

ORIGINAL ARTICLE

Co-effect of insulin resistance and biomarkers of inflammation and endothelial dysfunction on hypertension

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To explore the co-effects of inflammation and endothelial dysfunction and insulin resistance (IR) on hypertension in a large Asian population. Data on demographic characteristics, blood pressure and other variables were collected; additionally, fasting plasma glucose, insulin and biomarkers, including C-reactive protein (CRP), soluble intercellular cell adhesion molecule-1 (sICAM-1), soluble E-selectin (sE-selectin) and angiotensin II were examined among 2553 Mongolian adults aged ≥ 20 years. IR was assessed using the homeostasis model. The co-effects of elevated biomarkers of inflammation and endothelial dysfunction and IR on hypertension were analyzed. A total of 953 subjects were diagnosed with hypertension. Among hypertensive subjects, the levels of CRP (11.0 vs. 6.7 mg l⁻¹), sICAM-1 (348.3 vs. 335.9 ng ml⁻¹), sE-selectin (20.9 vs. 18.5 ng ml⁻¹) and angiotensin II (61.3 vs. 50.0 pg ml⁻¹) were significantly higher among subjects with IR than those without IR; among normotensives, levels of CRP (6.3 vs. 5.2 mg l⁻¹) and sE-selectin (20.1 vs. 17.8 ng ml⁻¹) were higher among IR subjects than those without IR. The prevalence of hypertension was significantly higher among subjects with IR and 2 elevated biomarkers (69.0%) and those with IR and ≥ 3 elevated biomarkers (79.3%) than among those with IR and no elevated biomarkers (45.9%) and those with IR and 1 elevated biomarker (50.6%). After adjusting for multivariate, the risk of hypertension was significantly associated with the coexistence of IR and any two or three elevated biomarkers (odds ratios (OR) (95% confidence intervals (CIs))=2.55 (1.60–4.06) and 3.19 (1.15–8.86), respectively). In this Mongolian population, IR and elevated biomarkers of inflammation and endothelial dysfunction were related to hypertension and the coexistence of IR and elevated biomarkers of inflammation and endothelial dysfunction increased the risk of hypertension.

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INTRODUCTION

Multiple cross-sectional studies^{1–4} and one cohort study⁵ have indicated that insulin resistance (IR) is associated with hypertension. Studies have also shown that inflammation and endothelial dysfunction are not only associated with atherosclerosis, cardiovascular disease and hypertension but also with IR in various settings.^{6–11} Inflammation and endothelial dysfunction may have an important role in the development of IR.¹² Biomarkers of inflammation and endothelial dysfunction, such as circulating C-reactive protein (CRP), interleukin-6, soluble intercellular cell adhesion molecule-1 (sICAM-1), soluble vascular cell adhesion molecule-1 and soluble E-selectin (sE-selectin), have been reported to be associated with IR.^{13–15} In addition, studies have demonstrated that both endothelial dysfunction and IR are related to cardiovascular risk factors among hypertensive patients.^{16–18} However, few studies investigating the co-effects of inflammation and endothelial

dysfunction and IR on hypertension in a large Asian population have been reported. The aim of this study was to investigate the co-effects of inflammation and endothelial dysfunction and IR on hypertension among a Mongolian population in Inner Mongolia, China.

METHODS

Study participants

From July 2002 to September 2003, a cross-sectional survey was conducted in 32 villages of two townships, Kezuohou Banner (county) and Naiman Banner, Inner Mongolia, China. These two adjacent townships are 100 km from Tongliao, a prefecture-level city in eastern Inner Mongolia, China. Most of the residents in the investigation field are Mongolian and have occupied the area for many generations. Of the 3475 Mongolians aged ≥ 20 years sampled, 2589 provided informed consent and participated in the study. This study was approved by the Soochow University Ethics Committee.

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Data collection and examination

Data on demographic characteristics, lifestyle risk factors, including cigarette smoking and alcohol drinking, as well as family and personal history of hypertension were collected using a standardized questionnaire administered by trained study staff. Cigarette smoking was defined as having smoked at least one cigarette per day for 1 year or more. Heavy alcohol consumption was defined as drinking at least 50 g of alcohol per day for 1 year or more.

