Association between Serum C-reactive Protein and Metabolic Syndrome in Mongolian Patients in Comparison to Japanese Patients

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Objective: Metabolic syndrome (MetS) is associated with chronic inflammation and cardiovascular disease. The present study's aim was to investigate the relationship between serum C-reactive protein (CRP) and MetS in the Mongolian population in comparison to the Japanese population.

Methods: Two-hundred and eighty-five Mongolian volunteers (males/females: 115/170, mean age 44.9 years) and 326 Japanese volunteers (males/females: 137/189, mean age 43.6 years) were recruited from health check-up settings. Cardiometabolic variables including CRP were measured. The patients were divided into three groups by the number of MetS risk factors (<1, 1–2 or ≥3).

Results: The percentages of patients with MetS were 39.6% in the Mongolians and 31.1% in the Japanese. The median CRP levels were .05, .12 and .19 mg/dL in the <1, 1–2 and ≥3 MetS risk factor groups among Mongolians, and .03, .05 and .07 mg/dL in these same groups among Japanese. The significance for the trend for CRP levels within each ethnic group was $P<.001$, and the significance for the difference in CRP levels between the respective groups by the MetS risk factors was $P=.03$ in subjects with <1, $P<.001$ in subjects with 1–2, $P<.001$ in subjects with ≥3. These results were similar in the subgroup analyses by sex.

Conclusions: While higher serum CRP levels were seen with increased MetS risk factors in both ethnic groups, in some cases we observed a higher serum CRP level increase in the Mongolian population than in the Japanese population. Mongolian people may be at greater risk for cardiovascular disease. (*Ethn Dis.* 2011;21:74–78)

Key Words: Chronic Inflammation, Ethnicity, Metabolic Risk Factor, Cardiovascular Disease

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Introduction

Metabolic syndrome (MetS) is a cluster of well-known risk factors of cardiovascular disease (CVD) such as obesity, high blood glucose, high blood pressure and dyslipidemia.[1–3] The accumulation of these risk factors has been shown to lead to an increased incidence of CVD.[3] It is of great public concern that MetS prevalence is increasing in the industrialized and developing countries.[4,5] While the biomarkers for assessing accumulated risk factors of MetS in association with CVD have been explored, C-reactive protein (CRP), a chronic systemic low-grade inflammatory marker, is regarded as another possible marker. Indeed, an increased level of serum CRP is reported to be found in MetS, possibly leading to CVD.[1,6]

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It is important to control the morbidity and mortality of CVD in Mongolia because of a 10.9% increase in deaths due to ischemic heart disease from 2000 to 2008; additionally, one in three individuals died due to CVD.[7] The nationwide prevalence of MetS in Mongolia has not been completely determined, and only one previous study has reported a relatively higher prevalence of MetS in Mongolian vs other Asians.[8] That study found the prevalence of MetS was 12% for Japanese, 13% for Koreans and 16% for Mongolians, according to the National Cholesterol Educational Program Expert Panel in Adult Treatment Panel III (NCEP - ATP III) definition, which had a minor modification of obesity criteria for Asians (body mass index [BMI] $\geq$ 25 kg/m^2).[8,9] Furthermore, our previous studies have reported that the atherogenic profiles with a higher serum CRP level are observed in the Mongolian population more than in the Japanese population,[10,11] but these studies did not take MetS into account.

Thus, there have been no studies on the relationship between serum CRP levels and MetS in the Mongolian people in comparison to the Japanese people. The comparison between the Mongolian and Japanese populations is reasonable, as these populations may share a similar genetic background (CRP and MetS are partially affected by genetic factors),[12] so the comparative studies concerning the relationship between CRP and MetS may provide new insights on the increased incidence of CVD in Mongolia. The aim of the present study was to investigate the hypothesis that serum CRP levels rise with the increased numbers of risk factors for MetS, and that the increased CRP levels are greater in Mongolians in comparison to the Japanese.

