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ORIGINAL ARTICLE

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건강검진 수진자들에서 성별, 나이 및 체질량지수에 따른 간효소치의 상세 분포 연구

최승호, 양종인, 이창현, 변희진, 강정묵, 김세룡[1], 임정윤

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Detailed Distribution of Liver Enzymes according to Gender, Age, and Body Mass Index in Health Check-up Subjects

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Background/Aims: The aim of this study was to examine the distribution of range of liver enzymes according to age and BMI in each gender using large-scale data.

Methods: Data were gathered from 65,715 subjects who underwent a routine health check-up and did not have HBsAg and anti-HCV. Boxplot analysis was used to examine the distribution of range of liver enzymes according to age and BMI in each gender. Multivariate linear regression analysis was performed for assessment of the association of liver enzymes with age and BMI, and to determine whether the range of liver enzymes was affected by risk factors for metabolic syndrome in each gender.

Results: ALT, AST, and GGT levels showed significant association with BMI in both male and female after adjusting for age. The range of ALT, AST, and GGT levels varied more widely according to the increase in BMI in males than in females, and this finding was more prominent in younger subjects than in older subjects. All risk factors for metabolic syndrome were shown to affect liver enzyme levels in male subjects. However, although most risk factors for metabolic syndrome affected liver enzyme levels, there might be weak or no effect of fasting hyperglycemia on AST, and low serum HDL-cholesterol level on GGT in female subjects.

Conclusions: Age, BMI, and other risk factors for metabolic syndrome had a significant effect on the distribution of range of liver enzymes in each gender, even in this study conducted from Korean health checkup subjects. **(Korean J Gastroenterol 2014;64:213-223)**

Key Words: Body mass index; Alanine aminotransferase; Aspartate aminotransferase; Gamma glutamyltranspeptidase; Metabolic syndrome X

INTRODUCTION

Liver, the largest internal organ, plays a central role in development of metabolic syndrome.[1] Continuous fat accumulation can contribute to development of nonalcoholic fatty liver disease (NAFLD) as an isolated disease entity. NAFLD, the most common chronic liver disease in Western countries, is associated with an increased cardiovascular risk and incidence of diabetes.[2-4] NAFLD may also be prevalent in Korea.[5] Metabolic syndrome is alleged to increase car-

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diovascular risk via insulin resistance and has the established risk factors of obesity, hyperglycemia, hypertension, and dyslipidemia.[6,7] Because abdominal obesity has a pathophysiology similar to that of metabolic syndrome and nonalcoholic fatty liver disease, adequate anthropometric measurements of body parameters should be considered for assessing the range of liver enzymes and metabolic risk factors.[7-9] BMI is regarded as a representative of body anthropometric measurement, which can be a good target for an intervention based on weight change.[10,11] Liver enzyme tests are usually the first choice of investigation for assessment of liver disease in clinics, and they include a battery of tests.[12,13]

The aim of this study was to examine the detailed distribution of range of liver enzymes according to age and BMI in each gender and to determine whether the risk factors for metabolic syndrome affect the range of liver enzymes using large-scale data from subjects who had undergone health check-ups at a single Korean health check-up specialized center established by national university hospital in Korea.

MATERIALS AND METHODS

1. Study subjects

A total of 68,183 subjects underwent a routine health check-up at the Seoul National University Hospital Healthcare System Gangnam Center (Seoul, Korea) between October 2003 and April 2011. Among these subjects, 2,354 subjects who were positive for serum hepatitis B surface antigen or for antibody to hepatitis C virus, and 114 additional subjects whose ALT or AST level was higher than 200 IU/L were excluded from this study to avoid the influence of acute or chronic liver injury on liver enzymes. Therefore, 65,715 subjects were selected as the final subjects for this study.

The study protocol was approved by the institutional review board of Seoul National University Hospital (IRB No. 1308-121-517). This study was a retrospective study that did not cause any harm to the study subjects; therefore, the requirement of informed consent was waived by the board.

2. Methods

Each subject answered questions about age and gender, underwent anthropometric assessment of systolic blood and diastolic blood pressure, body weight, height, and underwent laboratory testing on the same day of the health check-up. BMI was calculated by dividing the weight in kilograms by the square of the height in meters. Blood samples were collected from each subject before 10 AM after an overnight fast. All biochemical analyses of blood samples were performed in the same quality control laboratory according to standard laboratory methods. Laboratory tests included serum hepatitis B surface antigen; antibody to hepatitis C virus; concentrations of liver enzymes including ALT, AST, and GGT; fasting serum glucose; triglyceride; and HDL-cholesterol. Five risk factors for metabolic syndrome were defined as follows: BMI $\geq$25 kg/m^2 as most of our study subjects were Koreans; blood pressure $\geq$130 / $\geq$85 mmHg; fasting glucose $\geq$100 mg/dL; triglycerides $\geq$150 mg/dL; and, HDL-cholesterol $<$40 mg/dL in male and $<$50 mg/dL in female.[6]

3. Statistical analysis

Data are expressed as median and interquartile range because age, BMI, liver enzyme levels, and risk factors for metabolic syndrome were all skewed and did not fit a standard normal distribution. Kolmogorov-Smirnov test and Anderson-Darling test were used for the tests of normality. Boxplot analysis was performed to examine the detailed distribution of all liver enzymes in association with age and BMI in each gender after forming a total of 11 BMI groups based on two unit changes in BMI from below 16 to over 34 ($\leq$15.9, 16.0-17.9, 18.0-19.9, 20.0-21.9, 22.0-23.9, 24.0-25.9, 26.0-27.9, 28.0-29.9, 30.0-31.9, 32.0-33.9, $\geq$34.0). The association of each liver enzyme with age and BMI was determined by multivariate linear regression analysis. To evaluate the effect of risk factors for metabolic syndrome on the range of liver enzyme levels, Mann-Whitney U-test was performed if there were significant differences in the level of liver enzymes according to the existence of each risk factor for metabolic syndrome. The association of each liver enzyme with risk factors for metabolic syndrome was determined by multivariate linear regression analysis with adjustment for age and each risk factor of the metabolic syndrome. For all multivariate linear regression analysis in this study, we performed the log-transformation of liver enzymes since they were skewed and their residuals became fit for the regression analysis by log-transformation. This was confirmed by a statistician at Seoul National University Hospital Biomedical Research Institute. For correct comparison of the impact of each regression coefficient, both unstandardized and standardized

