

# Risk Factors of the Progression of Renal Function Deterioration Among Patients with Diabetic Nephropathy

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**Abstract:** *Objective:* To explore the risk factors for the progression of renal function deterioration in patients with diabetic nephropathy (DN). *Methods:* The clinical data and biochemical indexes of 100 diabetic patients admitted to our hospital from October 2021 to October 2022 were retrospectively analyzed. The patients were divided into a DN group, which consisted of 55 cases, and a nondiabetic nephropathy group (NDN), which consisted of 45 cases. The urinary microalbumin to creatinine ratio, the clinical data (gender, age, duration of the disease, and BMI), and the biochemical indexes (triglycerides [TG], low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C], total cholesterol [TC], glycated hemoglobin A1c [HbA1c], systolic blood pressure [SBP], diastolic blood pressure [DBP]) of the two groups were compared. Subsequently, the risk factors related to the progression of renal function deterioration in DN were analyzed through multifactorial logistic regression analysis. *Results:* No statistically significant difference was observed in the comparison of gender, age, BMI, LDL-C, and DBP between the two groups ( $P > 0.05$ ). The DN group demonstrated a longer disease duration and higher SBP, TC, HDL-C, HbA1c, and TG compared to the NDN group ( $P < 0.05$ ). Through multifactorial logistic regression analysis, it was found that the duration of the disease, the TC, the HDL-C, the HbA1c, the TG, and the SBP were independent risk factors of the deterioration of renal function in DN patients. *Conclusion:* Other than conventional indicators, TC, HDL-C, HbA1c, TG, and SBP are also crucial indicators in determining the progression of renal function deterioration in DN patients.

**Keywords:** Diabetic nephropathy; Renal function deterioration; Risk factors

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## 1. Introduction

Diabetic nephropathy (DN) is one of the most common chronic complications of diabetes mellitus, and its incidence has been increasing gradually as diabetes mellitus becomes more prevalent<sup>[1]</sup>. This condition greatly affects the quality of life of patients. Deterioration of renal function is one of the most important concerns for patients with DN. The deterioration of renal function may not only lead to uremia, but also require long-term

dialysis treatment, or even renal transplantation, which brings tremendous economic and social pressure to patients and their families [2]. Therefore, this paper aims to provide a theoretical basis for the prevention and treatment of DN by thoroughly investigating the risk factors for the progression of renal function deterioration in patients with DN [3].

## 2. General information and methods

### 2.1. General information

The clinical data and biochemical indexes of 100 diabetic patients admitted to our hospital from October 2021 to October 2022 were retrospectively analyzed. The patients were divided into a DN group, which consisted of 55 cases, and a nondiabetic nephropathy group (NDN), which consisted of 45 cases. The DN group consisted of 30 males and 25 females, while the NDN consisted of 28 males and 17 females.

Inclusion criteria: (1) Diagnosed with diabetes mellitus blood according to the World Health Organization's diagnostic criteria; fasting glucose of more than 7 mmol/L; (2) diagnosed with DN patients – urinary albumin excretion rate (UAER) >200 mg/24 h, persistent presence of proteinuria, urinary protein > 0.5 g/24h [4].

Exclusion criteria: (1) Acute complications of diabetes mellitus, (2) malignant tumors, (3) complicated with other primary or secondary renal diseases, (4) being treated with hormones, immunosuppressants, or other treatments that affect glucose metabolism and renal function, (5) presence of serious liver disease, heart disease, lung disease, or other chronic diseases.

### 2.2. Methods

The general information of the patients was collected including gender, age, body mass index (BMI), and the duration of disease. Besides, their laboratory test results were also gathered including triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), glycated hemoglobin A1c (HbA1c), systolic blood pressure (SBP), diastolic blood pressure (DBP), which are illustrated in **Table 1**.

