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ORIGINAL RESEARCH

Association Between Monocyte-to-High-Density Lipoprotein Ratio and Prediabetes: A Cross-Sectional Study in Chinese Population

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Background: The monocyte-to-high-density lipoprotein cholesterol (MHR) ratio has been linked to metabolic disorders. However, there is limited research on the predisposition to MHR and prediabetes. Hence, we conducted a study to investigate the relationship between MHR and the prevalence of prediabetes.

Methods: In total, 85,293 participants were included in our cross-sectional observational study. Multivariable regression analysis, subgroup analyses, and interaction testing were used to determine the relationship between MHR and prediabetes. To explore the non-linear association of MHR with prediabetes risk, generalized additive model (GAM) and smoothing splines were applied. The threshold effect analysis of MHR on the risk of prediabetes was further employed to identify the turning point.

Results: After controlling for covariates, the results indicated that a positive correlation persisted between MHR and prediabetes (odds ratio (OR) =1.64, 95% confidence interval (CI), 1.48–1.82), and subgroup analyses found a more robust correlation between MHR and prediabetes in individuals with lower age, SBP, DBP, TG, TC and higher values of BMI and LDL-C than in their counterparts. Additionally, the correlation between MHR and the risk of prediabetes was found to be non-linear, with a turning point of −0.4 (Log-Likelihood Ratio, P< 0.001). The impact of variables on the two sides of the turning point were 1.94 (1.72, 2.19) and 0.88 (0.69, 1.14).

Conclusion: The positive correlation between MHR and the risk of prediabetes in Chinese participants was observed to be non-linear, and MHR ≤ −0.4 was strongly positively correlated with prediabetes risk.

Keywords: prediabetes, monocyte-to-high-density lipoprotein ratio, non-linear relationship, inflammation

Introduction

Prediabetes refers to a stage where an individual's blood glucose levels are higher than the normal reference range, but have not yet reached the diagnostic criteria for diabetes.[1] According to the 2015–2017 epidemiological survey on diabetes in adults in China, the prevalence of prediabetes among Chinese adults was approximately 35.2% (95% CI, 33.5% to 37.0%).[2] As an important risk factor of developing diabetes, the annual conversion rate from prediabetes to diabetes was estimated to be around 5–10%,[3] although some patients with prediabetes remained stable or converted back to normal.[4] Significantly, individuals with prediabetes are at a heightened risk of developing numerous complications typically associated with diabetes in the future, including cardiovascular and diabetic kidney disease, diabetic retinopathy, and neuropathy.[5–8] The swiftly escalating global prevalence of prediabetes, coupled with its associated

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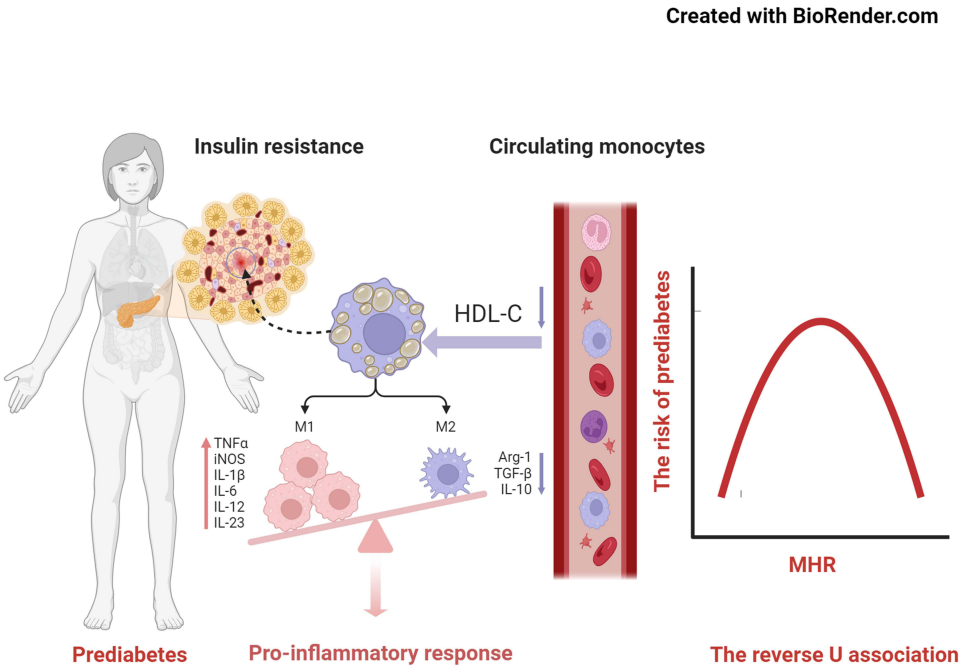
Graphical Abstract



complications, positions blood glucose disorders as a significant public health issue. Thus, it becomes crucial to pinpoint early interventions that could prevent the progression of prediabetes to diabetes and its subsequent complications.

