# Association Between Blood Lipid Profile and the Incident CKD in the General Chinese Population: A Retrospective Study

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**Research**

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## Abstract

Background: Prevalence of dyslipidemia in china is rising and the pattern of dyslipidemia in china is different from western countries. Our study aimed to investigate the association between hyperlipidemia and chronic kidney disease in the general population.

Methods: We conducted a retrospective, longitudinal cohort study of a health examination center database in China. Subjects who had at least three visits from 2011 to 2018 with normal baseline eGFR were enrolled. We evaluated the association of the lipid parameters with the incident chronic kidney diseases.

Results: Totally, 8087 participants without kidney damage were identified. After the mean 5.51 years follow-up, 211 participants developed chronic kidney disease. Compared to non-CKD, participants developing CKD had lower baseline HDL-c (1.35±0.36 vs 1.24±0.36 mmol/L, p<0.001) and higher Lg(triglyceride) (0.15±0.27 vs 0.19±0.24, p=0.037). There was no difference of LDL-c (2.72±0.72 vs 2.72±0.71 mmol/L, p= 0.971) and total cholesterol (4.86±0.92 vs 4.80±0.89 mmol/L, p= 0.329) in two groups. Multi-variable logistic analysis showed that lower HDL-c was an independent risk of incident CKD (OR [95%] =1.61[1.02, 2.55], P=0.04) in participants.

Conclusion: A lower HDL-c affects incident CKD in Chinese general population.


## Background:

The incidence of chronic kidney disease (CKD) in the world is increasing year by year. The latest epidemiological studies show that the prevalence of CKD is 10.8%~11.8% in China[1, 2]. Therefore, chronic kidney disease is an important public health problem. Moreover, dyslipidemia can cause cardiovascular disease. Studies have shown that different types of hyperlipidemia are related to CKD's occurrence. However, the prevalence of dyslipidemia in china is rising with low the proportion of awareness, treatment, and control[3]. The pattern of dyslipidemia in the general population in china is different from in western countries. While the main types of dyslipidemia in western countries were high cholesterol and high low-density lipoprotein cholesterol (LDL-c), low high-density lipoprotein cholesterol (HDL-c) and hypertriglyceridemia are two major types of dyslipidemia in Chinese adults[4, 5]. As we all know, serum cholesterol and LDL-c are major risk factors for coronary heart disease and ischemic stroke[6]. There are relatively few studies on the incident CKD among Chinese people with a specific type of dyslipidemia. Therefore, this study adopted a large center with repeated examination, and longitudinal analysis the relationship between dyslipidemia and CKD in the general Chinese population with normal renal function.

## Methods:

### Study design and covariates

The health examination center in Tonglu First People's Hospital is one of the healthcare centers in Tonglu, located in the eastern area of Zhejiang Province. We conducted a retrospective, longitudinal study from January 2011 to November 2018 in this center's clinical database[7]. Participants who were screened and identified by ID number, birthdates, and other identifiers. The participants who were older than 18 years old were included.

Blood samples were collected from the vein in the morning. All blood variables were measured using an autoanalyzer (Roche) at a central laboratory. Urine samples were collected for assessment of urinary protein. We used the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation to calculate eGFR [8]. The sex-specific criteria of serum UA defined HUA > 420 μmol/L in males and > 360 μmol/L in females.

### Statistical analysis

We used descriptive statistics to compare the characteristics of the cohorts stratified by quartiles. Data were checked for normal distribution by the Kolmogorov-Smirnov test. Continuous variables were described as the means (with standard deviations (SDs)) when appropriate, and nonnormally distributed variables described as medians and interquartile ranges (IQRs). Normally distributed continuous variables were compared using ANOVA, and nonnormally distributed variables were evaluated using the Kruskal-Wallis test.

The logistic model was used to assess the association between different groups and the onset of kidney disease. For logistic regression, age (age<65 years old as ref) was divided into two groups by 65-year-old. All analyses were performed using SPSS 20. A two-sided P value <0.05 was considered statistically significant.