Methods

A cross-sectional survey was conducted in a total of 285 Mongolian

volunteers (males/females: 115/170, mean age 44.9 years) and 326 Japanese volunteers (males/females: 137/189, mean age 43.6 years) in 2006–2008. The former group was recruited from the general health check-up settings at the Hospital Number 2 and State Mental Hospital of Mongolia in Ulaanbaatar city, Mongolia, and the latter group was recruited from the Jichi Medical University Hospital in Tochigi Prefecture, Japan. Patient eligibility required no history of CVD, no current medication use, no pregnancy nor acute infections (eg, common cold). This study was approved by the Ethnical Committee of Jichi Medical University and the Mongolian Ministry of Health, and each patient provided informed consent.

The volunteers were divided into the three groups by the number of risk factors for MetS (based on NCEP-ATP III criteria).[9] Each patient was assigned into a group with either: no MetS risk factors; 1 or 2 MetS risk factors; or ≥ 3 MetS risk factors . The MetS components were defined as: a BMI of >25 kg/m^2 (modified for Asians),[8] systolic blood pressure (SBP) of ≥135 mm Hg, diastolic blood pressure (DBP) ≥85 mm Hg, fasting serum triglyceride (TG) of ≥1.70 mmol/L, fasting serum high-density lipoprotein cholesterol (HDL-C) of <1.04 mmol/L in men and < 1.30 mmol/L in women, and fasting plasma glucose of ≥6.1 mmol/L.[9]

Current smoking habits were self-reported by a questionnaire. The BMI was calculated as the weight/height^2 as measured in light indoor clothing without shoes. Blood pressure was measured, after at least 5 minutes of rest, by a mercury sphygmomanometer. A 12-hour overnight fasting serum/plasma specimen was collected by venipuncture, and the samples were stored at −80°C until laboratory assays. All blood measurements were simultaneously performed at a single laboratory facility in Japan. The concentrations of serum total cholesterol (TC), TG, HDL-C and plasma glucose were measured enzymatically, and the concentration of insulin was measured by a sandwich enzyme immunoassay (TOSOH Co. Ltd., Tokyo, Japan). The CRP was measured using a latex agglutination immunoassay (EIKEN Chemical Co. Ltd, Tokyo, Japan).

Statistical Analyses

The data are presented as the mean ± standard deviation (SD). The variables with non-parametric distributions are presented as the median and interquartile range. Comparisons between the groups were performed using the unpaired t test (for continuous variables) and the χ^2-test (for categorical variables). The CRP levels were also examined using a general linear model with the adjustments on covariables as model 1 (adjusted for age and smoking), model 2 (adjusted for age, smoking and BMI) and model 3 (adjusted for all the measured variables). All non-parametric variables were log-transformed due to their skewed distribution. All statistical analyses were performed with the Statistical Package for Social Science (SPSS) software package, version 16.0 for Windows (SPSS Inc., Chicago, USA). A P <.05 was considered to be statistically significant.

RESULTS

In this study, the prevalence of subjects with MetS was 39.6% in the Mongolian patients and 31.3% in the Japanese (P=.005). As shown in Table 1, in the group with no MetS risk factors or with 1 or 2 MetS risk factors, the levels of BMI, DBP and CRP were significantly higher, while TC, TG, HDL-C and glucose levels were significantly lower in the Mongolian patients than in the Japanese patients. The Mongolians with no MetS risk factors also had a significantly higher percentage of current smoking and a higher level of insulin than the Japanese. In the patients with ≥3 MetS risk factors, the levels of BMI, SBP, DBP and CRP were significantly higher, while the HDL-C level was significantly lower in the Mongolians than in the Japanese.

When the difference in CRP levels between the Mongolian and Japanese was analyzed in the covariable-adjusted models, in the patients with no MetS risk factors, the difference in CRP was significant in model 1 (P=.04), but not in model 2 and model 3. In the patients with 1 or 2 MetS risk factors or with ≥ 3 MetS risk factors, the difference in CRP remained significant in all of the models (model 1 P<.001, model 2 P<.001, model 3 P<.001).

