Ten-year Time-trend Analysis of Dyslipidemia Among Adults in Wuhan

Man ZHANG, Zheng-ce WAN, Yong-man LV, Yuan-cheng HUANG, Liu HU, Hui XU, Xiao-mei LEI

Health Management Center, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China

Abstract
Objective: Dyslipidemia is associated with an increased risk of cardiovascular disease, the major cause of death in an aging population. This study aimed to estimate the prevalence of dyslipidemia for the past decade among adults in Wuhan, China.

Methods: We performed a serial cross-sectional study that recruited 705,219 adults from the Health Management Center of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology from 2010 to 2019. The diagnosis of dyslipidemia was based on the 2016 Chinese Guidelines for the Management of Dyslipidemia in Adults. Fixed effects and random effects models were applied to adjust the confounding variables (gender and age).

Results: The overall prevalence of dyslipidemia was 33.1% (46.2% in men and 14.7% in women) in 2019. The prevalence of dyslipidemia was significantly increased over 10 years [from 28.6% (95% CI: 28.2%–29.1%) in 2010 to 32.8% (95% CI: 32.6%–33.1%) in 2019; \( P < 0.001 \)], especially for hypo-high-density lipoprotein cholesterolemia [from 18.4% (95% CI: 18.0%–18.8%) in 2010 to 24.5% (95% CI: 24.3%–24.7%) in 2019; \( P < 0.001 \)]. In 2019, the prevalence of dyslipidemia was higher in participants with comorbidities, including overweight/obesity, hypertension, diabetes, hyperuricemia, or chronic kidney disease, and dyslipidemia was the most significant among participants aged 30–39 years.

Conclusion: This study demonstrated that dyslipidemia is on the rise in men, and more emphasis should be provided for the screening of dyslipidemia in young males for the primary prevention of cardiovascular and renal diseases.

Key words: dyslipidemia; prevalence; man; cardiovascular disease

According to the 2016 Chinese Guidelines for the Management of Dyslipidemia in Adults, dyslipidemia is defined as elevated levels of triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and total cholesterol (TC), as well as low high-density lipoprotein cholesterol (HDL-C) levels\(^1\)\(^-\)\(^3\). Specifically, hypertriglyceridemia was defined as \( \text{TG} \geq 2.26 \text{ mmol/L, high LDL-C as LDL-C} \geq 4.14 \text{ mmol/L, high TC as TC} \geq 6.22 \text{ mmol/L, and low HDL-C as HDL-C} <1.04 \text{ mmol/L}\)\(^3\). Importantly, an increasing body of evidence has suggested that the effects of dyslipidemia extend beyond a non-alcoholic fatty liver (NAFLD) and are positively associated with many chronic diseases, most notably cardiovascular disease (CVD), chronic kidney disease (CKD), and type 2 diabetes mellitus (T2DM)\(^4\)\(^-\)\(^8\). These diseases account for a significant global health burden with a high economic cost to healthcare systems and result from the same pathophysiological processes associated with visceral obesity, insulin resistance, atherosclerosis and chronic systemic inflammation\(^9\)\(^-\)\(^11\).

As the capital city of Hubei Province, Wuhan has the advantage of convenient transportation, and its economy and culture have undergone tremendous changes in the past few decades. Previous studies have shown that people in developing areas are under great mental and social stress\(^\)\(^12\) and are more likely to choose an unhealthy lifestyle that involves less physical activity, staying up late, smoking, and alcohol consumption to reduce stress. The most direct consequence is an increased incidence of CVD and dyslipidemia, and this association varies according to gender\(^\)\(^13\).

According to the China Health and Nutrition Survey, the prevalence of dyslipidemia increased from 18.6% in 2002 to 34% in 2010\(^14\). For a better understanding of the trends observed for dyslipidemia in adults in Wuhan over the decade from 2010 through 2019, stratification by gender and age was performed in this study to obtain more accurate findings. Importantly, findings of the present study could help estimate the future prevalence of dyslipidemia and its corresponding burden on the healthcare system. In addition, these data were necessary to assess and monitor the effectiveness of population-wide and community-level interventions in reducing the prevalence of dyslipidemia and its
adverse consequences.

