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An Association between Liver Markers and Physiological Variables: Comparison between Normal and Fatty Liver Subjects

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We evaluated whether liver markers such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma-glutamyltranspeptidase (GGT), and bilirubin have a relationship with other physiological factors in the normal (n=115) and fatty liver subjects (n=122) and there are differences between the two populations. Body indices were higher in the fatty liver group than in the normal group. Liver markers and blood pressure (BP) were greater in the fatty liver group than in the normal group. AST and ALT levels were positively correlated with body indices in the fatty liver group, but not in the normal group. AST, ALT and GGT levels in the fatty liver group had positive relationship with cardiovascular indices (CI). ALP and bilirubin levels were negatively associated with some of CI. Liver markers were negatively or positively correlated with inflammatory markers, thyroid hormones, or several biochemical markers levels. These findings suggest that abnormal changes in liver markers may be useful tool for diagnosis or prognosis of development of cardiovascular and/or inflammatory diseases as well as metabolic syndrome.

Key Words: Liver markers, Fatty liver, Body indices, Cardiovascular indices, Physiological variables

INTRODUCTION

Biochemical markers such as serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma-glutamyltranspeptidase (GGT) and bilirubin levels have been clinically utilized as important and routine markers for evaluating liver function and diagnosing hepatic disorder. Serum aminotransferases levels are considerations of hepatocellular health, whereas GGT also reflects biliary tract function. ALT is found primarily in the liver. AST and GGT are also found in other tissues and are less-specific markers of liver function. The liver plays an important role in maintaining normal glucose concentrations during fasting as well as postprandially, by producing digestive enzymes, and counteracting harmful substances. Liver markers are elevated in the serum with hepatic inflammation or injury. Therefore, they may be elevated in fatty liver. Although there is difference between alcoholic and nonalcoholic fatty liver in the pathogenesis, fatty liver disease refers to a wide spectrum of liver damage, ranging from simple steatosis to advanced fibrosis and cirrhosis (Byrne et al., 2009). Moreover, Adult disease, including metabolic syndrome results from fatty liver, which is associated with systemic disorders.

Recent studies have demonstrated that GGT, one of the hepatic enzymes may be associated with metabolic syndrome and/or cardiovascular risk (Liu et al., 2007; Martins et al., 2010). Especially, metabolic syndrome is a cluster of four major cardiovascular disease (CVD) risk factors; obesity, insulin resistance (hyperglycemia), hypertension and dyslipidemia where obesity and insulin resistance are the core elements (Reaven, 1988). Other important characteristics of metabolic syndrome include low-grade inflammation, endothelial dysfunction, plasma hypercoagulability and atherosclerosis. And yet, most of studies have focused

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on an association between liver markers and other variables in individuals with liver disorders and/or the adult disease (diabetes mellitus, obesity or CVD). Furthermore, although Choi et al. (2010) recently reported that AST and ALT were positively associated with the levels of cardiac markers (brain natriuretic peptide, troponin-I or creatine kinase isoenzyme 2) in the patients with CVD, we have a little data on the relationship between liver markers and other physiological variables in the normal and fatty liver populations. Actually, liver dysfunction may be associated with inflammatory response. More recent studies have demonstrated that dyslipidemia and fatty liver can influence thyroid function (Šamanc et al., 2010; Tagami et al., 2011).

Moreover, Ji and Shen (2010) have reported that uric acid potentially links the fatty liver and hypertension, resulting in CVD.

The present study was performed to clarify whether liver markers such as AST, ALT, ALP, GGT, and bilirubin have a relationship with other physiological factors in the normal and fatty liver populations and there are differences between the two populations.

MATERIALS AND METHODS

Study population

Volunteers of two hundred-thirty-seven adults participated in this study. According to the abdominal ultrasonography, they were divided into the normal group (n=115) and fatty liver group (n=122). This study was accepted and exempted from the Institutional Review Board for Human Research Dong-Eui University Hospital.

