Research Square

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Association of the triglyceride-to-high-density lipoprotein cholesterol ratio with diabetic peripheral neuropathy in hospitalized adults with type 2 diabetes and HbA1c ≤7.0%: a retrospective cross-sectional study

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Research Article

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Abstract

Background

Diabetic peripheral neuropathy (DPN) can be present in people with type 2 diabetes mellitus (T2DM) whose glycated hemoglobin (HbA1c) is ≤ 7.0%. We examined the cross-sectional association between the triglyceride-to-high-density lipoprotein cholesterol (TG/HDL-C) ratio and DPN in hospitalized adults meeting this HbA1c threshold.

Methods

This retrospective cross-sectional analysis included 276 hospitalized adults with T2DM and HbA1c ≤ 7.0% at Tianjin First Central Hospital between January 2023 and January 2024. Participants were classified as having DPN (n = 107) or not having DPN (n = 169) from the diagnosis documented in the medical record. Multivariable logistic regression was used to examine the association between the TG/HDL-C ratio and DPN. The ratio was also analyzed in quartiles using the same covariate set.

Results

DPN was identified in 107 of 276 participants (38.8%). The TG/HDL-C ratio was higher in the DPN group than in the non-DPN group [2.56 (2.00, 3.58) vs 1.44 (0.98, 1.91); P < 0.001]. After adjustment for age, sex, diabetes duration, body mass index, HbA1c, systolic blood pressure, smoking history, statin use, estimated glomerular filtration rate, and urinary albumin-to-creatinine ratio, each one-unit increase in the ratio was associated with higher odds of DPN (adjusted odds ratio, 6.11; 95% confidence interval, 3.47–10.77; P < 0.001). DPN prevalence across quartiles was 7.2%, 22.5%, 46.3%, and 79.7% (P for trend < 0.001).

Conclusions

Among hospitalized adults with T2DM and HbA1c ≤ 7.0%, a higher TG/HDL-C ratio was associated with prevalent DPN. The finding should be confirmed in prospective studies before the ratio is used for clinical risk stratification.

Background

Diabetic peripheral neuropathy (DPN) is one of the most common chronic complications of diabetes. Its clinical manifestations include limb numbness, pain, sensory loss, and gait instability; in severe cases, it can progress to foot ulceration and even amputation [1–3]. Recent Chinese and international consensus statements recommend incorporating DPN into comprehensive diabetes management and routine

screening, with particular attention to patients with a longer duration of diabetes or coexisting retinopathy or kidney damage [1, 2, 4].

HbA1c is central to the assessment of long-term glycemia, but it does not capture all pathways that may contribute to peripheral nerve injury. DPN can occur in patients whose HbA1c is within a commonly used treatment threshold, and observational studies have implicated glycemic variability and metabolic factors beyond average glucose exposure [5–7]. Dyslipidemia is of particular interest because it is routinely measured and potentially modifiable.

Diabetic dyslipidemia is typically characterized by elevated triglycerides (TG), reduced high-density lipoprotein cholesterol (HDL-C), and increased small dense low-density lipoprotein particles. The TG/HDL-C ratio can partly reflect this atherogenic lipid pattern and the underlying state of insulin resistance [8, 9]. Pathophysiologically, dysregulated lipid metabolism may aggravate peripheral nerve injury through oxidative stress, low-grade inflammation, endothelial dysfunction, and impaired microcirculatory perfusion of neural tissue [8, 9]. The ratio is also simple to calculate, readily available, and inexpensive, and has therefore attracted interest in the assessment of metabolic syndrome, cardiovascular risk, and diabetic microvascular complications [4, 10].

Earlier studies have reported associations between the TG/HDL-C ratio and DPN in broader T2DM populations [4, 8]. Less is known about this association among patients with HbA1c ≤ 7.0%, and published data on the shape of the association are limited. We therefore examined whether the TG/HDL-C ratio was associated with prevalent DPN in hospitalized patients who met this HbA1c threshold and explored the pattern of DPN prevalence across ratio quartiles.

