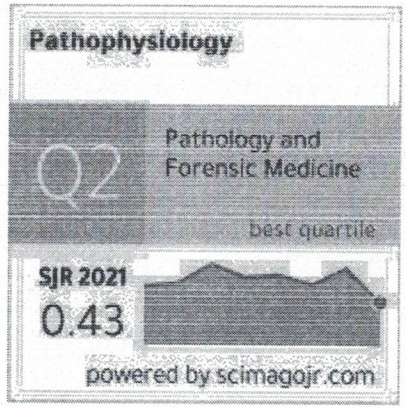
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TG/HDL-C Ratio Is a Risk Factor Associated with CKD: Use in Assessing the Risk of Progression of CKD

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Abstract: Background: Dyslipidemia is highly prevalent in patients with chronic kidney disease (CKD), and the relationship between dyslipidemia and renal function in these patients remains controversial. Our objectives were to determine the triglycerides/HDL-cholesterol ratio (TG/HDL-C), evaluate the correlation between TG/HDL-C and the urine albumin/creatinine ratio (ACR), and estimate the glomerular filtration rate (eGFR) according to MDRD in CKD patients. Methods: A descriptive cross-sectional study was conducted on 152 patients with CKD at the Endocrine Clinic, the University of Medicine and Pharmacy Hospital, Ho Chi Minh City, Vietnam. Study subjects were medically examined and recorded information on the data collection form. Subjects were tested for total cholesterol, triglycerides, HDL-C, LDL-C, urea, creatinine and albumin, urine creatinine, and eGFR according to the MDRD formula. Data were analyzed using SPSS Statistics version 20.0. Results: The average age was 58.08 ± 15.69 years, and the overweight and obesity rate was 54%. Most patients had comorbidities, among which the most common diseases were hypertension and diabetes mellitus. Among the subjects, 57.3% were CKD stage 3 patients, and ACR was in the range of 30–300 mg/g. According to the classification of CKD using GFR and ACR categories, 40.8% of patients were at very high risk. The average TG/HDL-C ratio was 5.09 ± 4.26. There was a medium negative correlation between TG/HDL-C and eGFR ($R = 0.44$, $p < 0.01$) and a weak positive correlation between TG/HDL-C and ACR ($R = 0.34$, $p < 0.01$). Conclusions: The TG/HDL-C ratio was a risk factor associated with CKD and was noticeable in monitoring and assessing the risk of progression of CKD.

Keywords: TG/HDL-C ratio; chronic kidney disease; eGFR; ACR; Vietnam

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1. Introduction

Chronic kidney disease (CKD) is a global health problem associated with high mortality; the principal outcome of CKD is a progressive loss of kidney function, leading to end-stage renal disease (ESRD) [1–3]. Therefore, identifying and managing risk factors associated with mild-to-severe stages of CKD is the best strategy to prevent and delay the progressive outcome of ESRD [4]. Several studies have suggested a vicious circle between loss of renal function and dyslipidemia in CKD, contributing to premature death from cardiovascular disease and other causes [5,6]. Abnormal lipoprotein metabolism has been

was and about 10 mL of urine were taken from each patient for testing. Serum urea, serum creatinine, total cholesterol, triglycerides, HDL-C, and LDL-C were quantified by enzymatic colorimetric method, whereby substances participate in color reactions with reagents to form complexes; then the absorbance of the complexes is at the appropriate wavelength [21]. Urine creatinine, urine urea, albumin, and urine protein were quantified by photometric method, whereby substances react with reagents to form colored complexes. The change in optical density measured at the appropriate wavelength was proportional to the concentration of the substance to be quantified in the sample [21].

The following patient characteristics were collected: age, gender, height, weight, BMI, and medical history (CKD, glomerulonephritis, diabetes, nephrotic syndrome, hypertension, systemic lupus erythematosus, and others). Clinical symptoms included edema, pale mucous membranes, hematuria, and others. Paraclinical characteristics included blood lipids (total cholesterol, triglycerides, HDL-C, LDL-C, and TG/HDL-C ratio) and parameters to evaluate kidney function (urea, albumin, creatinine, ACR, and eGFR according to MDRD) [19]. Classification of stages, prognosis assessment, and CKD progression were based on GFR and ACR.

