


Exploring the Incidence and Risk Factors of Diabetic Nephropathy in Type 1 Diabetes: Insights from a Retrospective Cohort Study in Northwest China

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Purpose: The study aimed to investigate the incidence of diabetic nephropathy (DN) and their relationship with certain risk factors in patients with type 1 diabetes (T1D) across hospitals in Gansu Province, China.

Methods: There were 434 T1D patients recruited from Gansu Province, China, in the present retrospective cohort study between January 2016 and December 2024. Patients were divided into two groups: (i) patients with T1D but without DN and (ii) type 1 diabetic nephropathy (T1DN). Eligibility for T1DN patients included a T1D diagnosis coupled with urine albumin to creatinine ratio ≥ 30 mg/g. Lifetable method helped determine the cumulative T1DN incidence, and Cox regression helped analyze the associated risk factors. The correlation between predictors (eg, age, serum creatinine (Scr)), and T1DN was assessed with restricted cubic spline curves depending on Cox proportional hazards regression models.

Results: The five-year cumulative incidence of T1DN was 29.89%. T1DN risk factors included diabetic ketosis/ketoacidosis (hazard ratio (HR): 1.623, 95% confidence interval (CI): 1.099–2.454, $P = 0.015$) and high Scr levels (HR: 1.003, 95% CI: 1.001–1.006, $P = 0.010$). However, age (HR: 0.534, 95% CI: 0.306–0.710, $P < 0.001$) and high-density lipoprotein cholesterol (HDL-C) (HR: 0.528, 95% CI: 0.261–0.851, $P = 0.013$) showed a negative association. Significant relationships were not observed with other variables studied, including hypertension, fasting plasma glucose, and postprandial glucose. The dose-response relationship suggested that age, HDL-C, and Scr levels were non-linearly associated with five-year cumulative DN incidences in patients with T1D.

Conclusion: Younger age and lower HDL-C levels were identified as risk factors for DN in patients with T1D. Additionally, diabetic ketosis/ketoacidosis and elevated Scr levels were associated with increased DN risk. Early diagnosis and treatment of dyslipidemia are warranted in patients with T1D. Furthermore, close monitoring of patients with diabetic ketosis/ketoacidosis or high Scr levels is crucial for DN management in these patients.

Keywords: cumulative incidence, risk factors, type 1 diabetes, type 1 diabetes nephropathy

Introduction

The autoimmune destruction of pancreatic β cells causes Type 1 diabetes (T1D), a chronic metabolic disease primarily diagnosed in children and adolescents.¹ The International Diabetes Federation (IDF) predicted that the diabetic

population will reach 537 million in 2030 and increase to 693 million by 2045.² However, in 2022, there were roughly 8.75 million diabetic patients, including 1.52 million below 20 years.³

Diabetic nephropathy (DN) is a common microvascular T1D complication and a leading cause of end-stage renal disease (ESRD).^{4,5} Moreover, kidney failure is 10 times more common in patients with diabetes.⁶ The prevalence of DN is expected to rise steadily over the next two decades because of the global diabetes pandemic. By then, the prevalence of T1DN is projected to reach 50% and may exceed 70% in certain populations, resulting in a considerable economic burden and increased mental stress.⁷ In patients with type 2 diabetes, the estimated incidence of DN is approximately 29.1%, based on a systematic review and meta-analysis of 20 cohorts.⁸ The incidence of DN and ESRD in patients with T1D varies by region. For example, in Taiwan Province, China, the cumulative incidence of DN exceeded 30% between 1999 and 2012.⁹ In contrast, in the United Kingdom, the crude incidence of DN is 0.5 per 100 person-years.¹⁰ Norway reports a cumulative ESRD incidence of 0.7% at 20 years, 2.9% at 30 years, and 5.3% at 40 years of diabetes duration.¹¹ Finland shows a cumulative risk of 2.2% at 20 years and 7.0% at 30 years after a diabetes diagnosis.¹² However, national and regional data on the incidence of T1DN in China are lacking.