Emerging evidence has suggested that inflammatory responses have a vital part in the pathogenesis of glucose metabolism disorders.[9] Prediabetes is a condition that characterized by high inflammatory burden.[10] Several inflammatory factors have been found to be connected with the risks of prediabetes, such as neutrophil-to-lymphocyte ratio(NLR),[11] white blood cell (WBC),[12] C-reactive protein (CRP),[13] NLRP3 inflammasome,[14] various interleukins (IL-1β, IL-6, TNF-α, and IL-18),[15–17] and an increase in number and activation of monocytes.[15,18] Similarly, high density lipoprotein (HDL) based inflammation markers are associated with inflammatory diseases such as hypertension,[19] hepatosteatosis,[20] diabetes mellitus type 2 (T2DM),[21] thyroiditis,[22] metabolic syndrome,[23] diabetic kidney disease,[24] and prediabetes.[25,26] Furthermore, MHR is also linked with inflammatory conditions.[27] Given these results, it would be reasonable to study MHR in prediabetes. However, the evidence regarding the role of MHR in the progression of prediabetes is unclear. To address this knowledge gap, we conducted a multi-centered, cross-sectional study to explore the association between MHR and prediabetes.

Materials and Methods

Study Population

The investigation was a national population-based, multi-centered and cross-sectional observational study, including the routine health checkup data of 3,652,054 participants, involving 49 hospitals from 10 provinces, covering widely seven geographic regions (North, North-East, Central, South, East, North-West, and South-West regions) in China. The data are available from 6 hospitals. A total of 135,299 study participants with measurements of MHR, Hemoglobin A1c (HbA1c) and fasting plasma glucose (FPG) were initially included in the survey. The following exclusion criteria were applied: 1) missing information for height and weight; 2) age < 18 years old or missing data; 3) history of diabetes or a diagnosis of diabetes; 4) pregnancy, infectious disease, cancer, or coronary artery disease; 5) severe liver or kidney diseases; 6)

extremely abnormal WBC (>20×10^9/L or <1.0×10^9/L); 7) abnormal or extreme values of MHR; 8) extreme body mass index (BMI) values (<15 or >55 kg/m^2). Finally, 85,293 subjects were included in the analysis. (Figure 1).

The Ethics Committee of Shandong Provincial Hospital granted ethical approval for this study, and all procedures were carried out according to the guidelines specified in the Declaration of Helsinki. In this research, participants were not required to provide written informed consent. Regarding the application for the waiver of informed consent, we have received approval from the Ethics Committee for Biomedical Research Involving Humans at Shandong Provincial Hospital (SWYX: NO. 2022–028). As the study was a retrospective analysis based on previously collected data, the need for formal patient consent was avoided. Throughout the study, it was particularly important that no areas related to patient privacy were violated or interfered with. The practice of this study strictly adheres to the ethical guidelines and management regulations related to the retrospective study. We have taken great care to ensure that the data we use is maintained to the maximum extent possible in terms of patient privacy and confidentiality.

Variables

The MHR can be assessed by dividing the monocyte count by the level of HDL. Based on the diagnostic criteria for prediabetes established by the Expert Consensus on Intervention for Prediabetes in Chinese Adults (2023 edition) according to the World Health Organization (WHO) in 1999 and the American Diabetes Association (ADA) 2022 guidelines,[3,28] the diagnostic criteria for prediabetes in Chinese adults are as follows: a fasting blood glucose level between 6.1mmol/L and <7.0mmol/L, or a glycated hemoglobin (HbA1c) level between 5.7% and 6.4%. If an individual meets either of these criteria, they can be diagnosed with prediabetes. However, if the fasting blood glucose level is <6.1mmol/L and the HbA1c level is <5.7%, it indicates a normal blood glucose (NG) level. The covariates included age, gender, BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), triglycerides (TG), low-density lipid cholesterol (LDL-C), serum creatinine (Scr), uric acid (UA), FPG and WBC. The data were collected through a standardized process.

