

Gender difference in the association of metabolic syndrome with hs-CRP Concentration of Blood

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The high sensitivity C-reactive protein (hs-CRP) as one of the typical acute phase reactants is used for predictive factor of the cardiovascular disease and diabetes mellitus. In addition, there are claims that must be included as factors of metabolic syndrome. This research examined the relationship between the concentration of hs-CRP in blood and risk factors of the metabolic syndrome by gender, and the rates of metabolic syndrome depending on the hs-CRP level based on the general public who took the comprehensive medical check-up at Chonbuk National University Hospital in the Jeonbuk province. The subjects aged 17-87 years were participated, and 2,000 people were included as the final subjects except the persons with more than 10 mg/L of the hs-CRP of blood level. The hs-CRP concentrations increased according to the number of risk factors of metabolic syndrome in both men and women. In regards to the risk ratio of metabolic syndrome based on hs-CRP level in blood according to gender, the risk ratio increased by 3.07 times in male and 4.55 times in female intermediate risk group and 3.60 times in male and 6.15 times in female high risk group compared to hs-CRP low risk group. As a result, there was a proportional relation between hs-CRP level and the occurrence of metabolic syndrome, and it occurs more frequently among women than men.

Key Words : hs-CRP, Metabolic syndrome, cardiovascular disease, diabetes mellitus

INTRODUCTION

Recently, the social interests about obesity and metabolic syndrome which are being increased in Korea are increasing caused by South Korea's rapid socio-economic development and change of dietary life, As an aging society, the death rate caused by cardiovascular disease and diabetes mellitus among causes of death in our country increased.

and the prevalence rate of metabolic syndrome that covers these risk factors is increased (Haffner, 1996).

The metabolic syndrome means that hypertension, hyperlipidemia, obesity are revealed in one individual at the same time due to chronic disturbance of metabolism like insulin resistance (Kim, 2010). This crowding phenomenon was called 'syndrome X' or 'insulin resistance syndrome' (Reaven, 1998). In 1998, the World Health Organization (WHO) named this complicated disease as metabolic syndrome because they could not identify this complicated disease and how to name this complication. Insulin resistance alone could not explain how it becomes complicated disease like glucose in tolerance, hypertension, hyperlipidemia, renal disease, etc (Grundy *et al*, 2005), These complicated diseases will eventually developed to cardiovascular disease and type 2 diabetes (McNeill *et al*, 2005). So

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the dangerous metabolic syndrome is not a single disease but the comprehensive disease by combining genetic predisposition and environmental factors. In 2007, according to the Public Health Nutrition study, Korean people over 30 years old who has the metabolic syndrome are 32.9% as men and 31.8% as women. In other study, they also compared the prevalence of metabolic syndrome adults in urban city with in rural areas and it came out to 22.3% in urban city, and 29.3% in rural area (Lim *et al*, 2006). The cause of metabolic syndrome is although not well known but generally, the insulin resistance is estimated as to act as root cause, but this cannot explain the onset of metabolic syndrome. The insulin resistance means the status that the amount of insulin which decreases glucose is normally secreted but the action of insulin is decreased. Therefore, the glucose cannot used in the muscle and liver by decrease of the action by insulin, so hyperglycemia is caused and the previous phase of diabetes or the diabetes are caused. In addition, the obesity is triggered by inducing the accumulation of fat, and the hyperlipidemia appears by increasing blood-level of triglycerides. The increase of blood-fat makes inflammatory easy so increases the risk of thrombosis. In other words, the insulin resistance is related to obesity, type II diabetes mellitus, hypertension, hyperlipidemia, cardiovascular disease. Therefore, all factors of metabolic syndrome are related to the insulin resistance. The insulin resistance is caused by environmental and genetic factors, and the environmental factors related to daily life habits such as obesity or lack of exercise which cause insulin resistance are known well. Especially the obesity is shown as the factor which has big effects on increasing risk of metabolic syndrome by the relevance with hyperlipidemia (Sower, 2003). But, the genetic factors were not disclosed yet. As more factors as cause of metabolic syndrome are included, the death rate due to total death rate and cardiovascular diseases will increase (Isomaa *et al*, 2001), and now increasing trend of metabolic syndrome is

shown around the world, and in our country, the prevalence rate of metabolic syndrome is increasing untiringly. The prevalence rate of metabolic syndrome and the death rate caused by coronary artery disease are expected to be increased by increase of ageing and obesity in our country in the future.