Methods

Analysis of variables

Body indices. Height, body weight, obesity degree, waist, body fat mass, waist-hip ratio, body mass index (BMI), and bone density in two groups were measured with FA-94H (Fanics Co., Korea) and Genivis-220 (Ja-Won medical Co., Korea).

Cardiovascular indices. Systolic and diastolic blood pressure (SBP and DBP, respectively), right and left cardio ankle vascular index (R-CAVI and L-CAVI, respectively), right and left ankle brachial pressure (R-ABI and L-ABI, respectively), and right and left intraocular pressure (R-IP and L-IP, respectively) in two groups were measured with MD202 (Medipia Co., Korea), Fukuda Denshi VS-1000 (Fukuda Co., Japan), and Canon TX10 (Canon Co., Japan).

Liver markers and biochemical indices. Three mL of the blood was separated into serum for analysis of biochemical markers. Serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma-glutamyltranspeptidase (GGT), and bilirubin (liver markers), blood urea nitrogen (BUN), creatinine (renal markers), total cholesterol (T-cholesterol), high density lipoprotein cholesterol (HDL), low density lipoprotein cholesterol (LDL), triglyceride (lipid metabolism), glucose and uric acid levels were measured by Autohumalyzer 9500 (Human Lab., Germany).

Inflammatory markers and alpha fetoprotein (AFP). Two mL of the blood was infused EDTA-containing CBC bottle for measuring leukocyte counts and they were determined by Sysmex XE-2100 (Sysmex Co., Japan). High sensitivity C-reactive protein (hs-CRP), amylase, rheumatoid factor and alpha fetoprotein (AFP) levels in serum were analyzed by Hitachi 7600-210 (Hitachi Co., Japan) with each commercial kit (Hitachi Co., Japan).

Thyroid hormones. Thyroid stimulation hormone (TSH), T_3 and free T_4 levels were analyzed by Eelcsys 2010 (Roche Inc., Germany) with commercial kit (Roche Inc., Germany).

Statistical analysis. Data were presented as mean ± SD (standard deviation). For comparison between Male- and Female-group, unpaired *t*-test was applied. Pearson's correlation-analysis was applied for the determination of association of serum levels of liver markers with other biochemical indices, or other physiological variables (SAS program). Statistical significance was accepted with $P \leq 0.05$.

Table 1. Demographic characteristics and body indices in the normal and fatty liver-group

Variable	Group		Normal range
	Normal	Fatty	
Sample size (n)	115	122	
Age (years)	47.89±10.76	47.44±11.30	
Gender (M : F)	70 : 45	79 : 43	
Height (cm)	169.70±6.54	170.44±6.95	
Weight (kg)	66.53±9.90	75.80±11.64‡	
Alcohol intake (mg)	15.02±8.17	47.89±29.54‡	
Obesity degree (%)	105.99±11.05	119.70±14.50‡	<120
Waist (cm)	79.83±6.92	88.58±7.38‡	
Body fat mass (%)	20.63±4.44	25.90±3.68‡	M<10~20; F<18~28
Waist-hip ratio	0.90±0.05	0.95±0.43‡	M<1.0; F<0.85
BMI (kg/m^2)	23.10±2.44	26.10±3.17‡	18.5~23
Bone density	-0.67±0.97	-0.45±1.15*	<−2.5

Data are expressed as mean ± SD.
*, P<0.05; ‡, P<0.0001 (compared with the normal group).
Abbreviation: Fatty, fatty liver group; BMI, body mass index; M, male; F, female.

Table 2. Cardiovascular indices in the normal and fatty liver group

Variable	Group		Normal range
	Normal	Fatty	
SBP (mmHg)	121.54±7.24	125.89±10.15†	<130
DBP (mmHg)	74.21±8.27	77.75±10.18†	<90
R-CAVI	7.50±0.83	7.50±0.99	0~9
L-CAVI	7.47±0.82	7.64±1.94	0~9
R-ABI	1.11±0.08	1.12±0.09	0.9~1.29
L-ABI	1.06±0.09	1.04±0.10	0.9~1.29
R-IP	15.14±2.78	15.71±2.42	
L-IP	15.39±2.84	15.15±2.31	

Data are expressed as mean ± SD.
†, P<0.001 (compared with Normal-group).
Abbreviations: Fatty, fatty liver group; SBP, systolic blood pressure; DBP, diastolic blood pressure; R-, right; L-, left; CAVI, cardio ankle vascular index; ABI, ankle brachial pressure index; IP, intraocular pressure.