Table 1. Baseline Characteristics of the Study Subjects

Characteristic	Total	Males	Females
Subjects (n)	65,715	34,915	30,800
Age (yr)[a]	47 (38-55)	47 (39-55)	47 (38-55)
Height (cm)[a]	164.8 (158.4-171.1)	170.6 (166.6-174.5)	158.2 (154.6-161.9)
Body weight (kg)[a]	63.0 (54.6-71.9)	70.7 (65.0-76.9)	54.6 (50.4-59.5)
BMI (kg/m^2)[a]	23.3 (21.2-25.4)	24.4 (22.7-26.1)	21.8 (20.0-23.9)
ALT (IU/L)[a]	20 (14-30)	25 (18-36)	16 (12-21)
AST (IU/L)[a]	21 (18-26)	23 (19-29)	20 (17-24)
GGT (IU/L)[a]	22 (15-37)	32 (22-51)	15 (12-20)
Systolic BP (mmHg)[a]	116 (106-128)	120 (111-130)	111 (102-123)
Diastolic BP (mmHg)[a]	75 (68-84)	80 (72-87)	70 (64-79)
Fasting glucose (mg/dL)[a]	95 (88-103)	98 (91-106)	92 (86-99)
Triglyceride (mg/dL)[a]	94 (67-138)	114 (81-165)	77 (59-107)
HDL-cholesterol (mg/dL)[a]	53 (44-63)	48 (41-56)	59 (50-68)
Obesity (BMI $\geq$25 kg/m^2)	18,749 (28.5)	13,955 (40.0)	4,794 (15.6)
BP $\geq$130 / $\geq$85 mmHg	20,056 (30.5)	13,914 (39.9)	6,142 (19.9)
Fasting glucose $\geq$100 mg/dL	22,176 (33.7)	15,316 (43.9)	6,860 (22.8)
Triglycerides $\geq$150 mg/dL	13,781 (21.0)	10,769 (30.8)	3,012 (9.8)
HDL-C $<$40 mg/dL (male); $<$50 mg/dL (female)	13,883 (21.1)	6,441 (18.5)	7,442 (24.2)

Values are presented as n only, median (interquartile range), or n (percentile).
BP, blood pressure.
[a]Data are expressed as median and interquartile range because age, BMI, liver enzyme levels, and risk factors for metabolic syndrome were all skewed and did not fit a standard normal distribution.

coefficients were calculated. Variance inflation factor for each risk factor for metabolic syndrome was calculated for quantification of the severity of multicollinearity in multivariate regression analysis. Variance inflation factor greater than 10 is regarded as suggesting the existence of collinearity. R-squared was calculated to determine how much the liver enzyme levels could be explained by the combination of age, gender, and risk factors for metabolic syndrome in each multivariate regression analysis. SAS version 9.3 (SAS Institute, Cary, NC, USA) was used for the statistical analysis. A two-tailed p-value less than 0.05 was considered statistically significant.

RESULTS

1. Baseline characteristics of the study population

Baseline characteristics of 65,715 subjects are summarized in Table 1. Of the study population, 34,915 were males and 30,800 were females. The median age was 47 years. The median BMI (kg/m^2) was 24.4 in males and 21.8 in females. The median ALT level was 25 IU/L in males and 16 IU/L in females. The median AST level was 23 IU/L in males and 20 IU/L in females. The median GGT level was 32 IU/L in males and 15 IU/L in females. The proportion of subjects with risk factors for metabolic syndrome was higher in males than in females.

2. Distribution of range of liver enzymes according to age and BMI in each gender

ALT, AST, and GGT levels were increased according to BMI (Figs. 1-6). ALT, AST, and GGT levels showed significant association with BMI in both male (Table 2) and female after adjusting for age (Table 3). The unstandardized coefficients showed that 1 unit change of age and 1 unit change of BMI resulted in −0.00211 IU/L and 0.07277 IU/L changes in log-transformed ALT level in each in male subjects; 1 unit change of age and 1 unit change of BMI resulted in 0.01045 IU/L and 0.03563 IU/L changes in log-transformed ALT level in each in female subject. When the unstandardized coefficients were calculated without log-transformation of ALT level, the unstandardized coefficients showed that 1 unit change of age and 1 unit change of BMI resulted in −0.13464 IU/L and 2.51567 IU/L changes in ALT level in each in male subjects; 1 unit change of age and 1 unit change of BMI resulted in 0.16897 IU/L and 0.89248 IU/L changes in ALT level in each in female subject. Comparison of standardized co-