Microalbuminuria, a hallmark during the early DN stage, is a crucial risk factor for albuminuria development in T1D patients.¹³ According to Chinese guidelines for the diagnosis and treatment of T1D (2022 edition), the estimated glomerular filtration rate (eGFR), urine albumin to creatinine ratio (UACR), and urinary albumin excretion rate are considered T1D diagnostic methods.¹⁴ Despite being the gold standard for diagnosing and prognostically evaluating DN patients, renal biopsy is only performed when other renal lesions are suspected.¹⁵ Simultaneously, diabetic patients with DN show a significantly elevated risk of chronic kidney disease, ESRD, cardiovascular disease (CVD), and mortality.^{16–18}

Perkins et al¹⁹ revealed that elevated mean glycemic exposure was the most vital DN determinant among the modifiable risk factors related to macroalbuminuria and reduced eGFR. A recent study by Mohammed et al²⁰ indicated that the glycemic control degree, T1D duration, and dyslipidemia were associated with enhanced microalbuminuria and reduced eGFR. To prevent or delay the occurrence and development of T1DN, in-depth relationship knowledge between T1DN development and relevant risk factors is of utmost importance in treating the disease. Therefore, the current study aimed to identify the risk factors and estimate a 5-year cumulative incidence, creating a dose-response relationship with predictors among T1DN patients.

Research Design and Methods

Study Participants

A hospital-based retrospective cohort study was conducted at three grade 3A hospitals in the Gansu Province, northwest of China. An electronic medical record system helped collect the data from patients diagnosed with T1D in the inpatient department between January 2016 and December 2024. Inclusion criteria: T1D patients of all ages with or without associated diabetes complications. Exclusion criteria: (1) those with latent autoimmune diabetes in adults, pregnancy, maturity-onset diabetes of the young, urinary tract infections, serious surgical history within the last half a year, and kidney damage due to non-diabetes; (2) an incomplete set of critical data (UACR). Since the study was retrospective, none of the patients were involved in its design, recruitment, or conduct. The Medical Ethics Committee of Gansu Provincial Hospital (No: 2022–473) approved this study, which was conducted in compliance with the tenets of the Declaration of Helsinki. Meanwhile, to ensure patient privacy, all records and information were de-identified and anonymized before analysis.

Collection of Clinical Data

The following data were collected by experienced physicians, including gender, age, the duration of T1D (time from T1D diagnosis to data collection), age at onset, family history, smoking history, drinking history, height, weight, body mass index (BMI) or Percentile-for-Age, systolic blood pressure, diastolic blood pressure. About laboratory examinations, after fasting for 8 to 10 h, a 3 mL venous blood sample was collected the following morning. Various biochemical parameters were measured using the Abbott ARCHITECT c16000 automated analyzer, including fasting plasma glucose (FPG), postprandial plasma glucose

(PPG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), alanine aminotransferase (ALT), aspartate aminotransferase, total bilirubin (TBIL), direct bilirubin (DBIL), total protein (TP), albumin (ALB), serum uric acid, and serum creatinine (Scr). The UACR was analyzed using the Abbott Ci16200 system. Glycated hemoglobin A1c (HbA_{1c}) was measured using the HLC-723G11 high-performance liquid chromatography system (Tosoh Corporation). Fasting C-peptide (FCP) and postprandial C-peptide (PCP) levels were quantified using the IMMULITE 2000 system (Abbott Laboratories), based on the chemiluminescence method. For adult patients, BMI was calculated based on measured height and weight. Our study includes 23 variables, with no evidence of collinearity among them ([Supplementary Table 1](#)).

Study Group and Design

The study population consisted of two groups: (i) patients with T1D but without DN (non-T1DN group) and (ii) patients with T1DN. Eligibility criteria for the T1DN group involved a T1D diagnosis along with a UACR ≥ 30 mg/g.