Methods

Study design and participants

This retrospective cross-sectional study included 276 adults with T2DM and HbA1c ≤ 7.0% who were hospitalized at Tianjin First Central Hospital between January 1, 2023, and January 31, 2024. The diagnosis of T2DM was taken from the electronic medical record. Of 324 records screened, 48 were excluded because HbA1c was > 7.0%, leaving 276 records for analysis. Participants were classified as having DPN (n = 107) or not having DPN (n = 169). Other exclusion criteria were type 1 diabetes, gestational diabetes, another specific type of diabetes, severe infection, malignancy, or an acute cardiovascular or cerebrovascular event. The 276 included records had complete data for all variables used in the analyses.

Diagnosis of DPN

DPN status was based on the clinical diagnosis recorded in the electronic medical record and was reviewed with reference to the 2021 Expert Consensus on the Diagnosis and Treatment of Diabetic

Neuropathy [1]. The clinical assessment considered a confirmed history of diabetes; symptoms or signs of peripheral neuropathy, such as numbness, pain, paresthesia, reduced or absent ankle reflexes, or impaired vibration, pinprick, temperature, or pressure sensation; and exclusion of other likely causes, including cervical or lumbar spine disease, Guillain–Barré syndrome, vitamin B12 deficiency, and alcohol-related neuropathy. Nerve-conduction testing was used as a supportive investigation, particularly when the presentation was atypical or the diagnosis was uncertain, but an abnormal result was not required for classification in every participant.

Data collection

Variables were extracted from the electronic medical record for the index hospitalization: age, sex, body mass index (BMI), duration of diabetes, blood pressure, smoking history, alcohol consumption, HbA1c, triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), statin use, glucose-lowering regimen, metabolic syndrome, estimated glomerular filtration rate (eGFR), urinary albumin-to-creatinine ratio (UACR), retinopathy, diabetic or high-risk foot, peripheral arterial disease, history of falls, gait abnormality, orthostatic hypotension, resting heart rate, heart-rate variability, neuropathic pain, and nerve-conduction abnormalities. The TG/HDL-C ratio was calculated by dividing TG by HDL-C; both values were expressed in mmol/L.

Statistical analysis

All tests were two-sided, and $P < 0.05$ was considered statistically significant. Approximately normally distributed continuous variables are presented as mean ± standard deviation and were compared using the independent-samples t test. Skewed continuous variables are presented as median (25th percentile, 75th percentile) and were compared using the Mann–Whitney U test. Categorical variables are presented as n (%) and were compared using the chi-square test or Fisher's exact test. DPN status was the dependent variable in logistic regression. Covariates were selected before modeling on clinical grounds and included age, sex, diabetes duration, BMI, HbA1c, systolic blood pressure, smoking history, statin use, eGFR, and log2-transformed UACR. The TG/HDL-C ratio was entered either as a continuous variable or as sample-based quartiles. Three nested models were fitted for the continuous analysis: model 1 adjusted for age, sex, diabetes duration, BMI, and HbA1c; model 2 additionally adjusted for systolic blood pressure, smoking history, statin use, and eGFR; and model 3 additionally adjusted for log2-transformed UACR. Quartile estimates used the model 3 covariate set, with Q1 as the reference. Trend was tested by entering the median TG/HDL-C value of each quartile as a continuous term. Linearity of the continuous TG/HDL-C term was assessed with a Box–Tidwell interaction, and multicollinearity was assessed with variance inflation factors. All 276 participants were included; no imputation was required. Analyses were performed in Python 3.12.

Use of generative AI-assisted technology

OpenAI Codex was used to translate the Chinese draft into English and to assist with language and formatting. The authors checked and revised the output and take responsibility for the final manuscript.

Results

Prevalence of DPN

Among the 276 hospitalized adults with T2DM and HbA1c ≤ 7.0%, 107 had DPN and 169 did not, corresponding to a DPN prevalence of 38.8%.

Comparison of baseline characteristics

Participants with DPN were older and had a higher BMI, a longer duration of diabetes, higher TG, lower HDL-C, and a higher TG/HDL-C ratio than participants without DPN. They also had lower eGFR, higher UACR, a higher resting heart rate, and lower heart-rate variability. Several vascular and microvascular comorbidities were more frequent in the DPN group (Table 1). HbA1c distributions were similar between groups (P = 0.636). Neuropathic pain and nerve-conduction abnormalities are reported descriptively because they overlap with the clinical assessment used to classify DPN.