When separating the results by sex (Table 2), Mongolian males with no MetS risk factors showed significantly higher levels of smoking, DBP and insulin, while TC, HDL-C and glucose levels were significantly lower than in Japanese males. In Mongolian males with 1 or 2 MetS risk factors, the CRP levels were significantly higher, while TC, HDL-C and glucose levels were significantly lower than in Japanese males. In Mongolian males with ≥3 MetS risk factors, BMI, SBP, DBP and CRP levels were significantly higher than in Japanese males. Furthermore, in Mongolian female subjects with no MetS risk factors, BMI, SBP, DBP, insulin and CRP levels were significantly higher, while TC, TG, HDL-C and glucose levels were significantly lower than in Japanese female subjects. In Mongolian females with 1 or 2 MetS risk factors, BMI, DBP and CRP levels were significantly higher, while TC, TG, HDL-C and glucose levels were significantly lower than in Japanese females. In Mongolian females with ≥ 3 MetS risk factors, SBP, DBP and CRP levels were significantly higher, while HDL-C and glucose levels were significantly lower than in Japanese females.

When the difference in CRP levels between the Mongolians and Japanese,

Table 1. Comparison of variables between the Mongolian and Japanese patients

	No MetS risk factors		1 or 2 MetS risk factors		≥3 MetS risk factors (MetS)	
	Mongolian (*n*=74)	Japanese (*n*=124)	Mongolian (*n*=98)	Japanese (*n*=100)	Mongolian (*n*=113)	Japanese (*n*=102)
Age, years	29.2 ± 13.5	28.9 ± 14.7	45.9 ± 13.8	48.9 ± 13.2	54.3 ± 10.6	56.3 ± 8.7
Sex, male, % (*n*)	36.5 (27)	34.7 (43)	34.7 (34)	38.0 (38)	47.8 (54)	54.9 (56)
Current smoking, % (*n*)	18.9 (14)	2.4 (3)**	22.4 (22)	38.0 (38)	24.8 (28)	19.6 (20)
BMI, kg/m^2	21.2 ± 2.1	20.6 ± 1.9*	25.2 ± 3.5	23.5 ± 3.5*	28.9 ± 4.7	26.3 ± 4.8**
SBP, mm Hg	113.3 ± 8.5	110.9 ± 9.3	127.8 ± 17.3	124.8 ± 13.5	149.6 ± 21.4	140.1 ± 16.4**
DBP, mm Hg	70.9 ± 6.5	66.5 ± 6.8**	79.8 ± 10.6	76.2 ± 9.8*	94.1 ± 12.3	87.0 ± 16.4**
TC, mmol/L	4.13 ± .68	4.67 ± .84*	4.59 ± .92	5.23 ± 1.02**	4.97 ± 1.10	5.17 ± 1.00
TG, mmol/L	.53 [.43–.41]	.64 [.46–.95]*	.88 [.61–1.25]	1.17 [.81–1.59]**	1.39 [.90–2.12]	1.40 [.96–2.10]
HDL-C, mmol/L	1.48 ± .25	1.70 ± .35**	1.34 ± .33	1.57 ± .44**	1.17 ± .26	1.32 ± .41**
Glucose, mmol/L	4.22 ± .50	4.95 ± .44**	4.69 ± 1.66	6.64 ± 3.13**	6.47 ± 3.26	7.21 ± 3.11
Insulin, μU/mL	6.3 [4.6–9.4]	4.9 [3.2–7.4]**	6.4 [4.1–11.4]	5.6 [3.9–8.0]	10.6 [6.6–16.4]	8.6 [5.1–14.8]
CRP, mg/dL	.05 [.02–.08]	.03 [.02–.06]*	.12 [.07–.32]	.05 [.02–.09]**	.19 [.08–.35]	.07 [.03–.12]**

Data are presented as the mean ± statistical deviation.

TG, insulin and CRP were presented as the median [interquartile range].

Significance level: *P<.05, **P<.01.