## Results

In total, we included 8,087 participants without kidney damage. The mean age of the sample 45.64 ± 15.18 years old (Table 1). The number of males was 4946. Mean eGFR was 101.37 ± 15.23 mL/min/1.73 m2. After the mean 5.51 years follow-up, 211 participants developed chronic kidney disease. Compared to non-CKD, participants developing CKD had lower baseline HDL-c (1.35 ± 0.36 vs 1.24 ± 0.36 mmol/L, p < 0.001) and higher Lg(triglyceride)(LgTG) (0.15 ± 0.27 vs 0.19 ± 0.24 mmol/L, p = 0.037). There was no difference of LDL-c (2.72 ± 0.72 vs. 2.72 ± 0.71 mmol/L,

p = 0.971) and total cholesterol (TC) (4.86 ± 0.92 vs. 4.80 ± 0.89 mmol/L, p = 0.329) in these two groups. We divided the participants into three groups according to LgTG, TC, HDL-c, and LDL-c (Tables 2 & 3). Participants in group3 of TG or TC or LDL-c and group1 of HDL-c were more likely to be older, a higher percentage of male, higher TC, higher HDL-c, higher UA, higher FPG, higher Scr and lower eGFR(p < 0.001). In group3 of TG and group 1 of HDL-c, the participants had a higher percentage of incidence of CKD (p = 0.015 for TG and p < 0.001 for HDL-c).

Table 1
Baseline characteristics of the total participants

| Parameters | Total |
|---|---|
| Age (year-old) | 45.64 ± 15.18 |
| Sex (%) | 61.00 |
| LgTG (mmol/L) | 0.15 ± 0.26 |
| TC (mmol/L) | 4.86 ± 0.92 |
| HDL-c (mmol/L) | 1.35 ± 0.36 |
| LDL-c (mmol/L) | 2.72 ± 0.72 |
| UA (umol/L) | 350.33 ± 94.27 |
| FPG (mmol/L) | 5.01 ± 1.06 |
| Scr (umol/L) | 71.15 ± 14.88 |
| eGFR (mL/min/1.73 m2) | 101.37 ± 15.23 |
| Continuous variables are presented as mean ± standard deviation, categorical variables as %. | |
| FPG: fasting plasma glucose; Total Cholesterol: TC; TG: triglyceride; eGFR: estimated glomerular filtration rate; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol; UA: uric acid; Scr: creatinine | |

Table 2
Baseline characteristics of participants in different groups by HDL-c or LDL-c.

| | HDL-c | | | | LDL-c | | | |
|---|---|---|---|---|---|---|---|---|
| | group1 | group2 | group3 | P value | group1 | group2 | group3 | P value |
| Age (year-old) | 46.55 ± 14.65 | 45.69 ± 15.10 | 44.66 ± 15.73 | P < 0.001 | 43.47 ± 15.8 | 45.50 ± 14.95 | 48.28 ± 14.31 | < 0.001 |
| Sex(%) | 76.40 | 64.20 | 41.90 | P < 0.001 | 53.70 | 61.70 | 68.30 | < 0.001 |
| LgTG (mmol/L) | 0.31 ± 0.27 | 0.14 ± 0.22 | 0.01 ± 0.21 | P < 0.001 | 0.12 ± 0.33 | 0.14 ± 0.24 | 0.19 ± 0.2 | < 0.001 |
| TC (mmol/L) | 4.73 ± 0.99 | 4.82 ± 0.87 | 5.04 ± 0.88 | P < 0.001 | 4.15 ± 0.76 | 4.83 ± 0.57 | 5.71 ± 0.72 | < 0.001 |
| HDL-c (mmol/L) | 0.99 ± 0.11 | 1.30 ± 0.09 | 1.76 ± 0.25 | P < 0.001 | 1.34 ± 0.4 | 1.34 ± 0.36 | 1.36 ± 0.3 | 0.031 |
| LDL-c (mmol/L) | 2.63 ± 0.72 | 2.81 ± 0.69 | 2.72 ± 0.74 | P < 0.001 | 1.96 ± 0.33 | 2.75 ± 0.2 | 3.55 ± 0.5 | < 0.001 |
| UA (umol/L) | 377.91 ± 92.33 | 354.46 ± 92.15 | 318.09 ± 88.49 | P < 0.001 | 334.41 ± 96.24 | 350.98 ± 92.27 | 367.62 ± 91.34 | < 0.001 |
| FPG (mmol/L) | 5.12 ± 1.22 | 4.99 ± 1.04 | 4.92 ± 0.89 | P < 0.001 | 4.95 ± 1.05 | 4.95 ± 0.90 | 5.14 ± 1.23 | < 0.001 |
| Scr (umol/L) | 74.90 ± 14.52 | 72.03 ± 14.75 | 66.45 ± 14.13 | P < 0.001 | 68.49 ± 14.76 | 71.89 ± 14.81 | 73.25 ± 14.68 | < 0.001 |
| eGFR (mL/min/1.73 m2) | 99.41 ± 14.79 | 100.98 ± 14.89 | 103.76 ± 15.70 | P < 0.001 | 104.46 ± 15.67 | 100.87 ± 15.01 | 98.47 ± 14.34 | < 0.001 |
| CKD (%) | 3.70 | 2.20 | 1.90 | P < 0.001 | 2.40 | 2.70 | 2.70 | 0.739 |

Continuous variables are presented as mean ± standard deviation, categorical variables as %.