These are several factors that the metabolic syndrome is closely related to the cardiovascular disease. The role of Pro-inflammatory cytokine such as Interleukin-6 (IL-6), Tumor necrosis factor- α (TNF- α) are directly related to the cardiovascular disease. Because these can dilate and constrict the blood vessel due to inflammatory activity is critical to the cardiovascular disease. In the addition, fibrinogen and plasminogen activator inhibitor-1 (PAI-1), and white blood cell are also directly related to the cardiovascular disease (Hotamisligil *et al*, 1993; Baumann and Gauldie, 1994; Mohamed *et al*, 1997; Imperatore *et al*, 1998). Among the inflammatory factors, the level of C-reactive protein is the first line of biomarker which shows the inflammatory activity since it is the acute phase reactant. It is sensitive to the acute inflammatory activity when the body systematically reacts with foreign subjects.

CRP is acute phase reactive protein which appears in the blood stream in response with inflammatory cytokine like interleukin-6 as the acute phase reactants generated from liver, and it is used as biomarker of systemic inflammatory reaction (Ridker *et al*, 2001). In addition, it is significantly increased in diseases such as inflammatory disease, necrosis of body tissues, and it has been related to cardiovascular diseases, obesity, insulin resistance (Albert, 2000), and it has been used for indicators to measure activity of the various inflammatory reactions and diseases. 10-50 mg/L CRP means mild inflammatory or virus infection, 50-200 mg/L means active inflammatory or bacterial infections, >200 mg/L means serious infection or wound. The high sensitivity C-reactive protein (hs-CRP) measures CRP which is included in healthy people or normal range, and

high precision can measure CRP in low range, so it causes light inflammatory, and it can be used as the predictive factor of the cardiovascular diseases, diabetes mellitus (Roberts, 2004). In addition, hs-CRP is the fine inflammatory markers to predict the occurrence of disease, so there is claim that it should be included as a factor of metabolic syndrome (Ridker *et al*, 2004). The hs-CRP is increased by hypertension, BMI, smoking, metabolic syndrome, high density Lipoprotein Cholesterol (HDL-C), diabetes mellitus, estrogen, chronic inflammation, chronic infection etc, and the moderate amounts of alcohol, exercise, weight loss are factors to decrease hs-CRP (Pearson *et al*, 2003). The metabolic syndrome is all related with inflammatory activity. As inflammatory activity increases, CRP level increases so risk of having cardiovascular diseases increases (Marroquin *et al*, 2004), due to constriction of blood vessel. It is important to detect at early stage of the disease to prevent such complications of the disease. According to the previous studies, there is a correlation between hs-CRP level in blood and risk factors for metabolic syndrome, and the occurrence of metabolic syndrome in high and intermediate risk group was two to four times higher than in low risk group, depending on the hs-CRP level. This research confirms the relationships between hs-CRP level and risk factors in different sexes, and tries to measure differences between men and women in the occurrence of metabolic syndrome through the relationship between hs-CRP level and metabolic syndrome.

MATERIALS AND METHODS

1. Participants and period

This study was based on Adults over the age of 17 from 87 who took comprehensive medical checkup in Chonbuk National University Hospital since January until August in 2011. The subjects of study were people residing in the

Jeonbuk province. 2,000 persons except subjects with more than 10 mg/L of hs-CRP level of blood were included in the final subjects of study.

2. Methods

1) Survey

The questionnaire examined population sociological variables (gender, age, family history, medical history, drinking status, smoking etc).

2) Somatometry

The somatometry was measured by using Inbody 3.0 (Biospace, Seoul, Korea) and Inbody 720 (Biospace, Seoul, Korea). As the anthropometry item, the height and weight, waist circumference, hip circumference were measured, and about the waist-hip ratio (WHR), the waist circumference measured by same equipment was calculated by dividing with hip circumference, the male was classified as abdominal obesity with more than 0.90, female was classified as abdominal obesity with more than 0.85. Body Mass Index (BMI) was calculated by dividing weight (kg) by the square of height (m), and more than 25 kg/m² (World Health Organization Western Pacific Region 2000) was defined as obesity. The blood pressure was measured by using Hem-907 (Omron, Kyoto, Japan) of subjects sat after taking 10 minutes to stabilize.

3) Blood Test

The blood was taken after fasting for 12 hours or more. The taken blood was took test by dividing serum by using centrifuge in Laboratory Medicine of Chonbuk National University Hospital Department. Relevant lab value findings were hs-CRP, total cholesterol: HDL-C, LDL-C, triglyceride and fasting glucose levels. All these blood testing was done by laboratory medicine department in Chonbuk National University Hospital, the testing equipment was Advia 2400 (SIEMENS, Berlin & Munich, Germany). In the

testing, a spectrophotometry was used, the principle of the spectrophotometry is explained below. A small amount of serum that is segregated from the blood was added into a reagent. This combined reagent then forms a new chemical structure solution which increases molecule reactivity. This vigorous reaction solution changes into a dense color which will be transmitted more light in the spectrophotometer. The spectrophotometer absorbs more color at various wavelengths to detect its concentrations.