MetS: metabolic syndrome, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, TC: total cholesterol, TG: triglyceride, HDL-C: high density lipoprotein cholesterol, CRP: C-reactive protein.

by sex, was analyzed in the covariables-adjusted models, in Mongolian and Japanese males with no MetS risk factors, the difference in CRP was not significant in all of the models. In males with 1 or 2 MetS risk factors, the difference in CRP remained significant in all models (model 1 P=.001, model 2 P=.001, model 3 P=.004). In males with ≥3 MetS risk factors, the difference in CRP remained significant in all models (model 1 P<.001, model 2 P=.001, model 3 P=.003). In the females with no MetS risk factors, the difference in CRP remained significant in model 1 (P=.03), but not in model 2 nor model 3. In females with 1 or 2 MetS risk factors, the difference in CRP remained significant in all models (model 1 P<.001, model 2 P<.001, model 3 P=.001). In females with ≥3 MetS risk factors, the difference in CRP remained significant in all models (model 1 P<.001, model 2 P=.001, model 3 P=.01).

DISCUSSION

To date, the ethnic differences in serum CRP levels have been characterized for various populations. The highest level of CRP is in Aboriginal people, the lowest in Japanese people, and moderate levels in South Asian, Chinese and Europeans people.[13,14] Our study found that the serum CRP levels were higher overall in the Mongolian population than in the Japanese, regardless of MetS. This is identical with previous results observed in patients with hypertension and diabetes mellitus and in healthy younger populations.[10,11] In general, CRP is secreted from hepatocytes and arterial endothelial cells,[15,16] and adipose tissue can increase serum CRP through the stimulation of proinflammatory cytokines.[17] The serum CRP is also induced by oxidative stress concomitant to MetS and its components.[15] This physiological response is a possible explanation of the increases in CRP with increases in MetS risk factors, and the reason that serum CRP levels can be predictive for MetS and its related CVD.[1,6] More importantly, the present study disclosed that with increased numbers of MetS risk factors, the increase in CRP in the Mongolian patients became higher in comparison to the Japanese. Whereas this may be influenced in part by worsening levels of each MetS risk factor in the Mongolians vs the Japanese, the differences in CRP between Mongolian and Japanese patients was not altered even by the covariables-adjusted model analyses. These data suggest the possibility that Mongolian people may be at a greater risk for CVD in comparison to the Japanese people.

The present study showed the higher prevalence of MetS in Mongolians than in the Japanese. This prevalence appears high in comparison to an earlier report conducted in workplace settings.[8] This may be partly explained by the study methods, including the recruitment settings (our settings were hospital-based, even though the recruitments were performed in health check-ups).

There are several limitations in our study. For example, the cross-sectional

Our study found that the serum CRP levels were higher overall in the Mongolian population than in the Japanese, regardless of MetS.

Table 2. Comparison of variables between the Mongolian and Japanese patients by sex