Statistical Analysis

Based on whether the data follows a normal distribution, continuous variables are shown as mean ± SD or median (interquartile range). Categorical variables are presented as frequencies and percentages. The MHR was a skewed distribution, when the MHR was log10-transformed, a normality analysis was conducted in the study. For comparisons between groups, Student's *t*-test or Mann–Whitney *U*-test for continuous variables, the chi-square tests for categorical

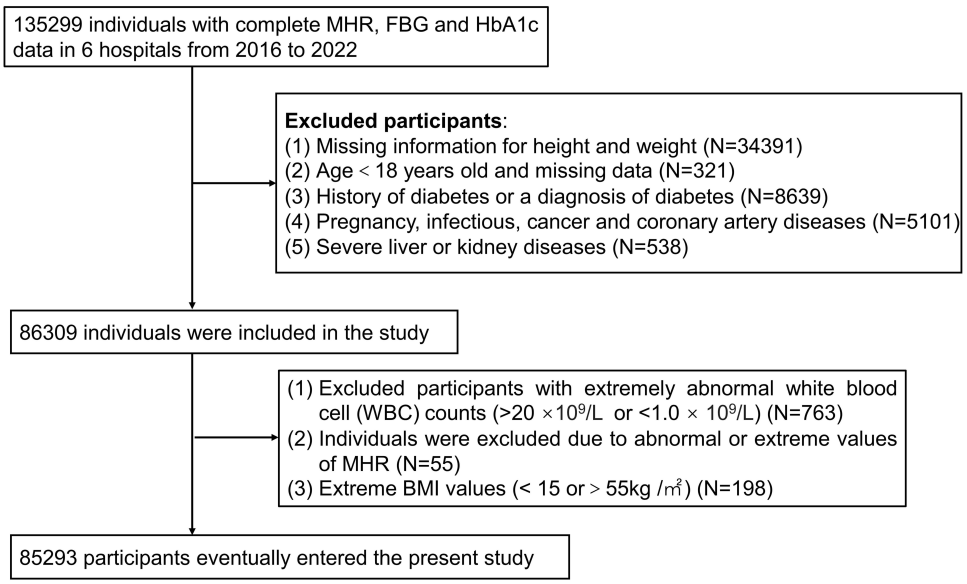


Figure 1 Study flow chart.

variables. The relationship between MHR and prediabetes was assessed via multivariate logistic regression to calculate OR and 95% CI. Model 1 was unadjusted data. In Model 2, the data were adjusted for age, gender, BMI. In Model 3, the results were adjusted for age, gender, BMI, SBP, DBP, Scr, UA, TG, TC, LDL-C, FPG, WBC.

We performed subgroup analyses using stratified factors, including age (<45, 45–60, >60 years), gender, BMI (18.5–23.9, 24–27.9, >28kg/m²), SBP (<140, ≥140 mmHg), DBP (<90, ≥90 mmHg), TG (<1.7, ≥ 1.7 mmol/L), TC (<5.2, ≥5.2mmol/L), LDL-C (<3.4, ≥3.4 mmol/L). The interaction test in the logistic regression model was employed to compare the OR among the various examined subgroups. A generalized additive model (GAM) with penalized smoothing splines was leveraged to investigate the nonlinear association between MHR and prediabetes. To dissect the threshold effect, we used the piecewise regression model and the logarithmic likelihood ratio test with the goal of identifying the inflection points on the curve and analyzing the effect in a piecewise manner. Subgroup analyses also employed a GAM.

Statistical analyses were performed using R software (version 4.2.3, http://www.R-project.org/) and SPSS (v.25.0; IBM Corporation, Armonk, New York, USA). Two-tailed P value below 0.05 was considered statistically significant.

Results

Sample Characteristics

The clinical attributes of 85,293 participants were classified based on the presence or absence of prediabetes. The mean age was 50.29 ± 13.24 years and 63.88% were male. 33,992 participants (39.85%) were diagnosed with prediabetes. Compared with NG, patients with prediabetes tended to be older, female, higher levels of BMI, SBP, DBP, HbA1c, FPG, Scr, ALT, TG, UA, WBC and MHR. (Table 1). Subjects were also divided into four groups based on MHR quartiles. Compared with the low MHR group, the high MHR group were older and had higher levels of BMI, SBP, DBP, HbA1c, FPG, Scr, ALT, TG, UA, WBC, and monocytes, but had lower levels of TC, LDL-C, HDL-C (Supplementary Table 1). Furthermore, the prevalence of prediabetes was higher with increasing MHR quartile (Figure 2).