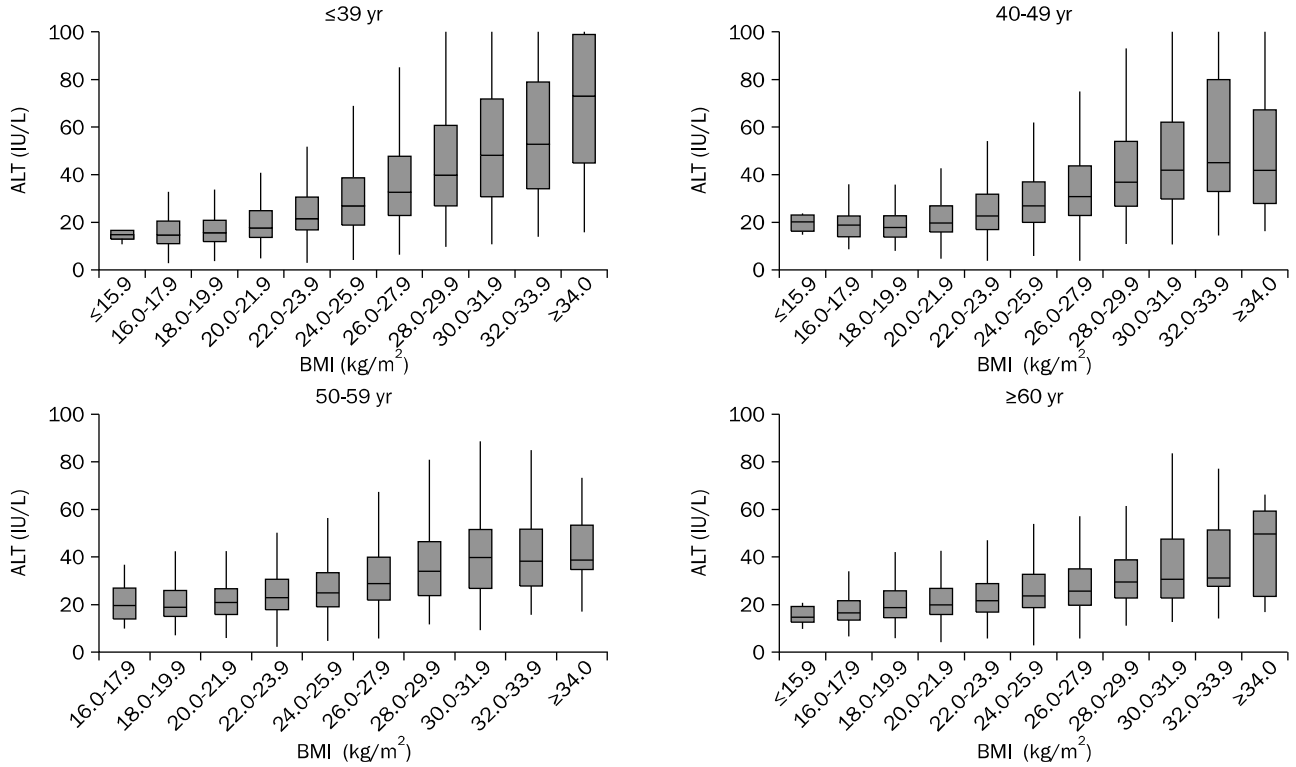

Fig. 1. The distribution of range of ALT levels according to age and BMI in male subjects. The range of ALT level varied widely according to the increase in BMI, and this finding was more prominent in younger subjects than in older subjects.

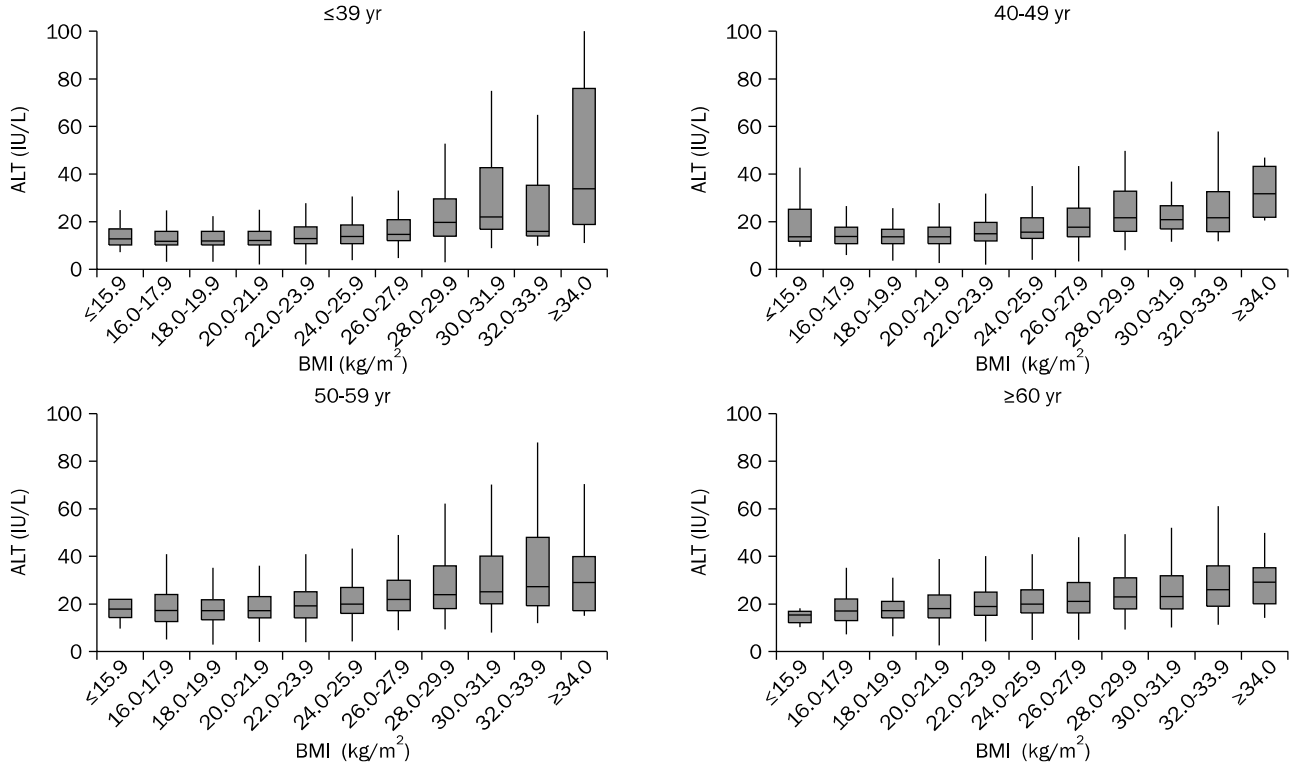

Fig. 2. The distribution of range of ALT levels according to age and BMI in female subjects. The range of ALT level varied more widely according to the increase in BMI in males than in females, and this finding was more prominent in younger subjects than in older subjects.