4) Metabolic syndrome

The diagnosis criteria of American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) was applied for the diagnosis criteria of metabolic syndrome except abdominal obesity. In case of abdominal obesity, WHR (waist-hip ratio) was measured and men over 0.90 and women over 0.85 were classified as abdominal obesity since the criteria for abdominal obesity is different according to countries and regions.

Criteria of metabolic syndrome

- (1) Abdominal obesity (WHR) : men $0.90 \geq$, women $0.85 \geq$
- (2) Triglyceride : ≥ 150 mg/dL
- (3) HDL-C : men < 40 mg/dL , women < 50 mg/dL
- (4) Blood Pressure : $\geq 130/85$ mmHg
- (5) FBS : ≥ 100 mg/dL

The group with 3 or more metabolic syndrome risk factors out of 5 was determined to have metabolic syndrome.

5) High sensitivity C-reactive protein (hs-CRP)

High sensitivity-CRP is a biomarker of inflammation. The hs-CRP level alerts in atherosclerosis and endothelial cell disorder whether they turn on the inflammatory activity or not. This inflammatory biomarker is also used to cardiovascular disease and type 2 diabetes mellitus (Tracy *et al*, 1997; Koenig *et al*, 1999; Rohde *et al*, 1999). The hs-CRP has high sensitivity and high precision at inflammatory activity, it can detect at minimum inflammatory event (Ridker

et al, 2003). Generally, hs-CRP level greater than 10 mg/L is considered as inflammation which is excluded in this study. The hs-CRP level greater than 3 mg/L are high risk group, below 1.0 mg/L are low risk group and between 1 and 3 mg/L are intermediate risk group that are classified by American Heart Association and Center for Disease Control Center (Pearson *et al*, 2003).

3. Data Analysis

All analysis were performed by using Excel 2007 and WIN (ver. 12.0), and it was analyzed by using statistical methods as follows. The risk group of metabolic syndrome were divided into 5 subcategories : 0-5, means 0 at the lowest risk and 5 at the highest risk. The hs-CRP value determined the risk group, CRP level less than 1.0 mg/L are the low risk group, CRP level between 1-3 mg/L are the intermediate group and CRP level greater than 3 mg/L are the high risk group. Property of population sociology, biological and physical were analyzed by Chi-Square test. The correlation coefficient of metabolic syndrome risk factors (TG, HDL-C, FBS, WHR, BP) and TC, LDL-C, BMI and hs-CRP was calculated by Pearson correlation analysis, hs-CRP level related to metabolic syndrome was analyzed by Logistic Regression Analysis.

Result

1. Age distribution of the study subjects

As a result of analyzing of age distribution of subjects, there were 1,000 men and women respectively. Looking into the distribution of age, the most targets were in their 40's (30.5%) followed by 50's (28.9%). The least targets were under 30's (3.0%) and over 70's (4.3%). Comparing the distribution of men and women, the most targets were in their 40's for both men (32.2%) and women (28.8%) and the least targets were under 30's for both men (2.7%) and

women (3.3%) (Table 1).

2. Distribution of metabolic syndrome and hs-CRP level in blood of the study subjects

Among 2,000 research targets, 585 (29.3%) had metabolic syndrome and there were 342 men (34.2%) and 243 women (24.3%). Also, in regards to the distribution of hs-CRP in blood, there were 1,598 (79.9%) in low risk group, 259 (12.9%) in intermediate risk group, and 143 (7.2%) in high risk group (Table 2, 3).

3. Distribution of the number of metabolic syndrome by gender and age of the study subjects

As a result of dividing the number of possessing risk

factors for metabolic syndrome into 0~5 and examining in accordance with gender, the highest distribution was presented in group with 2 risk factors in both men (25.3%) and women (30.3%) and the lowest distribution was presented in group with 5 risk factors in both men (2.4%) and women (2.3%). In regards to the age group, 1 and 2 risk factors of metabolic syndrome presented highest distribution in age under 30 and in 30's respectively. 2 and 3 risk factors of metabolic syndrome were presented in 25.1% and 18.9% respectively for targets in 40's, 32.2% and 22.1% respectively in 50's, 35.8% and 27.0% respectively in 60's, and 29.1% and 25.6% respectively in 70's. It was revealed that the number of possessing risk factors for metabolic syndrome increased with the increase in age and it was

