Original Article

Relationship of Inflammation and Endothelial Dysfunction with Risks to Cardiovascular Disease among People in Inner Mongolia of China*

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Abstract

Objective To explore the relationship of inflammation and endothelial dysfunction with risks to cardiovascular disease (CVD).

Methods Blood pressure, body weight, body height, waist circumference and lifestyle risk factors were measured and studied among 2589 participants in Inner Mongolia of China, and biomarkers of inflammation and endothelial dysfunction including high-sensitivity C-reactive protein (hsCRP), soluble inter-cellular adhesion molecule-1 (sICAM-1), soluble E-selectin (sE-selectin), and angiotensin II were investigated.

Results Subjects with metabolic risk factors for CVD had higher levels of hsCRP, sE-selectin and sICAM-1 than those without such risk factors (all $P<0.05$). Levels of all biomarkers positively and significantly increased with aggregation of the metabolic risk factors among the subjects (all P for trend <0.001). Data from the multivariate analysis showed that participants with high levels of hsCRP [odds ratio (OR): 1.96, 95% confidence interval (CI): 1.52-2.53], sE-selectin (OR: 1.35, 95% CI: 1.05-1.72), and angiotensin II (OR: 1.81, 95% CI: 1.40-2.33) were more likely to develop hypertension; participants with high levels of hsCRP (OR: 2.33, 95% CI: 1.85-2.94), sE-selectin (OR: 1.24, 95% CI: 1.00-1.54), and sICAM-1 (OR: 1.70, 95% CI: 1.30-2.22) were more likely to develop dyslipidemia, and those with high levels of hsCRP (OR: 2.95, 95% CI: 2.27-3.83) and sICAM-1(OR: 2.80, 95% CI: 2.06-3.80) were more likely to develop hyperglycemia.

Conclusion Biomarkers of inflammation and endothelial dysfunction were separately associated with relevant metabolic risk factors for CVD. And appropriate measures should be taken to control inflammation and improve endothelial function among individuals with different metabolic risk factors for CVD.

Key words: Cardiovascular disease; Endothelial dysfunction; Inflammation; Risk factors

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INTRODUCTION

Cardiovascular disease (CVD) has become a prevalent health concern worldwide that results in major health care costs[1]. Hypertension, hyperglycemia, dyslipidemia, and obesity are well recognized as the major metabolic risk factors for CVD[2] and are the leading global causes of death[1,3].

The endothelium is the organ targeted by metabolic risk factors for CVD and may be the origin of vascular inflammation reactions[4]. Recent studies showed that inflammation and endothelial dysfunction were the novel risk factors related to atherosclerosis and CVD[5-6]. Moreover, it was demonstrated that CVD risk factors were associated with inflammation and endothelial dysfunction[7-11]. However, most of these studies mentioned above were conducted in populations in Western countries and failed to take all the known confounders such as alcohol consumption[7], obesity[9], and hyperglycemia[10] into consideration. The exclusive relationships of inflammation and endothelial dysfunction with metabolic risk factors for CVD have not been extensively studied in Asian populations. Most of endothelial proteins lack exclusive expression and its formation is conditionally based on different stimulations[12]. Clear understanding of the relationships of inflammation and endothelial dysfunction with metabolic risk factors related to CVD is necessary and may help promote CVD prevention. The aim of the present study is therefore to explore the relationships between plasma levels of high-sensitivity C-reactive protein (hsCRP), soluble inter-cellular adhesion molecule-1 (sICAM-1), soluble E-selectin (sE-selectin) and angiotensin II, and metabolic risk factors for CVD among people in Inner Mongolia of China.