Body weight and height were measured with subjects wearing light clothing and without shoes by trained staff. The body mass index was calculated as weight in kilograms divided by the square of height in meters. The waist circumference was measured at the level of 1 cm above the umbilicus. Overweight was defined as body mass index $\geq 25 \text{ kg m}^{-2}$, and central obesity was defined as waist circumference $\geq 85 \text{ cm}$ for males and $\geq 80 \text{ cm}$ for females.¹⁹

Three blood pressure (BP) measurements were taken by four trained doctors using a standard mercury sphygmomanometer, and the mean of the three measurements was used in the analysis. Hypertension was defined as a systolic BP ≥ 140 and/or a diastolic BP $\geq 90 \text{ mm Hg}$ and/or use of antihypertensive medication within the previous 2 weeks.

Fasting blood samples were collected from all participants the morning after at least 8 h of fasting. Serum was subsequently isolated from the whole blood, and all serum samples were frozen at -80°C until testing. Fasting plasma glucose was measured using a modified hexokinase enzymatic method. The concentrations of total cholesterol (TC), HDL-C (high-density lipoprotein-cholesterol) and triglycerides (TGs) were assessed enzymatically on a Beckman Synchron CX5 Delta Clinical System (Beckman Coulter, Fullerton, CA, USA) using commercial reagents, and LDL-C (low-density lipoprotein-cholesterol) concentration was calculated by means of the Friedewald equation for participants who had $<4.52 \text{ mmol l}^{-1}$ (400 mg dl^{-1}) TG.²⁰ High TG levels were defined as TG $\geq 1.70 \text{ mmol l}^{-1}$, high TC was defined as TC $\geq 5.18 \text{ mmol l}^{-1}$, high LDL-C was defined as LDL-C $\geq 3.37 \text{ mmol l}^{-1}$ and low HDL-C was defined as HDL-C $<1.04 \text{ mmol l}^{-1}$. CRP was determined with immunoturbidimetry on a Beckman Synchron CX5 Delta Clinical System using commercial reagents. sE-selectin and sICAM-1 were measured by an enzyme-linked immunosorbent assay (R&D Systems, Minneapolis, MN, USA), which employs the quantitative sandwich enzyme immunoassay technique.^{21,22} Quantitative determination of immunoreactive angiotensin II was performed by a double antibody radioimmunoassay after reversed-phase sample extraction by means of phenylsilylsilica columns following the method previously reported by Emanuel *et al.*²³ and a commercial radioimmunoassay kit.

The homeostasis model assessment method was used to calculate the insulin resistance index (HOMA-IR): $\text{HOMA-IR} = (\text{insulin (mU l}^{-1}) \times \text{glucose (mmol l}^{-1}) / 22.5)^{24}$ and IR was defined as $\text{HOMA-IR} > 3.76 \text{ mU} \times \text{mmol l}^{-2}$ (the fifth quintile). Elevated CRP, elevated sICAM-1, elevated sE-selectin and elevated angiotensin II were defined in this study sample as values of these markers that were greater than the top quintiles.

Statistical analysis

The mean values (standard deviations) or medians (quartile intervals) of continuous variables were calculated and compared using a Student's *t*-test or Wilcoxon rank test between subjects with IR and without IR across the hypertensive and normotensive groups. The prevalence and 95% confidence intervals (95% CI) for categorical variables were calculated, and χ^2 -tests were performed to compare between two groups.

The age and gender-adjusted prevalence of IR, high CRP, sICAM-1, sE-selectin and angiotensin II were computed using a direct standardized method and compared using weighted χ^2 -tests. The associations between hypertension and IR, biomarkers of inflammation and endothelial dysfunction were analyzed using a logistic regression model. Statistical analyses were conducted using SAS 9.1 statistical software (SAS Institute Inc., Cary, NC, USA), and all *P*-values were based on two-side tests with the significance level set to 0.05.