1 MATERIALS AND METHODS

This study was conducted at the Health Management Center in Tongji Hospital (China) from January 1, 2010 to December 31, 2019. All the participants in this study underwent a thorough health check-up and provided overnight fasting blood samples. The exclusion criteria consisted of patients under 18 years and pregnant women. Participants were stratified into different age groups: 20 to 29 years, 30 to 39 years, 40 to 49 years, 50 to 59 years, 60 to 69 years, and 70 years and older. The weight and height were measured, and the body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. The participants were stratified into three groups based on the BMI: normal (BMI <24), overweight (BMI=24–27.9), and obesity (BMI ≥28)[15, 16]. Blood lipid concentrations were determined by enzyme colorimetry using an automated analyzer (Roche, Switzerland). Quality control was performed for each test according to the standard laboratory procedures. Moreover, the method of lipid concentration measurement did not change during the whole study period. The study was approved by the Ethics Committee of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology. Written informed consent was obtained from all participants.

1.1 Assessment of Hypertension, Diabetes, Hyperuricemia, and Chronic Kidney Disease

The blood pressure (BP) was measured with an automatic brachial sphygmomanometer (Omron Corporation, China). In this study, hypertension was defined as systolic blood pressure (SBP) of ≥140 mmHg or diastolic blood pressure (DBP) of ≥90 mmHg or taking antihypertensive medication[17]. Diabetes mellitus (DM) was defined as fasting plasma glucose (FPG) ≥7.0 mmol/L or 2 h PG in a 75 g OGTT ≥11.1 mmol/L or taking glucose-lowering therapies according to the International Expert Committee[18]. Hyperuricemia was defined as serum urate (SUA) level ≥7 mg/dL (416 μmol/L) in males and ≥6 mg/dL (357 μmol/L) in females according to the 2015 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) gout classification criteria[19]. The glomerular filtration rate (GFR) is widely acknowledged as a reliable indicator of overall kidney function in health and disease. Normal levels of GFR vary by age, gender, and body size. It has been established that GFR levels below 60 mL/min per 1.73 m² represent the loss of half or more of the normal adult kidney function level. Below this level, the complication rate of chronic kidney disease would increase[20]. Accordingly, we divided all participants into two groups: normal (eGFR ≥60 mL/min/1.73 m²) and CKD (eGFR <60 mL/min/1.73 m²).

1.2 Statistical Analyses

The annual prevalence of dyslipidemia was calculated as the ratio of the records of dyslipidemia to the total number of records available in that year. Descriptive statistics, including the mean values and 95% confidence intervals (CI), were used to describe and visualize the trend changes in the prevalence of dyslipidemia over 10 years. The trend of dyslipidemia during this period was examined by a non-parametric test. Confounding variables including age and gender were adjusted using a multivariable logistic mixed-effects model, and changes associated with repeated tests or annual changes for the same person over 10 years were taken into account. In this model, the “dyslipidemia status” was considered a response variable, “year” was considered a categorical predictor, and “age” and “gender” were included as confounding factors.

Given that an individual could be tested multiple times over the 10-year period, we included the individual identity card number (ID) as a random effect to account for this redundancy. In addition, we analyzed the trends by incorporating “observed years” as a continuous variable into linear or logistic regression models. All statistical analyses were performed using Stata V.12.0 (StataCorp LP, USA). The graph was drawn using the R software (V.3.6.1) package “ggplot2”. χ² tests were used to compare the categorical variables, and unconditional logistic regression analysis was used to analyze the risk factors. A P-value <0.05 was statistically significant.