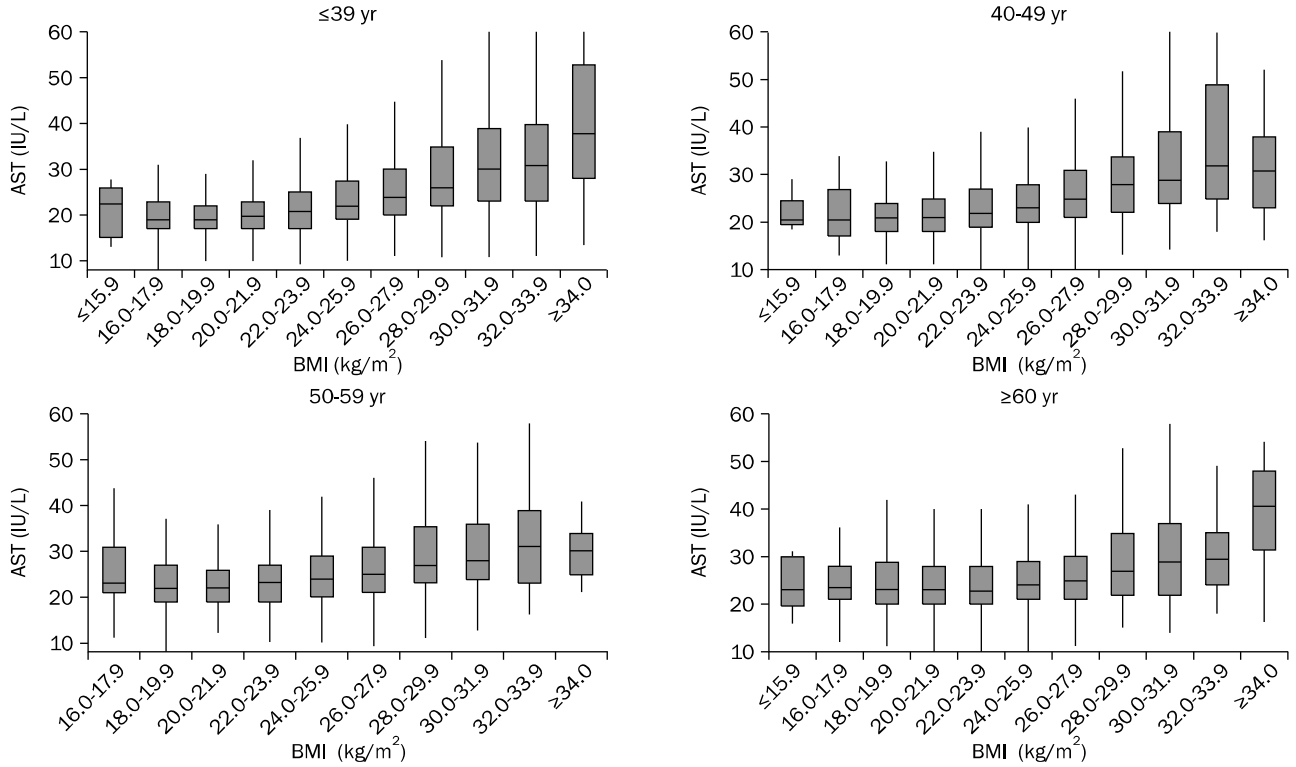

Fig. 3. The distribution of range of AST levels according to age and BMI in male subjects. The range of AST level varied widely according to the increase in BMI in male subjects, and this finding was more prominent in younger subjects than in older subjects.

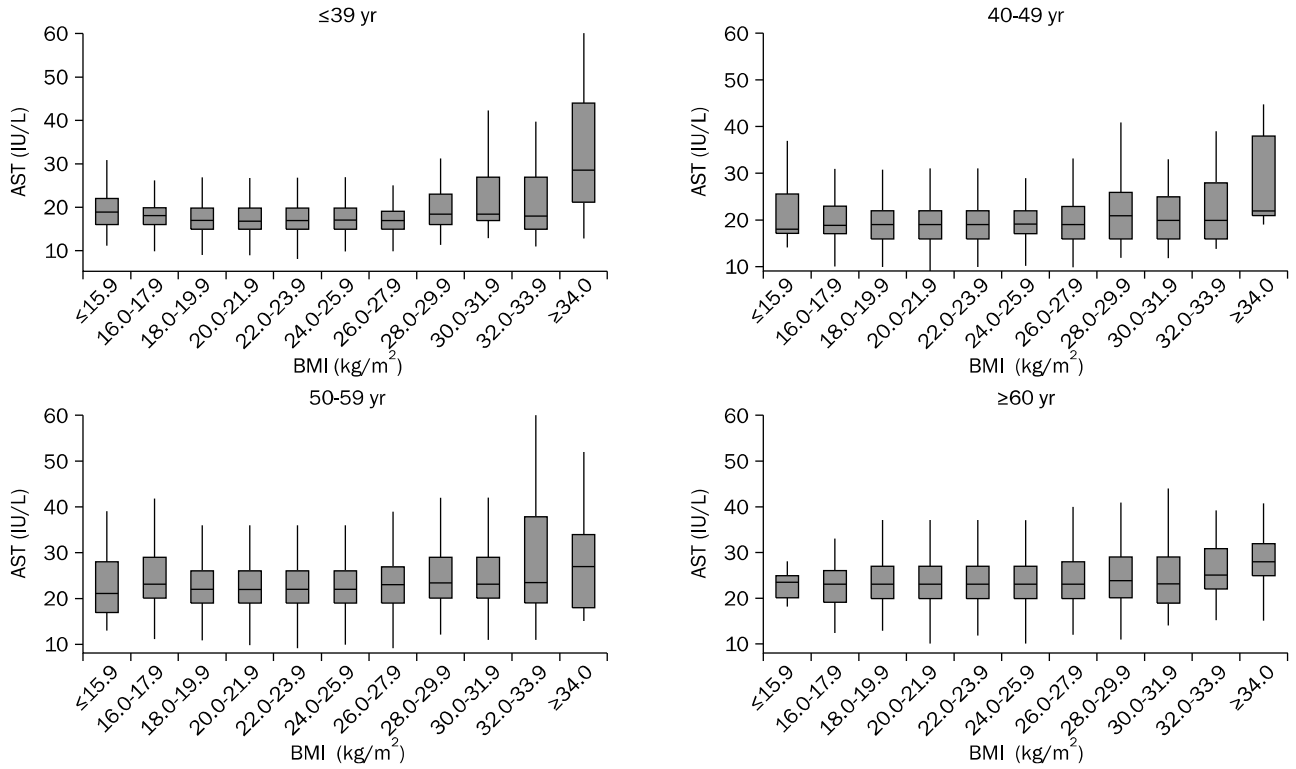

Fig. 4. The distribution of range of AST levels according to age and BMI in female subjects.