RESULTS

Of the 2589 participants initially recruited, 2553 subjects were included in the analysis, and 36 subjects were excluded due to absence of fasting plasma glucose or insulin data. There were 953 hypertensive participants and 1600 normotensive participants in the sample of 2553 individuals.

Table 1 presents the comparison of characteristics between subjects with IR and without IR, grouped by BP status. In the hypertension group, subjects with IR were more likely to have higher prevalence of overweight, central obesity, high TG, high TC, and higher average levels of CRP, sICAM-1, sE-selectin and angiotensin II compared with those without IR. Similarly, among the normotensive group, the prevalence of overweight, central obesity and high TG, as well as the average levels of CRP and sE-selectin were significantly greater among subjects with IR than those without IR. In addition, hypertensive

Table 1 Characteristics of subjects grouped by both blood pressure and IR status

Variables	Hypertension		Normotension	
	IR (n=234)	Non-IR (n=719)	IR (n=276)	Non-IR (n=1324)
Age (age), M (Q _L -Q _U)	51 (42-60)	51 (43-60)	41 (35-50) ^a	41 (35-51) ^a
Male, % (95% CI)	51.3 (44.8-57.7)	49.7 (46.0-53.3)	35.5 (29.8-41.2) ^a	35.6 (33.1-38.2) ^a
Family history of hypertension, % (95% CI)	23.1 (17.6-28.5)	25.3 (22.1-28.5)	8.0 (4.7-11.2) ^a	5.7 (4.4-6.9) ^a
Smoking, % (95% CI)	44.8 (38.5-51.3)	49.4 (45.7-53.0)	36.6 (30.9-42.3)	43.4 (40.8-46.1)
Drinking, % (95% CI)	41.3 (35.9-48.7)	45.1 (41.5-48.7)	26.8 (21.6-32.1) ^a	27.0 (24.6-29.4) ^a
Overweight, % (95% CI)	44.4 (38.0-50.9)	24.7 (21.5-27.8) ^b	25.0 (19.9-30.1) ^a	12.5 (10.8-14.3) ^{a,b}
Central obesity, % (95% CI)	64.1 (57.9-70.3)	50.2 (46.5-53.9) ^b	48.2 (42.3-54.1) ^a	31.4 (28.9-33.9) ^{a,b}
High TG, % (95% CI)	34.8 (28.6-40.9)	23.1 (20.0-26.2) ^b	22.5 (17.6-27.5) ^a	10.3 (8.7-12.0) ^{a,b}
High TC, % (95% CI)	21.5 (16.1-26.8)	13.0 (10.6-15.5) ^b	8.7 (5.4-12.1) ^a	7.0 (5.6-8.4) ^a
High LDL-C, % (95% CI)	24.6 (19.0-30.1)	17.8 (15.0-20.7)	13.5 (9.4-17.5) ^a	10.0 (8.4-11.7) ^a
Low HDL-C, % (95% CI)	47.8 (44.4-54.3)	35.5 (32.0-39.1) ^b	37.1 (31.3-42.8) ^a	36.3 (33.7-38.9)
CRP (mg l ⁻¹), M (Q _L -Q _U)	11.0 (5.2-18.8)	6.7 (4.4-13.3) ^b	6.3 (4.1-12.1) ^a	5.2 (3.5-8.9) ^{a,b}
sICAM-1 (ng ml ⁻¹), $\bar{x} \pm s$	348.3 \pm 102.1	335.9 \pm 97.7 ^b	320.2 \pm 95.1 ^a	322.9 \pm 96.9 ^a
sE-selectin (ng ml ⁻¹), M (Q _L -Q _U)	20.9 (16.9-27.8)	18.5 (15.2-24.6) ^b	20.1 (15.2-26.9)	17.8 (14.1-23.6) ^b
Angiotensin II (pg ml ⁻¹), M (Q _L -Q _U)	61.3 (43.0-97.0)	50.0 (40.0-77.0) ^b	49.9 (40.0-69.8) ^a	47.0 (39.2-66.1) ^a

Abbreviations: CRP, C-reactive protein; HDL-C, high density lipoprotein-cholesterol; IR, insulin resistance; LDL-C, low-density lipoprotein-cholesterol; M, median; Q_L, lower quartile; Q_U, upper quartile; sE-selectin, soluble sE-selectin; sICAM-1, soluble intercellular cell adhesion molecule-1; TC, total cholesterol; TG, triglycerides; 95% CI, 95% confidence interval.