MATERIALS AND METHODS

Participants

A cross-sectional study was conducted between 2002 and 2003 in Inner Mongolia, an autonomous region in north China, bordering Mongolia and Russia. The selection of the participants and data collection were based on the methods as previously reported[13]. A survey was conducted in 32 villages in two adjacent townships located in Kezuohou Banner county and Naiman Banner of Inner Mongolia. The majority of local residents were Mongolians who had lived there for many generations and maintained their traditional diet and lifestyle. The study population consisted of both farmers and herdsmen whose diets were high in fat and salt. A previous study reported a mean (standard deviation) of dietary sodium intake to be about 16.3 (12.6) grams per day in the population for the present study[14]. The selection criteria for the participants are as followed: (1) age: ≥20 years, (2) ethnicity: Mongolian, (3) no clinical evidence of end-organ damage, such as angina pectoris, myocardial infarction, heart failure, stroke, hypertensive encephalopathy, retinal hemorrhage, and renal failure, (4) no chronic renal diseases or tumors. Out of 3475 eligible individuals who lived in the villages, a total of 2589 of them were selected to participate in the present study. This study was approved by the Soochow University Ethics Committee and other corresponding regulatory institutions in China. Written informed consent was obtained from all the participants.

Data Collection

Data on demography, lifestyle, family history of hypertension and personal medical records were collected using a standard questionnaire by trained staffs. Smokers among the participants were defined as smoking at least one cigarette per day for 1 year or more. Alcohol consumers were defined as consuming one or more alcoholic drinks per week during the last three years.

Body weight and height were measured by using a regularly calibrated stadiometer and balance-beam scale with participants wearing light clothing and no shoes. Body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters. Waist circumference (WC) was measured at the level of 1 cm above the umbilicus. For this analysis, overweight or obesity was defined as BMI ≥24 kg/m^2 and central obesity was defined as WC ≥85 cm for men and as WC ≥80 cm for women, referring to the recommendations of the Working Group on Obesity in China[15]. Three sitting consecutive blood pressure (3 min between each) measurements were done by trained observers using a standard mercury sphygmomanometer according to a standard protocol after a rest for 30 min. The first and fifth Korotkoff sounds were recorded as systolic blood pressure (SBP) and diastolic blood pressure (DBP), respectively. The mean of the three readings was calculated for onwards analysis. Hypertension was defined as SBP at least 140 mmHg and/or DBP at least 90 mmHg

and/or under antihypertensive medication in the last 2 weeks[16].

Blood samples were collected in the morning after at least 8 h of fasting. All plasma and serum samples were frozen at -80 °C until laboratory use. Fasting plasma glucose (FPG) was measured using a modified hexokinase enzymatic method and hyperglycemia was defined as FPG ≥5.6 mmol/L or having already been diagnosed with diabetes[17]. Concentrations of total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), and triglycerides (TG) were assessed enzymatically on a Beckman Synchrony CX5 Delta Clinical System (Beckman Coulter, Fullerton, California, USA) using commercial reagents, and low density lipoprotein cholesterol (LDL-C) concentration was calculated by means of the Friedewald equation for participants who had less than 400 mg/dL TG[18]. Dyslipidemia was defined as TC ≥6.22 mmol/L and/or TG ≥2.26 mmol/L and/or LDL-C ≥4.14 mmol/L and/or HDL-C <1.04 mmol/L[19]. The value of hsCRP was determined by an immunoturbidimetric assay on a Beckman Synchron CX5 Delta Clinical System using commercial reagents. The value of sE-selectin and sICAM-1 was measured by an ELISA assay (R&D Systems, Minneapolis, Minnesota, USA) which employed the quantitative sandwich enzyme immunoassay technique.

For plasma angiotensin II, blood samples were collected into ice chilled tubes containing EDTA. Plasma was immediately separated by centrifugation at 4 °C and stored at -80 °C for onwards analysis. The quantitative determination of immunoreactive angiotensin II was performed by a double antibody RIA after reversed-phase sample extraction by means of phenylsilylsilica columns following the method previously reported by Emanuel et al.[20] and a commercial RIA kit. The cross-reactivity between the antiserum of angiotensin I and II was less than 0.1%. Inter-assay and intra-assay coefficients of variation were less than 5.0% and 10%, respectively. All assays were performed by professionals of Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences (Beijing, China).