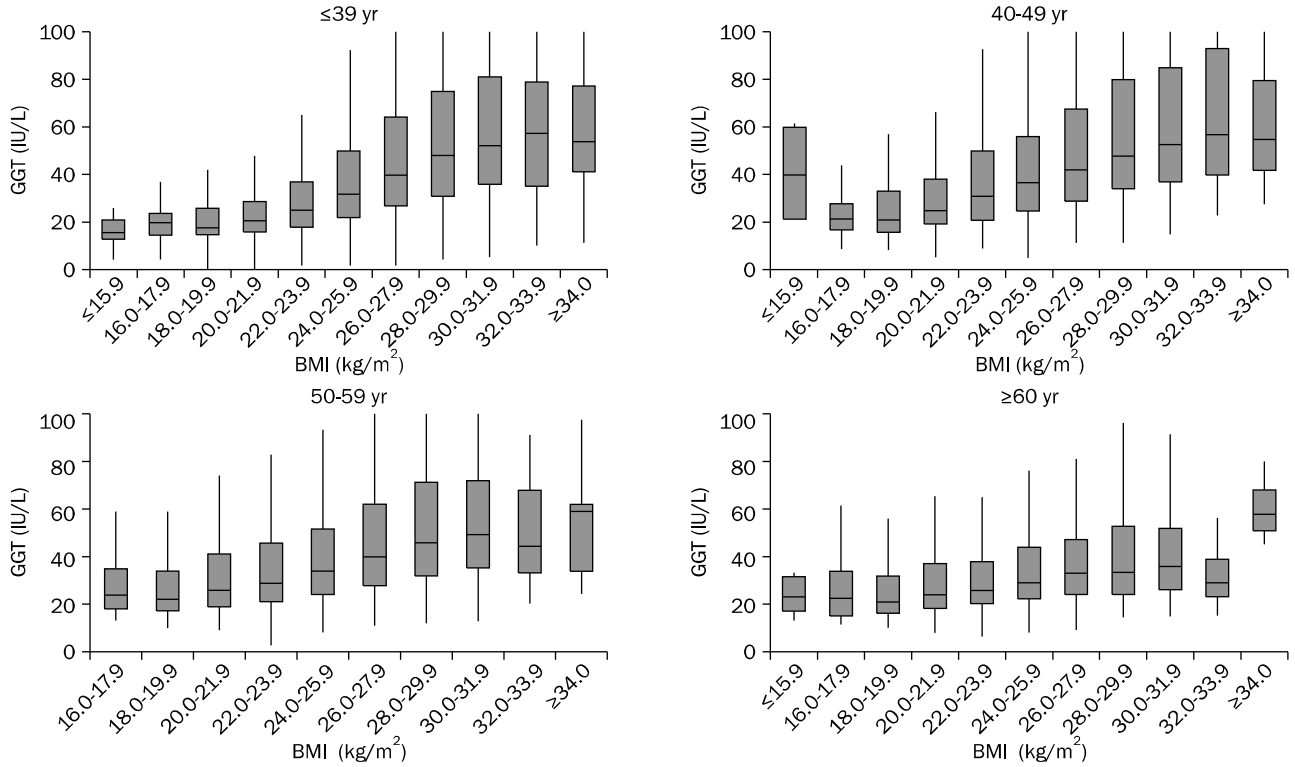

Fig. 5. The distribution of range of GGT levels according to age and BMI in male subjects. The range of GGT level varied widely according to the increase in BMI, and this finding was more prominent in younger subjects than in older subjects.