T1D was defined as the initial event, whereas T1DN was the terminal event. The time from T1D to T1DN was considered the survival time. The study endpoint time was defined within 5 years after T1D diagnosis.

Sample Size and Power Calculation

The incidence of DN in patients with T1D varies across regions. Hence, this study was based on an initial sample-size estimation using age as the exposure factor, dichotomized at 18 years. The primary outcome of interest was DN development. The sample size was calculated using the formula: $n = \frac{(Z_{\alpha}\sqrt{2pq} + Z_{\beta}\sqrt{p_0q_0 + p_1q_1})^2}{(p_1 - p_0)^2}$, where $\alpha = 0.05$, $Z_{\alpha} = 1.96$, $\beta = 0.20$, $Z_{\beta} = 0.84$, $\text{power} = 1 - \beta$, $p_0 = 0.20$, $p_1 = 0.37$, $p = \frac{p_1 + p_0}{2}$, $q = 1 - p$, $q_1 = 1 - p_1$, and $q_0 = 1 - p_0$. This calculation yielded a final sample size of 110 individuals, which was considered adequate. Detailed calculations are provided in [Supplementary Table 2](#).

Statistical Analysis

Descriptive data were summarized with the mean \pm SD for normally distributed continuous variables. The interquartile range (IQR) for nonnormally distributed values was represented as the median and proportion for categorical variables. The clinical characteristics were compared between T1DN and non-T1DN patients with the *t*-test or Mann–Whitney *U*-test for continuous variables and χ^2 test for categorical variables. The cumulative incidence T1DN probability in five years was estimated with the lifetable method. To identify T1DN predictors, Log rank tests and univariate and multivariate Cox proportional hazards models were conducted.

To measure the hazard ratio (HR) for each predictor, Cox proportional hazard regression models were utilized. The results are depicted as the HR with 95% CI. Multivariable models were adjusted for age, nutritional condition, HbA_{1c}, FCP, HDL-C, DBIL, TBIL, Scr, and diabetic ketosis/ketoacidosis. Schoenfeld residuals helped assess the proportional-hazards assumption.

The non-linear association between predictor and outcome was denoted as a spline cubic polynomial. In this study, four knots helped analyze the association between predictor and outcome and placed on the 20th, 40th, 60th, and 80th percentile of the predictor value range. Due to the large dispersion of Scr levels among the T1D patients in the study, the Scr of percentile P10–P90 (37.5, 80.5) helped establish the restricted cubic spline (RCS). Statistical analyses were performed using Stata version 12 statistical software (Computer Resource Center, USA).

Results

Characteristics of the Study Population

Of the 434 participants recruited in this study, 51.6% were males. The age ranged from 2 to 70 years, with a median age of 25. Of these, 326 individuals were in the non-T1DN group, and 108 were in the T1DN group, with a following period of five years ([Table 1](#)).

