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The association between monocyte to high-density lipoprotein cholesterol ratio and chronic kidney disease in a Chinese adult population: a cross-sectional study

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ABSTRACT

Background: Monocyte to high-density lipoprotein cholesterol ratio (MHR) was confirmed as a novel inflammatory marker and strongly associated with the risk of several diseases. This study aimed to investigate the relationship between MHR and chronic kidney disease (CKD) in a Chinese adult population.

Methods: In this cross-sectional study, 232,775 community-dwelling adults in Binhai who completed health checkups in 2021 were enrolled. Participants were categorized based on the MHR quartiles. Clinical characteristics of participants across different groups were compared using one-way ANOVA, Kruskal-Wallis *h*-test, and Chi-squared test as appropriate. Univariate and multivariable logistic regression analyses were taken to assess the relationship between MHR and the presence of CKD, as well as its association with low estimated glomerular filtration rate (eGFR) and proteinuria. Subgroup analyses were further executed to confirm the reliability of this relationship.

Results: A total of 21,014 (9.0%) individuals were diagnosed with CKD. Characteristic indicators including waist circumference, body mass index (BMI), blood pressure (BP), serum uric acid (SUA), triglyceride, and fasting blood glucose (FBG) showed a gradual increase with higher MHR quartiles, whereas parameters such as age, total cholesterol, high-density lipoprotein cholesterol (HDL-C), and eGFR decreased ($p < .001$). In the multivariable logistic regression analysis, we observed independent associations between MHR (per 1 SD increase) and CKD, as well as low eGFR and proteinuria, with odds ratio (ORs) and 95% confidence intervals (95%CIs) of 1.206 (1.186–1.225), 1.289 (1.260–1.319), and 1.150 (1.129–1.171), respectively ($p < .001$). Similar conclusions were confirmed in subgroup analysis stratified by gender, age, BMI, central obesity, hypertension, and diabetes mellitus, after justification for confounding factors.

Conclusion: Elevated MHR level was independently associated with the presence of CKD, suggesting that it might serve as a useful clinical tool for risk stratification, offering valuable insights to inform preventive and therapeutic approaches for clinicians in their routine medical practice.

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Chronic kidney disease; inflammation; monocyte to high-density lipoprotein cholesterol ratio; dyslipidemia

Introduction

Chronic kidney disease (CKD) is acknowledged as a critical threat to public health worldwide. According to the Global Burden of Disease Study, CKD and its impact on cardiovascular disease have a major effect on global health. It is responsible for approximately 35.8 million disability-adjusted life years (DALYs) and 2.6 million deaths every year all over the world [1]. Patients with CKD are more likely to develop atherosclerosis as the disease often accompanies inflammation, oxidative stress, and disturbed lipid metabolism [2].

Inflammation is typically accompanied by several alterations in lipid metabolism, including elevated triglyceride levels and reductions in high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C). Moreover, it also affects the functionality of lipoproteins, which could lead to an increased risk of atherosclerosis.[3]. As a proinflammatory state, CKD is also expected to have

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changes in lipids, lipoproteins, and lipoprotein-associated proteins. Indeed, the lipidome in CKD patients differs from that of healthy individuals with increased levels of triglycerides and N-acyltaurines, and decreased levels of phosphatidylcholines, plasmenyl ethanolamines, sulfatides, ceramides, and cholesterol sulfate [4,5]. Animal model studies have shown that CKD promotes lipid accumulation in the artery wall and kidney, leading to atherosclerosis, glomerulosclerosis, and tubulointerstitial fibrosis [6,7].

Monocyte to high-density lipoprotein cholesterol ratio (MHR) is a composite biomarker reflecting the balance between inflammation, oxidative stress, and lipid metabolism [8,9]. Its level has been revealed to be related to the risk of diabetes mellitus (DM) [10], hypertension (HTN)[11], coronary heart disease [12], atrial fibrillation [13,14], fatty liver disease [15,16], and cardiovascular mortality [17,18]. Although high MHR level has been known as a prognostic marker for diabetic nephropathy (DN), acute kidney injury, and renal dysfunction [10,19–21], limited data has been presented on the relationship between MHR and CKD. Our research aimed to investigate the association between MHR and CKD in a Chinese community population.