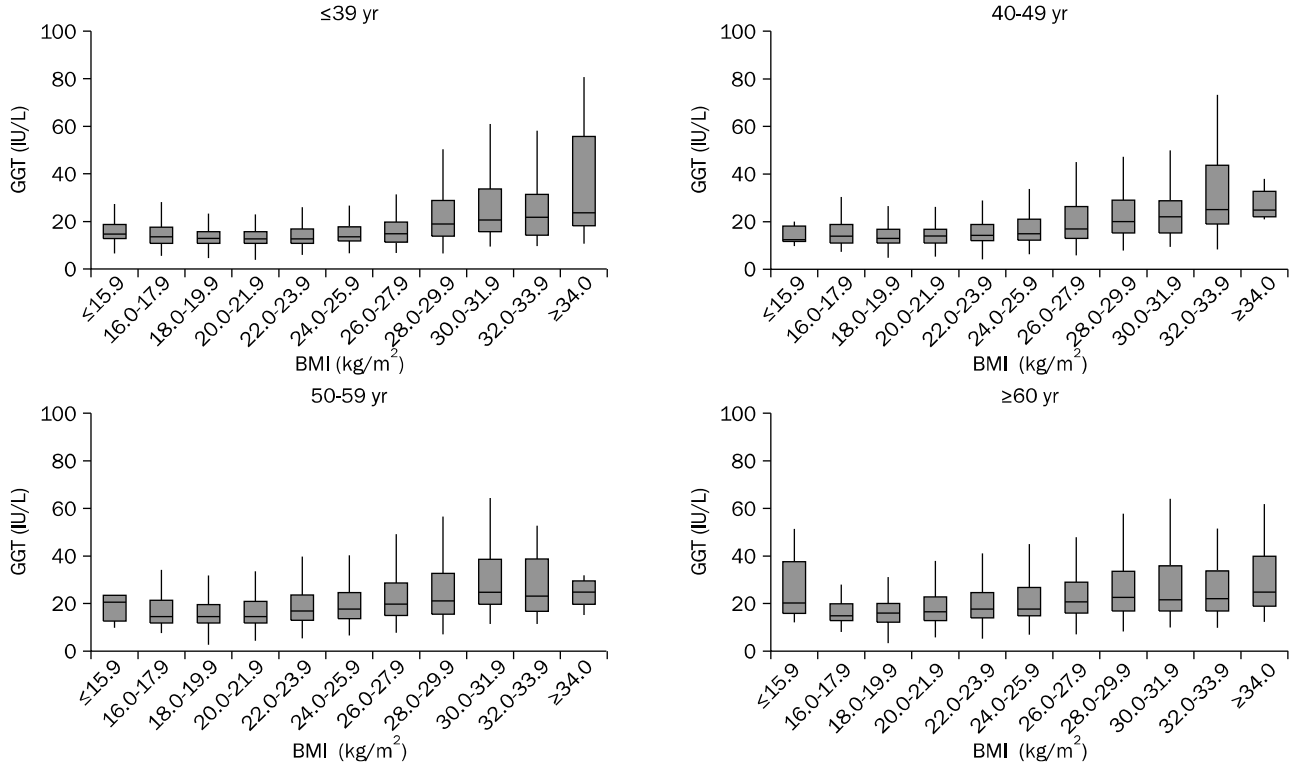

Fig. 6. The distribution of range of GGT levels according to age and BMI in female subjects. The range of GGT level varied more widely according to the increase in BMI in males than in females, and this finding was more prominent in younger subjects than in older subjects.

efficient showed that BMI had a more significant effect than age on liver enzymes in male subjects (Table 2). The coefficient of age might become a minus value because the coefficients of age and BMI were calculated simultaneously in the same multivariate regression analysis to reflect the simultaneous effect of age and BMI on ALT level in male subjects and the coefficient of BMI was large enough. By contrast, age had a more significant effect than BMI on liver enzymes in female subjects (Table 3). The range of ALT level varied more widely according to the increase in BMI in males than in females, and this finding was more prominent in younger subjects than in older subjects (Figs. 1, 2). Similar changes were observed in the distribution of AST but with a narrower range of variation than that in ALT according to age (Figs. 3, 4). The variation in the GGT level was similar to that in the ALT level (Figs. 5, 6).

3. Effect of risk factors for metabolic syndrome on the range of liver enzymes in each gender

In univariate analysis using Mann-Whitney U-test, significantly higher liver enzyme levels were observed in subjects who had a risk factor for metabolic syndrome in both male (Table 4) and female (Table 5). In male subjects, multivariate linear regression analysis showed that all risk factors for metabolic syndrome affected liver enzyme levels (Table 4). As the standard coefficient of obesity was 0.24616, that of hypertension was 0.05595, that of fasting hyperglycemia was 0.05907, that of hypertriglyceridemia was 0.18187, and that of low serum HDL-cholesterol level was 0.05470, obesity had the most significant effect on ALT level in male subjects. Similar comparisons of the standard coefficients suggested that obesity had the most significant effect on AST level and hypertriglyceridemia had the most significant effect on GGT level in male subjects. In female subjects, multivariate linear regression analysis showed that although most risk factors for metabolic syndrome affected liver enzyme levels, there might be weak or no effect of fasting glucose $\geq$100 mg/dL on AST, and HDL-cholesterol $<$50 mg/dL on GGT (Table 5). As the standard coefficient of obesity was 0.13896, that of hypertension was 0.01827, that of fasting hyperglycemia

Table 2. Multivariate Linear Regression Coefficients of Age and BMI to Log-Transformed Liver Enzyme Levels in Male Subjects

	Age			BMI			R-squared[c]
	Unstandardized coefficient (SD)[a]	Standardized coefficient (95% CI)[b]	p-value	Unstandardized coefficient (SD)[a]	Standardized coefficient (95% CI)[b]	p-value	
ALT	−0.00211 (0.00022)	−0.04812 (−0.05775-−0.03849)	<0.0001	0.07277 (0.00090)	0.39591 (0.38629-0.40554)	<0.0001	0.1605
AST	0.00279 (0.00014)	0.10044 (0.09035-0.11053)	<0.0001	0.03086 (0.00060)	0.26439 (0.25431-0.27448)	<0.0001	0.0777
GGT	0.00102 (0.00027)	0.01884 (0.00887-0.02881)	0.0002	0.07133 (0.00115)	0.31547 (0.30550-0.32543)	<0.0001	0.0993

[a]Calculated by multivariate regression analysis using log-transformed liver enzyme levels as a dependent variable, and age and BMI as independent variables.
[b]Calculated by multivariate regression analysis after standardizing the independent variables to make their variances into 1. Standardized coefficient enables comparison of the effect of independent variables with different units on the dependent variables.
[c]Introduced for estimation of the percentage of explanatory power of each multivariate regression analysis for each liver enzyme.

Table 3. Multivariate Linear Regression Coefficients of Age and BMI to Log-Transformed Liver Enzyme Levels in Female Subjects

	Age			BMI			R-squared[c]
	Unstandardized coefficient (SD)[a]	Standardized coefficient (95% CI)[b]	p-value	Unstandardized coefficient (SD)[a]	Standardized coefficient (95% CI)[b]	p-value	
ALT	0.01045 (0.00023)	0.26233 (0.25115-0.27350)	<0.0001	0.03563 (0.00092)	0.22127 (0.21011-0.23244)	<0.0001	0.1646
AST	0.00872 (0.00014)	0.35123 (0.33992-0.36254)	<0.0001	0.00608 (0.00058)	0.06053 (0.04922-0.07183)	<0.0001	0.1440
GGT	0.00860 (0.00024)	0.20698 (0.19544-0.21853)	<0.0001	0.03075 (0.00099)	0.18303 (0.17149-0.19458)	<0.0001	0.1069

[a]Calculated by multivariate regression analysis using log-transformed liver enzyme levels as a dependent variable, and age and BMI as independent variables.
[b]Calculated by multivariate regression analysis after standardizing the independent variables to make their variances into 1. Standardized coefficient enables comparison of the effect of independent variables with different units on the dependent variables.
[c]Introduced to estimate the percentage of explanatory power of each multivariate regression analysis for each liver enzyme.