Table 1 The Characteristics of 434 Individuals Included in the Study

Variates	Total Participants (434)	T1DN Group (108)	Non-T1DN Group (326)	P
Gender (male, %)	224 (51.6)	51 (47.2)	173 (53.1)	0.292
Age (years)	25 (17, 36)	20 (13, 28)	28 (18, 39)	< 0.001***
BMI (kg/m ²)	19.09 (17.15, 20.77)	18.05 (15.80, 19.92)	19.08 (17.58, 21.09)	0.001***
SBP (mmHg)	110.0 (101.0, 122.0)	110.0 (100.0, 123.5)	110.0 (101.0, 122.0)	0.588
DBP (mmHg)	73.0 (65.0, 80.0)	70.0 (65.00, 80.0)	73.0 (65.0, 80.0)	0.336
FPG (ng/mL)	0.21 (0.02, 0.46)	0.28 (0.07, 0.58)	0.20 (0.02, 0.43)	0.027*
PCP (ng/mL)	0.58 (0.06, 0.76)	0.61 (0.12, 0.91)	0.57 (0.04, 0.72)	0.531
FPG (mmol/L)	11.89 (7.86, 15.28)	12.27 (8.89, 15.90)	11.80 (7.80, 15.06)	0.355
PPG (mmol/L)	14.80 (9.90, 19.16)	15.15 (9.86, 19.60)	14.11 (10.00, 18.66)	0.237
HbA _{1c} (%)	8.98 (7.86, 13.20)	11.65 (9.20, 14.00)	8.90 (10.80, 12.90)	0.075
TG (mmol/L)	1.13 (0.80, 1.68)	1.21 (0.86, 1.78)	1.08 (0.78, 1.64)	0.526
TC (mmol/L)	4.13 (3.48, 4.90)	4.04 (3.46, 4.81)	4.16 (3.48, 4.91)	0.127
LDL-C (mmol/L)	2.43 (1.83, 3.01)	2.51 (1.97, 3.19)	2.37 (1.81, 2.97)	0.193
HDL-C (mmol/L)	1.27 (1.04, 1.49)	1.21 (0.99, 1.39)	1.29 (1.05, 1.53)	0.009***
ALT (U/L)	18.00 (12.00, 31.00)	18.50 (13.00, 28.06)	18.00 (12.00, 31.00)	0.729
AST (U/L)	20.00 (15.00, 26.00)	20.00 (15.00, 26.91)	20.00 (15.00, 26.00)	0.488
TBIL (μmol/L)	13.70 (9.87, 18.80)	12.45 (8.55, 17.40)	14.20 (10.20, 19.40)	0.023*
TP (g/L)	67.75 (62.00, 73.25)	68.00 (62.20, 72.55)	67.28 (62.00, 73.60)	0.760
ALB (g/L)	41.75 (37.80, 45.43)	42.60 (37.85, 45.60)	41.35 (37.80, 45.40)	0.395
DBIL (μmol/L)	4.10 (2.80, 5.60)	3.25 (1.90, 4.75)	4.35 (2.20, 6.00)	<0.001***
SUA (μmol/L)	263.5 (203.8, 344.0)	281.0 (188.0, 365.5)	261.5 (206.0, 337.0)	0.859
Scr (μmol/L)	52.3 (41.3, 63.3)	50.3 (37.2, 60.3)	53.0 (42.0, 63.4)	0.144
Diabetic ketosis/ketoacidosis (n, %)	182 (41.9)	57 (52.8)	125 (38.3)	0.008**

Notes: * $P < 0.05$, ** $P < 0.01$, and *** $P < 0.001$.

Abbreviations: ALB, serum albumin; ALT, glutamic pyruvic transaminase; AST, glutamic oxaloacetic transaminase; BMI, body mass index; DBIL, direct bilirubin; DBP, diastolic blood pressure; FCP, fasting C peptide; FPG, fasting plasma glucose; HbA_{1c}, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PCP, 2-h C peptide; PPG, postprandial glucose; SBP, systolic blood pressure; Scr, serum creatinine; SUA, Serum uric acid; TBIL, total bilirubin; TC, total cholesterol; TG, triglycerides; TP, total protein; T1DN, type 1 diabetes nephropathy.

Cumulative Incidence Probability of T1DN

The data showed that Lifetable helped estimate the five-year cumulative incidence of T1DN to be 29.89% (Table 2). Patients were divided into two subgroups (<18y and ≥18y) based on age. The incidence in the <18y subgroup (49.57%) was significantly larger than the ≥18y subgroup (24.24%) ($P < 0.001$) (Table 2 and Figure 1A). In this study, 41.9% of patients suffered from diabetic ketosis/ketoacidosis (Table 1). The results indicated that the five-year cumulative T1DN incidence was 42.75% in diabetic ketosis/ketoacidosis patients compared to 22.90% in non-diabetic ketosis/ketoacidosis patients ($P < 0.001$) (Table 2 and Figure 1B).