Statistical Analysis

Participants with one or more of the following risk factors were defined as the participants with metabolic risk factors for CVD: (1) hypertension, (2) hyperglycemia, (3) dyslipidemia, (4) overweight or obesity, (5) central obesity, while participants with none of the above mentioned risk factors were defined as the participants without metabolic risk factors for CVD. Mean and standard deviation (SD) of normally distributed continual variables, median and interquartile range (IQR) of non-normally distributed continual variables, and proportions of categorical variables were calculated for participants with and without metabolic risk factors for CVD. And the comparison in means between these two groups was performed using a Student's *t*-test. The comparison in medians was performed using a Wilcoxon rank-sum test, and the comparison in proportions was tested using the Chi-square statistic. Age-adjusted average levels of the biomarkers of inflammation and endothelial dysfunction were calculated for participants with and without overweight or obesity, central obesity, hypertension, dyslipidemia, and hyperglycemia, respectively. For normally distributed biomarkers (sICAM-1), mean (SD) and *P* value was calculated using an age-adjusted ANOVA model. hsCRP, sE-selectin, and angiotensin II had skewed distributions, therefore medians (IQR) for each group were presented. *P* values were computed using rank order ANOVA calculations adjusting for age. In addition, all the participants were categorized into four mutually exclusive groups based on the metabolic risk factors for CVD: with no risk factors, with 1 risk factors, with 2 risk factors, and with 3 or more risk factors. The age-adjusted levels of each biomarker were calculated and the linear trend associations between the risk factors and the level of each biomarker were assessed by using an age-adjusted ANOVA model. Furthermore, all the participants were divided into three groups (<25 percentile, 25-75 percentile and >75 percentile) according to quartiles of the values of each biomarker. Odds ratio (OR) and 95% confidence interval (CI) of hypertension, dyslipidemia, hyperglycemia, overweight or obesity, and central obesity for participants with 25-75 percentile and >75 percentile of each biomarker were computed with multivariate non-conditional logistic regression models, respectively, compared with those with <25 percentile of each biomarker. Trends of increasing levels of each biomarker and ORs were assessed with categories of each biomarker as an ordinal variable. In addition to groups of each biomarker, variables like age, gender, smoking, alcohol consumption, family history of CVD, hypertension, hyperglycemia, dyslipidemia, overweight or obesity, and central obesity were used in the multivariate models. All *P* values were 2-tailed and statistical significance was defined as $P \leq 0.05$. SAS statistical software (version 9.1, Cary, North

Carolina) was used for the statistical analysis in this study.

RESULTS

Baseline characteristics of participants were presented by two exclusive categories: with and without metabolic risk factors for CVD (Table 1). Overall, 2133 participants (82%) had one or more metabolic risk factors. Participants with metabolic risk factors for CVD were older and had higher levels of FPG, TC, TG, LDL-C, SBP, DBP, BMI, WC, and lower HDL-C. They were also more likely to have increased alcohol consumption and family history of CVD, compared to those participants without metabolic risk factors. The median of hsCRP, sE-selectin, and the mean level of sICAM-1 were significantly higher among participants with risk factors for CVD. However, the median plasma concentration of angiotensin II in the participants with CVD risks factors showed no difference from those without such factors.

Age-adjusted means of inflammatory and endothelial dysfunction biomarkers were calculated for individuals with and without a metabolic risk factor for CVD. As shown in Table 2, a higher level of hsCRP, sE-selectin and sICAM-1, rather than of angiotensin II, was observed among the participants with CVD risk factors compared with those without any CVD risk factors. Levels of hsCRP and sICAM-1 were significantly higher among subjects with high level of TC, LDL-C or FPG than those without these risk factors. There was no significant difference in levels of sE-selectin and angiotensin II between participants with and without each of the three CVD risk factors. Levels of all biomarkers were significantly increased among the participants with hypertension or a high level of TG. And these results demonstrated that there was an association of different metabolic risk factors with relevant biomarkers of inflammation and endothelial dysfunction. Age-adjusted mean levels of inflammatory and endothelial dysfunction biomarkers were therefore evaluated for the participants according to the number of CVD risk factors (Table 3). The mean values of hsCRP, sE-selectin and sICAM-1 progressively and significantly increased with the number of CVD metabolic risk factors the participants had, but the level of angiotensin II was otherwise.