2 RESULTS

2.1 Characteristics of the Study Population of 2019

The overall prevalence of dyslipidemia in 2019 and the prevalence stratified in terms of gender, age group, and presence of comorbidities, such as BMI, hypertension, diabetes, hyperuricemia, and eGFR (≥60 mL/min/1.73 m² or <60 mL/min/1.73 m²) are shown in Table 1. The overall crude prevalence of dyslipidemia was 33.1% (95% CI; 32.8%–33.3%); it was 46.2% (95% CI; 45.8%–46.6%) for men and 14.7% (95% CI; 14.4%–15.1%) for women (P<0.05). The mean age of the male and female groups was 42.54±12.72 and 41.59±12.75 years, respectively, and there was no statistical difference between them. The prevalence of dyslipidemia was higher in the 30–39 age group than in the 20–29 age group [32.5% (95% CI; 32.0%–33.0%) vs. 22.5% (95% CI; 21.9%–23.1%); P<0.05]. When stratified by the BMI, dyslipidemia was only increased among participants with a BMI of 28 or greater compared to participants with a BMI of less than 24 [62.7% (95% CI; 61.9%–63.5%) vs. 18.0% (95% CI; 17.7%–18.3%); P<0.05].
Many chronic diseases are associated with the dysregulation of the lipid profile and hence result into dyslipidemia. In participants with dyslipidemia, a higher prevalence of hypertension was observed [56.5% (95% CI: 55.2%–57.9%); P<0.05], compared with non-hypertension [47.3% (95% CI: 46.7%–47.9%)]. The proportion of diabetic patients was 56.5% (95% CI: 55.2%–57.9%; P<0.05), compared with non-diabetics [31.9% (95% CI: 31.6%–32.2%)]. Moreover, the prevalence of hyperuricemia [54.9% (95% CI: 54.4%–55.5%; P<0.05)] was significantly higher than that of non-hyperuricemia [25.1% (95% CI: 24.1%–25.3%)]. The incidence of dyslipidemia in CKD patients (eGFR <60 mL/min/1.73 m²) was significantly higher [51.1% (95% CI: 48.4%–53.8%); P<0.05] than that in participants with normal eGFR (eGFR ≥60 mL/min/1.73 m²; 32.9% (95% CI: 32.6%–33.1%)).

Detailed information on the trend changes in the prevalence of dyslipidemia from 2010 to 2019 is shown in table 2.

### 2.2 Trends in Age- and Sex-adjusted Prevalence (95% CI) of Dyslipidemia Among Adults in Wuhan from 2010–2019

The number of tests increased gradually from 2010 (n=32 952) to 2019 (n=116 369). Using a multivariable logistic mixed-effects model, we examined the annual change in prevalence after adjusting the confounding factors (age and gender) and random effects (participants repeatedly tested over 10 years and patients with annual changes in lipid levels). The studied population consisted of an equal number of males and females with slightly more records identified for men (54.1%–60.9% males). The mean age ranged from 41.38±12.53 to 43.77±13.42 years during the 10-year period.