^aHypertension vs. normotension, *P* < 0.05.

^bNon-insulin resistance vs. insulin resistance, *P* < 0.05.

subjects were, regardless of IR or non-IR status, more likely to be older, male, have a family history of hypertension, report drinking, be overweight, have central obesity, high TG, high TC and low HDL-C as well as have higher average levels of CRP, sICAM-1 and angiotensin II compared with normotensive subjects.

The unadjusted and age–gender-adjusted prevalence of IR, elevated CRP, elevated sICAM-1, elevated sE-selectin, elevated angiotensin II and prevalence of coexistence of IR with elevated inflammatory and endothelial biomarkers are presented in Table 2. Both the unadjusted and age–gender-adjusted prevalence of IR, elevated CRP, elevated sICAM-1, elevated angiotensin II, prevalence of coexistence of IR with elevated CRP, elevated sICAM-1, elevated sE-selectin and elevated angiotensin II, but not sE-selectin, were higher among hypertensive subjects than among normotensive subjects. Furthermore, unadjusted and age–gender-adjusted prevalence of IR and coexistence of IR with 1, 2 or ≥ 3 elevated biomarkers of inflammation and endothelial dysfunction were all significantly greater among hypertensive participants than among normotensive participants.

The prevalence of hypertension in subjects without IR and without elevated biomarkers, among subjects with IR, and among subjects with the coexistence of IR and 1, 2 or ≥ 3 elevated inflammatory and endothelial biomarkers are shown in Figure 1. The prevalence of hypertension among subjects without IR and without elevated biomarkers, with IR, with the coexistence of IR and 1 elevated biomarkers, coexistence of IR and 2 elevated biomarkers, coexistence of IR and ≥ 3 elevated biomarkers were 29.9, 45.9, 50.6, 69.0 and 79.3%, respectively. The prevalence of hypertension was significantly greater among subjects with IR than in those without IR and without elevated biomarkers; the prevalence of hypertension was significantly greater in subjects with IR and 1, 2 or ≥ 3 elevated biomarkers than among those without IR and without elevated biomarkers. The prevalence of hypertension was significantly greater in subjects with IR and 2 or ≥ 3 elevated biomarkers than in those with IR alone. However, there was no significant difference in the prevalence of hypertension between subjects with IR and ≥ 3 elevated biomarkers and those with IR and 2 elevated biomarkers.

Normotensive participants served as the control in this study. Odds ratios (ORs) and 95% CIs for hypertension associated with IR, elevated biomarkers of inflammation and endothelial dysfunction

are presented in Table 3. Compared with those without IR and without elevated biomarkers, subjects with IR or elevated CRP, sICAM-1, sE-selectin or angiotensin II had a greater risk of hypertension before adjusting for age, gender and other factors. Furthermore, coexistence of IR with elevated CRP, elevated sICAM-1, elevated sE-selectin or elevated angiotensin II increased the risk of hypertension, especially when IR was accompanied with two or three elevated biomarkers. After adjusting for age, gender, family history of hypertension, smoking, drinking, overweight and high TG, the risk of hypertension associated with IR alone, elevated CRP alone, elevated sICAM-1 alone, elevated angiotensin II alone and with the coexistence of IR and elevated CRP or elevated angiotensin II remained significant. Moreover, the risk of hypertension associated with the coexistence of IR and any two or any three elevated biomarkers was highly significant; the ORs (95% CI) were 2.55 (1.60–4.06) and 3.19 (1.15–8.86), respectively.

