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Original Article

Correlations between metabolic syndrome, serologic factors, and gallstones

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Abstract. [Purpose] This study investigated the serologic factors associated with metabolic syndrome and gallstones. [Subjects and Methods] The study evaluated subjects who visited a health promotion center in Seoul from March 2, 2013 to February 28, 2014, and had undergone abdominal ultrasonography. Height, weight, and blood pressure were measured. Blood sampling was performed for high-density lipoprotein cholesterol, triglyceride, fasting blood glucose, total bilirubin, direct bilirubin, indirect bilirubin, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, uric acid, total cholesterol, low-density lipoprotein cholesterol, thyroid stimulating hormone, and red and white blood cell counts. We conducted logistic regression analysis to assess the risk factors associated with metabolic syndrome. [Results] The risk factors for metabolic syndrome in men, in order of decreasing weight, were red blood cell count, body mass index, maximum size of gallstones, white blood cell count, waist circumference, and uric acid level. The factors in women, in order of decreasing weight, were red blood cell count, presence/absence of gallstones, uric acid level, body mass index, fasting blood glucose, and waist circumference. [Conclusion] Most serum biochemical factors and gallstone occurrence could be used to indicate the presence or absence of metabolic syndrome, independent of gender.
Key words: Metabolic syndrome, Gallstones, Hematologic relevant factors

INTRODUCTION

Due to lower fertility rates and advances in medical technology and services, the average age of the population is increasing worldwide. An aging society has a higher rate of various chronic diseases including abdominal obesity, type 2 diabetes, cardiac and cerebrovascular disease, and cancers[1–5]. In particular, obesity is a primary factor in the etiology of diabetes mellitus (DM), hypertension, hyperlipidemia, and arthritis, and contributes to a reduced quality of life and shorter life expectancy[6]. Obesity-induced blood lipid accumulation causes chronic inflammation and tissue damage, and induces insulin resistance and hyperinsulinemia; these stimulate excessive secretion of cholesterol by the liver, consequently triggering excessive secretion of bile, with subsequent increases in the size of the gallbladder and deterioration of gallbladder contractility[7, 8]. It has been reported that reduction in gallbladder motility is associated with gallstones[9]. The presence of gallstones is the most common disease of the biliary system. In Western countries, the prevalence of gallstones in females is 2 times greater than that in males, and in both genders, the prevalence increases with age; by the age of 70, the prevalence is approximately

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30%[10]). Abdominal ultrasonography is relatively cost-effective and is widely used for the diagnosis of gallstones. There is a high prevalence of asymptomatic gallstones. Gallstones are said to be closely associated with metabolic syndrome[11]). To this end, we examined serologic factors associated with metabolic syndrome in relation to the occurrence of gallstones.

SUBJECTS AND METHODS

Subjects who visited a health promotion center in Seoul from March 2, 2013 to February 28, 2014 and had undergone abdominal ultrasonography were included in the study. All participants signed a written informed consent form approved by the Institutional Review Board of the Hallym University of Graduate Studies. Of a total of 428 subjects, 256 males and 172 females were selected at random and divided into 3 groups: those with a gallstone and concurrent metabolic syndrome during the study period, those with metabolic syndrome without a gallstone, and a normal group who did not have either a gallstone or metabolic syndrome. The diagnosis of metabolic syndrome was made when an individual met 3 or more of the following components of the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) diagnostic criteria: (1) abdominal obesity (waist circumference ≥90 cm for Asian men or ≥80 cm for Asian women); (2) triglycerides ≥150 mg/dl; (3) HDL cholesterol ≤40 mg/dl for men or 50 mg/dl for women; (4) systolic/diastolic blood pressure ≥130/85 mmHg or receiving drug treatment; and (5) fasting plasma glucose ≥100 mg/dl[11]). Subjects under 20 years of age or with factors that could affect metabolic syndrome such as insufficient data, or past surgical history involving the liver or biliary system were excluded. Height, weight, and blood pressure were measured using an Automatic Anthropometric Machine; the body mass index (BMI) was calculated according to [Weight (kg)/Height (m^2)], and the degree of obesity was assessed according to [(Current Weight (kg)/Standard Weight (kg) ×100 (%)].Waist circumference was the smallest measurement taken with a tape measure at a point between the lowest rib and the iliac crest. Venous blood sampling was performed after a fast of at least 12 hours. The items measured included high-density lipoprotein (HDL) cholesterol, triglyceride, fasting blood glucose, total bilirubin, direct bilirubin, indirect bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), uric acid, total cholesterol, low-density lipoprotein (LDL) cholesterol, thyroid stimulating hormone (TSH), red blood cell (RBC) count, and white blood cell (WBC) count. Diagnosis of gallstones was made by 3 independent skilled medical radiology specialists using abdominal ultrasonography. Any migration of the echo with positional changes accompanied by shadowing toward the posterior of the gallbladder was diagnosed as having gallstones. Those with gallbladder diseases other than gallstones were excluded from the study. The numbers of gallstones were determined through imaging and interpretation of abdominal ultrasonography. When the number of stones was more than 10, the subject was considered to have 10 stones. The largest gallstones were measured using ultrasonic equipment (SSD-σ7; Aloka Company). Collected data were analyzed by using SPSS, version 18.0 for Windows (SPSS, Chicago, IL, USA). An independent t-test was conducted for correlations between the serum biochemical assay factors and occurrence of cholelithiasis in males and females with and without metabolic syndrome. Logistic regression analysis was performed to assess metabolic syndrome risk factors. Statistical significance was set at p<0.05.