Table 1. Characteristics of the Participants with and without Metabolic Risk Factors[a] for Cardiovascular Disease

Variables	without Risk Factor	with Risk Factors	*P* Value
No. of subjects	456	2133	
Age, years	41.63 (10.97)	47.55 (12.49)	<0.001
Male, %	42.76	40.74	0.426
Current smoking, %	46.27	44.02	0.380
Current drinking, %	29.17	34.36	0.033
Family history of CVD, %	5.04	14.77	<0.001
Body mass index, kg/m^2	20.41 (1.83)	22.74 (3.64)	<0.001
Waist circumference, cm	75.35 (5.57)	82.66 (9.91)	<0.001
Systolic blood pressure, mmHg	114.0 (10.6)	133.2 (25.6)	<0.001
Diastolic blood pressure, mmHg	76.2 (7.0)	86.3 (13.2)	<0.001
Total cholesterol, median (IQR)	3.36 (2.90-3.90)	3.67 (2.99-4.52)	<0.001
Triglycerides, median (IQR)	0.76 (0.57-1.03)	0.99 (0.69-1.52)	<0.001
LDL cholesterol, median (IQR)	1.93 (1.51-2.43)	2.25 (1.63-2.98)	<0.001
HDL cholesterol, median (IQR)	1.25 (1.14-1.37)	1.09 (0.91-1.37)	<0.001
Fasting glucose, median (IQR)	4.4 (4.0-4.8)	5.0 (4.4-5.6)	<0.001
hsCRP, median (IQR)	4.62 (3.31-6.80)	6.49 (4.14-12.63)	<0.001
sE-selectin, median (IQR)	17.10 (13.26-23.21)	18.92 (15.17-25.14)	<0.001
Angiotensin II, median (IQR)	49.6 (39.5-72.4)	49.0 (40.0-71.1)	0.544
sICAM-1, ng/mL	301.37 (92.33)	335.01 (98.09)	<0.001

Note. Data are expressed with mean (SD) unless otherwise noted. [a]metabolic risk factors for cardiovascular disease included hypertension, hyperglycemia, dyslipidemia, overweight or obesity and central obesity. IQR, interquartile range; hsCRP, high-sensitivity C-reactive protein; sE-selectin, soluble E-selectin; sICAM-1, soluble intercellular adhesion molecule 1.

Table 2. Levels of the Inflammation and Endothelial Dysfunction Biomarkers Associated with the Metabolic Risk Factors for CVD

Risk Factor	hsCRP	sE-selectin	Angiotensin II	sICAM-1
Body mass index (BMI)				
BMI<24 kg/m^2	5.51 (3.69-10.11)	17.93 (14.38-23.74)	49.0 (40.0-71.2)	323.90 (96.62)
BMI≥24 kg/m^2	7.46 (4.78-15.41)	20.69 (15.96-27.39)	49.0 (39.0-71.3)	342.76 (100.21)
P value	<0.001	<0.001	0.771	<0.001
Waist circumference (WC)				
Low WC	5.36 (3.56-9.39)	17.62 (14.19-23.51)	48.6 (40.0-71.1)	324.95 (95.87)
High WC	7.01 (4.54-14.64)	20.10 (15.37-26.53)	49.2 (40.0-71.8)	334.52 (100.56)
P value	<0.001	<0.001	0.882	0.004
Blood pressure status				
Non-hypertensive	5.39 (3.60-9.40)	18.15 (14.31-24.26)	47.0 (39.3-66.6)	322.62 (96.67)
Hypertensive	7.43 (4.57-15.07)	19.11 (15.37-25.48)	52.0 (40.5-83.3)	339.38 (99.13)
P value	<0.001	0.001	<0.001	<0.001
Total cholesterol (TC)				
TC<6.22 mml/L	5.85 (3.92-11.16)	18.50 (14.78-24.83)	49.0 (40.0-71.0)	327.38 (97.77)
TC≥6.22 mml/L	11.63 (6.62-19.86)	19.11 (15.88-23.91)	51.0 (40.0-80.0)	377.76 (90.20)
P value	<0.001	0.227	0.592	<0.001
Triglycerides (TG)				
TG<2.26 mmol/L	5.56 (3.83-9.97)	18.15 (14.58-24.04)	48.0 (40.0-70.0)	327.22 (96.93)
TG≥2.26 mmol/L	13.64 (7.90-23.60)	22.60 (16.55-29.56)	57.8 (44.0-80.0)	343.31 (105.28)
P value	<0.001	<0.001	<0.001	0.002
Low density lipoprotein cholesterol (LDL-C)				
LDL-C<4.14 mmol/L	5.79 (3.90-10.94)	18.50 (14.78-24.96)	49.0 (40.0-71.3)	325.93 (97.42)
LDL-C≥4.14 mmol/L	11.19 (6.15-19.48)	19.21 (15.17-24.08)	46.9 (40.0-66.3)	381.20 (92.07)
P value	<0.001	0.323	0.679	<0.001
High density lipoprotein cholesterol (HDL-C)				
HDL-C≥1.04 mmol/L	5.38 (3.70-9.37)	17.93 (14.31-23.91)	49.4 (40.0-73.0)	321.25 (96.44)
HDL-C<1.04 mmol/L	7.61 (4.43-14.39)	19.70 (15.57-26.18)	48.0 (40.0-69.0)	343.20 (99.11)
P value	<0.001	<0.001	0.620	<0.001
Fast plasma glucose (FPG)				
FPG<5.6 mmol/L	5.50 (3.85-9.42)	18.33 (14.48-24.96)	49.6 (40.0-72.0)	317.4 0 (96.32)
FPG≥5.6 mmol/L	9.98 (4.83-17.58)	19.11 (15.57-24.44)	47.0 (40.0-69.0)	371.02 (92.06)
P value	<0.001	0.059	0.931	<0.001