2.3. Data Analysis

Data were analyzed using SPSS Statistics version 20.0. Difference were considered statistically significant when $p < 0.05$. Qualitative variables were described by frequency and percentage, and quantitative variables were presented as mean ± standard deviation. The relationship between two qualitative variables was compared by testing (Chi-squared); between two quantitative variables by *t*-test with 95% confidence. The correlation coefficients of two quantitative variables were determined by the Pearson correlation coefficient if the variables were normally distributed and by the Spearman correlation coefficient if the variables non-normally distributed. The convention proposed by Guilford (1965) was used to interpret the correlation coefficients of the sample (Table 1).

Table 1. Guilford's interpretation of the magnitude of significant correlations (1956).

|R|	Interpretation
<0.20	Almost no relationship
0.20–0.40	Low correlation
0.40–0.70	Moderate correlation
0.70–0.90	High correlation
>0.90	Very high correlation

2.4. Ethics Approval

The council of Ho Chi Minh University of Medicine and Pharmacy approved our study (No. 91/ĐHYD-HĐĐĐ, dated 30 March 2017). All study participants gave their consent and agreed that their personal information would be kept private. This study did not harmed the patients' health.

3. Results

3.1. Patient Characteristics

Among 152 patients, 55% were men; the mean age was 58.08 ± 15.69. The average BMI was 23.45 ± 3.07 kg/m^2, and the overweight/obesity rate accounted for 54% of subjects. The main clinical symptom was pale mucous membranes; less common symptoms included edema and hematuria. Most patients had comorbidities, the most common of which were hypertension (63%) and diabetes (24%). The group of patients with TG/HDL-C < 4 accounted for 53.3% of subjects—higher than that of TG/HDL-C ≥ 4. A proportion of 57% of subjects were CKD stage 3 patients, and the urine ACR was in the range of 30–300 mg/g. According to the classification of CKD using GFR and ACR categories, 41% of patients were at very high risk (Table 2).

Table 2. *Cont.*

General Characteristics	Frequency	Percentage (%)
Classification of CKD based on GFR and ACR		
Low risk	0	0
Moderate risk	53	35
High risk	37	24
Very high risk	62	41

3.2. Characteristics of Patients with TG/HDL-C < 4 and ≥ 4

The difference was statistically significant in BMI, triglycerides, HDL-C, eGFR, and ACR between two groups of patients with TG/HDL-C < 4 and ≥ 4 ($p < 0.05$). TG/HDL-C < 4 occurred most commonly among patients at moderate risk of kidney disease; TG/HDL-C ≥ 4 was primarily associated with the very high-risk group ($p < 0.05$). Patients with TG/HDL-C < 4 mostly had stages 1 and 2 CKD; in contrast, TG/HDL-C ≥ 4 was more common in patients with stages 3, 4, and 5 CKD ($p < 0.05$) (Table 3).

Table 3. Characteristics of patients with TG/HDL-C < 4 and ≥ 4.

Characteristic	TG/HDL-C		*p*
	<4 (*n* = 81)	≥4 (*n* = 71)	
	n (%)	*n* (%)	
Average age (mean ± SD)	57.85 ± 17.46	58.34 ± 13.50	0.85
BMI (mean ± SD)	22.91 ± 3.26	24.07 ± 2.73	0.02
Blood lipids (mg/dL)			
Cholesterol	193.33 ± 57.18	192.18 ± 60.21	0.90
Triglycerides	123.60 ± 43.10	304.99 ± 151.44	<0.01
HDL-C	54.48 ± 15.58	38.94 ± 8.60	<0.01
LDL-C	120.80 ± 44.91	121.23 ± 44.23	0.95
Parameters to evaluate kidney function			
eGFR (ml/min/1.73 m^2)	59.38 ± 19.33	44.65 ± 20.16	<0.01
ACR (mg/g)	397.50 ± 103.30	842.27 ± 201.54	0.04
Stage of CKD			
Stages 1 and 2	34 (42%)	14 (20%)	0.003
Stages 3, 4, and 5	47 (58%)	57 (80%)	
Classification of CKD based on GFR and ACR			
Moderate risk	34 (42%)	19 (27%)	
High risk	23 (28.4%)	14 (20%)	<0.05
Very high risk	24 (29.6%)	38 (53%)	

3.3. Correlation of Blood Lipids and TG/HDL-C with eGFR and ACR

There was a medium negative correlation between TG/HDL-C and eGFR (R = 0.44, $p < 0.01$) and a weak positive correlation between TG/HDL-C and ACR (R = 0.34, $p < 0.01$) (Table 4).

Table 4. Correlation of blood lipids and TG/HDL-C with eGFR and ACR.