RESULTS

In male subjects, the mean age of those with metabolic syndrome was 43.59 ± 9.46 years and the mean BMI was 28.28 ± 3.02 kg/m^2; these values were greater than in those without metabolic syndrome. In both males and females, those with metabolic syndrome had systolic and diastolic blood pressure (BP) higher than those without metabolic syndrome (p<0.05) (Table 1). In male subjects, those with metabolic syndrome showed the following: mean AST 31.5 ± 16 u/l, mean cholesterol 208.42 ± 54.89 mg/dl, mean fasting blood glucose 116.0 ± 3 mg/dl, mean RBC count 5.07 ± 0.3 × 10^3/mm^3, mean duration of smoking 14.6 ± 10 years, and mean maximum size of gallstones 1.35 ± 0.51 cm. All of the values represent significant differences from those of the group without metabolic syndrome (p<0.05). In female subjects, those with metabolic syndrome showed the following: mean total bilirubin 0.66 ± 0.3 mg/dl, mean cholesterol 201.1 ± 32 mg/dl, mean HDL cholesterol 45.7 ± 9 mg/dl, and mean WBC count 6.5 ± 1.7 × 10^3/mm^3. All of the values represent significant differences from those of the group without metabolic syndrome (p<0.05) (Table 2). In male subjects with metabolic syndrome, age was 1.029 times, weight was 1.205 times, HDL cholesterol was 0.922 times, triglyceride was 1.027 times, fasting blood glucose was 1.076 times, RBC count was 3.790 times, and WBC count was 1.824 times greater than in those without metabolic syndrome (p<0.05) (Table 3).

DISCUSSION

This study was conducted to investigate metabolic syndrome using 2005 American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) criteria, and 2005 Abdominal Obesity Criteria published by the Korean Society for the Study of Obesity. The study also analyzed the association between biochemical factors and gallstones by gender, and the relative risks by factor for the presence of metabolic syndrome. In male subjects, metabolic syndrome was associated with age,

Table 1. General indicators of metabolic syndrome by gender

Gender	Variable	Presence or absence of metabolic syndrome	Average	Gender	Variable	Presence or absence of metabolic syndrome	Average
Male	Age	No	40.9 ± 10.1	Female	Age	No	36.5 ± 10.2
		Yes	43.5 ± 9.4			Yes	44.0 ± 9.5
	Height	No	173.6 ± 5.1		Height	No	161.3 ± 5.8
		Yes	172.9 ± 8.1			Yes	159.9 ± 5.3
	Weight	No	69.5 ± 7.4		Weight	No	56.8 ± 8.7
		Yes	85.2 ± 10.5			Yes	71.7 ± 10.2
	BMI	No	23.0 ± 2.4		BMI	No	21.7 ± 2.9
		Yes	28.2 ± 3.0			Yes	28.0 ± 3.7
	Degree of obesity	No	104.9 ± 11.6		Degree of obesity	No	103.2 ± 14.2
		Yes	129.2 ± 13.9			Yes	131.9 ± 20.9
	Waist circumference	No	80.6 ± 6.4		Waist circumference	No	71.7 ± 7.0
		Yes	95.1 ± 6.6			Yes	90.2 ± 9.2
	Systolic BP	No	114.3 ± 10.6		Systolic BP	No	106.7 ± 10.9
		Yes	126.3 ± 13.9			Yes	123.7 ± 13.2
	Diastolic BP	No	72.0 ± 8.9		Diastolic BP	No	66.1 ± 7.8
		Yes	80.2 ± 10.0			Yes	78.0 ± 9.7