Note. For normally distributed variables (sICAM-1), values are presented as means (SD) and *P* values were computed with an age-adjusted ANOVA test; for non-normally distributed variables (hsCRP, sE-selectin, and angiotensin II), values are presented as medians (interquartile range) and *P* values were computed using rank order ANOVA test for the difference in medians adjusted for age. Low WC was defined as <85 cm for men and as <80 cm for women; high WC was defined as ≥85 cm for men and as ≥80 cm for women.

Multivariate adjusted ORs of hypertension, dyslipidemia, hyperglycemia, overweight or obesity, and central obesity by the levels of inflammatory and endothelial dysfunction biomarkers, were presented in Table 4. As the levels of hsCRP, sE-selectin, and angiotensin II were elevated, ORs of hypertension significantly increased. Nevertheless, the association between the increasing levels of sICAM-1 and ORs of hypertension was not significant. With the lowest quartile of hsCRP, sE-selectin and sICAM-1 as a reference, ORs of dyslipidemia for other levels of the biomarkers were significantly and gradually increased, but the association between dyslipidemia and levels of angiotensin II was not observed. Subjects with elevated levels of hsCRP and sICAM-1 were more likely to have hyperglycemia. Participants among the lowest and highest quartile of hsCRP and sICAM-1 reported ORs of hyperglycemia as 2.95 and 2.80, respectively. Overweight or obesity and central obesity were only associated with levels of hsCRP and sE-selectin.

Table 3. Levels of the Inflammation and Endothelial Dysfunction Biomarkers Associated with the Number of CVD Risk Factors

No. of Risk Factors	hsCRP	sE-selectin	Angiotensin II	sICAM-1
No risk factor	4.62 (3.31-6.80)	17.10 (13.26-23.21)	49.6 (39.5-72.4)	301.37 (92.33)
1 risk factor	5.23 (3.56-8.59)	17.62 (14.38-23.45)	48.0 (40.0-68.5)	321.37 (96.69)
2 risk factors	6.24 (4.06-11.76)	18.52 (14.91-24.53)	48.6 (40.0-70.0)	329.91 (93.20)
≥3 risk factors	9.32 (5.18-17.51)	20.59 (16.05-26.71)	49.3 (40.0-75.5)	352.80 (100.70)
P value for trend	<0.001	<0.001	0.186	<0.001

Note. For normally distributed variables (sICAM-1), values are presented as means (SD) and *P* values were computed with an age-adjusted ANOVA test; for non-normally distributed variables (hsCRP, sE-selectin, and angiotensin II), values are presented as medians (interquartile range) and *P* values were computed using rank order ANOVA test for the difference in medians adjusted for age.