Table 1
Comparison of clinical characteristics between groups

Variable	Overall (n = 276)	DPN (n = 107)	Non-DPN (n = 169)	P value
Age, years	61.7 ± 9.2	63.7 ± 8.5	60.5 ± 9.5	0.005
Male sex, n (%)	176 (63.8)	67 (62.6)	109 (64.5)	0.752
BMI, kg/m²	26.0 ± 3.2	26.6 ± 3.2	25.5 ± 3.2	0.006
Diabetes duration, years	7.1 (3.9, 10.7)	10.5 (7.0, 14.9)	5.1 (3.0, 8.5)	< 0.001
Systolic blood pressure, mmHg	131.3 ± 14.2	135.5 ± 13.7	128.7 ± 14.0	< 0.001
Diastolic blood pressure, mmHg	80.5 ± 10.3	81.6 ± 10.7	79.8 ± 10.0	0.179
Smoking history, n (%)	83 (30.1)	38 (35.5)	45 (26.6)	0.117
Alcohol consumption, n (%)	51 (18.5)	25 (23.4)	26 (15.4)	0.096
HbA1c, %	6.6 (6.4, 6.8)	6.6 (6.4, 6.8)	6.6 (6.4, 6.8)	0.636
TG, mmol/L	1.90 (1.41, 2.60)	2.40 (1.86, 3.29)	1.69 (1.20, 2.17)	< 0.001
HDL-C, mmol/L	1.09 ± 0.24	0.94 ± 0.19	1.19 ± 0.21	< 0.001
TG/HDL-C ratio	1.82 (1.18, 2.52)	2.56 (2.00, 3.58)	1.44 (0.98, 1.91)	< 0.001
LDL-C, mmol/L	2.81 ± 0.72	2.92 ± 0.68	2.74 ± 0.74	0.053
TC, mmol/L	4.77 ± 0.85	4.92 ± 0.85	4.68 ± 0.84	0.021
Statin use, n (%)	165 (59.8)	72 (67.3)	93 (55.0)	0.043
Metabolic syndrome, n (%)	127 (46.0)	59 (55.1)	68 (40.2)	0.016
eGFR, mL/min/1.73 m²	75.8 ± 19.3	70.4 ± 21.6	79.2 ± 16.8	< 0.001
UACR, mg/g	35.3 (20.7, 63.9)	52.0 (28.5, 90.6)	27.0 (18.3, 50.8)	< 0.001
Retinopathy, n (%)	57 (20.7)	35 (32.7)	22 (13.0)	< 0.001

Data are presented as mean ± standard deviation, median (25th percentile, 75th percentile), or n (%). Normally distributed continuous variables were compared using the independent-samples t test; non-normally distributed continuous variables were compared using the Mann-Whitney U test; categorical variables were compared using the chi-square test or Fisher's exact test. BMI, body mass index; DPN, diabetic peripheral neuropathy; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides; UACR, urinary albumin-to-creatinine ratio.

Variable	Overall (n = 276)	DPN (n = 107)	Non-DPN (n = 169)	P value
Diabetic/high-risk foot, n (%)	10 (3.6)	7 (6.5)	3 (1.8)	0.050
Peripheral arterial disease, n (%)	36 (13.0)	24 (22.4)	12 (7.1)	< 0.001
History of falls, n (%)	31 (11.2)	19 (17.8)	12 (7.1)	0.006
Gait abnormality, n (%)	48 (17.4)	30 (28.0)	18 (10.7)	< 0.001
Orthostatic hypotension, n (%)	37 (13.4)	24 (22.4)	13 (7.7)	< 0.001
Resting heart rate, beats/min	79.0 ± 12.1	82.9 ± 13.5	76.5 ± 10.5	< 0.001
Heart-rate variability, ms	30.4 (20.7, 39.5)	22.5 (15.3, 29.5)	35.4 (26.6, 44.1)	< 0.001
Neuropathic pain, n (%)	72 (26.1)	57 (53.3)	15 (8.9)	< 0.001
Abnormal nerve conduction, n (%)	109 (39.5)	83 (77.6)	26 (15.4)	< 0.001