Table 1. Age distribution of the study subjects

Variables	Number of tests		Total (%)
	Men (%)	Women (%)	
Age (year)			
< 30	27 (2.7)	33 (3.3)	60 (3.0)
30-39	165 (16.8)	194 (19.4)	359 (17.9)
40-49	322 (32.2)	288 (28.8)	610 (30.5)
50-59	308 (30.8)	270 (27.0)	578 (28.9)
60-69	143 (14.3)	164 (16.4)	307 (15.4)
70 ≤	35 (3.5)	51 (5.1)	86 (4.3)
Total (%)	1,000 (100.0)	1,000 (100.0)	2,000 (100.0)

Table 2. Distribution of metabolic syndrome of the study subjects

Variables	Metabolic syndrome Distribution		
	Men (%)	Women (%)	Total (%)
0	164 (16.4)	202 (20.0)	366 (18.3)
1	241 (24.1)	252 (25.2)	493 (24.6)
2	253 (25.3)	303 (30.3)	556 (27.8)
3	225 (22.5)	162 (16.2)	387 (19.4)
4	93 (9.3)	58 (5.8)	151 (7.5)
5	24 (2.4)	23 (2.3)	47 (2.4)
Total (%)	1,000 (100.0)	1,000 (100.0)	2,000 (100.0)

Table 3. Distribution of hs-CRP concentration in blood of the study subjects

Variables	Distribution of hs-CRP Concentration		
	Men (%)	Women (%)	Total (%)
< 1	772 (77.2)	826 (82.6)	1,598 (79.9)
1-3	142 (14.2)	117 (11.7)	259 (12.9)
> 3	86 (8.6)	57 (5.7)	143 (7.2)
Total (%)	1,000 (100.0)	1,000 (100.0)	2,000 (100.0)

Table 4. Distribution of the number of metabolic syndrome by gender and age of the study subjects

Variables	Number of components of metabolic syndrome						Total (N)
	0 (N=366)	1 (N=493)	2 (N=556)	3 (N=387)	4 (N=151)	5 (N=47)	
Gender							
Men	164 (43.4)	241 (24.1)	253 (25.3)	225 (22.5)	93 (9.3)	24 (2.4)	1,000
Women	202 (20.2)	252 (25.2)	303 (30.3)	162 (16.2)	58 (5.8)	23 (2.3)	1,000
Age (year)							
< 30	26 (43.4)	23 (38.3)	6 (10.0)	5 (8.3)	0 (0.0)	0 (0.0)	60 ()
30-39	120 (33.4)	113 (31.5)	76 (21.2)	34 (9.5)	14 (3.8)	2 (0.6)	359 ()
40-49	139 (22.8)	158 (25.9)	153 (25.1)	115 (18.9)	35 (5.7)	10 (1.6)	610 ()
50-59	63 (10.9)	134 (23.2)	186 (32.2)	128 (22.1)	51 (8.8)	16 (2.8)	578 ()
60-69	14 (4.6)	51 (16.6)	110 (35.8)	83 (27.0)	37 (12.1)	12 (3.9)	307 ()
70 <							

statistically significant ($p < 0.001$, Table 4).

4. Distribution of hs-CRP group based on the number of risk factors of metabolic syndrome

Looking into the distribution of hs-CRP based on the number of possessing risk factors for metabolic syndrome, the distribution of hs-CRP in low risk group was very high presenting over 80% in case of possessing 0-2 risk factors of metabolic syndrome ($p < 0.001$). In case of possessing 3 risk factors of metabolic syndrome, the distribution was 71.0%, 20.2%, and 8.8% for low, intermediate, and high risk group for hs-CRP respectively. In case of 4 risk factors, the distribution was 46.4%, 31.1%, and 22.5% for low, intermediate, and high risk group respectively. In case of 5 risk factors, the distribution was 44.7%, 23.4%, and 31.9%

for low, intermediate, and high risk group respectively. Therefore, it was revealed that the distribution in intermediate and high risk group for hs-CRP increased with the increase in number of possessing risk factors for metabolic syndrome. According to the distribution chart, there is no significant difference between gender when the number of risk factors are 0 to 3, but when the number increases to 4, women show more intermediate risk group, and when it increases to 5, men show more high risk group ($p < 0.001$, Table 5).