Table 4. Multivariate Adjusted OR (95% CI) of Cardiovascular Risk Factors Associated with Inflammation and Endothelial Dysfunction Biomarkers

Biomarkers (levels)	Hypertension	Dyslipidemia	Hyperglycemia	Overweight or Obesity	Central Obesity
hsCRP, mg/L					
<3.95	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
3.95-11.38	1.32 (1.05, 1.66)	0.98 (0.81, 1.19)	0.80 (0.62, 1.03)	1.87 (1.48, 2.39)	1.82 (1.48, 2.25)
>11.38	1.96 (1.52, 2.53)	2.33 (1.85, 2.94)	2.95 (2.27, 3.83)	3.27 (2.50, 4.27)	3.34 (2.62, 4.26)
Trend *P* value	<0.001	<0.001	<0.001	<0.001	<0.001
sE-selectin, ng/mL					
<14.78	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
14.78-24.83	1.40 (1.13, 1.73)	1.12 (0.94, 1.35)	1.39 (1.11, 1.74)	1.11 (0.89, 1.37)	1.14 (0.94, 1.39)
>24.83	1.35 (1.05, 1.72)	1.24 (1.00, 1.54)	1.09 (0.83, 1.43)	2.10 (1.64, 2.67)	1.82 (1.45, 2.29)
Trend *P* value	0.013	0.048	0.291	<0.001	<0.001
Angiotensin II, pg/mL					
<40.0	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
40.0-71.3	1.26 (1.01, 1.57)	0.96 (0.79, 1.16)	1.50 (1.18, 1.91)	0.85 (0.69, 1.06)	1.00 (0.82, 1.21)
>71.3	1.81 (1.40, 2.33)	0.86 (0.69, 1.08)	1.17 (0.88, 1.56)	0.93 (0.72, 1.19)	1.05 (0.83, 1.33)
Trend *P* value	<0.001	0.189	0.306	0.543	0.683
sICAM-1, ng/mL					
<230.96	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
230.96-426.78	1.03 (0.83, 1.29)	1.05 (0.87, 1.27)	1.24 (0.96, 1.59)	0.99 (0.79, 1.23)	0.92 (0.75, 1.12)
>426.78	1.29 (0.96, 1.73)	1.70 (1.30, 2.22)	2.80 (2.06, 3.80)	1.36 (1.02, 1.82)	1.23 (0.86, 1.48)
Trend *P* value	0.126	0.001	<0.001	0.070	0.557

***Note*.** The multivariate model included biomarkers groups, age, gender, current smoking, current drinking, family history of CVD, hypertension, hyperglycemia, dyslipidemia, overweight or obesity, and central obesity. The three levels of all the biomarkers were categorized as the low/up quartiles: <25%, 25%-75%, and >75%.

DISCUSSION

The present study, has demonstrated that different biomarkers of inflammation and endothelial dysfunction were associated with different metabolic risk factors for CVD among people of Inner Mongolia in China. Biomarker levels of inflammation and endothelial dysfunction between participants without CVD risks and with one or more risk factors for CVD were also compared. And we observed that subjects with CVD risk factors had higher levels of hsCRP, sE-selectin, and sICAM-1 than those without them. We also evaluated

associations of levels of inflammation and endothelial dysfunction biomarkers with amount of risk factors. With the increasing number of risk factors, values of hsCRP, sE-selectin and sICAM-1 were significantly raised, implying that levels of hsCRP, sE-selectin, and sICAM-1 might be associated with CVD risk factors. Furthermore, associations between CVD risk factors and levels of all biomarkers were investigated independently as shown below:

hsCRP, sE-selectin and angiotensin II were associated with hypertension.

hsCRP, sE-selectin and sICAM-1 were associated with dyslipidemia.

hsCRP, and sICAM-1 were associated with hyperglycemia.

hsCRP and sE-selectin were associated with both obesity and central obesity.

These findings further demonstrated that inflammation and endothelial dysfunction might play a role in the development of the metabolic risk factors for CVD.