FPG: fasting plasma glucose; Total Cholesterol: TC; TG: triglyceride; eGFR: estimated glomerular filtration rate; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol; UA: uric acid; Scr: creatinine

Table 3
Baseline characteristics of participants in different groups by TC or TG.

| | TC | | | | TG | | | |
|---|---|---|---|---|---|---|---|---|
| | group1 | group2 | group3 | P value | group1 | group2 | group3 | P value |
| Age (year-old) | 42.89 ± 16.31 | 45.9 ± 15.04 | 48.17 ± 13.59 | < 0.001 | 42.53 ± 16.40 | 47.4 ± 15.34 | 47.21 ± 13.04 | < 0.001 |
| Sex (%) | 56.20 | 62.10 | 64.60 | < 0.001 | 43.50 | 63.90 | 76.40 | < 0.001 |
| LgTG (mmol/L) | 0.05 ± 0.23 | 0.14 ± 0.24 | 0.27 ± 0.28 | < 0.001 | -0.11 ± 0.11 | 0.12 ± 0.07 | 0.45 ± 0.19 | < 0.001 |
| TC (mmol/L) | 3.92 ± 0.38 | 4.8 ± 0.20 | 5.87 ± 0.69 | < 0.001 | 4.50 ± 0.79 | 4.85 ± 0.81 | 5.25 ± 1.00 | < 0.001 |
| HDL-c (mmol/L) | 1.27 ± 0.31 | 1.35 ± 0.35 | 1.42 ± 0.39 | < 0.001 | 1.53 ± 0.37 | 1.36 ± 0.29 | 1.15 ± 0.29 | < 0.001 |
| LDL-c (mmol/L) | 2.11 ± 0.42 | 2.72 ± 0.41 | 3.35 ± 0.68 | < 0.001 | 2.51 ± 0.64 | 2.87 ± 0.66 | 2.80 ± 0.80 | < 0.001 |
| UA (umol/L) | 334.08 ± 91.41 | 349.78 ± 91.02 | 367.39 ± 97.35 | < 0.001 | 309.28 ± 83.15 | 349.91 ± 84.74 | 393.86 ± 94.62 | < 0.001 |
| FPG (mmol/L) | 4.89 ± 0.88 | 4.96 ± 0.96 | 5.17 ± 1.28 | < 0.001 | 4.85 ± 0.76 | 4.97 ± 0.94 | 5.21 ± 1.37 | < 0.001 |
| Scr (umol/L) | 69.30 ± 14.88 | 71.72 ± 14.80 | 72.46 ± 14.79 | < 0.001 | 66.38 ± 14.09 | 72.44 ± 14.65 | 74.88 ± 14.63 | < 0.001 |
| eGFR (mL/min/1.73 m2) | 104.52 ± 15.9 | 100.83 ± 14.88 | 98.72 ± 14.29 | < 0.001 | 105.70 ± 15.80 | 99.32 ± 14.92 | 98.84 ± 13.91 | < 0.001 |
| CKD (%) | 2.70 | 2.60 | 2.50 | 0.903 | 1.90 | 3.10 | 2.90 | 0.015 |

Continuous variables are presented as mean ± standard deviation, categorical variables as %.

FPG: fasting plasma glucose; Total Cholesterol: TC; TG: triglyceride; eGFR: estimated glomerular filtration rate; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol; UA: uric acid; Scr: creatinine

Table 4 showed an association between lipid parameters and baseline eGFR by linear regression. High level of TG (p = 0.044) and low level of HDL-c (p = 0.001) were a risk factor for low eGFR independent of the other parameters.