5. Correlation between risk factors of metabolic syndrome and hs-CRP concentration in blood

In regards to the correlation between risk factors of metabolic syndrome such as TG, HDL-C, LDL-C, TC,

Table 5. Distribution of hs-CRP group based on the number of risk factors of metabolic syndrome

Variables	Number of components of metabolic syndrome						Total (%)
	0 (N=366)	1 (N=493)	2 (N=556)	3 (N=387)	4 (N=151)	5 (N=47)	
hs-CRP (mg/L)							
Men	< 1	143 (87.2)	208 (86.3)	206 (81.4)	160 (71.1)	45 (48.3)	10 (41.7)
	1-3	13 (7.9)	20 (8.3)	32 (12.6)	50 (22.2)	23 (24.7)	4 (16.6)
	> 3	8 (4.9)	13 (5.4)	15 (6.0)	15 (6.7)	25 (27.0)	10 (41.7)
Women	< 1	197 (96.0)	224 (88.9)	257 (84.8)	115 (71.0)	25 (43.1)	11 (47.8)
	1-3	5 (2.5)	22 (8.7)	31 (10.2)	28 (17.3)	24 (41.4)	7 (30.4)
	> 3	3 (1.5)	6 (2.4)	15 (5.0)	19 (11.7)	9 (15.5)	5 (21.8)
Total	< 1	337 (92.0)	432 (87.6)	463 (83.3)	275 (71.0)	70 (46.4)	21 (44.7)
	1-3	18 (5.0)	42 (8.5)	63 (11.3)	78 (20.2)	47 (31.1)	11 (23.4)
	> 3						

Table 6. Correlation between risk factors of metabolic syndrome and hs-CRP concentration in blood

	TG	HDL-C	FBS	SBP	DBP	WHR	LDL-C	TC
TG	1.00	-0.38	0.19**	0.23**	0.24**	0.33**	0.05**	0.27**
HDL-C		1.00	-0.15	-0.13	-0.09	-0.36	-0.06	0.09**
FBS			1.00	0.16**	0.12**	0.21**	0.03	0.12**
SBP				1.00	0.71**	0.34**	0.12**	0.10**
DBP					1.00	0.26**	0.15**	0.12**
WHR						1.00	0.25**	0.18**
LDL-C							1.00	0.58**
TC								1.00
BMI								
hs-CRP								

* $p < 0.05$, ** $p < 0.01$

FBS, and others and hs-CRP concentration in blood, TG presented positive correlation in most of factors including TC ($r=0.27$), WHR ($r=0.33$), and BMI ($r=0.33$) and Systole blood pressure presented strong positive correlation with diastole blood pressure ($r=0.71$) and WHR ($r=0.34$). In addition, WHR presented strong positive correlation with BMI ($r=0.84$) and LDL-C presented highly positive correlation with TC ($r=0.58$). HDL-C that poses risk when its concentration in blood is low different from other risk factors pre-

sented negative correlation with other risk factors except DBP, LDL-C, and TC. hs-CRP presented weak negative correlation with HDL-C and weak positive correlation with other risk factors of metabolic syndrome including TG, FBS, Systole BP, WHR and BMI (Table 6). The correlations between hs-CRP level in blood and risk factors of metabolic syndrome were similar between gender.

Table 7. Ratio for risk occurrence of metabolic syndrome based on hs-CRP level in blood

Variables	Univariate analysis	
	Hazard ratio (95% CI)*	<i>p</i> -value [†]
hs-CRP (mg/L)		
< 1	1.00	
1-3	3.72 (2.84-4.88)	< 0.001
> 3	4.66 (3.28-6.62)	< 0.001

*95% confidence interval, [†]*p*-value by logistic regression analysis

Table 8. Ratio for risk occurrence of metabolic syndrome based on hs-CRP level in blood

Variables	Univariate analysis			
	Men		Women	
	Hazard ratio (95% CI)*	<i>p</i> -value [†]	Hazard ratio (95% CI)*	<i>p</i> -value [†]
hs-CRP (mg/L)				
< 1	1.00			
1-3	3.07 (2.13-4.42)	< 0.001		
> 3		< 0.001		

6. Ratio for risk occurrence of metabolic syndrome based on hs-CRP level in blood

In regards to the ratio of metabolic syndrome risk based on level of hs-CRP in blood, the ratio for intermediate risk group (1.0~3.0 mg/L) was 3.72 times and high risk group (≥ 3.0 mg/L) was 4.66 times compared to hs-CRP low risk group (< 1.0 mg/L) (Table 7).

7. Ratio for risk occurrence of metabolic syndrome based on hs-CRP level in blood by gender

In regards to the ratio of metabolic syndrome risk based on the concentration level of hs-CRP in blood according to gender, the ratio for intermediate risk group was 3.07 times as men, 4.55 times as women and high risk group was 3.60 times as men, 6.15 times as women compared to hs-CRP low risk group (Table 8).

