| DN                               | 0.326 (0.150–0.711) | 0.005*|
| DPN                              | 0.848 (0.479–1.501) | 0.571 |

*Statistical significance. OR: Odds ratio; CI: Confidence interval; HbA1c: Hemoglobin A1c; C-P: C-peptide; TC: Total cholesterol; TG: Triglyceride; eGFR: Estimated glomerular filtration rate; DR: Diabetic retinopathy; DN: Diabetic nephropathy; DPN: Diabetic peripheral neuropathy.

In conclusion, our study suggested that lower serum zinc level in T2D patients was related to higher prevalence of diabetic microvascular complications and represented as an independent risk factor for DN. Patients with lower serum zinc level were more likely to have a longer duration of diabetes, poorer glucose control, and worse β-cell function. Older age, longer diabetes duration, higher HbA1c level, and the prevalence of DN were risk factors related to the lower serum zinc level.

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Conflicts of interest
There are no conflicts of interest.

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