Table 2 Cumulative Incidence of Type 1 Diabetic Nephropathy

Times (Year)	Cumulative Incidence (%)				
	Overall	Age < 18	Age ≥18	Diabetic Ketosis/Ketoacidosis	Without Diabetic Ketosis/Ketoacidosis
1	16.26	28.57	11.43	21.43	12.30
2	19.62	33.55	14.63	25.31	15.66
3	22.44	40.94	16.43	29.70	17.76
4	24.32	45.94	17.81	32.13	19.42
5	29.89	49.57	24.24	42.75	22.90

Notes: The 5-year cumulative incidence of type 1 diabetic nephropathy is expressed as percentages (%). Incidence is reported for the overall population and stratified by the age group (<18 years and ≥18 years) and by the presence of diabetic ketosis/ketoacidosis.

Predictors Associated with T1DN

All the variables satisfied the proportional hazards assumption ($P = 0.825$). Depending on the univariate Cox regression analysis ([Supplementary Table 3](#)), a multivariate Cox proportional hazards regression model was prepared to assess the relationship between T1DN and predictors ([Table 3](#)). The results indicated that age, diabetic ketosis, Scr, and HDL-C level were independent predictors for T1DN patients. Age (HR: 0.466, 95% CI: 0.306–0.710, $P < 0.001$) and HDL-C level (HR: 0.472, 95% CI: 0.261, 0.851, $P = 0.013$) were negative factors. In contrast, diabetic ketosis (HR: 1.623, 95% CI: 1.099–2.454, $P = 0.015$) and Scr levels (HR: 1.003, 95% CI: 1.001–1.006, $P = 0.010$) were factors positively associated with T1DN.

The Dose-Response Relationship Between Predictors and Five-year Cumulative Incidence Among T1DN Patients

Non-linear restricted cubic spline models helped estimate the dose-response relationship between predictors and five-year cumulative incidence among T1DN patients. The RCS curve of age depicted a declined shape. The increased relative risk (RR) trends were shown in patients younger than 18 years, and a declining trend was observed in patients older than 18 by setting 18 years as a reference point ([Figure 2A](#), [Supplementary Table 4](#)). The RCS curve of Scr also depicted a declined shape. The curve's nadir was 56.7 $\mu\text{mol/L}$, without significant association with RR of T1DN in concentrations < 56.7 $\mu\text{mol/L}$. A positive association was observed in concentrations > 56.7 $\mu\text{mol/L}$ ([Figure 2B](#), [Supplementary](#)