The rate of dyslipidemia at 10 years showed an upward trend in HDL-C [from 18.4% (95% CI: 18.0%–18.8%) in 2010 to 24.5% (95% CI: 24.3%–24.7%) in 2019, P<0.001] and in TG [from 12.3% (95% CI: 12.0%–12.7%) in 2010 to 13.8% (95% CI: 13.7%–14.0%) in 2019, P<0.001]. In contrast, TC exhibited a downward trend [from 5.1% (95% CI: 4.9%–5.3%) in 2010 to 2.8% (95% CI: 2.7%–2.9%) in 2019, P<0.001]. LDL-C exhibited a slight descending trend [from 4.8% (95% CI: 4.6%–5.0%) in 2010 to 4.1% (95% CI: 4.0%–4.2%) in 2019, P<0.001]. After stratified in terms of gender, the prevalence of dyslipidemia was increased more significantly in males [from 39.7% (95% CI: 39.1%–40.4%) to 46.3% (95% CI: 45.9%–46.6%), P<0.001], but not in females [from 14.1%
| Variables | 2010  | 2011  | 2012  | 2013  | 2014  | 2015  | 2016  | 2017  | 2018  | 2019  | P for trend |
|-----------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------------|
| n         | 32492 | 43619 | 47777 | 53912 | 55518 | 64465 | 77830 | 99942 | 112835 | 116369 |             |
| Men, n (%)| 20062 | 25113 | 28683 | 30350 | 31793 | 34877 | 44034 | 55849 | 64644  | 67790  | <0.001      |
| Age (years)| 43.77±13.42 | 42.37±12.65 | 42.75±12.96 | 42.21±12.94 | 43.08±13.24 | 42.50±12.86 | 41.38±12.53 | 41.88±12.83 | 42.41±12.82 | 42.18±12.72 | <0.001      |
| Hyper TG  |       |       |       |       |       |       |       |       |       |       |             |
| Total     | 12.3  | 13.8  | 13.5  | 13.5  | 13.5  | 13.5  | 13.5  | 13.5  | 13.5  | 13.5  | <0.001      |
| Men       | 18.1  | 20.0  | 19.5  | 19.5  | 19.5  | 19.5  | 19.5  | 19.5  | 19.5  | 19.5  | <0.001      |
| Women     | 4.7   | 5.6   | 5.3   | 5.5   | 5.5   | 5.5   | 5.5   | 5.5   | 5.5   | 5.5   | <0.001      |
| Hyper TC  |       |       |       |       |       |       |       |       |       |       |             |
| Total     | 5.1   | 5.6   | 5.4   | 5.4   | 5.4   | 5.4   | 5.4   | 5.4   | 5.4   | 5.4   | <0.001      |
| Men       | 5.4   | 6.0   | 5.7   | 5.7   | 5.7   | 5.7   | 5.7   | 5.7   | 5.7   | 5.7   | <0.001      |
| Women     | 4.7   | 4.6   | 4.3   | 4.3   | 4.3   | 4.3   | 4.3   | 4.3   | 4.3   | 4.3   | <0.001      |
| Hypo HDL  |       |       |       |       |       |       |       |       |       |       |             |
| Total     | 18.4  | 17.7  | 17.7  | 17.7  | 17.7  | 17.7  | 17.7  | 17.7  | 17.7  | 17.7  | <0.001      |
| Men       | 27.5  | 27.0  | 27.0  | 27.0  | 27.0  | 27.0  | 27.0  | 27.0  | 27.0  | 27.0  | <0.001      |
| Women     | 6.4   | 5.4   | 5.4   | 5.4   | 5.4   | 5.4   | 5.4   | 5.4   | 5.4   | 5.4   | <0.001      |
| Hyper LDL |       |       |       |       |       |       |       |       |       |       |             |
| Total     | 4.8   | 4.5   | 4.5   | 4.5   | 4.5   | 4.5   | 4.5   | 4.5   | 4.5   | 4.5   | <0.001      |
| Men       | 5.6   | 5.1   | 5.1   | 5.1   | 5.1   | 5.1   | 5.1   | 5.1   | 5.1   | 5.1   | <0.001      |
| Women     | 3.7   | 3.7   | 3.7   | 3.7   | 3.7   | 3.7   | 3.7   | 3.7   | 3.7   | 3.7   | <0.001      |
| Dyslipidemia | 28.6  | 28.8  | 28.8  | 28.8  | 28.8  | 28.8  | 28.8  | 28.8  | 28.8  | 28.8  | <0.001      |
| Men       | 39.7  | 40.2  | 40.2  | 40.2  | 40.2  | 40.2  | 40.2  | 40.2  | 40.2  | 40.2  | <0.001      |
| Women     | 14.1  | 13.6  | 13.9  | 13.9  | 13.9  | 13.9  | 13.9  | 13.9  | 13.9  | 13.9  | 0.150       |

Age is presented as a mean (95% confidence interval), and dyslipidemia is presented as a percentage (95% confidence interval). The trend is significant at P<0.05.

TG: triglycerides; TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol
were well recognized risk factors for dyslipidemia than in women, since obesity and alcohol consumption prevalence of obesity and alcohol consumption in men hypothesis. Two other explanations were the higher studies would be required to assess the veracity of this to the influence of estrogen. Accordingly, further

**3 DISCUSSION**

The present study demonstrated that the prevalence of dyslipidemia in adults in Wuhan in 2019 was significantly higher in males (46.2%) than in females (14.7%). In addition, the prevalence of hyper TG and hypo HDL-C and hyper LDL-C was higher in men than in women, which was inconsistent with the literature. Previous studies demonstrated that the prevalence of lipids in postmenopausal women was significantly higher than in men[21] and was attributed to the influence of estrogen. Accordingly, further studies would be required to assess the veracity of this hypothesis. Two other explanations were the higher prevalence of obesity and alcohol consumption in men than in women, since obesity and alcohol consumption were well recognized risk factors for dyslipidemia[22, 23]. Furthermore, the present study showed that the prevalence of dyslipidemia varied according to age, BMI, hypertension, diabetes, hyperuricemia, and CKD. Moreover, we found that the trend in the prevalence of dyslipidemia was significantly different between males and females, which was consistent with the literature[24]. We found that the prevalence of dyslipidemia was significantly increased in men [from 39.7% (95% CI: 39.1%–40.4%) in 2010 to 46.3% (95% CI: 45.9%–46.6%) in 2019, P=0.001]; however, no significant increase was observed in women [from 14.1% (95% CI: 13.6%–14.7%) in 2010 to 14.6% (95% CI: 14.3%–14.9%) in 2019, P=0.15]. This finding suggested that males are nowadays at an increased risk of dyslipidemia and should be screened earlier.