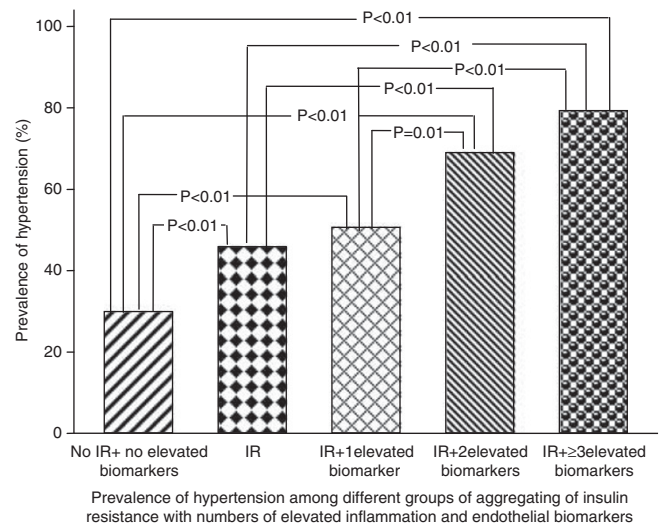


Figure 1 Prevalence of hypertension among different groups of aggregating of insulin resistance with numbers of elevated inflammation and endothelial biomarkers.

Table 2 Prevalence of IR and elevated inflammation and endothelial biomarkers in hypertensives and normotensives

Variables	Hypertensives		Normotensives	
	Unadjusted	Age–gender adjusted	Unadjusted	Age–gender adjusted
IR, %	24.5 (21.8–27.3)	26.3 (23.1–29.5)	17.3 (15.4–19.1) ^a	17.0 (15.2–18.8) ^b
Elevated CRP, %	28.9 (26.0–31.7)	27.1 (24.2–30.0)	14.7 (13.0–16.5) ^a	15.7 (13.9–17.6) ^b
Elevated sICAM-1, %	24.6 (21.7–27.4)	23.1 (20.3–25.9)	17.6 (15.6–19.5) ^a	17.8 (15.9–19.6) ^b
Elevated sE-selectin, %	21.9 (19.2–24.6)	20.3 (17.6–22.9)	18.8 (16.9–20.8)	19.2 (17.2–22.2)
Elevated angiotensin II, %	25.7 (23.0–28.5)	25.5 (22.8–28.4)	16.0 (14.2–17.8) ^a	15.9 (14.2–17.6) ^b
IR+elevated CRP, %	10.2 (8.3–12.2)	9.7 (7.7–11.7)	3.6 (2.7–4.5) ^a	3.7 (2.8–4.7) ^b
IR+elevated ICAM-1, %	7.2 (5.5–8.9)	7.1 (5.3–8.9)	3.3 (2.4–4.2) ^a	3.2 (2.3–4.1) ^b
IR+elevated E-selectin, %	7.2 (5.5–8.9)	7.0 (5.2–8.8)	4.2 (3.2–5.2) ^a	4.2 (3.1–5.0) ^b
IR+elevated angiotensin II, %	8.2 (6.4–9.9)	7.8 (5.9–9.7)	2.9 (2.1–3.7) ^a	3.2 (2.2–4.1) ^b
IR+1 elevated biomarker, %	39.6 (34.9–44.3)	37.0 (33.2–40.7)	21.5 (18.5–24.4) ^a	21.3 (18.6–23.9) ^b
IR+2 elevated biomarkers, %	27.7 (30.0–32.4)	25.1 (21.8–28.5)	6.8 (4.9–8.8) ^a	7.1 (5.3–9.0) ^b
IR+≥3 elevated biomarkers, %	8.2 (5.0–11.5)	6.1 (3.8–8.3)	1.0 (0.2–1.8) ^a	0.9 (0.2–1.6) ^b

Abbreviations: CRP, C-reactive protein; IR, insulin resistance; sE-selectin, soluble sE-selectin; sICAM-1, soluble intercellular cell adhesion molecule-1.

^aCompared with hypertensives for unadjusted prevalence, $P < 0.05$.

^bCompared with hypertensives for age–gender-adjusted prevalence, $P < 0.05$.