RESULTS

Demographic characteristics and body indices

Table 1 shows demographic characteristics and body indices in the normal group and fatty liver group. The weight, alcohol intake, obesity degree, waist, body fat mass, waist-hip ratio, BMI were greater, whereas bone density was less in the fatty liver group than in the normal group (P<0.05 or P<0.001, respectively).

Table 3. Biochemical markers in the normal and fatty liver-group

Variable	Group		Normal range
	Normal	Fatty	
AST (IU/L)	27.18±1.75	28.36±15.86	0~33
ALT (IU/L)	24.21±17.72	37.72±22.86‡	0~38
ALP (IU/L)	168.10±39.96	172.04±47.77	77~293
GGT (IU/L)	35.89±20.19	50.42±39.64*	M<56; F<38
T-bilirubin (mg/dL)	0.84±0.30	0.84±0.32	0.3~1.7
Glucose (mg/dL)	96.07±14.23	109.84±11.93‡	70~99
Triglyceride (mg/dL)	116.03±25.01	171.94±105.47‡	10~149
T-cholesterol (mg/dL)	180.85±32.78	199.52±33.39‡	98~199
HDL (mg/dL)	49.30±8.76	46.23±8.20†	M, 40~99; F, 50~99
LDL (mg/dL)	109.97±27.81	116.81±31.60*	1~99
BUN (mg/dL)	14.66±3.60	15.60±3.29*	6.2~23.30
Creatinine (mg/dL)	0.97±0.11	1.06±0.20†	0.6~1.2
Uric acid (mg/dL)	5.71±1.17	6.61±1.51‡	M, 2.8~7.7; F, 2.1~6.7
LDH (IU/L)	353.09±61.27	359.36±48.67	100~360
CK (IU/L)	156.95±85.16	183.09±178.27	50~250

Data are expressed as mean ± SD.
*, P<0.05; †, P<0.001; ‡, P<0.0001 (compared with Normal-group).
Abbreviations: Fatty, fatty liver group; AST, Aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; GGT, gamma-glutamyltranspeptidase; T-, total; HDL, high density lipoprotein; LDL, low density lipoprotein; BUN, blood urea nitrogen; LDH, lactic dehydrogenase; CK, creatine kinase.

Cardiovascular indices

Cardiovascular indices in both the groups were summarized in Table 2. Although SBP and DBP in both groups were within normal ranges, those in the fatty liver group were higher than those of the normal group (P<0.05). The other variables were no significant differences between the both groups.

Liver markers and biochemical indices

Table 3 displays liver markers and biochemical indices

in both the groups. All indices were within normal ranges. However, AST, GGT, glucose, triglyceride, total cholesterol, LDL, BUN, creatinine and uric acid levels were higher, whereas HDL levels were lower in the Fatty liver-group than in the normal group (P<0.05, P<0.001, or P<0.0001).

Inflammatory markers, alpha fetoprotein (AFP), and thyroid hormones

Inflammatory markers and AFP in both groups were summarized in Table 4. All indices were within normal ranges. However, the Fatty liver-group had greater leukocyte count compared with the normal group (P<0.0001). hs-CRP, CK and TSH levels in the fatty liver group tended to be higher than those of the normal group, but not statistically significant.