Data are presented as mean ± standard deviation, median (25th percentile, 75th percentile), or n (%). Normally distributed continuous variables were compared using the independent-samples t test; non-normally distributed continuous variables were compared using the Mann-Whitney U test; categorical variables were compared using the chi-square test or Fisher's exact test. BMI, body mass index; DPN, diabetic peripheral neuropathy; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides; UACR, urinary albumin-to-creatinine ratio.

Multivariable logistic regression analysis

The association between TG/HDL-C and DPN was similar across the three nested models. The adjusted OR per one-unit increase in TG/HDL-C was 6.40 (95% CI, 3.79–10.80) in model 1, 6.39 (95% CI, 3.69–11.07) in model 2, and 6.11 (95% CI, 3.47–10.77) in model 3; all P < 0.001 (Table 2). In model 3, longer diabetes duration, higher BMI, and higher UACR were also associated with DPN. The Box–Tidwell interaction for TG/HDL-C was not statistically significant (P = 0.073), and the maximum variance inflation factor was 1.14.

Table 2
Multivariable logistic regression analysis of factors associated with DPN

Variable	OR	95% CI	P value
TG/HDL-C ratio: model 1 (per 1 unit)	6.397	3.790–10.797	< 0.001
TG/HDL-C ratio: model 2 (per 1 unit)	6.391	3.690–11.070	< 0.001
TG/HDL-C ratio: model 3 (per 1 unit)	6.111	3.467–10.771	< 0.001
Age (per 5 years)	1.206	0.955–1.522	0.116
Male sex	0.687	0.287–1.645	0.399
Diabetes duration (per 5 years)	5.667	3.178–10.104	< 0.001
BMI (per 1 kg/m²)	1.234	1.078–1.414	0.002
HbA1c (per 1%)	3.385	0.788–14.541	0.101
Systolic blood pressure (per 10 mmHg)	1.275	0.946–1.719	0.110
Smoking history	1.986	0.805–4.900	0.136
Statin use	1.385	0.602–3.187	0.444
eGFR (per 10 mL/min/1.73 m²)	0.841	0.665–1.062	0.146
UACR (per doubling)	2.105	1.381–3.208	< 0.001

DPN status was the dependent variable. Model 1 adjusted for age, sex, diabetes duration, BMI, and HbA1c. Model 2 additionally adjusted for systolic blood pressure, smoking history, statin use, and eGFR. Model 3 additionally adjusted for log2-transformed UACR. Covariate estimates shown after the three TG/HDL-C rows are from model 3. BMI, body mass index; CI, confidence interval; DPN, diabetic peripheral neuropathy; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; OR, odds ratio; UACR, urinary albumin-to-creatinine ratio.

Association across TG/HDL-C ratio quartiles

DPN was present in 5 of 69 participants in Q1, 16 of 71 in Q2, 31 of 67 in Q3, and 55 of 69 in Q4. The corresponding prevalences were 7.2%, 22.5%, 46.3%, and 79.7%. After adjustment using the model 3 covariate set, the ORs relative to Q1 were 5.34 (95% CI, 1.32–21.67) for Q2, 14.84 (95% CI, 3.76–58.65) for Q3, and 147.20 (95% CI, 29.14–743.53) for Q4 (P for trend < 0.001; Table 3).

Table 3
Association between TG/HDL-C ratio quartiles and DPN prevalence

Quartile	TG/HDL-C range	n	DPN, n (%)	Crude OR	Crude 95% CI	Adjusted OR (95% CI)	P value
Q1	≤ 1.1775	69	5 (7.2)	1.00	Reference	1.00 (Reference)	—
Q2	> 1.1775 to 1.8200	71	16 (22.5)	3.72	1.28–10.82	5.34 (1.32–21.67)	0.019
Q3	> 1.8200 to 2.5175	67	31 (46.3)	11.02	3.94–30.85	14.84 (3.76–58.65)	< 0.001
Q4	> 2.5175	69	55 (79.7)	50.29	17.03–148.50	147.20 (29.14–743.53)	< 0.001
P for trend	—	—	—	—	—	—	< 0.001

Q1 was the reference group. Adjusted estimates used the model 3 covariate set. Trend was tested by entering the median TG/HDL-C value of each quartile as a continuous term. CI, confidence interval; DPN, diabetic peripheral neuropathy; HDL-C, high-density lipoprotein cholesterol; OR, odds ratio; TG, triglycerides.