Materials and methods

Study population

A retrospective cross-sectional study was conducted in Binhai, Jiangsu Province, China. The prevalence of CKD in this region, located in Eastern China, was 8.1% (7.2%–8.9%) from 2018 to 2019[22]. Binhai was selected because of its universal coverage of free primary care and an integrated electronic health information system. The annual health examination program conducted by the local government was free of charge for all the residents there. Its information was disseminated through various media channels such as the Internet, television, newspapers, and others before the health examination took place. All the community residents in Binhai were eligible to participate in the health examination freely by presenting their identification cards. Finally, a total of 261,510 individuals participated in the health examination project from 1st January 2021 to 31st December 2021 in Binhai. We excluded participants who lacked urine measurement data ($n = 1,625$), monocyte or HDL-C count ($n = 26,768$), or serum creatinine (Scr) measurements ($n = 189$). Additionally, Considering the impact of inflammation-malnutrition syndrome and the potential effects of dialysis technique on lipid homeostasis, patients with CKD stage G5 ($n = 153$) were excluded due to their distinct pathophysiology [23]. A total of 232,775 participants aged ≥18 years were finally enrolled in this study. The flow chart in Figure 1 shows the inclusion and exclusion criteria for participants. Informed consent was obtained from each participant before data collection.

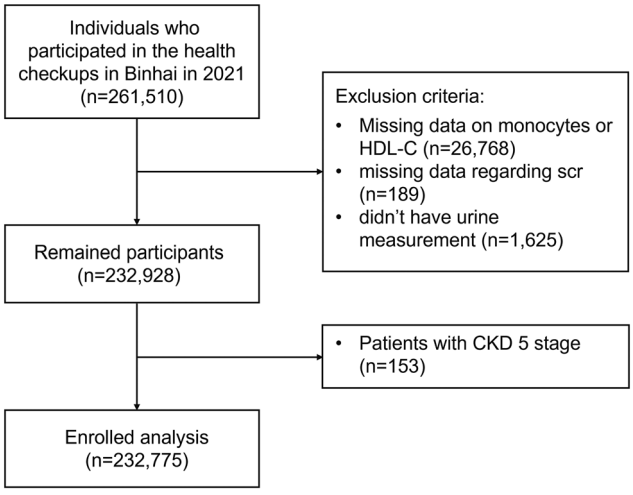

Figure 1. The flowchart of the study.

Data collection

All data were collected by trained nurses using questionnaires and anthropometric measures. Height, weight, and waist circumference were all measured twice and averaged for analysis. The average of three blood pressure (BP) measurements made by the nurses was documented. Blood samples were obtained after overnight fasting and examined with automatic analyzers (Beckman Coulter AU5800 and Sysmex XN-350). MHR was calculated by the count of circulating monocytes divided by serum HDL-C level. A random spot urine sample was collected and assessed using a urine dipstick test to detect urinary protein. The results were shown as negative, trace, +1, +2, or +3.

Definition of metabolic variables

Systolic BP (SBP) ≥140 mmHg or diastolic BP (DBP) ≥90 mmHg, or the present antihypertensive treatment, was used as the diagnostic criteria for HTN. Pre-HTN was defined as either SBP 120–139 mmHg or DBP 80-89 mmHg [24]. Fasting blood glucose (FBG) level was classified into three groups: <5.6 mmol/L (no-DM), 5.6–6.9 mmol/L (pre-DM), and ≥7.0 mmol/L (DM) [25]. Participants with a waist circumference of ≥80 cm for females and ≥90 cm for males were identified to have central obesity [26]. The criteria set by the Working Group on Obesity in China were as follows: overweight with a body mass index (BMI) of 24.0–27.9 kg/m^2, and obesity with a BMI of ≥28.0 kg/m^2 [27].

Definition of CKD and CKD stages

The CKD epidemiology collaboration creatinine equation (CKD-EPI) was used to report the estimated glomerular filtration rate (eGFR) in this study [28]. Despite widespread awareness of urinary albumin/creatinine ratio (UACR) as one of the gold standards for assessing CKD, the urine dipstick test remains widely used as a screening tool for proteinuria evaluation, especially in large-scale population health screenings, due to its low cost, simplicity, and ability to provide rapid

point-of-care information [29]. The proteinuria was evaluated with a urine dipstick test in this study, which was classified as normal (negative or trace), mild (+1), or heavy (≥+2) [30]. Referencing previous epidemiological research methods and the Kidney Disease Improving Global Outcomes (KDIGO) 2012 Clinical Practice Guideline, CKD was diagnosed based on low eGFR [<60 mL·min^{-1}·(1.73 m^2)$^{-1}$] and/or proteinuria (≥+1)[31–33]. CKD stages are defined as follows: Stage G1, proteinuria with eGFR ≥ 90 mL·min^{-1}·(1.73 m^2)$^{-1}$; Stage G2, proteinuria with eGFR of 60–89 mL·min^{-1}·(1.73 m^2)$^{-1}$; Stage G3, an eGFR of 30–59 mL·min^{-1}·(1.73 m^2)$^{-1}$; Stage G4, an eGFR of 15–29 mL·min^{-1}·(1.73 m^2)$^{-1}$; Stage G5, eGFR < 15 mL·min^{-1}·(1.73 m^2)$^{-1}$[33].