Table 4. Inflammatory and cardiac markers, and thyroid hormones in the normal and fatty liver group

Variable	Group		Normal range
	Normal	Fatty	
Leukocyte (10^3/μL)	5.80±1.35	6.64±1.61‡	4.00~10.80
hs-CRP (mg/dL)	0.13±0.19	0.24±0.38	0.099~0.30
Amylase (IU/L)	63.86±27.52	57.09±17.89	28~117
RF (IU/mL)	13.94±10.25	13.27±13.66	0~18
AFP (ng/mL)	3.01±2.11	2.98±1.44	0~8.90
LDH (IU/L)	353.09±48.67	359.3±61.276	360
CPK (IU/L)	156.95±85.16	183.09±303.20	50~250
T_3 (ng/mL)	1.13±0.11	1.11±0.15	0.80~2.90
Free T_4 (ng/dL)	1.40±0.20	1.34±0.54	0.80~1.90
TSH (μ/IU)	1.99±1.55	3.11±0.15	0.27~4.20
AFP (ng/mL)	3.15±1.00	3.21±2.19	<10 ng/mL

Data are expressed as mean ± SD.
‡, P<0.0001 (compared with Normal-group).
Abbreviations: Fatty, fatty liver group; hs-CRP, high sensitivity C-reactive protein; RF, rheumatoid factor; AFP, alpha fetoprotein; TSH, thyroid stimulation hormone; LDH, lactate dehydrogenase; CPK, creatine kinase.

Correlation of liver markers to body indices

Table 5 shows correlation of liver markers to body indices in the both groups. AST in the Fatty liver-group had a positive relationship with obesity degree and BMI (P<0.05 or P<0.01), but a negative correlation with bone density (P<0.0001). ALT in the Fatty liver-group was positively associated with weight, obesity degree, waist, body fat mass, waist-hip ratio and BMI (P<0.0001). ALP in both groups had negative with bone density relationships (P<0.0001). The other liver markers in the normal group did not have any correlation with other body indices.

Correlation of liver markers to cardiovascular indices

Table 6 shows correlation of liver markers to cardiovascular indices in both groups. In the normal group, ALP was negatively correlated with R- and L-ABI, or R-IP (P< 0.05 or P<0.01), while bilirubin was negatively associated with DBP (P<0.05). In the fatty liver group, AST had a positive relationship with L-ABI (P<0.05). ALT had positive relationship with R-CAVI or R-ABI (P<0.05). GGT had a positive with DBP (P<0.05). Bilirubin was positively

Table 5. Correlation of liver marker (LM) to body indices (BI) and comparison between the normal and fatty liver group

Group / LM / BI	Normal vs. Fatty				
	AST (r)	ALT (r)	ALP (r)	GGT (r)	Bilirubin (r)
Height	ns vs ns	ns vs ns	ns vs ns	ns vs ns	ns vs ns
Weight	ns vs ns	ns vs 0.44‡	ns vs ns	ns vs ns	ns vs ns
Obesity degree	ns vs 0.23**	ns vs 0.49‡	ns vs ns	ns vs ns	ns vs ns
Waist	ns vs ns	ns vs 0.32‡	ns vs ns	ns vs ns	ns vs ns
Body fat mass	ns vs ns	ns vs 0.35‡	ns vs ns	ns vs ns	ns vs ns
Waist-hip ratio	ns vs ns	ns vs 0.33‡	ns vs ns	ns vs ns	ns vs ns
BMI	ns vs 0.22*	ns vs 0.51‡	ns vs ns	ns vs ns	ns vs ns
Bone density	ns vs -0.35‡	ns vs ns	-0.30‡ vs -0.39‡	ns vs ns	ns vs ns

r, correlation coefficient.
*, P<0.05; **, P<0.01; ‡, P<0.0001 (statistically significant correlation).
Abbreviations: Fatty, fatty liver group; ns, not significant; AST, Asparate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; GGT, gamma-glutamyltranspeptidase.