Table 4. The Significant Effect of the Risk Factors for Metabolic Syndrome on the Range of Liver Enzyme Levels in Male Subjects

Liver enzyme	Risk factor of metabolic syndrome	Median of liver enzyme levels	Mann-Whitney U-test[a]	Slope				
		Risk factor for MS positive *vs.* negative	p-value	Unstandardized coefficient (SD)[b]	Standardized coefficient (95% CI)[c]	Variantion inflation factor[d]	p-value	R-squared[e]
ALT	Obesity (BMI≥25 kg/m^2)	31 *vs.* 22	<0.0001	0.26245 (0.00548)	0.24616 (0.23608-0.25624)	1.08482	<0.0001	0.1491
	Blood pressure ≥130/≥85 mmHg	27 *vs.* 24	<0.0001	0.05968 (0.00546)	0.05595 (0.04592-0.06598)	1.07344	<0.0001	
	Fasting glucose ≥100 mg/dL	27 *vs.* 24	<0.0001	0.06216 (0.00548)	0.05907 (0.04886-0.06927)	1.11206	<0.0001	
	Triglycerides ≥150 mg/dL	31 *vs.* 23	<0.0001	0.20565 (0.00594)	0.18187 (0.17156-0.19217)	1.13342	<0.0001	
	HDL-cholesterol <40 mg/dL	29 *vs.* 24	<0.0001	0.07365 (0.00689)	0.05470 (0.04468-0.06473)	1.07173	<0.0001	
AST	Obesity (BMI≥25 kg/m^2)	25 *vs.* 22	<0.0001	0.11608 (0.00363)	0.17145 (0.16094-0.18195)	1.08483	<0.0001	0.0761
	Blood pressure ≥130/≥85 mmHg	24 *vs.* 22	<0.0001	0.04308 (0.00361)	0.06359 (0.05314-0.07404)	1.07344	<0.0001	
	Fasting glucose ≥100 mg/dL	24 *vs.* 23	<0.0001	0.02511 (0.00363)	0.03757 (0.02694-0.04821)	1.11206	<0.0001	
	Triglycerides ≥150 mg/dL	25 *vs.* 22	<0.0001	0.09288 (0.00393)	0.12935 (0.11861-0.14008)	1.13344	<0.0001	
	HDL-cholesterol <40 mg/dL	24 *vs.* 23	<0.0001	−0.01500 (0.00456)	−0.01755 (−0.02799-−0.00710)	1.07173	0.001	
GGT	Obesity (BMI≥25 kg/m^2)	40 *vs.* 27	<0.0001	0.22062 (0.00661)	0.16821 (0.15833-0.17809)	1.08488	<0.0001	0.1828
	Blood pressure ≥130/≥85 mmHg	37 *vs.* 29	<0.0001	0.12213 (0.00658)	0.09307 (0.08325-0.10290)	1.07354	<0.0001	
	Fasting glucose ≥100 mg/dL	37 *vs.* 28	<0.0001	0.16222 (0.00661)	0.12529 (0.11530-0.13529)	1.11178	<0.0001	
	Triglycerides ≥150 mg/dL	45 *vs.* 28	<0.0001	0.40950 (0.00717)	0.29437 (0.28427-0.30447)	1.13338	<0.0001	
	HDL-cholesterol <40 mg/dL	34 *vs.* 31	<0.0001	−0.11024 (0.00830)	−0.06656 (−0.07638-−0.05673)	1.07178	<0.0001	

MS, metabolic syndrome.

[a]Mann-Whitney U-test was performed if there were significant differences in the level of liver enzymes according to the existence of each risk factor for metabolic syndrome.

[b]Calculated by multivariate regression analysis using log-transformed liver enzyme levels as a dependent variable, and age and each risk factor for metabolic syndrome as independent variables.

[c]Calculated by multivariate regression analysis after standardizing the independent variables to make their variances into 1. Standardized coefficient enables comparison of the effect of independent variables with different units on the dependent variables.

[d]Variance inflation factor for each risk factor for metabolic syndrome was calculated to quantify the severity of multicollinearity in multivariate regression analysis. There may be no colinearity among the risk factors for metabolic syndrome because variance inflation factor greater than 10 is regarded as suggesting the existence of collinearity.

[e]R-squared was introduced to estimate the percentage of explanatory power of each multivariate regression analysis for each liver enzyme.

Table 5. The Significant Effect of the Risk Factors for Metabolic Syndrome on the Range of Liver Enzyme Levels in Female Subjects