Statistical analysis

Statistical analyses were performed with SPSS version 23 (SPSS Inc, Chicago, Illinois). Continuous variables were described using mean ± standard deviation (SD) or interquartile range (IQR) and analyzed with one-way ANOVA or the Kruskal–Wallis *H*-test, where applicable. Categorical variables were expressed as numbers with percentages, and the difference was determined by the Chi-squared test. The missing rates for all variables were below 0.25%, and regression estimation was used to deal with the missing data. The quantitative variable MHR was chosen to be divided into quartiles to explore potential non-linear relationships between MHR and baseline clinical features more flexibly within this population. We examined the unadjusted association between latent variables and CKD in a univariate logistic regression analysis. The association between MHR (per 1 SD increase) and the presence of CKD as well as low eGFR and proteinuria was measured using multivariate logistic regression analysis. Variables in model 1 were unadjusted. Gender and age were adjusted in model 2. In addition, various clinical variables such as BMI, FBG, SBP, DBP, WBC, platelet, hemoglobin, total cholesterol, serum uric acid (SUA), triglyceride, waist circumference, and LDL-C were further adjusted in model 3. Moreover, subgroup analyses were further conducted to examine the robustness of this relationship. The Bonferroni correction was used to adjust *p* values for interaction in the subgroup analyses. The formula for a Bonferroni Correction is as follows: $\alpha_{new} = \alpha_{original}/n$, where $\alpha_{original}$=0.05, and n represents the total number of comparisons or tests being performed.

Results

Clinical characteristics of the population

The clinical characteristics of the study population grouped by quartiles of MHR are shown in Table 1. A total of 232,775 individuals were included in the study, with an average age of 58.39 ± 14.35 years, 44.9% were male. Participants were divided into four subgroups according to MHR quartiles

Table 1. Clinical characteristics of the population by MHR quartiles.

		Quartiles of MHR				
Characteristic	Total	Q1 (< 0.1769)	Q2 (≥0.1769 and <0.2453)	Q3 (≥0.2453 and~ <0.3383)	Q4 (≥0.3383)	*p* value
Number, *n* (%)	232,775 (100.0)	58,213 (25.0)	58,262 (25.0)	58,079 (25.0)	58,221 (25.0)	
Demographics						
Age (years)	58.39 ± 14.35	59.65 ± 13.26	58.57 ± 14.01	58.12 ± 14.55	57.21 ± 15.37	<.001
Male, *n* (%)	104,596 (44.9)	19,301 (33.2)	22,722 (39.0)	27,009 (46.5)	35,564 (61.1)	<.001
Metabolic variables						
Waist circumference (cm)						
Men	83.00 ± 6.81	82.39 ± 6.74	82.80 ± 6.77	82.99 ± 6.83	83.47 ± 6.82	<.001
Woman	80.32 ± 7.26	80.15 ± 7.11	80.16 ± 7.29	80.39 ± 7.26	80.79 ± 7.45	<.001
BMI (kg/m^2)	24.68 ± 3.02	24.12 ± 2.94	24.46 ± 2.93	24.81 ± 2.98	25.33 ± 3.11	<.001
SBP (mmHg)	130.14 ± 15.97	129.05 ± 15.76	129.64 ± 15.87	130.53 ± 16.15	131.34 ± 15.98	<.001
DBP (mmHg)	78.88 ± 9.49	78.01 ± 9.34	78.55 ± 9.29	79.16 ± 9.44	79.81 ± 9.78	<.001
FBG (mmol/L)	5.78 ± 1.90	5.58 ± 1.72	5.68 ± 1.77	5.82 ± 1.91	6.04 ± 2.13	<.001
SUA (μmol/L)	317.26 ± 88.63	291.60 ± 79.13	307.52 ± 83.37	323.38 ± 87.13	348.10 ± 94.64	<.001
total cholesterol (mmol/L)	4.99 ± 1.00	5.08 ± 0.98	5.04 ± 0.98	4.98 ± 0.99	4.86 ± 1.04	<.001
triglyceride (mmol/L)	1.46 (1.01,2.15)	1.27 (0.90,1.82)	1.37 (0.97,1.97)	1.51 (1.06,2.20)	1.79 (1.22,2.64)	<.001
LDL-C (mmol/L)	2.70 ± 0.81	2.68 ± 0.79	2.74 ± 0.81	2.74 ± 0.81	2.64 ± 0.82	<.001
HDL-C (mmol/L)	1.34 ± 0.36	1.61 ± 0.40	1.41 ± 0.28	1.27 ± 0.25	1.09 ± 0.24	<.001
Complete blood count						
WBC (10^9/L)	6.05 ± 1.79	5.07 ± 1.48	5.68 ± 1.55	6.23 ± 1.48	7.21 ± 1.90	<.001
Hemoglobin (g/L)	137.03 ± 17.02	132.58 ± 15.78	135.54 ± 16.24	137.98 ± 16.82	142.01 ± 17.75	<.001
Platelet (10^9/L)	178.73 ± 62.09	162.51 ± 56.17	174.33 ± 58.99	182.99 ± 61.10	195.12 ± 66.96	<.001
Kidney function						
Scr (μmol/L)	67.92 ± 18.31	63.35 ± 16.01	66.08 ± 16.58	68.85 ± 18.02	73.40 ± 20.73	<.001
eGFR (ml·min^{-1}·(1.73 m^2)$^{-1}$)	93.60 ± 18.11	94.91 ± 16.76	94.17 ± 17.38	93.21 ± 18.25	92.11 ± 19.78	<.001
Proteinuria, n (%)						
Neg/Trace	219,756 (94.4)	55,769 (95.8)	55,358 (95.0)	54,812 (94.4)	53,817 (92.4)	<.001
1+	8522 (3.7)	1654 (2.8)	1887 (3.2)	2155 (3.7)	2826 (4.9)	
≥2+	4497 (1.9)	790 (1.4)	1017 (1.7)	1112 (1.9)	1578 (2.7)	