Blood Lipids	eGFR		ACR	
	Correlation	*p*	Correlation	*p*
Cholesterol	R = −0.14	0.09	R = 0.22	<0.01
Triglycerides	R = 0.20	0.02	R = 0.33	<0.01
HDL-C	R = −0.23	<0.01	R = −0.05	0.55
LDL-C	R = −0.13	0.12	R = 0.21	<0.05
TG/HDL-C	R = −0.44	<0.01	R = 0.34	<0.01

by Chih-I Ho (2.3 ± 2.6) [22]. This could be because our study was conducted with a small sample size of patients with CKD, whereas Chih-I Ho's study was performed on a large population to screen health check-ups and CKD surveys.

In addition, we found that the average eGFR was 52.50 ± 20.10 mL/min/1.73 m^2, of which stage 3 of CKD was the most common (57%). This was similar to the results of a study by Le Quoc Tuan and Dang Huynh Anh Thu (2017), who recorded the rate of stages 1-5 CKD as 18%, 30%, 36%, 10%, and 6%, respectively [25]. The urine ACR was within the range of 30–300 mg/g (41%) in this study. Microscopic hematuria was one of the symptoms of glomerular damage. According to an annual report on CKD in the United States, the percentage of ACR > 10 mg/g was 32%, whereas the rates of ACR 30–300 mg/g and ACR > 300 mg/g were 8.5% and 1.4%, respectively. With respect to evaluation of the overall distribution of eGFR and ACR, the report also showed that elevated ACR was associated with reduced renal function [15]. Similarly, according to the classification of CKD using GFR and ACR categories in this study, up to 41% of patients were at very high risk.

4.2. *Characteristics of Patients with TG/HDL-C < 4 and ≥ 4*

When considering two groups of patients with TG/HDL-C ratios < 4 and ≥ 4, we found a significant difference in BMI, triglycerides, HDL-C, eGFR, and ACR ($p < 0.05$). TG/HDL-C ≥ 4 was found primarily in the very high-risk group ($p < 0.05$) and was more common in patients with stage 3 and higher CKD ($p < 0.05$). Research by Chih-I Ho et al. (2015) showed increases from the lowest to the highest quartile of the TG/HDL-C ratio. Men and women in the highest TG/HDL-C ratio quartile (>2.76) had a 1.4-fold and 1.74-fold greater risk of CKD than those in the lowest quartile (≤1.04), respectively, independent of confounding factors. Therefore, A TG/HDL-C ratio ≥2.76 may be helpful in clinical practice to detect subjects with worsened cardiometabolic profiles who require monitoring to prevent CKD [22].

4.3. *Correlation of Blood Lipids and TG/HDL-C with eGFR and ACR*

There was a medium negative correlation between TG/HDL-C and eGFR (R = −0.44, $p < 0.01$). Dyslipidemia might decrease the glomerular filtration rate and accelerate the rate of progression of kidney disease by several mechanisms [7]. First, phospholipid and cholesterol reabsorption in renal tubular epithelial cells released inflammatory factors and tissue damage [22]. Second, lipoproteins stimulated the formation of inflammatory cytokines and induced renal atherosclerosis [26]. The loss of renal function facilitated hypertriglyceridemia and accelerated dyslipidemia, resulting in a vicious cycle between dyslipidemia and decreased renal function [22,26]. Moreover, the research results of Kazuhiko Tsuruya not only emphasized the vital role of Triglyceride/HDL-C as a factor related to CKD progression, especially in patients with diabetes and hypertension, but also noted the benefit of positive management of dyslipidemia in preventing the morbidity and progression of renal failure [14]. This research showed a weak positive correlation between TG/HDL-C and ACR (R = 0.34, $p < 0.01$). Many studies have demonstrated that a high TG/HDL-C ratio is a valuable marker for proteinuria abnormalities [27–29]. Abnormalities in lipid metabolism are believed to contribute to the progression of kidney disease [30,31].

This study is subject to some limitations. First, the observational nature of the cross-sectional research reduced the reliability of establishing a cause-and-effect relationship. Second, the short study period and small sample size might not be sufficient to comprehensively assess the impact of dyslipidemia on renal function. Third, some potential risk factors were not analyzed, such as the history of lipid-lowering drugs and other comorbidities. Therefore, we recommended that further studies be conducted with larger sample sizes in patients with annual physical examinations and simultaneously consider the potential risk factors mentioned above to evaluate the role of TG/HDL-C for CKD in the general population. Otherwise, the MDRD and CKD-EPI equations are the most popular methods for estimating GFR in patients aged 18 years and older. Both of these methods may allow us to observe that CKD is present despite a serum creatinine concentration that appears to fall

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