**Table 1.** General information and preliminary laboratory test results of the patients

Variability	Group NDN (n = 45)	Group DN (n = 55)	$t/\chi^2$ -value	P-value
Gender (male/female)	28/17	30/25	3.596	> 0.05
Age (years)	65.2 ± 8.21	66.2 ± 9.15	0.569	> 0.05
Duration of the illness (years)	6.5 ± 2.2	8.2 ± 2.5	3.569	< 0.01
BMI	23.25 ± 2.56	22.58 ± 2.35	1.362	> 0.05
TC (mmol/L)	2.35 ± 0.89	3.56 ± 1.25	5.458	< 0.01
LDL-C (mmol/L)	3.06 ± 1.21	3.36 ± 1.21	1.234	> 0.05
HDL-C (mmol/L)	1.36 ± 0.34	1.21 ± 0.22	2.662	< 0.01
HbA1c (mmol/L)	7.25 ± 1.36	7.85 ± 1.47	2.099	< 0.05
TG (mmol/L)	1.82 ± 1.53	2.54 ± 1.71	2.195	< 0.05
SBP (mm/Hg)	135.26 ± 14.25	150.28 ± 22.81	3.844	< 0.05
DBP (mm/Hg)	82.58 ± 10.28	84.25 ± 12.15	0.732	> 0.05

### 2.3. Statistical analysis

SPSS 20.0 was used to analyze the data. The measurement data were expressed as mean  $\pm$  standard deviation; independent samples *t*-test was used for those conforming to normal distribution, and the rank sum test was used to compare data that were not normally distributed. The count data were expressed as percentages and compared using a  $\chi^2$ -test. These indexes were then subjected to multifactorial logistic regression analysis.  $P < 0.05$  indicates a statistically significant difference.

## 3. Results

### 3.1. Baseline data

There were no significant differences in terms of gender, age, BMI, LDL-C, or DBP between the two groups ( $P > 0.05$ ). The difference in terms of disease duration, SBP, TC, HDL-C, HbA1c, and TG between the two groups was statistically significant ( $P < 0.05$ ); the DN group demonstrated a longer disease duration and higher SBP, TC, HDL-C, HbA1c, and TG compared to the NDN group ( $P < 0.05$ ), as shown in **Table 1**.

### 3.2. Multifactorial logistic regression analysis

A multifactorial logistic regression analysis was performed with the presence of diabetic nephropathy as the dependent variable and various clinical factors as independent variables. The results revealed that the duration of diabetes mellitus, TC, HDL-C, HbA1c, TG, and SBP were identified as independent risk factors contributing to the deterioration of renal function in diabetic nephropathy, as shown in **Table 2**.

**Table 2.** Multifactorial logistic regression analysis of risk factors for renal function impairment in diabetic nephropathy patients

Related factors	$\beta$ -value	OR	95% CI	<i>P</i> -value
Duration of the diabetic disease (years)	0.072	1.075	1.012–1.142	0.022
TC (mmol/L)	0.535	1.712	1.098–2.662	0.019
HDL-C (mmol/L)	0.736	2.086	1.013–4.297	0.048
HbA1c (mmol/L)	0.435	1.542	1.030–2.309	0.035
TG (mmol/L)	0.358	1.433	0.032–1.989	0.017
SBP (mm/Hg)	0.015	1.015	1.004–1.022	0.003

## 4. Discussion

Diabetes mellitus is a lifelong chronic disease, and as the standard of living and life expectancy increases, diabetes mellitus comorbidities are also increasing year by year. Statistics show that millions of people around the world develop diabetes every year, and a large proportion of these diabetic patients develop comorbidities<sup>[5]</sup>.

In clinical practice, diabetes is often accompanied by a series of conditions such as hypertension, hyperglycemia, nephropathy, etc., with DN being one of the most common and dangerous chronic complications in diabetic patients<sup>[6]</sup>. The possibility of developing DN increases with the progression of diabetes. Studies have shown that 30% to 40% of diabetic patients in China will develop DN<sup>[7]</sup>. The deterioration of renal function is an important risk factor in DN, and many studies have been done on the factors influencing the deterioration of renal function in DN. A study showed that eGFR, cystatin-C, ACR, ALB, and HGB influence the deterioration of renal function in DN<sup>[3]</sup>. Another study demonstrated that diabetes disease duration, Hb A1c, and eGFR are

influential factors in the progressivity of renal function<sup>[8]</sup>. FBG, HbA1c, TC, TG, HDL-C, Hcy, Cys-C, and Vit B6 have also been shown to be independent risk factors for the deterioration of renal function in patients with type 2 DN<sup>[9]</sup>. The findings of the studies are generally consistent with this study.