Values are mean ± SD for normally distributed data and median and interquartile range for skewed distributed data, or *n* (%) for categorical variables.
BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; FBG: fasting blood glucose; eGFR: estimated glomerular filtration rate; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; Scr: Serum creatinine; SUA: serum uric acid; WBC: white blood cell.

using the following cutoff values (Q1: <0.1769, Q2: 0.1769–0.2452, Q3: 0.2453–0.3382, Q4: ≥0.3383). The proportion of male participants increased as MHR quartiles increased. The levels of waist circumference, BMI, SBP, DBP, SUA, triglyceride, FBG, white blood cell (WBC), hemoglobin, platelet, and Scr increased significantly across the increasing quartiles, whereas age, total cholesterol, and HDL-C decreased with higher MHR in this study. Notably, eGFR decreased gradually from Q1 to Q4, which were 94.91 ± 16.76, 94.17 ± 17.38, 93.21 ± 18.25, and 92.11 ± 19.78 mL·min^{-1}·(1.73 m^2)$^{-1}$ ($p < .001$), respectively. The prevalence and severity of proteinuria also increased across the increasing quartiles ($p < .001$).

The prevalence of CKD across different quartiles of MHR groups

The prevalence of CKD and the distribution of its components across the four MHR quartiles are illustrated in Figure 2. Overall, 21,014 (9.0%) individuals were diagnosed with CKD, which is consistent with previous epidemiological findings in this region. In groups from Q1 to Q4, the prevalence of CKD was 6.6%, 7.8%, 9.2%, and 12.5%, respectively. With the increase of MHR quartiles, the proportion of advanced CKD also gradually increased, especially the CKD stage G3 and stage G4. In Q3 and Q4 groups, the proportions of patients with CKD stage G3 were 3.9% and 5.6%, respectively, while the proportions of patients with CKD stage G4 were 0.2% and 0.4%, which were significantly higher than those of the lower quartile groups ($p < .001$).

The association between CKD and clinical characteristics

We performed a univariate analysis of the association between CKD and the relevant covariates (Table 2). The development of CKD in this study was positively correlated with age, BMI, SBP, DBP, SUA, FBG, total cholesterol, triglyceride, WBC, monocytes, and MHR. No significant difference was observed between males and females. Individuals with central obesity had a higher risk of CKD. Furthermore, we discovered a substantial negative correlation between CKD and relevant variables such as hemoglobin, platelet, HDL-C, and LDL-C.