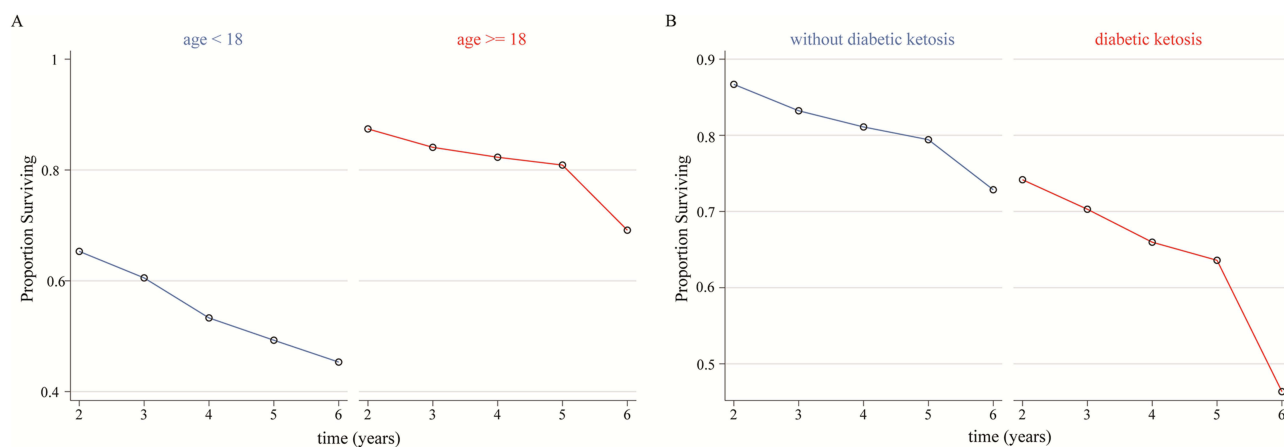


Figure 1 Cumulative incidence of type 1 diabetic nephropathy estimated in different groups using the life-table method. (A) Age <18 years (blue line) and age ≥18 years (red line). (B) Patients without (blue line) and with (red line) diabetic ketosis.

Table 3 Cox Proportional Hazards Regression Model to Establish the Association Between Type 1 Diabetic Nephropathy and Predictors

Variates	HR (95% CI)	P-value
Age	0.466 (0.306, 0.710)	<0.001***
Diabetic ketosis/ketoacidosis	1.623 (1.099, 2.454)	0.015*
FCP	1.223 (0.783, 1.910)	0.377
HbA _{1c}	1.031 (0.962, 0.105)	0.390
HDL-C	0.472 (0.261, 0.851)	0.013*
TBIL	1.003 (0.967, 1.041)	0.857
DBIL	0.912 (0.818, 1.017)	0.098
Scr	1.003 (1.001, 1.006)	0.010**

Notes: * $P < 0.05$, ** $P < 0.01$, and *** $P < 0.001$.

Abbreviations: DBIL, direct bilirubin; FCP, fasting C peptide; HbA_{1c}, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; Scr, serum creatinine; TBIL, total bilirubin; HR, hazard ratio; CI, confidence interval.

Table 5). The RCS curve of HDL-C indicated a negative association with the RR of T1DN. The curve's nadir was 2.94 nmol/L (Figure 2C, Supplementary Table 6).

Discussion

The study of 434 T1D patients from three grade 3A hospitals in Gansu Province, northwest of China, observed cumulative incidence in T1D patients with nephropathy, which increased annually. Age, diabetic ketosis/ketoacidosis, Scr, and HDL-C level could be potential and independent T1DN factors. Furthermore, the findings demonstrated an elevated risk of T1DN occurrence was associated with younger individuals, diabetic ketosis/ketoacidosis, and a low HDL-C level. Intriguingly, Scr level $> 56.7 \mu\text{mol/L}$ could be a potential predictive factor for T1DN. These novel findings can help predict the occurrence of DN in T1D patients in clinical practice.

Possible Explanations for Our Findings

The association between younger T1D patients and an increased T1DN risk could be explained. Renal function with diabetes duration of early age-onset in T1D patients was significantly reduced compared to those with a later onset.¹⁶ Although this study used the current age and not the age of onset, young patients are more susceptible to T1DN. d'Annunzio et al¹⁷ reported that younger age at T1D diagnosis is related to a greater DN risk. Meanwhile, early-