Table 6. Correlation of liver marker (LM) to cardiovascular indices (CI) and comparison between the normal and fatty liver group

Group / LM / CI	Normal vs. Fatty				
	AST (*r*)	ALT (*r*)	ALP (*r*)	GGT (*r*)	Bilirubin (*r*)
SBP	ns vs ns	ns vs ns	ns vs ns	ns vs ns	ns vs ns
DBP	ns vs ns	ns vs ns	ns vs ns	ns vs 0.20*	-0.20* vs ns
R-CAVI	ns vs ns	ns vs 0.23*	ns vs ns	ns vs ns	ns vs ns
L-CAVI	ns vs ns	ns vs ns	ns vs ns	ns vs ns	ns vs ns
R-ABI	ns vs ns	ns vs 0.26*	-0.32** vs ns	ns vs ns	ns vs 0.45‡
L-ABI	ns vs 0.21*	ns vs ns	-0.26 vs ns	ns vs ns	ns vs ns
R-IP	ns vs ns	ns vs ns	-0.24* vs ns	ns vs ns	ns vs ns
L-IP	ns vs ns	ns vs ns	ns vs ns	ns vs ns	ns vs 0.23*

r, correlation coefficient.
*, $P<0.05$; **, $P<0.01$; ‡, $P<0.0001$ (statistically significant correlation).
Abbreviations: Fatty, fatty liver group; ns, not significant; SBP, systemic blood pressure; DBP, diastolic blood pressure; R-, right; L-, left; CAVI, cardio ankle vascular index; ABI, ankle brachial pressure index; IP, intraocular pressure.

Table 7. Correlation of liver marker (LM) to other variables (OV) and comparison between the normal and fatty liver group

Group / LM / OV	Normal vs. Fatty				
	AST (*r*)	ALT (*r*)	ALP (*r*)	GGT (*r*)	Bilirubin (*r*)
Leukocyte	ns vs ns	ns vs ns	ns vs ns	ns vs ns	-0.46‡ vs -0.23*
hs-CRP	ns vs ns	ns vs ns	ns vs ns	ns vs ns	ns vs
Amylase	0.31† vs 0.66‡	ns vs 0.28*	ns vs ns	0.27* vs ns	ns vs -0.38†
RF	ns vs ns	ns vs 0.35†	ns vs ns	0.27* vs ns	ns vs -0.22*
AFP	0.25* vs 0.34†	0.32** vs ns	ns vs ns	0.39† vs 0.32†	ns vs 0.23*
T_3	-0.20* vs -0.20*	-0.20* vs -0.21*	0.45† vs -0.35†	ns vs ns	ns vs ns
Free T_4	-0.28** vs -0.21*	-0.25** vs -0.20*	ns vs ns	-0.20* vs ns	ns vs ns
TSH	0.23* vs 0.20*	0.23* ns vs ns	ns vs ns	ns vs ns	ns vs ns
Glucose	ns vs ns	ns vs ns	ns vs ns	ns vs ns	ns vs ns
Triglyceride	ns vs ns	0.20* vs ns	ns vs 0.24*	ns vs ns	ns vs -0.20*
T-cholesterol	ns vs ns	ns vs ns	ns vs ns	ns vs ns	ns vs ns
HDL	ns vs ns	ns vs ns	ns vs -0.25**	-0.32** vs -0.21*	ns vs 0.25**
LDL	ns vs ns	ns vs ns	ns vs ns	ns vs ns	ns vs ns
BUN	ns vs 0.20*	ns vs ns	ns vs ns	ns vs ns	ns vs ns
Creatinine	0.24* vs ns	0.27† vs ns	ns vs ns	ns vs ns	ns vs ns
Uric acid	ns vs 0.20*	0.20* vs 0.20*	ns vs ns	0.29** vs 0.20*	- 0.23* vs ns
LDH	0.52‡ vs 0.55‡	ns vs ns	ns vs ns	ns vs 0.26*	ns vs -0.24*
CK	ns vs 0.28**	ns vs ns	ns vs ns	ns vs ns	ns vs ns

r, correlation coefficient.
*, $P<0.05$; **, $P<0.01$; †, $P<0.001$; ‡, $P<0.0001$.
Abbreviations: Fatty, fatty liver group; ns, not significant; hs-CRP, high sensitivity C-reactive protein; RF, rheumatoid factor; AFP, alpha fetoprotein; TSH, thyroid stimulation hormone;T-, total; HDL, high density lipoprotein; LDL, low density lipoprotein; BUN, blood urea nitrogen.

associated with R-ABI or L-IP ($P<0.0001$ or $P<0.05$).