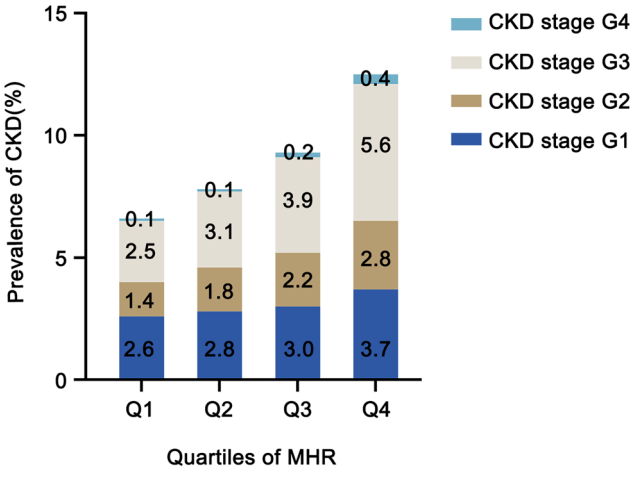

Figure 2. Prevalence of CKD according to the quartile of MHR. The prevalence of CKD according to the quartiles of MHR was shown in different colored bars (dark blue: CKD stage G1, brown: CKD stage G2, gray: CKD stage G3, light blue: CKD stage G4). MHR: monocyte to high-density lipoprotein cholesterol ratio; CKD: chronic kidney disease.

The association between MHR and CKD

Multivariate regression analysis was further performed to clarify the association between MHR and the presence of CKD (Table 3). In model 2, after adjusting for age and gender, a significant association was observed between higher MHR levels and the risk of CKD, as well as low eGFR and proteinuria ($p < .001$). In model 3, confounding factors such as waist circumference, BMI, FBS, SBP, DBP, total cholesterol, SUA, triglyceride, WBC, platelet, hemoglobin, and LDL-C were further adjusted. Independent associations were observed between MHR(per 1 SD increase) and CKD, as well as low eGFR and proteinuria. The odds ratio (ORs) and 95% confidence intervals (95%CIs) were 1.206(1.186–1.225), 1.289(1.260–1.319), and 1.150 (1.129–1.171) in model 3, respectively ($p < .001$).

Higher levels of MHR were associated with the risk of CKD in subgroup analysis

Subgroup analysis was further performed to explore the robustness of the association between MHR (per 1 SD increase) and CKD using multivariate analysis (Figure 3). In

Table 2. Univariate logistic analysis of the relationships between the other variables and CKD.

Variables	Effect size(β)	OR (95%CI)	*p* value
Gender			
Male	Ref		
Female	−0.008	0.992 (0.964,1.021)	.586
Age (per-1 year increase)	0.038	1.039 (1.038,1.040)	<.001
BMI (kg/m^2)	0.047	1.048 (1.043,1.053)	<.001
Central obesity			
No	Ref		
Yes	0.132	1.141 (1.109,1.174)	<.001
SBP (mmHg)	0.020	1.020 (1.020,1.021)	<.001
DBP (mmHg)	0.023	1.024 (1.022,1.025)	<.001
SUA (μmol/L)	0.005	1.005 (1.005,1.005)	<.001
FBG (mmol/L)	0.132	1.414 (1.135,1.148)	<.001
Total cholesterol (mmol/L)	0.085	1.089 (1.074,1.104)	<.001
Triglyceride (mmol/L)	0.093	1.098 (1.089,1.107)	<.001
LDL-C (mmol/L)	−0.040	0.961 (0.944,0.978)	<.001
HDL-C (mmol/L)	−0.312	0.732 (0.702,0.763)	<.001
WBC (10^9/L)	0.110	1.117 (1.108,1.125)	<.001
Hemoglobin (g/L)	−0.007	0.993 (0.992,0.994)	<.001
Platelet (10^9/L)	−0.001	0.999 (0.999,1.000)	<.001
Monocyte(10^9/L)	1.748	5.742 (5.241,6.291)	<.001
MHR (per-1 SD increase)	0.236	1.266 (1.250,1.281)	<.001

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; FBG: fasting blood glucose; WBC: white blood cell; SUA: serum uric acid; MHR: monocyte to high-density lipoprotein cholesterol ratio.

Table 3. Multivariate logistic analysis of the association between MHR (per-1 SD increase) and the presence of CKD, low eGFR, and proteinuria.

	CKD		Low eGFR		Proteinuria	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Model 1	1.266(1.250,1.281)	<.001	1.293(1.273,1.314)	<.001	1.227(1.210,1.245)	<.001
Model 2	1.310(1.293,1.326)	<.001	1.362(1.338,1.386)	<.001	1.224(1.206,1.243)	<.001
Model 3	1.206(1.186,1.225)	<.001	1.289(1.260,1.319)	<.001	1.150(1.129,1.171)	<.001

Model 1: No variables were adjusted. Model 2: Age and gender were adjusted. Model 3: Age, gender, BMI, FBS, SBP, DBP, TC, SUA, TG, central obesity, WBC, platelet, hemoglobin, and LDL-C were adjusted. ORs reflected the associations between MHR (per 1SD increase) and different indicators of kidney damage.

MHR: monocyte to high-density lipoprotein cholesterol ratio; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate.