Table 1 Baseline Characteristics of Study Participants

Characteristics	NG (n=51,301)	Prediabetes (n=33,992)	P value
Age (years)	47.58±12.87	54.38±12.74	<0.001
Gender			
Male	32,477 (63.31%)	22,005 (64.74%)	<0.001
Female	18,824 (36.69%)	11,987 (35.26%)	<0.001
BMI (kg/m²)	24.23 (22.08, 26.37)	24.88 (22.85, 27.00)	<0.001
SBP (mmHg)	124.38±17.32	128.95±18.17	<0.001
DBP (mmHg)	77.07±12.14	78.92±11.96	<0.001
HbA1c (%)	5.37±0.22	5.92±0.20	<0.001
FPG (mmol/L)	5.03±0.46	5.29±0.62	<0.001
Scr (μmol/L)	69.60 (59.20, 79.00)	70.00 (60.00, 79.60)	<0.001
ALT (U/L)	20.00 (14.00, 29.00)	21.00 (15.00, 30.00)	<0.001
TG (mmol/L)	1.32 (0.93, 1.90)	1.46 (1.06, 2.08)	<0.001
TC (mmol/L)	4.81±0.95	4.93±1.03	<0.001
HDL-C (mmol/L)	1.30±0.32	1.27±0.31	<0.001
LDL-C (mmol/L)	2.91±0.79	3.02±0.85	<0.001
UA (μmol/L)	342.18±88.66	352.55±88.12	<0.001
WBC (10^9/L)	5.70 (4.83, 6.70)	5.82 (4.95, 6.88)	<0.001
MHR	0.30 (0.21, 0.40)	0.32 (0.23, 0.42)	<0.001

Note: Data are shown as number (%) for categorical variables and mean ± SD or median (interquartile range) for continuous variables.

Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, Hemoglobin A1c; FPG, fasting plasma glucose; Scr, serum creatinine; ALT, alanine aminotransferase; TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipid cholesterol; UA, uric acid; WBC, white blood cell; MHR, monocyte-to-high-density lipoprotein ratio.