Discussion

CRP is one of generalized acute inflammation reactive substances and it is known as the risk factor and predictive factor of cardiovascular disease (Freeman *et al*, 2002). Also, as the marker of atherosclerosis and qualitative disorders of endothelial cell, it is reported to be related to percent body fat and risk factors of cardiovascular diseases (Ridker *et al*, 2001). Moreover, it is protein that is generated in inflammation, neoplasm, or serum with abnormality. It precipitates polysaccharide of pneumococcus and used to diagnose the condition of various inflammations. Especially, hs-CRP concentration in blood presents the degree of minor inflammation and more attention is paid to it as a predictive factor for the onset of cardiovascular disease and diabetes mellitus. Therefore, the relation between hs-CRP concentration in blood which is one of indexes for inflammation in human body and each risk factor of metabolic

syndrome will be looked into in this study. Also, the purpose of this study lies in revealing the risk ratio of metabolic syndrome based on the level of hs-CRP risk groups and relevant risk factors including drinking and smoking among general traits. The diagnosis criteria of AHA/NHLBI was applied for the diagnosis criteria of metabolic syndrome except abdominal obesity (Grundy *et al*, 2005). In case of abdominal obesity, WHR was measured and men over 0.90 and women over 0.85 were classified as abdominal obesity since the criteria for abdominal obesity is different according to countries and regions. Then, the group with 3 or more metabolic syndrome risk factors out of 5 was determined to have metabolic syndrome.

As a result of analysis, 585 (29.3%) had metabolic syndrome among 2,000 research targets and the prevalence was 34.2% and 24.3% for men and women respectively. Also, in regards to the distribution of hs-CRP in blood, there were 1,598 (79.9%) in low risk group, 259 (12.9%) in intermediate risk group, and 143 (7.2%) in high risk group. Looking into the distribution for number of risk factors for metabolic syndrome diagnosis criteria based on age of study subjects, the distribution was concentrated in 2 and 3 metabolic syndrome risk factors for the age group of 40~70. The prevalence of metabolic syndrome increased with the increase in age. The prevalence started to increase in 30's for both men and women. It implies that it is necessary to prevent metabolic syndrome by actively managing it from early age. In study, the most distribution was presented in 2 metabolic syndrome risk factors presenting the distribution of 25.3% and 30.3% for men and women respectively in 2 metabolic syndrome risk factors and 22.5% and 16.2% for men and women respectively in 3 metabolic syndrome risk factors. It signifies high probability for potential metabolic syndrome thus it is critical to prevent and manage all stages of metabolic syndrome.

Same as previous study which revealed that the increase in number of metabolic syndrome risk factors causes the

increase in hs-CRP level thereby increase risk for the onset of cardiovascular disease and diabetes mellitus (Soly-moss *et al*, 2004), and insulin resistance (Meshkani *et al*, 2006), the average level of hs-CRP concentration in blood increased when the number of possessing risks factors for metabolic syndrome was 3 or more regardless of the fact that most inflammation reactive targets were excluded from the target of analysis when hs-CRP was over 10mg/L which generally signifies the condition of inflammation. As seen above, hs-CRP concentration in blood is the index for generalized micro immune reaction and it reveals that hs-CRP is important influencing factor of metabolic syndrome. Also, in regards to the distribution of hs-CRP concentration in blood, the distribution of hs-CRP high risk group was higher as the number of risk factors for metabolic syndrome increased. As a result of this study, it can be noticed that the increase in number of possessing risk factors for metabolic syndrome causes the increase in hs-CRP concentration in blood thereby increase micro inflammation. Also, it suggests that generalized inflammation is progressed with the increase in number of possessing risk factors for metabolic syndrome in hs-CRP high risk group.

In previous studies, it was reported that there is negative correlation between hs-CRP and HDL-C (Nakanishi *et al*, 2005). Also, the relation between metabolic syndrome elements such as BP, FBS, TG, BMI, TC, WHR, and others and hs-CRP has been reported (Frohlich *et al*, 2000). In this study, negative correlation between hs-CRP and HDL-C was presented as well and positive correlation was presented between hs-CRP and other metabolic syndrome factors. Also, this study revealed the influence of various environmental factors of metabolic syndrome. Age, obesity, smoking, and others were presented to be principal risk factors of metabolic syndrome and hs-CRP (Sower, 2003). Among them, low HDL-C was reported with the increase in amount of smoking and the increase in risk of coronary artery disease was reported with metabolic syndrome and

increase in hs-CRP concentration (Aguilar *et al*, 2006). In this study, the decrease in HDL-C was also reported with the increase in number of risk factors for metabolic syndrome. In study by Framingham (Castelli, 1998), low prevalence of cardiovascular disease was presented in both men and women with high HDL-C. In study targeting Koreans, as a result of conducting 13 year follow-up study on over 100,000 general population regarding the correlation between HDL-C level and risk of cardiovascular disease, it was revealed that the risk for the onset of ischaemic heart disease increased with the decrease in HDL-C level (KIMS POC, 2007). Therefore, HDL-C is very important matter to be controlled together with other metabolic syndrome risk factors and long-term follow-up study shall be conducted for more accurate epidemiology study.