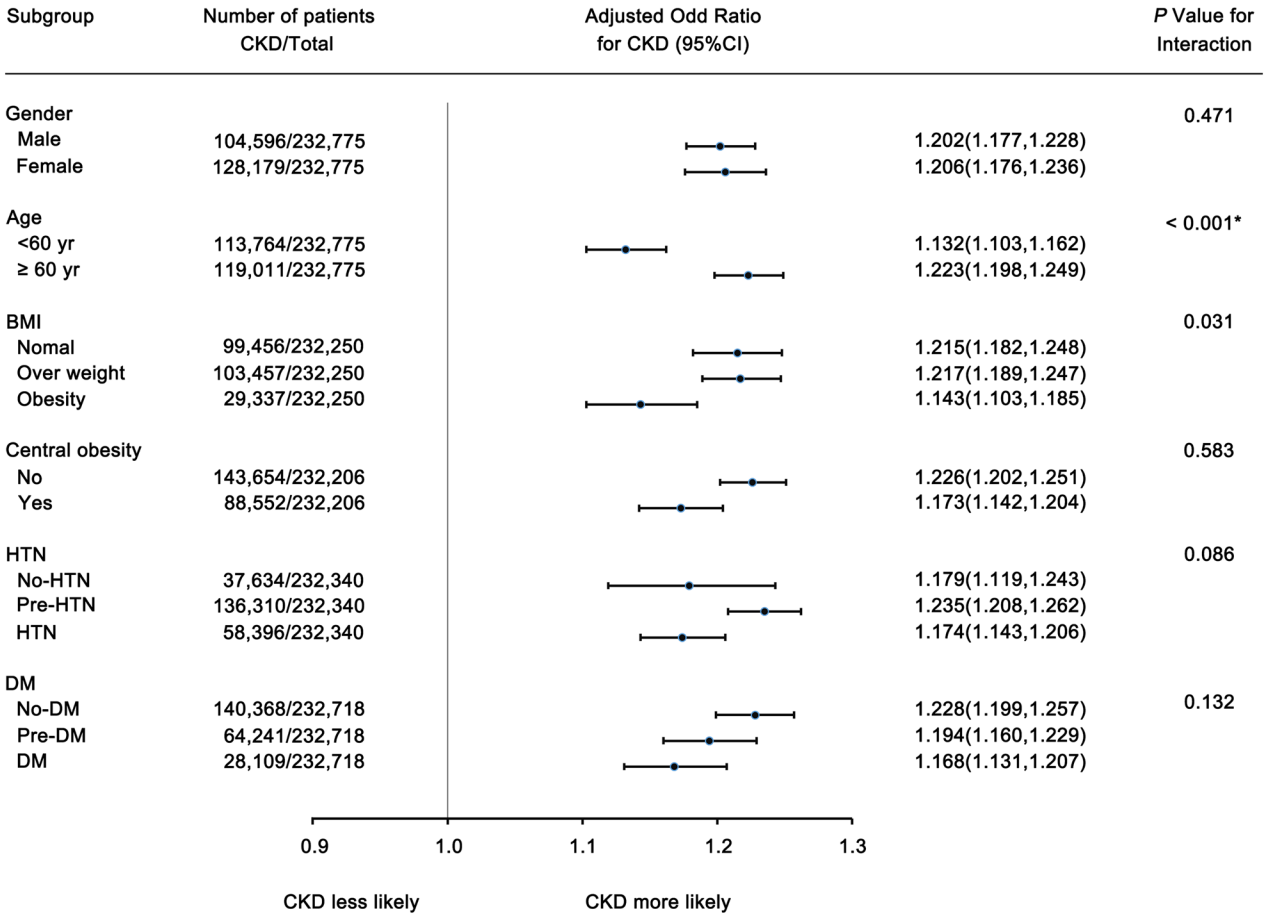

Figure 3. The odds ratio (95% CI) of MHR (per 1 SD increase) for CKD in subgroups. The odds ratio (95% CI) of per 1 SD increase of MHR for CKD, were adjusted for age, gender, BMI, FBS, SBP, DBP, total cholesterol, SUA, triglyceride, central obesity (yes or no), Hb, WBC, PLT, and LDL-C. *represents statistical significance after the Bonferroni Correction.

this analysis, the population was stratified based on demographic and clinical characteristics and further adjusted for age, gender, platelet, hemoglobin, WBC, FBG, SUA, BMI, BP, total cholesterol, triglycerides, central obesity, and LDL-C.