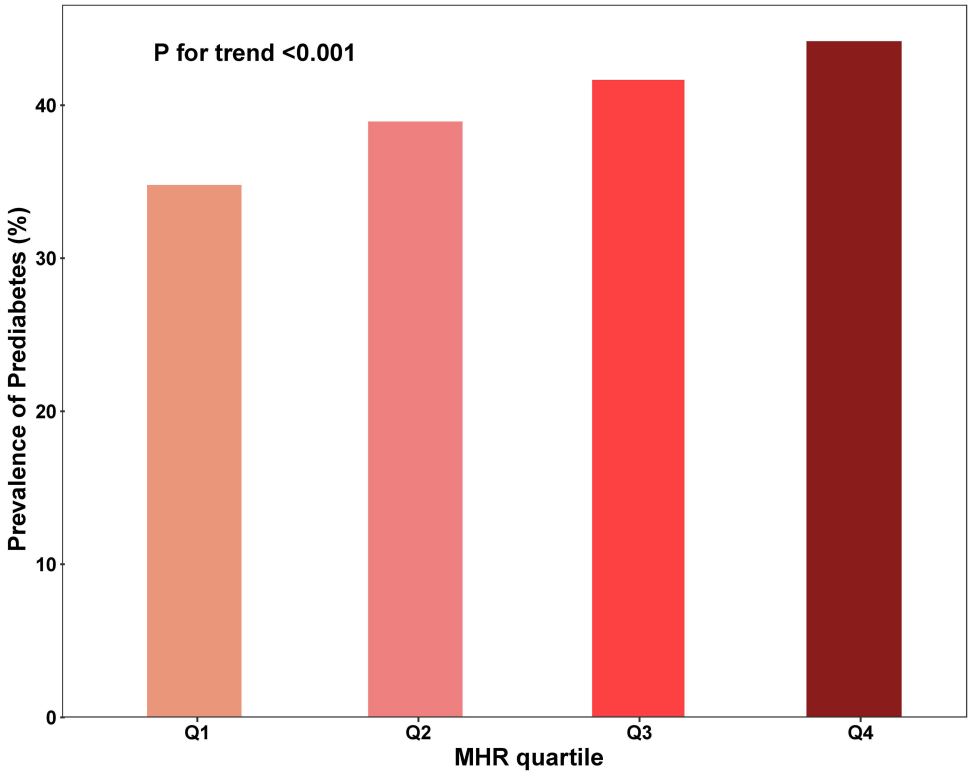


Figure 2 Prevalence of Prediabetes stratified according to MHR categories.
Notes: MHR was divided into quartiles with the following values: Q1 ≤ −0.67; −0.67 < Q2 ≤ −0.52; −0.52 < Q3 ≤ -0.39; Q4 > −0.39.
Abbreviations: MHR, monocyte-to-high-density lipoprotein ratio, MHR value was log10-transformed.

Relationship Between MHR and Prediabetes

Table 2 showed the results of the multivariable regression analysis between MHR and prediabetes. This relationship was expressed to be significant in both the non-adjusted model (OR= 2.19; 95% CI), 2.04–2.31; P < 0.001) and the minimally-adjusted model (OR = 1.72; 95% CI, 1.59–1.87; P < 0.001). A positive correlation between MHR and prediabetes was still evident in the fully controlled model (OR = 1.64; 95% CI, 1.48–1.82, P < 0.001). This means that a one-unit increase in MHR corresponded to a 64% increase in prediabetes prevalence. Moreover, the trend remained statistically significant

Table 2 The Association Between MHR and Prediabetes

	Model 1		Model 2		Model 3	
	ORs (95% CI)	**P value**	**ORs (95% CI)**	**P value**	**ORs (95% CI)**	**P value**
Log-MHR	2.19(2.04,2.34)	<0.001	1.72(1.59,1.87)	<0.001	1.64(1.48,1.82)	<0.001
Q1 (≤ −0.67)	Ref		Ref		Ref	
Q2 (−0.67, −0.52)	1.20(1.15,1.25)	<0.001	1.12(1.08,1.17)	<0.001	1.10(1.05,1.15)	<0.001
Q3 (−0.52, −0.39)	1.34(1.29,1.40)	<0.001	1.22(1.17,1.28)	<0.001	1.19(1.13,1.25)	<0.001
Q4 (> -0.39)	1.49(1.43,1.55)	<0.001	1.22(1.17,1.28)	<0.001	1.22(1.15,1.29)	<0.001
P for trend	<0.001		<0.001		<0.001	

Notes: Model 1: non-adjusted model; Model 2: adjusted for age, gender, BMI; Model 3: additionally adjusted for SBP, DBP, Scr, UA, TG, TC, LDL-C, FPG, WBC.
Abbreviations: ORs, odds ratios; CI, confidence interval; Ref, reference; MHR, monocyte-to-high-density lipoprotein ratio, MHR value was log10-transformed.

when MHR was converted into a categorical variable (quartiles). Compared with Q1 in the unadjusted model, the MHR in Q4 was connected with an increased risk of prediabetes (crude OR, 1.49; 95% CI, 1.43–1.55, P < 0.001). After accounting for confounders, the association has been impaired but still remains significant (adjusted OR=1.29; 95% CI, 1.23–1.35, P < 0.001) (adjusted OR=1.22; 95% CI, 1.15–1.29, P < 0.001).

Subgroup Analyses

The subgroup analysis identified variations in the association between MHR and the risk of prediabetes across diverse stratified factors. A slightly stronger association was observed in individuals with lower age, SBP, DBP, TG, TC and higher levels of BMI and LDL-C than in their counterparts. On the other hand, a weaker correlation was observed in participants with higher levels of age, SBP, DBP, TG, TC and lower levels of BMI and LDL-C. Interaction tests were used to evaluate how age, BMI, SBP, DBP, TG, TC, and LDL influenced the positive relationship between MHR and prediabetes. The results showed that these variables produced statistically significant interactions (All P for interaction < 0.05) (Table 3).

The Non-Linear Association Between MHR and Prediabetes

We employed GAM with smoothing splines to further analyze the correlation between MHR and prediabetes risk. After adjusting for several confounding factors (age, gender, BMI, SBP, DBP, Scr, UA, TG, TC, LDL-C, FPG, WBC), we discovered a significant nonlinear connection between MHR and prediabetes (Figure 3), with an inverted U-shaped curve. Simultaneously, we identified the inflection point of MHR was −0.4 by two-piecewise linear regression model (P < 0.001).