Table 4
The association between lipid and baseline eGFR by linear regression

| | B value | 95%CI | P value |
|---|---|---|---|
| age | -0.68 | [-0.70, -0.66] | < 0.001 |
| LgTG | -1.42 | [-2.81, -0.04] | 0.044 |
| TC | 0.50 | [-0.03, 1.02] | 0.062 |
| HDL-c | 1.45 | [0.59, 2.30] | 0.001 |
| LDL-c | -1.18 | [-1.73, -0.62] | < 0.001 |
| UA | -0.03 | [-0.03, -0.03] | < 0.001 |
| BUN | -1.61 | [-1.78, -1.44] | < 0.001 |
| Alb | -0.15 | [-0.25, -0.05] | 0.003 |
| FPG | 1.10 | [0.89, 1.31] | < 0.001 |

FPG: fasting plasma glucose; Total Cholesterol: TC; TG: triglyceride; eGFR: estimated glomerular filtration rate; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol; UA: uric acid; Scr: creatinine

In the HDL-c group, logistic regression analysis for incident CKD showed that univariable and age for the outcome in group1 were significantly higher than ORs in group 3. We also calculated ORs after adjustment for age (age < 65-year-old as ref), gender (male as ref), baseline eGFR, HUA, and other metabolic parameters (FPG and other lipid parameters), and group1 was still a risk for CKD (Table 5).

Table 5
The relationship between blood lipid levels and CKD by logistic analysis

| | HDL-c | OR[95%CI] | P value | LDL-c | OR[95%CI] | P value | TC | OR[95%CI] | P value | TG | OR[95%CI] | P value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Crude | Group1 | 2.05[1.45, 2.88] | < 0.001 | Group1 | Ref | | Group1 | Ref | | Group1 | Ref | |
| | Group2 | 1.17[0.80, 1.71] | 0.42 | Group2 | 1.13[0.82, 1.58] | 0.453 | Group2 | 0.94[0.68, 1.31] | 0.720 | Group2 | 1.63[1.15, 2.32] | 0.006 |
| | Group3 | Ref | | Group3 | 1.11[0.78, 1.57] | 0.571 | Group3 | 0.93[0.67, 1.30] | 0.680 | Group3 | 1.51[1.06, 2.16] | 0.022 |
| Model1 | Group1 | 1.99[1.38, 2.87] | < 0.001 | Group1 | Ref | | Group1 | Ref | | Group1 | Ref | |
| | Group2 | 1.16[0.78, 1.73] | 0.47 | Group2 | 1.05[0.74, 1.49] | 0.78 | Group2 | 1.03[0.72, 1.46] | 0.893 | Group2 | 1.43[0.99, 2.07] | 0.057 |
| | Group3 | Ref | | Group3 | 0.96[0.66, 1.38] | 0.817 | Group3 | 0.90[0.63, 1.29] | 0.565 | Group3 | 1.73[1.19, 2.51] | 0.004 |
| Modle2 | Group1 | 1.89[1.31, 2.74] | < 0.001 | Group1 | Ref | | Group1 | Ref | | Group1 | Ref | |
| | Group2 | 1.11[0.75, 1.68] | 0.59 | Group2 | 0.93[0.65, 1.32] | 0.685 | Group2 | 1.24[0.86, 1.77] | 0.250 | Group2 | 1.22[0.84, 1.77] | 0.306 |
| | Group3 | Ref | | Group3 | 0.82[0.56, 1.19] | 0.292 | Group3 | 0.97[0.68, 1.40] | 0.886 | Group3 | 1.46[0.99, 2.15] | 0.052 |
| Model3 | Group1 | 1.61[1.02, 2.55] | 0.04 | Group1 | Ref | | Group1 | Ref | | Group1 | Ref | |
| | Group2 | 1.04[0.67, 1.61] | 0.87 | Group2 | 1.05[0.7, 1.55] | 0.826 | Group2 | 0.88[0.57, 1.35] | 0.549 | Group2 | 1.16[0.78, 1.72] | 0.457 |
| | Group3 | Ref | | Group3 | 0.92[0.54, 1.57] | 0.759 | Group3 | 0.98[0.55, 1.75] | 0.940 | Group3 | 1.04[0.66, 1.62] | 0.875 |
| model1: adjusted for age (age < 65-year-old as ref) and gender (male as ref) | | | | | | | | | | | | |
| model2: adjusted for age (age < 65-year-old as ref), gender (male as ref) and baseline eGFR | | | | | | | | | | | | |
| model3: adjusted for age (age < 65-year-old as ref), gender (male as ref), baseline eGFR, HUA and other metabolic parameters (FPG and the other lipid parameters) | | | | | | | | | | | | |

In the TG group, logistic regression analysis for the onset of CKD showed that univariable OR for CKD in group1 and group2 were significantly higher than ORs in groups 1 and 2. After adjusted for age (age < 65-year-old as ref), gender (male as ref), baseline eGFR, HUA, and other metabolic parameters (FPG and other lipid parameters), TG was not a risk factor for CKD. We also did the logistic regression analysis in TC and LDL-c groups, but TC and LDL-c were not risk factors for incident CKD in our study.