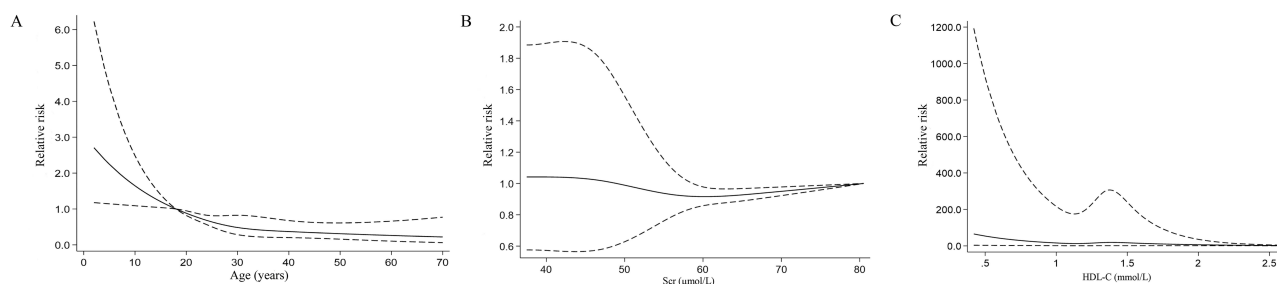


Figure 2 Restricted cubic spline (RCS) analysis of the association between predictors and the risk of type 1 diabetic nephropathy. (A) Association between age and the risk of diabetic nephropathy. (B) The relationship with serum creatinine (Scr), and (C) the association with high-density lipoprotein cholesterol (HDL-C). Four knots are placed at the 20th, 40th, 60th, and 80th percentiles of the predictor value range. Solid lines represent the fitted RCS curves, whereas dashed lines indicate the 95% confidence intervals. X-axes represent the continuous predictor variables, and Y-axes represent the relative risk of diabetic nephropathy.

onset diabetes confers the highest lifetime risk of ESRD, albeit with slower ESRD progression.²¹ A national study in Israel suggested that T1D is associated with a younger age of ESRD onset.²² Additionally, puberty—characterized by rapid growth, hormonal changes (particularly in growth hormone and sex hormones), and deteriorating glycemic control—may accelerate chronic diabetes complications.^{23,24} In younger patients with T1D, C-peptide levels decline more rapidly, suggesting the loss of residual islets β cell function.^{25,26} This phenomenon may result in earlier T1DN onset.

Currently, Scr is an indispensable indicator to estimate GFR. Niu et al revealed that the DN stage is closely related to the Scr level.²⁷ Mendelian randomization analysis did not demonstrate a risk relationship between the Scr level and DN.²⁸ Furthermore, Colombo et al advocated that serum biomarkers (KIM-1 and TNFR1 or CD27) easily measured with Scr may outperform UACR for predicting renal disease progression in T1D, necessitating urine testing.²⁹ Due to the small sample size, this study did not explore DN in stages. However, prospective studies involving a larger population of T1D patients can confirm the study findings.

In recent years, growing studies have targeted the relationship between HDL-C levels and microvascular complications of T1D patients.^{30,31} Even though diabetes patients have achieved the recommended blood pressure and blood glucose objectives, a low HDL-C level could be an independent risk factor for DN development and progression.^{32,33} In this study, high levels of HDL-C could protect T1D patients from DN development.

Albuminuria is one of the earlier markers of DN.¹³ A retrospective study comprising 2345 children with T1DM revealed that a significantly elevated risk of microalbuminuria development and acute kidney injury (AKI) occurrence were closely related during diabetic ketoacidosis. Moreover, AKI contributed to T1DN development during the diabetic ketoacidosis.³⁴ In their study, the AKI stage was determined by the SCr level. In addition, eGFR is determined using Scr and helps diagnose the DN stage in diabetes patients. Therefore, AKI and DN cannot be distinguished by the Scr level alone, particularly in retrospective data. Diabetic ketosis/ketoacidosis contributes to DN development, consistent with our findings. However, whether diabetic ketosis/ketoacidosis increases DN risk by leading to AKI or causes kidney injury via a separate mechanism with similar endpoints needs questioning. This should be further confirmed through animal models. Berot et al indicated that the number of T1D diagnoses enhanced more than three-fold between 1997 and 2019 at the Reims University Hospital. The clinical features at diagnosis deteriorated during this period for patients under 15 with increased diabetic ketosis/ketoacidosis.³⁵ Previous studies have shown a significant increase in diabetic ketoacidosis and severe ketoacidosis while diagnosing diabetes in children and adolescents during the COVID-19 pandemic.^{36,37} Therefore, T1D patients diagnosed during COVID-19 or those with ketosis or ketoacidosis should be monitored promptly for renal function changes.