The rate of occurrence of metabolic syndrome was higher in intermediate risk group and high risk group than low risk group depending on the hs-CRP level, and women show high more occurrence rate than men when they belong to the intermediate and high risk group. In conclusion, overall relations between metabolic syndrome and hs-CRP is confirmed. Therefore, if hs-CRP level in blood belong to the intermediate or high risk group level, need to conduct the examination of metabolic syndrome, and it is more necessary to women. In study on relation between dietary habit and CRP, Blake & Ricker suggested that there is relation between the folic acid intake & sound lifestyle and the decrease in CRP concentration (Blake and Ricker, 2003). Therefore, in order to prevent metabolic syndrome, comprehensive management shall be carried out by integrating such risk factors and it is necessary to clarify whether the increase in hs-CRP concentration in blood is followed by risk factors of metabolic syndrome or minor inflammation. Since this study has the limitation in clarifying the relation among the prevalence of metabolic syndrome, hs-CRP, risk factors of metabolic syndrome, and other factors because of unbalanced age group, short

research period, and selection of complete physical examination recipients as target, it is necessary to carry out more accurate and extensive study by applying newly introduced diagnosis criteria for metabolic syndrome, and others in the future.

References

1. Aguilar D, Fisher MR, O'Connor CM, Dunne MW, Muhlestein JB, Yao L, *et al*. Metabolic syndrome, C-reactive protein, and prognosis in patients with established coronary artery disease. *Am Heart J*. 2006, 152:298-304.
2. Albert MA. The role of C-reactive protein in cardiovascular disease risk. *Curr Cardiol Rep*. 2000, 2(4):274-279.
3. Baumann H, Gauldie J. The acute phase response. *Immunol Today*. 1994, 15:74-80.
4. Blake GJ, Ricker PM. C-reactive protein and other inflammatory risk markers in acute coronary syndrome. *J Am College Cardiology*. 2007, 41(4):37-42.
5. Castelli WP. Cholesterol and lipids in the risk of coronary heart disease: The framingham heart study. *Can J Cardiol*. 1998, 4:5A-10A.
6. Freeman DJ, Norrie J, Caslake MJ, Gaw A, Ford I, Lowe GD, *et al*. C-Reactive protein is an independent predictor of risk for the development of diabetes in the west of scotland coronary prevention study. *Diabetes*. 2002, 51(5):1596-1600.
7. Frohlich M, Imhof A, Berg G, Hutchinson WL, Pepys MB, Boeing H, *et al*. Association between C-reactive protein and features of the metabolic syndrome: a population-based study. *Diabetes Care*. 2000, 23(12):1835-1839.
8. Grundy SM, Cleeman JL, Daniels SR, Donato KA, Eckel RH, Franklin BA, *et al*. American heart association; national heart, lung, and blood institute, diagnosis and management of themetabolic syndrome: an American heart association/national heart, lung, and blood institute scientific statement. *Circulation*. 2005, 112:2735-2752.
9. Haffner SM. The insulin resistance syndrome revisited. *Diabetes Care*. 1996, 19:275-7.
10. Hotamisligil GS, Shargill NS, Spiegelman BM. Adipose expression of tumor necrosis factor-alpha: direct role in obesitylinked insulin resistance. *Science*. 1993, 259:87-91.
11. Imperatore G, Riccardi G, Iovine C, Rivellese AA, Vaccaro O. Plasma fibrinogen: a new factor of the metabolic syndrome. A population-based study. *Diabetes Care*. 1998, 21:649-54.