In addition, it is widely acknowledged that obesity is a risk factor for dyslipidemia[25]. We found that the prevalence of dyslipidemia was paralleled by the increased BMI in both genders. Due to the growing global obesity epidemic, available evidence has suggested that in most countries, 20% to 30% of the adult population has been diagnosed with metabolic syndrome (MetS)[26, 27]. MetS is a multiplex risk factor for CVD and results from the interplay of obesity and metabolic susceptibility. In addition to dyslipidemia, hypertension, and T2DM, MetS is associated with a prethrombotic state and a pro-inflammatory state, which are related to CVD and CKD[28–30]. In recent years, an increasing number of studies have focused on microRNAs and their potential use as biomarkers of dyslipidemia, especially proprotein convertase subtilisin/Kexin type 9 (PCSK9) and sphingosine-1-phosphate (S1P), as key regulators of the metabolism of low-density lipoproteins (LDL) and high-density lipoprotein (HDL) particles[31]. It is highly conceivable that more studies could focus on developing targeted molecular therapy approaches against dyslipidemia in the future.

It is not surprising that many studies have highlighted the association between dyslipidemia and chronic diseases, involving increased serum triglycerides, small dense LDL-C and low HDL-C[32–34]. Furthermore, it has been established that low HDL-C and high LDL-C levels are independent risk factors for CVD[35, 36]. In our data, the incidence of high LDL-C was more pronounced in men than in women from 2010 to 2019, which would be possible that men were associated with high concentrations of oxidized, small, cytotoxic LDL lipoproteins. Therefore, men were more susceptible to CVD than women. Moreover, dyslipidemia has been reported in 20% to 80% of cases of a NAFLD. Each 1.0 mg/dL increase in HDL-C was correlated with a 2%–3% reduction in the incidence of coronary heart disease[37, 38]. Our results showed that the incidence of hypo HDL-C was significantly higher in both genders; however, the prevalence of hyper TC exhibited a declining trend among adults. Interestingly, we found that the upward trend in dyslipidemia was limited to men, especially at a mean age of >30 years. This finding emphasized the need to target young men during screening and risk management of CVD and CKD.

To date, more than 4.13 million people in 215 countries have died from coronavirus disease-19 (COVID-19), which is having a profound health socio-economic impact. Therefore, we conducted a cross-sectional study of a 10-year time trend analysis of dyslipidemia among adults in Wuhan. Interestingly, studies have shown that men were more likely to be infected with COVID-19[39], similar to the prevalence of dyslipidemia in 2019, which could be attributed to genetic, hormonal factors and gender-specific...
behavior. Hence, further studies are required for a better understanding of this phenomenon.

Several limitations were present in our study. First, our findings were based on data from the Health Management Center of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, and most participants were government officials or worked in different industries. Accordingly, our findings may not reflect the crude prevalence of dyslipidemia in Wuhan. Therefore, we estimated the prevalence of dyslipidemia after controlling several confounding factors, which helped to reduce the bias through statistical analysis. Second, in the study population, there were participants who had multiple health checks during the study period. Their multiple medical records were included in the analysis, which could ultimately affect the accuracy of our results. Nonetheless, our results were representative of any individual who had had a lipid test in the province over the past 10 years and could be used as a reliable indicator of dyslipidemia-related diseases in the local population. Moreover, the incidence of dyslipidemia was assessed based on the blood lipid test results of the examinee, but the effect of potential confounding factors, such as lipid-lowering drugs, was not considered. Additionally, the present study did not account for other factors, such as diet, education level, lifestyle, and physical activity level that might influence dyslipidemia[40]. In addition to alcohol consumption, smoking and lifestyle habits were identified as risk factors for dyslipidemia. Over the past decade, there has been a modest increase in alcohol consumption, frequency of drinking, and rates of heavy drinking among men, especially young men[41], which may help explain our results.

In summary, the findings of the present study revealed the increased prevalence of dyslipidemia during the past 10 years, especially in young males. This trend may be attributed to men being increasingly susceptible to MetS and CVD. However, further research would be needed to increase the robustness of our findings and improve the chronic disease outcomes in the local population.

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Conflict of Interest Statement
The authors declare no conflict of interest.

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