Table 3 Subgroup Analysis for the Association Between MHR and Prediabetes

Characteristic	No. of Participants	OR (95% CI)	P value	P for Interaction
Age (years)				<0.001
<45	27,412	3.27(2.76,3.87)	0.001	
45–60	40,605	1.60(1.39,1.86)	<0.001	
>60	17,276	1.25(1.02,1.52)	0.028	
Gender				0.487
Male	30,811	1.67(1.46,1.90)	<0.001	
Female	54,482	1.66(1.43,1.93)	<0.001	
BMI (kg/m²)				<0.001
18.5–23.9	35,419	1.67(1.45,1.91)	<0.001	
24–27.9	35,922	1.53(1.30,1.79)	<0.001	
≥28	12,019	2.09(1.61,2.72)	<0.001	
SBP (mmHg)				<0.001
<140	67,377	1.74(1.55,1.96)	<0.001	
≥140	17,916	1.34(1.08,1.67)	0.008	
DBP (mmHg)				<0.001
<90	70,946	1.74(1.55,1.94)	<0.001	
≥90	14,347	1.40(1.11,1.78)	0.005	
TG (mmol/L)				<0.001
<1.7	55,659	1.70(1.49,1.93)	<0.001	
≥1.7	29,634	1.53(1.29,1.81)	<0.001	
TC (mmol/L)				<0.001
<5.2	56,783	1.83(1.62,2.07)	<0.001	
≥5.2	28,510	1.70(1.44,2.00)	<0.001	
LDL-C(mmol/L)				
<3.4	22,954	1.71(1.42,2.06)	<0.001	<0.001
≥3.4	62,339	1.82(1.63,2.04)	<0.001	

Notes: Each model was adjusted for age, gender, BMI, SBP, DBP, FPG, Scr, TG, TC, LDL-C, UA, WBC. In each case, the model is not adjusted for the stratification variable. MHR value was log10-transformed.

Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglycerides; TC, total cholesterol; LDL-C, low-density lipid cholesterol; MHR, monocyte-to-high-density lipoprotein ratio.

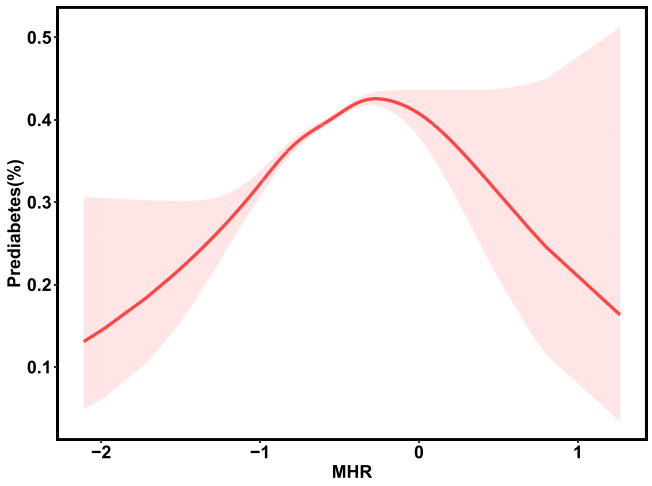


Figure 3 Association between MHR and the prevalence of prediabetes.
Notes: GAM with smooth curve fitting for the nonlinear association between MHR and the prevalence of prediabetes. Adjusted for age, gender, BMI, SBP, DBP, Scr, UA, TG, TC, LDL-C, FPG, WBC.
Abbreviations: MHR, monocyte-to-high-density lipoprotein ratio, MHR value was log10-transformed.

When the turning point was ≤ −0.4, MHR had a positive connection with prediabetes risk (OR=1.94; 95% CI, 1.72–2.19, P < 0.001). However, it is important to note that when the turning point was above −0.4, the correlation between MHR and prediabetes did not demonstrate statistical significance (OR = 0.88; 95% CI 0.69–1.14; P = 0.348), as evidenced by the data presented in Table 4. Besides, in the subgroup analysis stratified by age, gender, BMI, SBP, DBP, TG, TC, and LDL, the non-linear relationships between MHR and the risk of prediabetes still existed (Supplementary Figure 1).