The risk of CKD increased by 20.6% (95%CI, 17.6%–23.6%) per 1 SD increase in MHR in females while 20.2% (95%CI, 17.7%–22.8%) in males. The association between MHR and CKD was not significantly different between the two groups ($p = .471$ for interaction). Increased MHR was linked to a greater risk of CKD in the elderly (OR = 1.223, per 1 SD increase in MHR, 95%CI, 1.198–1.249), compared to those younger than 60 years (OR = 1.132, per 1 SD increase in MHR, 95%CI, 1.103–1.162) ($p < .001$ for interaction).

After stratification according to BMI, the ORs of CKD for the overweight population was 1.217 (per 1 SD increase in MHR, 95%CI, 1.189–1.247), while the ORs for the normal group was 1.215 (per 1 SD increase in MHR, 95%CI, 1.182–1.248), which were slightly higher than that for the obese population (OR = 1.143, per 1 SD increase in MHR, 95%CI, 1.103–1.185) ($p = .031$ for interaction). However, after Bonferroni correction, there was no significant statistical significance observed in the *p* for interaction among these three subgroups. In addition, a higher level of MHR was consistently and independently associated with the risk of CKD regardless of whether individuals were comorbid with central obesity, HTN, or abnormal FBG, with no statistically significant difference in ORs between these subgroups. Positive

correlations were further observed between MHR (per 1 SD increase) and the presence of low eGFR and proteinuria in individuals in different subgroups (Supplement Figure 1).

Discussion

Previous studies suggest that the development of CKD is associated with inflammation and disturbed lipid metabolism [34–37]. Patients even with mild renal dysfunction tend to have elevated monocyte counts and reduced serum HDL-C concentration [38,39]. MHR has been recognized as an emerging marker of inflammation with abnormal lipid metabolism and the prognostic predictor of numerous diseases. To date, it is strongly associated with the risk of several metabolic diseases such as diabetes [10], HTN [11], obesity [40], and target organ damage [12,18,19,41].

In this study, we observed a significant decrease in eGFR as MHR levels increased, while a notable increase in the prevalence and severity of proteinuria within a large general population. Importantly, a higher level of MHR was consistently and independently associated with the risk of CKD, low eGFR, and proteinuria. This association remained robust even after adjusting for confounding variables, regardless of whether individuals were comorbid with HTN, diabetes, obesity, or central obesity, as shown in the subgroup analysis.

It is well known that inflammation can lead to various alterations in lipid and lipoprotein metabolism. Elevated triglyceride levels and reductions in HDL-C are the most common changes associated with the inflammatory state. Moreover, a sustained increase in small dense LDL and Lp(a) levels, along with decreased LDL-C levels, can be observed. Additionally, inflammation affects the functionality of lipoproteins, such as diminishing the anti-inflammatory, antioxidant, and anti-atherosclerotic capacity of HDL-C. This dysfunctional HDL-C leads to an increase in oxidized LDL-C and loses its ability to promote cholesterol efflux from cells [3].

As a proinflammatory state, CKD is expected to have a similar adverse impact on lipid balance. In recent years, the relationship between MHR and the risk of CKD has received increasing attention. Previous studies confirmed that elevated MHR levels were associated with the presence and severity of proteinuria and renal insufficiency, which is consistent with our conclusion [20,42]. Moreover, MHR was found to be independently linked with urine albumin excretion in patients with diabetic nephropathy, suggesting that it may serve as a biomarker for diabetic renal injury [10,19]. In our study, a positive correlation was observed between MHR and the presence of proteinuria and low eGFR regardless of whether individuals have diabetes. Furthermore, studies have shown that MHR was independently related to several comorbidities and the outcome in patients with CKD. Kanbay et al. showed that higher MHR values were related to both composite cardiovascular events [hazard ratio (HR)=4.91, 95%CI, 2.88-6.94] and higher mortality rate (HR = 2.24, 95%CI, 1.85-2.39) in patients with CKD [43]. MHR may also be associated with multiple anti-HTN treatments and refractory HTN in CKD patients [44]. Furthermore, two clinical studies suggested that patients undergoing peritoneal dialysis (PD) had an increased risk of cardiovascular disease and death from all causes when their MHR was elevated [45,46].

As well known, peripheral monocyte count has been demonstrated as a powerful predictor of atherosclerosis, especially in individuals with CKD [47,48]. The elevated number of circulating monocytes and their differentiation into lipid-laden macrophages are known to be critical in plaque formation. Monocytes also play key roles in immune surveillance and the maintenance of kidney homeostasis [49]. It has been proven that interfering with monocyte recruitment prevented renal injury and subsequent scarring in most settings [50,51]. The ability of HDL-C to reverse cholesterol transport and its antioxidant and anti-inflammatory activities are essential protective factors in atherosclerosis formation. However, compared to healthy individuals, patients with CKD exhibit decreased levels and impaired maturation of HDL-C. This leads to decreased antioxidative and anti-inflammatory activities of HDL-C in patients [52]. HDL-C abnormalities contribute to lipid accumulation in the artery wall and kidney tissue, which subsequently cause glomerulosclerosis, tubulointerstitial, and atherosclerosis injury in CKD [53,54].