## Discussion

In the present study, we examined the involvement of dyslipidemia at baseline with eGFR in the general population. We also found that the involvement of low HDL-c at baseline with the onset of CKD in the same cohort, indicating that lower HDL-c is an independent risk factor for the incident CKD. This finding suggests that low levels of HDL-c might induce CKD.

The incidence of CKD increases year by year, and hyperlipidemia is a risk factor for the occurrence and progression of chronic kidney disease. We found that HDL-c is an independent risk factor for CKD in the Chinese population, while LDL-c, TC, and TG have no such effect. Many studies found an association between dyslipidemia and the development and progression of CKD. However, there are different opinions on the types of hyperlipidemia that cause CKD. Hypertriglyceridemia was independently associated with the development of CKD in the general Japanese population[9]. Increased LDL-C levels are associated with the development of incident CKD and eGFR decline in young to middle-aged working men[10]. Studies have also shown that lower HDL-c levels are associated with a higher risk of CKD, and there is no statistically significant association between LDL-c levels and the risk of CKD[11]. In non-CKD patients, low levels of HDL-C are an essential risk factor for renal insufficiency in healthy people[12]. In diabetic patients, low HDL-C and high triglyceride levels are independent risk factors for diabetic nephropathy[13]. In type 2 diabetes, low-density lipoprotein/high-density lipoprotein ratio and low levels of apoA/HDL related to the occurrence of diabetic nephropathy[14]. An observational study with nearly 2 million male participants found that HDL-C < 30 mg/dL increases the risk of CKD[15]. Also, Mendelian randomization studies have shown that HDL-c may be related to CKD's occurrence [16]. However, we only found a

relation between HDL-c and CKD in the general Chinese population. Different type of dyslipidemia of dyslipidemia might explain part of this phenomenon. Unlike other countries, low HDL-C and high TG are two significant types of dyslipidemia in Chinese adults.

HDL-c is an important one of lipoproteins and an important factor in anti-atherosclerosis. Its key role is to participate in the reverse transport of cholesterol to the liver and anti-thrombosis. Besides, HDL-c can prevent LDL-c from being oxidized by active oxygen and prevent oxidized LDL-c from adversely affecting the endothelium[17]. The role of HDL-c in CKD patients is different from its role in incident CKD. In CKD patients, HDL-c was dysfunctional[18, 19] and has different composition[20, 21]. In CKD patients, HDL reverse cholesterol efflux capacity cannot predict CVD occurrence [22], while in the general population, HDL reverse cholesterol efflux capacity is related to the occurrence of CVD[23]. Accumulating evidence supports the hypothesis that prolonged metabolic imbalance of lipids leads to ectopic fat distribution in the kidney, causing inflammation, endoplasmic reticulum stress, etc. Therefore, for the general population, lipid toxicity might cause renal injury[24]. However, the RCT study of the protective effect of Anacetrapib on cardiovascular events has not benefited[25]. Therefore, the causal relation between HDL-c and chronic kidney disease is still controversial and needs further exploration.

The present study was limited by the following points. The most important limitation of our study is that the participants in this study are from a health examination center leading to a self-selected population and the lack of data on the use of medications of diabetes mellitus, hypertension, and other data. Second, the outcome of the present study was based on incident CKD, and we did not include the UACR end. Third, because we included only participants with an eGFR $\geq$ 60 ml/min per 1.73 m2, we cannot make conclusions about participants with an eGFR < 60 ml/min per 1.73 m2. Besides, this study was an observational design, which makes it impossible to infer causality between the observed associations between dyslipidemia and the development of CKD.

## Conclusions

In conclusion, we found that low HDL-c is associated with CKD development in the general population. This study demonstrated that dyslipidemia might contribute to reduced renal dysfunction.

## Abbreviations

CKD: chronic kidney disease.

FPG: fasting plasma glucose.

Total Cholesterol: TC.

TG: triglyceride.

eGFR: estimated glomerular filtration rate.

HDL-c: high-density lipoprotein cholesterol.

LDL-c: low-density lipoprotein cholesterol.

UA: uric acid.

Scr: creatinine

## Declarations

### Ethics declarations

### Ethics approval and consent to participate

This study was approved by the Institutional Review Board of the Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, and was in accordance with the principles of the Helsinki Declaration II.

### Consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

### Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.


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### Contributions

WWM designed the work. JL and WWM drafted the manuscript or substantively revised it. JL, GPY, XLY and YZL analyzed and interpreted the study data. All authors read and approved the final manuscript.


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