Discussion

In this hospital-based cross-sectional sample, 38.8% of participants had DPN despite an HbA1c of ≤ 7.0%. The TG/HDL-C ratio differed substantially between DPN and non-DPN groups and remained associated with DPN after adjustment for the covariates included in the model. By contrast, HbA1c showed little variation within this restricted sample and was not associated with DPN.

The TG/HDL-C ratio is a practical summary of an atherogenic lipid pattern characterized by higher TG and lower HDL-C [8, 9]. Lipid-related oxidative stress, inflammation, endothelial dysfunction, and impaired microvascular perfusion are biologically plausible contributors to nerve injury, although these pathways were not measured here [8, 9]. The present findings are consistent with earlier observational reports linking lipid abnormalities and the TG/HDL-C ratio to DPN [4, 8], but they do not establish a causal mechanism.

DPN prevalence increased across TG/HDL-C quartiles, and the graded pattern remained after adjustment. The estimates, particularly for Q4, were large and imprecise because only five DPN cases occurred in the reference quartile. The upper quartile boundary of 2.5175 is therefore a sample-derived cut point rather than a clinically validated threshold.

The DPN group also had higher UACR, lower eGFR, and more frequent retinopathy, peripheral arterial disease, falls, gait abnormality, and orthostatic hypotension. These differences describe a clinically complex inpatient population with multiple complications. They may reflect shared disease duration, vascular burden, or other confounding factors rather than a single underlying pathway. Because the

TG/HDL-C ratio is available from routine lipid testing, it may be useful for identifying patients who warrant closer neurological assessment, but its incremental value beyond established clinical factors was not evaluated in this study.

Several limitations affect interpretation. First, the single-center inpatient sample is vulnerable to referral and selection bias and may not represent community or outpatient populations. Second, exposure and outcome were assessed during the same hospitalization, so temporal ordering and causality cannot be established. Third, DPN classification relied on diagnoses documented in existing records rather than a uniform prospective screening protocol; abnormal nerve conduction was recorded in 83 of 107 participants with DPN and 26 of 169 without DPN, so some misclassification is possible. Fourth, residual confounding remains possible despite covariate adjustment. Finally, only five DPN cases occurred in Q1, producing wide confidence intervals for the higher-quartile estimates. Odds ratios should not be interpreted as risk ratios, and the observed quartile boundaries should not be treated as clinical cutoffs.

Conclusions

In hospitalized adults with T2DM and HbA1c ≤ 7.0%, a higher TG/HDL-C ratio was associated with prevalent DPN after covariate adjustment, and DPN prevalence increased across ratio quartiles. The cross-sectional design does not establish causality or validate a clinical threshold. Prospective multicenter studies are needed to determine whether the ratio adds useful information to established DPN risk factors.

Abbreviations

BMI, body mass index; CI, confidence interval; DPN, diabetic peripheral neuropathy; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; OR, odds ratio; T2DM, type 2 diabetes mellitus; TC, total cholesterol; TG, triglycerides; UACR, urinary albumin-to-creatinine ratio.

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the Medical Ethics Committee of Tianjin First Central Hospital (approval no. 2026-236) and was conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived by the committee because of the retrospective design.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are not publicly available because they contain potentially identifiable clinical information, but de-identified data may be available from the corresponding author on reasonable request and subject to institutional and ethics approval.

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

WJ conceived and designed the study, collected and analyzed the data, interpreted the findings, and drafted the manuscript. JL contributed to the interpretation of the findings and critically revised the manuscript for important intellectual content. Both authors read and approved the final manuscript.

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