Inflammatory processes and endothelial dysfunction play a fundamental role in the pathogenesis and progression of hypertension[21]. Recent studies have shown that basic inflammatory biomarkers, such as hsCRP, are involved in mechanisms that lead to hypertension[22-23]. However, a few studies reported controversial association between hypertension and sE-selectin[24-26]. In a community-based study of 664 men and women living in England, Miller and colleagues[24] reported that plasma level of sE-selectin was significantly associated with blood pressures in women. However, the significant association was not found in other studies[25-26]. Our study showed a significant and independent association between sE-selectin and hypertension. Consistent with previous studies[27-28], findings from our study indicated that individuals with a higher level of angiotensin II were more likely to develop hypertension.

Atherosclerosis, as the underlying cause of CVD, can be characterized as an inflammatory condition linked with dyslipidemia[29]. In atherogenesis, endothelial cells are stimulated by various risk factors, expressing adhesion and chemoattractant molecules that recruit inflammatory monocytes into the vascular wall. In this stage, endothelial dysfunction is also associated with the introduction of extracellular lipid into the intimal layer of the arterial wall. Therefore, inflammation and endothelial dysfunction are correlated with dyslipidemia. A cross-sectional study of 507 Iranian women revealed[30] that hsCRP and sE-selectin were associated with dyslipidemia. And this association was also observed in our present study. A self-controlled trial study[31] reported that the value of sICAM-1 significantly increased with serum TG and HDL triglyceride content after intra lipid infusion, indicating that dyslipidemia induced excretion of sICAM-1. A significant association between sICAM-1 and dyslipidemia was also observed in our study population.

Recent progress showed that pathophysiological mechanisms leading to β-cell damage, insulin resistance, and the vascular complications of diabetes included an activation of the inflammation cascade, endothelial dysfunction, and procoagulant imbalance. It appeared that many circulating biomarkers of inflammation pathways, such as TNF alpha, IL-6, hsCRP, vascular cellular adhesion molecule-1, sICAM-1, E- and P-selectins, von Willebrand factor, plasminogen activator inhibitor-1, fibrinogen and adiponectin, might be associated with the pathogenesis of type 2 diabetes and even with type 1 diabetes[32]. In addition, it has been reported that hyperglycemia might lead to endothelial dysfunction[33]. As our results showed, biomarkers of inflammation and endothelial dysfunction, such as hsCRP and sICAM-1 were associated with hyperglycemia. In contrast, a significant association between sE-selectin and hyperglycemia in our study population was not observed.

Obesity also had a profound impact on endothelial function as demonstrated in a study (n=397) on the impact of BMI on coronary vasomotor response[34]. Increased plasma concentration of sE-selectin has been reported in overweight and obese individuals[10]. Additionally, hsCRP and sE-selectin were also reported to be significantly higher in individuals with higher BMI and WC[35]. In the present study, the associations between hsCRP, sE-selectin and obesity and central obesity were also demonstrated.

The present study has a number of limitations. First, this was a cross-sectional study, and consequently a causal relationship of inflammation and endothelial dysfunction with the metabolic risk factors for CVD could not be established. Second, approximately 25% of the eligible population from the study villages were reluctant to participate in the study, which might produce selection bias. However, we believe that these bias is negligible because it is unlikely that the reason why the participants were

reluctant to participate in the study was due to their biomarker levels. Furthermore, several important biomarkers of inflammation and endothelial dysfunction, such as tumor necrosis factor-alpha (TNF-a), IL-6 and VCAM-1 were not investigated in our study.

Despite the above limitations the present study is the largest study so far to examine the associations of the biomarkers of inflammation and endothelial dysfunction with metabolic risk factors for CVD in people of Inner Mongolia in China. The study participants were homogeneous in regard with the genetic background and environmental exposures. Data of this study were collected with quality control and covariates were measured and controlled in the data analysis.

Most endothelial proteins lack exclusive expression and their formation is conditional based on different stimulations. Clear understanding of the associations of biomarkers of inflammation and endothelial dysfunction with risk factors for CVD is therefore crucial for the prevention and clinical treatment of CVD. By exploring the association of the biomarkers of inflammation and endothelial dysfunction with risk factors for CVD (hypertension, hyperglycemia, dyslipidemia, overweight or obesity, and central obesity) the present study has suggested that individuals who are at risk to CVD should receive appropriate anti-inflammatory actions so as to prevent and treat CVD.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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