Discussion

For the first time, this cross-sectional study demonstrated that a higher value of MHR was connected with the escalated risk of prediabetes in a Chinese sample. Besides, the results of the subgroup analyses and interaction testing indicated that lower levels of age, SBP, DBP, TG, TC and higher levels of BMI and LDL-C strengthened MHR-associated prediabetic risks. An inverted U-shape relationship between MHR and prediabetes was also discovered, with an inflection point of −0.4. When MHR ≤ −0.40, MHR is an independent risk factor for prediabetes.

The pathological characteristics of prediabetes, particularly insulin resistance (IR) and β-cell dysfunction, make it a crucial period for early intervention and prevention.[29,30] Previous evidence suggested that inflammation contributed to the development of IR and impaired pancreatic β-cell function.[31–33] Proteomics indicated that the changes in pancreatic function during prediabetes was largely associated with the activation of immune cells from congenital and acquired immunity.[34] Long-term chronic inflammation associated with glucose and lipid metabolism can recruit monocytes in the circulation to migrate to tissues and organs which regulate insulin sensitivity, and then differentiate into tissue-resident

Table 4 Threshold Effect Analysis of MHR on Prediabetes Using a Two-Piecewise Linear Regression Model

	Prediabetes OR (95% CI)	P value
Fitting model by standard linear regression	1.64 (1.48, 1.82)	<0.001
Fitting model by two-piecewise linear regression		
Inflection points of MHR	−0.40	
≤ −0.40	1.94 (1.72, 2.19)	<0.001
> −0.40	0.88 (0.69, 1.14)	0.348
P for log likelihood ratio test	0.001	

Note: Each model was adjusted for age, gender, BMI, SBP, DBP, Scr, UA, TG, TC, LDL-C, FPG, WBC.
Abbreviations: OR, odds ratio; CI, confidence; MHR, monocyte-to-high-density lipoprotein ratio, MHR value was log10-transformed.

macrophages to exacerbate inflammatory responses and tissue function damage.[35] Consequently, circulating monocytes may be important indicators for reflecting tissue-related inflammation activation.

As the MHR rose, there was a corresponding increase in risks for metabolic syndrome, diabetes mellitus, coronary artery disease, and nonalcoholic fatty liver disease.[36–40] Recent observational studies suggested that the MHR as an independent factor could predict long-term prognosis in Takayasu arteritis.[41] In addition, MHR has been indicated to have greater diagnostic significance in conditions such as tuberculosis and osteoarthritis.[42,43] In the prediabetic stage, an increase in monocytes count and pro-inflammatory subtypes has been observed.[18] In a 5-year cohort study, it was found that the dysregulation of circulating immune cells and inflammatory factors was associated with dynamic disruptions in glucose metabolism. In particular, innate immune cells, such as granulocytes and monocytes, exhibited a significant and progressively increasing risk for prediabetes and diabetes.[15] It has been observed that there was an increase in pro-inflammatory CD14 and CD18 monocytes, as well as recruiting factors and inflammatory cytokines such as CRP and TNF-α in prediabetes and diabetes.[44] When HDL-C levels was low, there was an accumulation of cholesterol within monocytes, leading to enhanced activation of signaling pathways and resulting in a more severe inflammatory response produced by monocytes.[45–47] A large prospective cohort study in Tangshan, North China, has shown that metabolic inflammation evaluated by the Cumulative MHR, was a valuable complement to hsCRP for a more thorough evaluation of inflammatory risk in the development of T2DM.[38] Simultaneously, interventions targeting inflammation have demonstrated efficacy in improving IR and potentially reversing prediabetes. Several studies suggested that interventions like exercise, weight loss, dietary modifications, and medication interventions can effectively reduce inflammation and immune responses in individuals with prediabetes.[48–51] Therefore, MHR might contribute to the progression of prediabetes and its conversion to T2DM.

In the present study, we found that each unit in the MHR increased the risk of prediabetes by 64% (OR: 1.64 95% CI 1.48–1.82, P<0.001), after adjusting for age, gender, BMI, SBP, DBP, Scr, UA, TG, TC, LDL-C, FPG, WBC. It was the first study to find a correlation between MHR and prediabetes, which may provide valuable insight into the primary prevention of prediabetes.

Additionally, in subgroup analyses, a more robust correlation was noticed in individuals with lower age, SBP, DBP, TG and TC, and higher values of BMI and LDL-C than in their counterparts. These variables may change the association between MHR and prediabetes. Clinically, by intervening with the levels of SBP, DBP, BMI, TG, TC, and LDL-C, it's feasible to lower the risk of prediabetes by changing the degree of the correlation between MHR and prediabetes.