Through a multifactorial analysis of risk factors for deterioration of renal function in patients with DN, we found that diabetes duration, TC, HDL-C, HbA1c, TG, and SBP were independent risk factors for deterioration of renal function in DN. This finding suggests that the deterioration of renal function in patients with DN is related to disease duration, blood glucose, blood lipids, and blood pressure<sup>[10]</sup>.

Hyperglycemia is one of the important factors leading to the deterioration of renal function among diabetic patients and is an important indicator of glycemic control that plays a crucial role in determining the development of DN and the risk of deterioration of renal function. A higher level of HbA1c implies poorer glycemic control<sup>[11]</sup>. HbA1c leads to an increase in reactive oxygen species (ROS) in the body, which causes oxidative stress. Oxidative stress can damage the microvessels of the kidneys, leading to a decline in renal function; in addition, HbA1c can damage the vascular endothelium, leading to vasoconstriction and diastolic dysfunction. Vascular endothelial dysfunction can exacerbate renal ischemia, which further worsens DN and accelerates the deterioration of renal function.

Disease duration also affects the deterioration of renal function of DN patients. As DN develops, the patient's blood glucose will remain high, and long-term high blood glucose will damage the renal microvessels, leading to the decline of renal function. DN patients are often in a state of glomerular hyperfiltration. Along with the advancement of the disease, the excessive filtration of water and protein substances causes the patient to be highly susceptible to kidney injury. In addition, the advancement of the disease also increases the probability of inflammation and renal fibrosis, which further leads to the deterioration of renal function.

As fatty compounds in the blood, the main function of TG and TC is to provide energy and protect cells. However, high levels of TG, and TC may lead to deterioration of renal function in patients with diabetic nephropathy<sup>[12]</sup>. High levels of TG and TC may lead to lipid deposition in the kidneys, which in turn causes changes in kidney structure and function, and lipid deposition in the kidneys may impair kidney filtration, leading to a decline in renal function. In addition, elevated levels of TC increase the probability of inflammation, and inflammation further exacerbates the process of renal fibrosis, which in turn triggers the deterioration of renal function<sup>[13]</sup>.

HDL-C is an important lipid indicator, which is usually considered beneficial for cardiovascular health. However, for DN patients, abnormal levels of HDL-C may lead to deterioration of renal function<sup>[14]</sup>. This is mainly because HDL-C can activate the inflammatory response and promote glomerulosclerosis and deterioration of renal function. It has been shown that low levels of HDL-C are associated with elevated inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6). This may accelerate glomerulosclerosis by mediating cytokines such as monocyte chemoattractant protein-1 (MCP-1) and intercellular adhesion molecule-1 (ICAM-1), which promote the recruitment and infiltration of renal monocytes<sup>[15]</sup>.

SBP is one of the most important indicators for assessing the risk of kidney disease in diabetic patients. Elevated SBP may lead to renal impairment in DN patients. Specifically, long-term elevated SBP may lead to increased intraglomerular pressure in the glomerular capsule, triggering glomerular hypertension, which can lead to glomerular hypertrophy, sclerosis, and decreased renal function. In addition, elevated SBP may also lead to proteinuria, which can lead to glomerular injury and decreased renal function.

## 5. Conclusion

In summary, disease duration, TC, HDL-C, HbA1c, TG, and SBP are independent risk factors for the deterioration of renal function of DN patients. Therefore, in the clinical treatment of diabetic nephropathy patients, it is necessary to strictly control patients' blood glucose, blood pressure, and blood lipids. To achieve that, the patient should be given proper medication and dietary interventions should be carried out focusing on low sugar, low salt, and low-fat consumption, as well as adopting a healthy lifestyle incorporating suitable exercise, alongside regular monitoring of renal function.

## Disclosure statement

The authors declare no conflict of interest.

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