Previous Study

Recently, most studies investigating the risk factors for T1DN provided different results. High blood pressure was a risk factor for DN in children and adolescents with T1D in Sudan.³⁸ Still, no relationship was found between blood pressure and DN, as blood pressure data was only collected once in this study. Similarly, resistant hypertension was associated with an elevated risk of DN progression in the Finnish.³⁹ Furthermore, an increased HbA_{1c} level as a chronic hyperglycemia marker could be the most established risk factor for nephropathy.^{40–42} In this study, HbA_{1c} levels were higher in T1DN patients than in T1D patients, but the difference was insignificant (Table 1). In a study by Lind et al involving 11009 T1D patients, HbA_{1c} levels of 7.0–7.4% (compared with 6.5–6.9%) were linked with an increased microalbuminuria risk.⁴³ No previous studies have focused on Scr concentration associated with T1DN risk. One study suggested that serum biomarkers and Scr could outperform UACR for predicting future eGFR.²⁹ Our study found that the Scr level (56.7 μ mol/L) was a node to predict T1DN, which larger samples of prospective clinical studies can confirm.

Clinical Importance

This study provides critical insights into the risk factors associated with the development of T1DN in patients with T1D. These findings necessitate early screening and monitoring to identify at-risk individuals and prevent the progression to kidney complications. Specifically, patients under 18 years of age and patients with a history of diabetic ketoacidosis/ketosis had the highest 5-year cumulative incidence of DN. These findings necessitate regular renal function assessment in younger patients with T1D, facilitating early intervention and preventive measures. In addition to age and metabolic

decompensation, dyslipidemia was identified as a major contributor to the development of DN. Low HDL-C levels were associated with an increased risk of kidney complications, necessitating the management of lipid profiles in patients with T1D. Clinicians should prioritize strategies to improve lipid control, particularly by raising HDL-C levels, to mitigate the risk of microvascular complications, including DN. Furthermore, Scr levels, particularly values exceeding 56.7 $\mu\text{mol/L}$, significantly predicted DN in our cohort. Regular Scr monitoring, particularly in high-risk patients, is essential to facilitate timely intervention and prevent further renal damage. Clinicians should closely monitor renal function in patients with T1D, particularly those with a history of diabetic ketosis/ketosis, lipid metabolism disorders, or elevated Scr levels, to implement targeted interventions aimed at preserving kidney health.

Limitations and Future Direction

The study limitations include the small number of T1D patients and retrospective cohort study design, the lack of more detailed information on insulin dosage, GAD antibody, family history, etc. The disease duration could only be determined in years. Moreover, information on quality of life was unavailable. Another limitation is that UACR levels were only obtained once. Therefore, other factors influencing UACR levels cannot be excluded. Finally, data were drawn from T1D patients enrolled in three hospitals. Consequently, they may not represent all the T1D patients across China.

To better explore the risk factors of T1DN in the future, conducting multi-regional and multi-hospital prospective studies in China and following up for a long time to observe T1D development and the progress of related complications would be conducive. Furthermore, at the molecular level, for instance, the human leukocyte antigen gene—the genetic risk of type 1 diabetes, or metabolites, the relationship between molecular typing and T1DN risk was analyzed to make a more accurate prediction, diagnosis, and personalized treatment through molecular markers using molecular typing of specific genes. This can help evaluate T1DN factors and identify more targets or better prevention, diagnosis, or treatment plans.

Conclusion

Therefore, age, diabetic ketosis/ketoacidosis, HDL-C concentration, and Scr levels were considered independent factors in this retrospective cohort study. Accordingly, our findings suggest that diabetes care should keep a watchful eye on long-term metabolic control and additional latent factor reduction.

Data Sharing Statement

Additional data are available from the corresponding author on reasonable request.

Ethics Statement

The protocol was reviewed and approved by the Ethics Committee of Gansu Provincial Hospital. The study was conducted in accordance with local legislation and institutional requirements. Given the retrospective nature of this study, the Ethics Committee waived the requirement for written informed consent.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that there are no conflicts of interest related to this work.

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