In addition, a potential association between abnormal HDL-C metabolism and monocyte counts in patients with CKD has been noted. Anjali Ganda et al. illustrated that low HDL-C was independently associated with monocytosis in individuals with mild renal dysfunction [39]. Studies indicated that monocytes were more likely to develop an inflammatory state in individuals with perturbed lipid profiles, and their cytokine production such as IL-1β was negatively correlated with HDL-C [55]. HDL-C showed an anti-atherosclerotic effect by compromising the pro-oxidative and pro-inflammatory effects of monocytes by suppressing macrophage migration and LDL-C oxidation, as well as cholesterol efflux from these cells. In addition, HDL-C can also decrease the proliferation and differentiation of monocyte progenitor cells [56].

It should be noted that patients with end-stage renal disease (ESRD) were excluded from this study because of their distinct pathophysiology. Differing from the general population, higher cholesterol concentrations are associated with improved clinical outcomes in patients with ESRD. This phenomenon might be explained by the interaction of inflammation and malnutrition [57]. Moreover, the dialysis technique, selection of dialysate, and repeated use of heparin may contribute to additional disruptions in lipid homeostasis among patients undergoing maintenance hemodialysis. Additionally, substantial protein loss and glucose loading from the peritoneal dialysate (PD) both have an impact on lipid metabolism in patients undergoing PD [23]. A specialized clinical cohort may be more suitable for the assessment of this subset of patients.

Our study confirmed the relationship between MHR and CKD risk in a general community population. More importantly, the association remained statistically significant after adjusting for confounding variables. These results were consistent with previous studies. However, previous studies have their limitations due to the small clinical sample sizes and different ethnic groups. According to our knowledge, this is

the first study to explore the relationship between MHR and the prevalence of CKD in a large general Chinese community population. This will help us identify high-risk groups of CKD early and then follow up.

We acknowledge several limitations in our research. Firstly, the definition of CKD was based on a single measurement in this study. Existing epidemiological studies aiming to investigate the prevalence of CKD usually assess the eGFR and proteinuria of each participant once due to practical considerations, as taking repeated measurements is time-consuming and expensive [31,32,58]. It's important to note that a single measurement of eGFR in CKD diagnosis has a false positive rate of approximately 30%, which is even higher for albuminuria [59]. Secondly, we assessed the proteinuria using a urine dipstick test in the study. However, many factors can influence the excretion of proteinuria including obesity, age, posture, and others, leading to wide fluctuations, hence false positivity of proteinuria [59]. Previous researches have substantiated that using a threshold of urine protein ≥1+ could significantly decrease the chances of false positives [60]. Thirdly, as a retrospective study, this research lacked information on certain potential confounding factors, such as acute infections, history of kidney transplantation, the presence of inflammatory diseases such as lupus or vasculitis, and inflammatory markers (C-reactive protein, etc.). Further investigations with additional data support are needed to assess the generalizability of our findings to other CKD populations. To address these shortcomings in this research, we have established a cohort to enhance the credibility and persuasiveness of the study's findings. The results from this validation cohort support our study's conclusions, with details available in the supplementary materials section.

In conclusion, we demonstrated that MHR values were independently associated with CKD prevalence in the general population of the Chinese community. Since MHR combines monocytes and HDL-C, an increased MHR can represent an enhanced inflammatory response and dyslipidemia response in CKD and may predict poor outcomes of CKD. As MHR measurement is cheap and convenient, it might serve as a useful clinical tool for risk stratification, offering valuable insights to inform preventive and therapeutic approaches for clinicians in their routine medical practice. Further prospective clinical research is necessary to verify the causal relationship and potential pathophysiological mechanisms between MHR and the progression of CKD in the future.

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Authors contributions

JY guaranteed the complete integrity of this research. JY, YZ, and PW designed this study. LX, DL, JL, and ZS were responsible for carrying out the clinical studies. LX, JL, DL, and ZS all contributed to gathering the data. Data analysis and manuscript writing were performed by LX and PW. The paper was revised by JY after being edited by YZ. All authors have reviewed and given their approval to the final manuscript. LX and DL contributed to this work equally.

Consent form

All coauthors and participants have approved this paper for publishing in Renal Failure.

Ethical approval

The Medical Ethics Committee of the Second Affiliated Hospital of Nanjing Medical University approved this study (ID: [2019]KY105).

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

The datasets used in this work are accessible upon reasonable request from the corresponding author.

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