weight, BMI, degree of obesity, waist circumference, systolic BP, diastolic BP, AST, ALT, uric acid, total cholesterol, HDL cholesterol, triglycerides, fasting blood glucose, RBC count, WBC count, presence of gallstones, and the size of gallstones. In female subjects, metabolic syndrome was associated with age, weight, BMI, degree of obesity, waist circumference, systolic BP, diastolic BP, total bilirubin, indirect bilirubin, AST, ALT, ALP, uric acid, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, fasting blood glucose, RBC count, and WBC count. In men, there were relatively more subjects with metabolic syndrome within each generation in their 30s, 40s, and 50s. In women, there were more subjects without metabolic syndrome within each generation in their 30s and 40s. These results are different from those reported by Son et al., who concluded that the reduction in male hormones in men and reduction of female hormones in menopausal women were associated with increased prevalence of metabolic syndrome with aging, in both men and women[12]. Park et al. reported that the lower the rate of obesity, weight, and BMI, the higher the concentration of adiponectin; they stated that adiponectin acted as a critical element in the development of insulin resistance, and that this information would be helpful for the treatment of diabetes[13]. Similarly, this study found that factors such as weight, BMI, and the degree of obesity were significantly greater in those with metabolic syndrome. In men, total, direct, and indirect bilirubin showed no statistical association with metabolic syndrome. However, in women with metabolic syndrome, total bilirubin was 0.66 ± 0.32 mg/dl and indirect bilirubin was 0.46 ± 0.24 mg/dl, whereas in women without metabolic syndrome, total bilirubin was 0.78 ± 0.31 mg/dl and indirect bilirubin was 0.56 ± 0.23 mg/dl, indicating a significant inverse reduction. These outcomes were consistent with a report by Jo et al. that indicated that total, direct, and indirect bilirubin were inversely associated with metabolic syndrome[14]. Choi et al. also reported that total bilirubin was inversely associated with metabolic syndrome[15], while Guzek et al. reported that bilirubin was inversely associated with metabolic syndrome, and affected antioxidation and inflammation[16]. There have been reports that AST, ALT, and ALP all reflected the degree of inflammation, and were associated with diabetes, impaired glucose tolerance, and metabolic syndrome[17]. In this study as well, AST and ALT were related to metabolic syndrome in both men and women. However, ALP was related to metabolic syndrome only in women; previous studies reported that this was because ALP is an osteogenic indicator in pre- and postmenopausal women, and is correlated with triglycerides and LDL cholesterol[18]. Such differences are expected, given the different physical developmental characteristics of men and women, and might also be due to the differences in age distributions within each study group. In particular, the RBC counts were found to have with substantially.

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Table 2. Serum biochemical indicators for metabolic syndrome by gender