12. Isomaa P, Almare P, Tuomi T, Forsen B, Lahti K, Nissen M. Cardiovascular morbidity and associated with the metabolic syndrome. *Diabetes Care*. 2001, 24(4):683-689.
13. Kim. The Association between hs-CRP Concentration of Blood and Metabolic Syndrome in the Residents of a Rural Community. *Korean J Community Nutr*. 2010, 15(6):796-805.
14. KIMS POC (Point of Care). Current data of HDL in Korean and new proposal to define role of HDL in Korean. 2007, Available from <http://www.kimsonline.co.kr>
15. Koenig W, Sund M, Frohlich M, Fischer HG, Lowel H, Doring A, *et al*. C-Reactive protein, a sensitive marker of inflammation, predicts future risk of coronary heart disease in initially healthy middle-aged men: results from the MONICA (Monitoring Trends and Determinants in Cardiovascular Disease) Augsburg Cohort Study, 1984 to 1992. *Circulation*. 1999, 99:237-42.
16. Lim S, Lee HK, Kim KC, Park C, Shin C, Cho NH. Submitted to journal of endocrinological investigation a ruralurban comparison of the characteristics of metabolic syndrome by gender in Korea: The Korea Health and Demome Study (KHGS). *J Endocrinol Invest*. 2006, 29(4):303-319.
17. Marroquin OC, Kip KE, Kelley DE, Johnson BD, shaw LJ, Bairey Merz CN, *et al*. Metabolic syndrome modifies the cardiovascular risk associated with angiographic coronary artery disease in women: A report from the women's ischemia syndrome evaluation. *Circulation*. 2004, 109(6):714-721.
18. McNeill AM, Rosamond WD, Girman CK, Golden SH, Schmidt ML, East HE, *et al*. (2005): The metabolic syndrome and 11-year risk of incident cardiovascular disease in the atherosclerosis risk in communities study. *Diabetes Care*. 2005, 28(2):385-390.
19. Meshkani R, Taghikhani M, Larijani B, Khatami B, Khatami S, Khoshbin E, *et al*. The relationship between homeostasis model assessment and cardiovascular risk factors in Iranian subjects with normal fasting glucose and normal glucose tolerance. *Clin Chim Acta*. 2006, 371(2):169-175.
20. Mohamed-Ali V, Goodrick S, Rawesh A, Katz DR, Miles JM, Yudkin JS, *et al*. Subcutaneous adipose tissue releases interleukin-6, but not tumor necrosis factor-alpha, in vivo. *J Clin Endocrinol Metab*. 1997, 82:4196-200.
21. Nakanishi N, shirishi T, Wada M. Association between fasting glucose and C-reactive protein in a Japanese population: the Minoh study. *Diabetes Research and Clinical Practice*. 2005, 69(1):88-98.
22. Pearson TA, Mensah GA, Alexander RW, Anderson JL, Cannon RO, Criqui M. Markers of inflammation and cardiovascular disease: Application to clinical and public health practice: A statement for healthcare professionals from the centers for disease control and prevention and the American heart association. *Circulation*. 2003, 107(3):499-511.
23. Reaven GM. Role of insulin resistance in human disease. *Diabetes*. 1998, 37(12):1595-1607.
24. Ridker PM, Buring JE, Cook NR, Rifai N. C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events: an 8-year follow-up of 14 719 initially healthy American women. *Circulation*. 2003, 107(3): 391-397.
25. Ridker PM, Stampfer MJ, Rifai N. Novel risk factors for systemic atherosclerosis: a comparison of C-reactive protein, fibrinogen, homocysteine, lipoprotein(a), and standard cholesterol screening as predictors of peripheral arterial disease. *JAMA*. 2001, 285(19):2481-2485.
26. Ridker PM, Wilson PW, Grundy SM. Should C-reactive protein be added to metabolic syndrome and to assessment of global cardiovascular risk. *Circulation*. 2004, 109(23):2818-2825.
27. Roberts WL. CDC/AHA workshop on markers of inflammation and cardiovascular disease: Application to clinical and public health practice: laboratory tests available to assess inflammation-performance and standardization. *Circulation*. 2004, 110(25):572-576.
28. Rohde LE, Hennekens CH, Ridker PM. Survey of C-reactive protein and cardiovascular risk factors in apparently healthy men. *Am J Cardiol*. 1999, 84:1018-22.
29. Solymoss BC, Bourassa MG, Campeau L, Sniderman A, Marcil M, Lesperance J, *et al*. Effect of increasing metabolic syndrome score on atherosclerotic risk profil and coronary artery disease angiographic severity. *Am J Cardiol*. 2004, 93(2):159-164.
30. Sower JR. Obesity as a cardiovascular risk factors. *Am J Med*. 2003, 115(8A):37-44.
31. Stern MP, Williams K, Haffer SM. Identification of persons at high risk for type 2 diabetes mellitus: Do we need the oral glucose tolerance test. *Ann Inter Med*. 2002, 136(8):575-581.
32. Tracy RP, Lemaitre RN, Psaty BM, Ives DG, Evans RW,ushman M, *et al*. Relationship of C-reactive protein to risk of cardiovascular disease in the elderly. Results from the cardiovascular health study and the rural health promotion project. *Arterioscler Th romb Vasc Biol*. 1997, 17:1121-7.