	No MetS risk factors		1 or 2 MetS risk factors		≥3 MetS risk factors (MetS)	
	Mongolian	Japanese	Mongolian	Japanese	Mongolian	Japanese
Male	*n*=27	*n*=43	*n*=34	*n*=38	*n*=54	*n*=56
Age, years	26.8 ± 13.3	28.9 ± 15.5	39.5 ± 17.1	43.4 ± 14.2	53.2 ± 10.8	56.4 ± 9.3
Current smoking, % (*n*)	37.0 (10)	2.3 (1)**	44.1 (15)	31.6 (12)	24.8 (28)	19.6 (20)
BMI, kg/m^2	21.4 ± 2.0	21.2 ± 1.5	23.7 ± 2.8	22.8 ± 2.8	29.1 ± 5.2	25.3 ± 2.6**
SBP, mm Hg	114.9 ± 8.9	115.8 ± 9.1	127.2 ± 18.6	123.6 ± 13.5	147.0 ± 17.0	139.3 ± 16.8*
DBP, mm Hg	71.3 ± 7.2	66.7 ± 6.6*	78.0 ± 10.4	76.0 ± 10.0	94.7 ± 10.7	86.8 ± 9.3**
TC, mmol/L	3.96 ± .74	4.31 ± .71*	4.30 ± .85	4.89 ± 1.04*	4.86 ± 1.11	4.99 ± 1.01
TG, mmol/L	.55 [.43–.78]	.63 [.41–1.02]	.93 [.60–1.24]	1.01 [.73–1.33]	1.63 [1.01–2.20]	1.66 [1.02–2.82]
HDL-C, mmol/L	1.33 ± .21	1.51 ± .27*	1.25 ± .33	1.49 ± .39*	1.14 ± .29	1.21 ± .39
Glucose, mmol/L	4.35 ± .57	5.06 ± .46**	4.92 ± 2.04	6.77 ± 3.47*	7.12 ± 3.65	7.05 ± 2.81
Insulin, μU/mL	6.3 [4.9–10.8]	3.9 [2.3–6.3]**	5.8 [3.2–12.4]	5.3 [3.2–9.5]	12.4 [6.8–18.6]	9.0 [4.8–16.1]
CRP, mg/dL	.05 [.02–.08]	.04 [.02–.08]	.09 [.04–.21]	.05 [.01–.11]*	.17 [.07–.41]	.08 [.03–.15]**
Female	*n*=47	*n*=81	*n*=64	*n*=62	*n*=59	*n*=46
Age, years	30.6 ± 13.5	28.8 ± 14.4	49.2 ± 10.6	52.4 ± 11.3	55.4 ± 10.4	56.3 ± 8.0
Current smoking, % (*n*)	8.5 (4)	2.5 (2)	10.9 (7)	11.3 (7)	15.3 (9)	10.9 (5)
BMI, kg/m^2	21.2 ± 2.1	20.3 ± 2.1*	26.0 ± 3.7	24.0 ± 3.8*	28.7 ± 4.2	27.4 ± 6.0
SBP, mm Hg	112.3 ± 8.3	108.3 ± 8.4*	128.1 ± 16.7	125.5 ± 13.6	152.0 ± 24.7	141.2 ± 15.8*
DBP, mm Hg	70.7 ± 6.1	66.4 ± 6.9*	80.8 ± 10.6	76.3 ± 9.8*	93.5 ± 13.6	87.1 ± 9.5*
TC, mmol/L	4.23 ± .64	4.85 ± .85**	4.75 ± .92	5.44 ± .96**	5.06 ± 1.08	5.39 ± .96
TG, mmol/L	.51 [.42–.69]	.64 [.48–.93]*	.87 [.62–1.25]	1.21 [.96–1.64]**	1.30 [.85–1.94]	1.30 [.81–1.72]
HDL-C, mmol/L	1.56 ± .23	1.81 ± .34**	1.39 ± .32	1.62 ± .46*	1.19 ± .23	1.45 ± .40**
Glucose, mmol/L	4.15 ± .45	4.88 ± .43**	4.58 ± 1.42	6.57 ± 2.92**	5.93 ± 2.75	133.4 ± 53.1*
Insulin, μU/mL	6.3 [4.4–8.7]	5.4 [3.6–7.7]*	6.7 [4.1–11.2]	5.7 [4.1–7.8]	9.3 [5.7–15.7]	7.7 [5.1–12.4]
CRP, mg/dL	.05 [.02–.08]	.03 [.02–.06]*	.16 [.08–.40]	.05 [.02–.09]**	.19 [.08–.33]	.07 [.04–.12]**

Data are presented as the mean ± statistical deviation.

TG, insulin and CRP were presented as the median [interquartile range].

Significance level: *$P<.05$, **$P<.01$.

MetS: metabolic syndrome, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, TC: total cholesterol, TG: triglyceride, HDL-C: high density lipoprotein cholesterol, CRP: C-reactive protein.

design did not determine the causality of the correlation between CRP and MetS risk factors. Our study settings relied on hospital-based health check-ups, so community-based surveys may be required for further generalization of results. In addition, our study did not detect atherosclerotic lesions in each subject. Research including the measurements of atherosclerosis itself should be considered in the future.

CONCLUSIONS

In summary, the present study showed higher serum CRP levels in the Mongolian population than in the Japanese population, and CRP increased at higher rates in the Mongolians than in the Japanese in correlation with the increased number of MetS risk factors. This may be related to the high incidence of CVD in the Mongolian people in comparison to the Japanese people. Further studies are needed to clarify the roles of CRP on vascular health in the Mongolian people.

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AUTHOR CONTRIBUTIONS

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