Table 3 ORs (95% CI) of hypertension associated with IR and elevated biomarkers of inflammation and endothelial dysfunction

Variables	Unadjusted OR (95%CI)	Multivariate-adjusted OR (95%CI)
Non-IR+low biomarkers	1.00	1.00
IR	1.50 (1.25–1.80) ^a	1.25 (1.00–1.58) ^a
Elevated CRP	2.74 (2.18–3.44) ^a	1.55 (1.17–2.04) ^a
Elevated ICAM-1	1.95 (1.54–2.45) ^a	1.35 (1.02–1.78) ^a
Elevated E-selectin	1.62 (1.28–2.04) ^a	1.09 (0.83–1.44)
Elevated angiotensin II	2.24 (1.79–2.82) ^a	1.76 (1.34–2.30) ^a
IR+elevated CRP	3.99 (2.79–5.71) ^a	1.81 (1.16–2.84) ^a
IR+elevated ICAM-1	3.06 (2.05–4.56) ^a	1.55 (0.97–2.56)
IR+elevated E-selectin	2.38 (1.63–3.47) ^a	1.35 (0.85–2.14)
IR+elevated angiotensin II	3.97 (2.68–5.88) ^a	2.23 (1.39–3.58) ^a
IR+1 elevated biomarker	2.40 (1.85–3.11) ^a	1.37 (1.00–1.88) ^a
IR+2 elevated biomarkers	5.22 (3.55–7.67) ^a	2.55 (1.60–4.06) ^a
IR+≥3 elevated biomarkers	8.98 (3.62–22.33) ^a	3.19 (1.15–8.86) ^a

Abbreviations: CRP: C-reactive protein; IR, insulin resistance; OR, odds ratio; sE-selectin: soluble sE-selectin; sICAM-1: soluble intercellular cell adhesion molecule-1; 95% CI, 95% confidence interval.

^aOthers compared with non-IR+low biomarkers group, $P < 0.05$.

DISCUSSION

We examined the relationships between biomarkers of inflammation and endothelial dysfunction and IR, biomarkers of inflammation and endothelial dysfunction and hypertension, IR and hypertension, and the co-effect of IR and biomarkers of inflammation and endothelial dysfunction on hypertension in a large Mongolian population. This study included multiple biomarkers of inflammation and endothelial dysfunction, including CRP, sICAM-1, sE-selectin and angiotensin II; of the four, CRP, sICAM-1 and sE-selectin reflect the status of inflammation or the status of endothelial dysfunction.^{25–27} In addition to its role as a vasoconstrictor, angiotensin II induces endothelial dysfunction and inflammation, resulting in accelerated progression of atherosclerosis.^{28,29} Our study found that IR was related to the biomarkers of inflammation and endothelial dysfunction, both in subjects with hypertension and those without hypertension. Subjects with IR (HOMA-IR > 3.76) had higher CRP, sICAM-1, sE-selectin and angiotensin II levels than those without IR. Elevated biomarkers of inflammation and endothelial dysfunction were related to hypertension in subjects with and without IR. Hypertensive subjects had higher CRP, sICAM-1 and angiotensin II levels than normotensive subjects. The coexistence of IR and elevated biomarkers of inflammation and endothelial dysfunction increased the risk of hypertension, and the risk of hypertension for subjects with IR+2 elevated biomarkers or IR+≥3 elevated biomarkers was greater than for those with only IR or with any one elevated biomarker. These findings suggest that not only are biomarkers of inflammation and endothelial dysfunction alone and IR alone associated with hypertension, but their co-effect may also be associated with hypertension.