Correlation of liver markers to other variables

Table 7 shows correlation of liver markers to other variables in both groups.

In the normal group, AST was positively correlated with amylase, AFP, TSH, creatinine, or LDH, ($P<0.05$), but negatively correlated with T_3 or free T_4 ($P<0.05$, $P<0.01$

or $P<0.0001$). ALT had positive correlation with AFP, TSH, triglyceride, creatinine, or uric acid, and had negative relationship with T_3 or free T_4 ($P<0.05$, $P<0.01$ or $P<0.001$). ALP had a positive correlation with T_3 ($P<0.001$). GGT was positively associated with amylase, RF, AFP, and uric acid, but negatively correlated with T_4 or HDL ($P<0.05$, $P<0.01$ or $P<0.001$). Bilirubin was negatively associated with leukocyte and uric acid ($P<0.05$ or $P<0.0001$).

In the Fatty liver-group, AST was positively correlated with amylase, AFP, TSH, BUN, uric acid, LDH, and CK ($P<0.05$, $P<0.01$, $P<0.001$ and $P<0.0001$, respectively), but negatively correlated with T_3 or free T_4 ($P<0.05$). ALT had positive correlation with amylase, RF, or uric acid, but had negative relationship with T_3 or free T_4 ($P<0.05$ or $P<0.001$). ALP was negatively correlated with T_3 or HDL, but positively associated with triglyceride ($P<0.05$, $P<0.01$ or $P<0.001$, respectively). GGT was positively associated with AFP, uric acid or LDH, but negatively correlated with HDL ($P<0.05$ or $P<0.001$). Bilirubin was negatively correlated with leukocytes, amylase, RF, triglyceride or LDH, but positively associated with HDL ($P<0.05$, $P<0.01$ or $P<0.001$, respectively).

DISCUSSION

This study was designed to investigate whether liver markers such as AST, ALT, ALP, GGT, and bilirubin have a relationship with other physiological factors in the normal and fatty liver subjects, and there are differences between the two populations. Interesting findings were observed. Most of body indices and biochemical variables together with liver markers were higher in the Fatty liver-group than in the normal group, being attributable to much alcohol intake and/or overweight. These findings suggest heavy drinking and/or overweight may have harmfully effects health and liver function, leading to adult disease and metabolic disease including dyslipidemia.

As is well known, obesity and heavy alcohol drinking can cause metabolic syndrome and adult diseases (Kim et al., 2006; Sidorenkov et al., 2010). The World Health Organization estimates that, worldwide, 1.6 billion adults are overweight (BMI > 25) and 400 million are obese (BMI > 30). Obesity and heavy alcohol drinking may contribute to elevation of blood pressure or hypertension (Hillbom et al., 2011; Kshatriya et al., 2011). The present data agree with such suggestion.

Furthermore, overweight, and obesity can lead to liver diseases. Especially, a finding which only Fatty liver-group had a negative relationship between AST and bone density may reflect that increased levels in liver markers may facilitate the development of osteoporosis in individuals with hepatic steatosis. Also, finding that bone density was less in the Fatty liver-group may suggest that obesity and fatty liver may be associated with osteoporosis.

In the correlation between liver markers and cardiovascular indices (CI), AST, ALT, GGT or bilirubin in the Fatty liver-group generally had positive correlations with several vascular indices, which are diagnostic indicators of cardiovascular disease including hypertension, coronary heart problem and/or stroke. These results indicate that elevated levels in liver markers can significantly predict incident arterial stiffness or hypertension. Mason et al. (2010) recently reported that GGT is becoming an important addition to the multimarker approach to cardiovascular risk evaluation.

These results indicate that elevated levels in liver markers can significantly predict incident arterial stiffness or hypertension. Mason et al. (2010) recently reported that GGT is becoming an important addition to the multimarker approach to cardiovascular risk evaluation. Especially, on the correlations between livers markers and cardiovascular indices, the Fatty liver-group had more frequent relationships than the normal group, suggesting that increased levels in liver markers (fatty liver) may be associated with atherosclerosis, hypertension and vascular diseases (Baou et al., 2007).