Liver enzyme	Risk factor of metabolic syndrome	Median of liver enzyme levels	Mann-Whitney U-test[a]	Slope				
		Risk factor for MS positive *vs.* negative	p-value	Unstandardized coefficient (SD)[b]	Standardized coefficient (95% CI)[c]	Variantion inflation factor[d]	p-value	R-squared[e]
ALT	Obesity (BMI ≥25 kg/m^2)	20 *vs.* 15	<0.0001	0.18416 (0.00737)	0.13896 (0.12806-0.14987)	1.13875	<0.0001	0.1640
	Blood pressure ≥130/≥85 mmHg	18 *vs.* 15	<0.0001	0.02197 (0.00680)	0.01827 (0.00718-0.02936)	1.17735	0.0012	
	Fasting glucose ≥100 mg/dL	19 *vs.* 15	<0.0001	0.06556 (0.00647)	0.05678 (0.04580-0.06775)	1.15455	<0.0001	
	Triglycerides ≥150 mg/dL	21 *vs.* 15	<0.0001	0.15030 (0.00906)	0.09293 (0.08195-0.10390)	1.15399	<0.0001	
	HDL-cholesterol <40 mg/dL	17 *vs.* 15	<0.0001	0.02409 (0.00617)	0.02146 (0.01068-0.03224)	1.11202	<0.0001	
AST	Obesity (BMI ≥25 kg/m^2)	22 *vs.* 19	<0.0001	0.05057 (0.00464)	0.06120 (0.05019-0.07221)	1.13879	<0.0001	0.1482
	Blood pressure ≥130/≥85 mmHg	21 *vs.* 19	<0.0001	0.01047 (0.00428)	0.01397 (0.00277-0.02516)	1.17733	0.0145	
	Fasting glucose ≥100 mg/dL	21 *vs.* 19	<0.0001	0.00037728 (0.00407)	0.00052397 (−0.01055-0.01160)	1.15442	0.9261	
	Triglycerides ≥150 mg/dL	22 *vs.* 19	<0.0001	0.05487 (0.00570)	0.05440 (0.04333-0.06548)	1.15387	<0.0001	
	HDL-cholesterol <40 mg/dL	20 *vs.* 19	<0.0001	−0.02418 (0.00388)	−0.03456 (−0.04543-−0.02368)	1.11193	<0.0001	
GGT	Obesity (BMI ≥25 kg/m^2)	19 *vs.* 14	<0.0001	0.15822 (0.00782)	0.11440 (0.10331-0.12548)	1.13866	<0.0001	0.1355
	Blood pressure ≥130/≥85 mmHg	17 *vs.* 14	<0.0001	0.04232 (0.00722)	0.03372 (0.02245-0.04500)	1.17742	<0.0001	
	Fasting glucose ≥100 mg/dL	18 *vs.* 14	<0.0001	0.12433 (0.00686)	0.10317 (0.09202-0.11433)	1.15418	<0.0001	
	Triglycerides ≥150 mg/dL	21 *vs.* 15	<0.0001	0.24552 (0.00961)	0.14545 (0.13430-0.15661)	1.15371	<0.0001	
	HDL-cholesterol <40 mg/dL	16 *vs.* 15	<0.0001	−0.00639 (0.00655)	−0.00545 (−0.01641-0.00550)	1.11200	0.3293	

MS, metabolic syndrome.

[a]Mann-Whitney U-test was performed if there were significant differences in the level of liver enzymes according to the existence of each risk factor for metabolic syndrome.

[b]Calculated by multivariate regression analysis using log-transformed liver enzyme levels as a dependent variable, and age and each risk factor for metabolic syndrome as independent variables.

[c]Calculated by multivariate regression analysis after standardizing the independent variables to make their variances into 1. Standardized coefficient enables comparison of the effect of independent variables with different units on the dependent variables.

[d]Variance inflation factor for each risk factor for metabolic syndrome was calculated to quantify the severity of multicollinearity in multivariate regression analysis. There may be no colinearity among the risk factors for metabolic syndrome because variance inflation factor greater than 10 is regarded as suggesting the existence of collinearity.

[e]R-squared was introduced to estimate the percentage of explanatory power of each multivariate regression analysis for each liver enzyme.

was 0.05678, that of hypertriglyceridemia was 0.09293, and that of low serum HDL-cholesterol level was 0.02146, obesity had the most significant effect on ALT level in female subjects. Similar comparisons of the standard coefficients suggested that obesity had the most significant effect on AST level and hypertriglyceridemia had the most significant effect on GGT level in female subjects.

DISCUSSION

Our results provide a detailed distribution of liver enzymes according to age, BMI, and gender.[11,14] This study was conducted using data from mostly Korean subjects, which were measured and analyzed using uniform protocols at a single health check-up specialized center established as a part of a major tertiary hospital by a national university hospital in Korea; thus, we believe that it can provide accurate information on the detailed distribution of liver enzymes according to BMI, age, and gender without racial or measurement bias.[15-17]

In this study, liver enzyme levels were increased according to BMI even after adjusting for age in each gender. Our findings also showed that risk factors for metabolic syndrome affected the liver enzyme levels. Recent studies have reported direct association of liver enzyme levels with increased risk of diabetes and metabolic syndrome; therefore, liver enzymes and risk factors for metabolic syndrome may need to be analyzed and managed simultaneously.[18-20] The variation of ALT level according to BMI was more prominent in male subjects than in female subjects. This may be due to alcohol consumption and the effect of sex hormones.[21] Liver enzyme levels showed significant association with the existence of risk factors for metabolic syndrome, except that the AST level in female subjects failed to show an association with high fasting glucose level in multivariate regression analysis. GGT was analyzed with importance in this study in order to explore the association of GGT with the risk factors for metabolic syndrome, including BMI, in Korean subjects. In the previous study, GGT showed even stronger association with increased diabetic risk than ALT and AST.[22] This may coincide with the results of our study because the standardized coefficients of high fasting glucose for GGT levels were higher than those for ALT and AST levels. In this study, GGT showed strong association with all risk factors for metabolic syndrome in male subjects and all risk factors for metabolic syndrome, except low HDL-cholesterol level in female subjects.

The limitation of this study is that it did not represent the entire Korean population because the subjects visited voluntarily for a routine health check-up and most were healthy. Regional distinctiveness may also limit the results of this study to represent the entire Korean population considering that our health check-up center is located in Gangnam district, an area with high socioeconomic status in Korea, and median value of BMI in this study may be higher than that in the Korean population.[11] Because there was no information regarding alcohol intake, it is difficult to interpret the meaning of AST and GGT. No information about medication for hypertension, diabetes, and dyslipidemia may be a major limitation for interpreting the affect by the risk factors for metabolic syndrome. This study also has the limitation of a retrospective study. However, a large sample size may help to overcome these limitations by reducing error and reflect the status of liver enzymes in the general Korean population.

In conclusion, our results showed that the distribution of range of liver enzymes was affected not only by gender, age, and BMI, but also by risk factors for metabolic syndrome in Koreans.

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