Gender	Variable	Presence or absence of metabolic syndrome	Average	Gender	Variable	Presence or absence of metabolic syndrome	Average
Male	Total bilirubin	No	0.95 ± 0.35	Female	Total bilirubin	No	0.78 ± 0.31
		Yes	0.93 ± 0.39			Yes	0.66 ± 0.32
	Direct bilirubin	No	0.29 ± 0.12		Direct bilirubin	No	0.22 ± 0.10
		Yes	0.27 ± 0.12			Yes	0.20 ± 0.11
	Indirect bilirubin	No	0.65 ± 0.24		Indirect bilirubin	No	0.56 ± 0.23
		Yes	0.66 ± 0.28			Yes	0.46 ± 0.24
	AST	No	21.71 ± 15.94		AST	No	20.81 ± 23.29
		Yes	31.50 ± 16.61			Yes	28.76 ± 19.05
	ALT	No	24.59 ± 25.65		ALT	No	18.72 ± 16.25
		Yes	48.47 ± 34.86			Yes	38.00 ± 34.59
	ALP	No	84.07 ± 47.99		ALP	No	73.13 ± 46.84
		Yes	87.88 ± 49.51			Yes	105.50 ± 57.61
	Uric acid	No	6.04 ± 1.20		Uric acid	No	4.35 ± 0.91
		Yes	6.97 ± 3.58			Yes	5.27 ± 1.25
	Cholesterol	No	188.27 ± 30.21		Cholesterol	No	183.26 ± 29.62
		Yes	208.42 ± 54.89			Yes	201.16 ± 32.39
	HDL cholesterol	No	58.03 ± 13.99		HDL cholesterol	No	66.15 ± 14.82
		Yes	45.52 ± 10.76			Yes	45.70 ± 9.75
	LDL cholesterol	No	109.54 ± 30.94		LDL cholesterol	No	100.15 ± 29.24
		Yes	113.59 ± 35.29			Yes	113.94 ± 30.38
	Triglyceride	No	106.47 ± 65.58		Triglyceride	No	89.39 ± 51.01
		Yes	268.53 ± 235.74			Yes	242.78 ± 164.59
	FBS	No	94.43 ± 9.33		FBS	No	89.42 ± 7.73
		Yes	116.08 ± 35.98			Yes	119.50 ± 38.90
	TSH	No	2.04 ± 1.05		TSH	No	2.46 ± 1.54
		Yes	2.12 ± 1.27			Yes	2.25 ± 1.10
	RBC count	No	4.90 ± 0.33		RBC count	No	4.41 ± 0.29
		Yes	5.07 ± 0.36			Yes	4.59 ± 0.35
	WBC count	No	5.82 ± 1.17		WBC count	No	5.86 ± 1.80
		Yes	7.07 ± 1.71			Yes	6.54 ± 1.75

AST: aspartate aminotransferase, ALT: alanine aminotransferase, ALP: alkaline phosphatase, HDL: high-density lipoprotein, LDL: low-density lipoprotein, FBS: fasting blood sugar, TSH: thyroid stimulating hormone, RBC: red blood cells, WBC: white blood cells

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Table 3. Metabolic syndrome and binominal logistic regression model by item in men

Variable	B	S.E.	OR	95%CI
Age	0.028	0.014	1.029	1.001–1.057
Height	−0.015	0.019	0.985	0.948–1.024
Weight	0.186	0.023	1.205	1.152–1.260
BMI	0.853	0.108	2.347	1.899–2.902
Degree of obesity	0.185	0.024	1.203	1.149–1.260
Waist circumference	0.39	0.05	1.477	1.340–1.628
Systolic BP	0.079	0.013	1.082	1.055–1.110
Diastolic BP	0.096	0.017	1.1	1.064–1.137
Total bilirubin	−0.131	0.342	0.877	0.449–1.715
Direct bilirubin	−1.554	1.034	0.211	0.028–1.605
Indirect bilirubin	0.054	0.485	1.056	0.408–2.733
AST	0.084	0.019	1.087	1.048–1.128
ALT	0.062	0.011	1.064	1.041–1.087
ALP	0.002	0.003	1.002	0.996–1.007
Uric acid	0.323	0.097	1.382	1.143–1.670
Cholesterol	0.013	0.004	1.013	1.005–1.021
HDL cholesterol	−0.082	0.013	0.922	0.899–0.945
LDL cholesterol	0.004	0.004	1.004	0.996–1.011
Triglyceride	0.027	0.004	1.027	1.020–1.035
FBS	0.074	0.014	1.076	1.047–1.107
TSH	0.062	0.114	1.064	0.850–1.331
RBC count	1.332	0.398	3.79	1.736–8.275
WBC count	0.601	0.111	1.824	1.466–2.269
Gallstones	−0.723	0.267	0.485	0.287–0.819
Maximum size of gallstones	0.757	0.355	2.131	1.064–4.269
Number of gall stones	−0.019	0.053	0.981	0.884–1.089

AST: aspartate aminotransferase, ALT: alanine aminotransferase, ALP: alkaline phosphatase, HDL: high density lipoprotein, LDL: low density lipoprotein, FBS: fasting blood sugar, TSH: thyroid stimulating hormone, RBC: red blood cells, WBC: white blood cells

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