ALT is found mainly in the liver and is elevated with hepatic inflammation or injury. AST is located in both hepatocytes and muscle cells and elevated in the serum with hepatic cell involvement, skeletal muscle fiber inflammation, and myocardial cell injury. ALP is found in the hepatobiliary tract and is markedly elevated with biliary track obstruction.

Several studies have also demonstrated that increased AST and ALT were strongly associated with adiposity and

other features of metabolic syndrome and that ALT was a predictor for the development of CVD (Clark et al., 2003; Schindhelm et al., 2007). Furthermore, Iacobellis et al. (2008) proposed that serum AST and ALT activity were significantly correlated with epicardial fat thickness. However, the present findings that the other liver markers, excepting ALP (negative correlation) had no relationships with CI suggest that population without fatty liver may have lower risk of hypertension and/or vascular disease. On the other hand, bilirubin level in the normal group was inversely related with vascular indices, suggesting a useful role for cardiovascular system. Bilirubin is a potent physiological antioxidant that may provide important protection against atherosclerosis, CAD, and inflammation (Ghem et al., 2010). Bilirubin has a powerful scavenging of peroxyl radicals, which cause lipid peroxidation and inflammation and thereby the development of CVD events.

In the correlation between liver markers and other variables, both groups had some correlations of liver markers to inflammatory (amylase and RF) and cardiac markers (LDH and CK), or AFP, indicating that elevated levels in liver markers may be associated with inflammation, cardiovascular disease or liver disorders. AFP is a glycoprotein that is normally generated during conception by the fetal liver and yolk sac. In clinical practice, AFP levels are elevated in various clinical situations, which include hepatocellular carcinoma, acute, or chronic viral hepatitis, chronic liver disease, and gonadal tumors (Collier and Sherman, 1998). Recently, Babali et al. (2009) have reported that subjects with nonalcoholic fatty liver disease (having increased AST, ALT, cholesterol, triglyceride and glucose levels) have higher AFP levels than those without nonalcoholic fatty liver disease and that AFP levels rise as the grade of liver steatosis increases.

T_3 and free T_4 levels (which are thyroid hormones) were negatively associated, whereas they were positively correlated with liver markers. These observations imply that increased levels in liver markers may be associated with decrease of thyroid function.

Some of liver markers were positively correlated with triglyceride, but negatively associated with HDL, suggesting elevated levels in liver markers can cause dyslipidemia. A decreased level of HDL due to increased levels of liver markers is very important for the development of cardiovascular disease because it prevents an elevation of LDL, which can lead to cardiovascular disease. AST or ALT in the both group had positive relationships with BUN, creatinine, or uric acid. These results suggest that changed levels in hepatic enzymes (liver markers) can be involved in renal disorder. Especially, uric acid is involved in cardiovascular disorders, including hypertension (Cannon et al., 1996; Galvan et al., 1995), metabolic syndrome (Ford et al., 2007), coronary artery disease (Tuttle et al., 2001) and cerebrovascular disease as well as kidney disease (Siu et al., 2006; Talaat et al., 2007).

As earlier mentioned, bilirubin have physiologically good effects as it was negatively correlated with all of inflammatory markers, triglyceride, uric acid or LDK, but positively associated with HDL. However, bilirubin had a positive relationship with AFP, indicating that it is a double-sword. Therefore, serum level of bilirubin should be normal range.

In conclusion, this study reveals that serum liver markers, even in healthy adults with nonfatty liver to near normal range, may be associated with the potential development of chronic low-grade inflammation, endocrine and renal disorder, dyslipidemia, gout, cardiovascular risk, or metabolic syndrome and that there is a difference between the normal and fatty liver populations in the relationships. Moreover, the present study has demonstrated that liver markers are higher in population with fatty liver, suggesting that they may have a higher possibility to be exposed to adult disease. However, this study has a limitation because the population was not distinguished into nonalcoholic or alcoholic fatty liver and the design was a cross-section study. Therefore, further studies should be performed.

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