CRP, as a biomarker of systemic inflammation, has been reported to be a strong independent predictor of myocardial infarction, ischemic stroke, type 2 diabetes and hypertension.^{6,22} Moreover, experimental and epidemiological data have indicated that the inflammatory process is associated with impaired insulin sensitivity and the development of dysglycemic conditions.³⁰ A study conducted in Peru among 1525 individuals³¹ found that elevated CRP were significantly and positively associated with increased mean fasting insulin concentrations and mean HOMA-IR ($P < 0.001$) in both women and men. Women with CRP concentrations > 2.53 mg l⁻¹ (upper tertile) had

a 2.18-fold increased risk of IR (OR=2.18; 95% CI 1.51–3.16) compared with those in the lowest tertile (< 0.81 mg l⁻¹). Among men, those in the upper tertile had a 2.54-fold increased risk of IR (OR=2.54; 95% CI 1.54–4.20) compared with those in the lowest tertile. Another study³² indicated that elevated sICAM-1 levels were independently associated with IR in a Taiwanese population. Chen *et al.*⁸ reported that the degree of IR was significantly correlated to concentrations of sE-selectin, sICAM-1 and soluble vascular cell adhesion molecule-1 among 28 healthy American volunteers. Ingelsson *et al.*³³ found that vascular cell adhesion molecule-1, E-selectin and CRP were independently associated with metabolic syndrome (MetS) and increased HOMA-IR. Park *et al.*⁷ examined the cross-sectional and longitudinal relationships between CRP and IR and found a significant positive association between CRP and IR, in both cross-sectional and longitudinal results, even after adjusting for adiposity measurements and oxidative stress markers. Xu *et al.*³⁴ found that CRP suppressed insulin signaling in endothelial cells. The studies by Park *et al.*⁷ and Xu *et al.*³⁴ appear to support the hypothesis that inflammation and endothelial dysfunction introduce IR. Additional results indicate that IR may in turn exacerbate inflammation by increasing cytokine and adipokine expression (including TNF- α , interleukin-6, leptin and others), elevating free fatty acid levels, and impairing endothelial nitric oxide synthase activity.^{35,36} Both inflammation and IR are two important links in the mechanism of hypertension; either systemic inflammation promotes the development of hypertension by introducing IR or IR promotes the development of hypertension by exacerbating inflammation. According to our findings that the coexistence of inflammation and IR increase the risk of hypertension, we presume that inflammation may partially and directly introduce hypertension by way of the inflammatory process in addition to IR; there is a co-effect between inflammation and IR on hypertension. Anuurad *et al.*³⁷ conducted a study among African Americans and Caucasians and found that the synergistic relationship between inflammation and IR was a risk factor in coronary artery disease. Matsumoto *et al.*³⁸ reported that among Japanese patients with type 2 diabetes mellitus and without a history of cardiovascular disease or stroke, the coexistence of IR and inflammation effectively predicted cardiovascular disease but not stroke.

In addition, results of multiple intervention studies indicated that lifestyle modification^{39,40} and pharmacologic treatment for hypertension,^{41,42} such as the angiotensin converting enzyme inhibitor, imidapril or the angiotensin II type 1 receptor antagonist, irbesartan, not only reduced BP values but also improved insulin sensitivity and endothelial function. Therefore, weight management or drug therapy may be necessary for hypertensive patients to reduce incidence of cardiovascular events.

There are limitations to the present study. First, it is a cross-sectional study, and the co-effect of IR with elevated biomarkers of inflammation and endothelial dysfunction on hypertension should be elucidated in a cohort study. Second, 25% of the eligible individuals did not participate in the study because they were away from home or refused to respond, which may have caused selection bias. However, area inhabitants who did not participate in the study were likely unaware of their serum insulin, plasma glucose, biomarker levels and BP values, which may partially attenuate the selection bias.

This study has several advantages that should be mentioned. To our knowledge, this is the largest study to examine the association between hypertension and the co-effect of IR with elevated biomarkers of inflammation and endothelial dysfunction in a general Asian population. In addition, the study participants were homogeneous with respect to their genetic background and environmental exposures.

The study data were collected with rigid quality control, and important co-variables were measured and controlled in the analysis.

In summary, in this Mongolian population, IR was associated with elevated biomarkers of inflammation and endothelial dysfunction; elevated biomarkers of inflammation and endothelial dysfunction were associated with hypertension, and the coexistence of IR and elevated biomarkers of inflammation and endothelial dysfunction increased the risk of hypertension.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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