Moreover, we observed a nonlinear relationship between MHR and the risk of prediabetes. The turning point was −0.4 after controlling for confounding variables (age, gender, BMI, SBP, DBP, Scr, UA, TG, TC, LDL-C, FPG, WBC). When the MHR was ≤ −0.4, a 1-unit increase in MHR levels was correlated to a 94% increase in adjusted OR of prediabetes risk (OR: 1.94, 95% CI: 1.72–2.19, P < 0.001). However, when MHR was > −0.4, there was no correlation with prediabetes risk (OR = 0.88, 95% CI 0.69–1.14; P = 0.348). The reason may be that variables other than MHR also affected prediabetes. In comparison with the MHR ≤ −0.4 group, participants in the MHR > −0.4 group displayed higher average levels of age, BMI, SBP, DBP, Scr, TG, LDL-C, UA, WBC and a greater percentage of males. Nevertheless, the noted indicators were strongly associated with prediabetes. When MHR was > −0.4, owing to the existence of these prediabetes risk factors, MHR had a mild impact on prediabetes risk. Conversely, when MHR was below −0.4, the lower levels of related risk factors such as age, BMI, SBP, DBP, Scr, TG, LDL-C, UA, and WBC were found in prediabetes, and the influence on prediabetes was lessened, during which the relative impact of MHR was seen to be strengthened (Supplementary Table 2).

In our study, we discerned a non-linear relationship and found a critical juncture between MHR and the risk of prediabetes. Notably, in individuals with a lesser metabolic risk profile, we observed a substantial relationship between MHR and prediabetes under mildly inflammatory conditions. Despite the high prevalence of prediabetes, it often remains undiagnosed in clinical practice. The practical application of MHR coupled with identifying the pivotal point, could prove to be invaluable tools for both prevention and early detection of prediabetes. Furthermore, our study provides compelling evidence for interventions aimed at addressing inflammation.

Prediabetes is a condition characterized by marked by heightened systemic inflammation.[10] This condition's link to the MHR, a key marker of inflammation, is therefore of notable interest. Monocytes can migrate to sites of inflammation

or infection, which amplifies the inflammatory response, leading to tissue damage and exacerbated insulin resistance, a cardinal trait of prediabetes.[15,18,32] On the other hand, HDL-C serves a crucial anti-inflammatory role.[52] A decline in HDL-C concentrations heightens the inflammatory status within the body. In essence, the association between prediabetes and MHR likely stems from inflammation, which reinforces the potential value of MHR in prediabetes, particularly in assessing the risks associated with inflammation.

Our research possesses several strengths. Firstly, we used a relatively large sample size and included individuals from different centers. Secondly, through the application of GAM and smoothing splines, our study primarily unveiled a significant non-linear relationship between MHR and the risk of prediabetes. Thirdly, we executed meticulous statistical adjustments to reduce the impact of potential confounders. Moreover, subgroup analyses were carried out to identify potential confounding variables which could change the relationship between MHR and prediabetes.

Our study has several limitations. Firstly, the absence of oral glucose tolerance tests (OGTTs) may lead to an underestimation of prediabetic cases. Secondly, given the cross-sectional design of the study, it was not feasible to determine a causal relationship between the variables studied. In the future, prospective research will be necessary to validate the potential causality. Thirdly, despite controlling for confounding factors such as SBP, DBP, BMI, TC, LDL-C, there could still be confounding factors that are not controlled or measured, including dietary habits, exercise, smoking and alcohol intake. These factors may influence the observed associations and should be considered in future research.

Conclusions

There was a threshold effect between MHR and prediabetes. When MHR was < -0.4, there was a substantial and positive correlation observed in relation to the risk of prediabetes. This study for the first time provided epidemiological insights into the association between MHR and prediabetes. Particularly in participants at low risk of prediabetes, targeted assessment and management of MHR can significantly decrease the risk of prediabetes when MHR is below the inflection point.

Ethics Statement

The Ethics Committee of Shandong Provincial Hospital granted ethical approval for this study, and all procedures were carried out according to the guidelines specified in the Declaration of Helsinki. In this research, participants were not required to provide written informed consent.

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Disclosure

The authors declare no competing interests in this work.

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