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Original Article

Analysis of Biochemical Markers Related to Fatty Liver Patients

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Abstract. [Purpose] This study was designed to study the correlation between biochemical tests and fatty liver. [Subjects and Methods] The study subjects were 242 people who received an abdominal ultrasound examination at a general hospital in Seoul, Korea, from March 2012 to March 2013. After the abdominal ultrasound examination, the subjects were categorized according to the presence or absence of fatty liver (n = 118 and 124, respectively). [Results] Comparison of biochemical markers revealed that glucose, total protein, aspartate transminase, alanine transaminase and triglyceride were higher in fatty liver patients. Risk analysis of general characteristics determined that hypertensive and diabetic patients had a 2.475- and 2.026-times greater risk of onset of fatty liver, respectively. The comparison of fatty liver with individual characteristics and biochemical markers revealed a 1.804-times greater chance of fatty liver when total protein was high, 0.964-times greater chance when high density lipoprotein was elevated and 1.204-times greater chance when triglyceride was elevated. When hypertension became severe, the chance of experiencing onset of fatty liver was 2.848 times higher. [Conclusion] Fatty liver is a representative disease of obese people in general and more active attention is necessary for its prevention and treatment. A direct cause of fatty liver was not found. Large-scale prospective studies will be required.
Key words: Fatty liver, Biochemical markers

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INTRODUCTION

Fatty liver is a disease characterized by deposition of fat in the liver. Onset of fatty liver disease is very closely related to obesity, especially abdominal obesity[1, 2)]. As the number of obese people continues to increase, the prevalence of fatty liver onset has and will continue to increase. A survey of 160,000 people in Seoul and Gyeonggi Province, conducted by the Korea Ministry of Food and Drug Safety, on the prevalence rate of fatty liver revealed an increased prevalence of fatty liver from 11.5% in 2004 to 23.6% in 2010 overall, with increases of 31.0% for men and 16.0% for women. In general, fatty liver patients also have accompanying metabolic disorders including obesity (60–95%) and diabetes (30–55%)[3–5)].

Diagnosis methods of fatty liver are liver biopsy, abdominal ultrasound, and radiologic examinations including computed tomography (CT) and magnetic resonance imaging (MRI). Liver biopsy is considered an absolute standard for the diagnosis of fatty liver and its severity, but due to its invasive nature, the risk of complications exists[6)]. CT and MRI are expensive and also entail the risk of side effects due to the use of contrast medium. Abdominal ultrasound examination is most frequently used for the diagnosis of fatty liver due to benefits that include safety, repeatability and economical cost[7–11)].

Factors related to fatty liver are closely related to dietary habits and metabolic syndrome. Especially, it was reported recently that serum uric acid, by itself, is related to metabolic syndrome[12)]. In one study, average serum uric acid level was higher in a group with fatty liver than a control group[4)].

Diet affects fatty liver[1)]. However, biochemical tests including blood test scores have been little studied. Therefore, the present study was undertaken to assess the correlation between biochemical markers and fatty liver.

SUBJECTS AND METHODS

Four hundred eighty-two people who visited a general hospital in Seoul from March 2012 to March 2013 for an abdominal ultrasound examination were initially selected for this study. After applying the exclusion criteria described below, they were categorized into those with fatty liver (non-alcoholic fatty liver only, n=118, 84 men and 34

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women, average age 64.43±11.30 years) or without fatty liver after the examination (n=124, 96 men and 28 women, average age 63.31±11.37 years).

All participants signed a written informed consent form approved by the Institutional Review Board of the Korea Veterans Hospital.

Non-alcoholic fatty liver was defined as fatty liver with the absence of hepatitis or severe hepatic dysfunctions, and only a moderate level of alcohol intake. Fatty liver patients with evidence of liver cirrhosis from the abdominal ultrasound examination, and those positive for hepatitis B surface antigen and hepatitis C virus were excluded. The normal subjects did not have fatty liver or other diseases. Abdominal ultrasound was conducted by a radiology specialist and the diagnosis of fatty liver was made for reflections equal in strength or higher than that of parenchyma. A retrospective survey was performed to complete individual indicators, using data from charts. The four assessed items were smoking habit, blood pressure level, alcohol consumption, and diabetes. After fasting for at least 12 hours, systolic blood pressure, diastolic blood pressure were recorded, and blood and urine were collected for biochemical analyses of glucose, blood urea nitrogen/creatinine (BUN/Cr) ratio, total protein, albumin, total bilirubin, alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), creatinine, hemoglobin, total cholesterol, high density lipoprotein-cholesterol (HDL), low density lipoprotein-cholesterol (LDL) and triglyceride. Student's t-test was used to compar e the presence and absence of fatty liver with the biochemical markers of the selected individuals. The χ^2 test was performed to compare general characteristics and risk levels. To find variables independently related to fatty liver, partial correlation coefficients with a restriction on age were used. Accurate correlation with related variables was attained using a binomial logistic regression model. Statistical analysis was performed using SPSS software ver. 18.0 (ver. 18.0, Chicago, USA). The significance level was chosen as 0.05.

RESULTS

Compared to normal subjects, those with fatty liver had significantly ($p<0.05$) higher levels of glucose (145.92±70.17 mg/dl), total protein (7.00±0.52 g/dl), AST (39.23±33.98 U/l), ALT (40.89±26.15 U/l) and triglyceride (199.31±111.95 U/l). The value of HDL in subjects with fatty liver (43.13±12.88 mg/dl) was significantly lower ($p<0.05$) than that of normal subjects (Table 1). One hundred thirty-two subjects (54.5%) had hypertension and 110 subjects (45.5%) did not have hypertension. Hypertensive patients were 2.475 times more likely to have onset of fatty liver. One hundred one (41.7%) subjects had diabetes and 141 subjects (58.3%) did not. Diabetic patients were 2.026 times more likely to have onset of fatty liver ($p<0.05$) (Table 2). Correlation analysis of the presence or absence of fatty liver with individual characteristics and biochemical markers showed a positive correlation of 0.250 for glucose, 0.195 for total protein, 0.175 for AST, 0.234 for ALT, 0.505 for triglyceride, 0.237 for blood pressure, and 0.187 for diabetes; HDL displayed a negative correlation of −0.308. All correlations were significant ($p<0.05$) (Table 3). A logistic regression model based on the presence/absence of fatty liver, individual characteristics, and biochemical markers revealed 1.804, 1.204 and 2.848 greater chances of fatty liver if total protein, or triglyceride was high and hypertension was present, respectively (all $p<0.05$), and a 0.964 times lower chance if HDL was high (Table 4).

Table 1. Comparison of biochemical markers based on the presence or absence of fatty liver

Division	Presence of fatty liver	Average
Glucose (mg/dl)	Normal	117.43±41.45
	fatty liver	145.92±70.17
BUN (mg/dl)	Normal	17.39±6.25
	fatty liver	16.23±5.97
Total protein (g/dl)	Normal	6.77±0.65
	fatty liver	7.00±0.52
Albumin (g/dl)	Normal	4.33±0.40
	fatty liver	4.40±0.41
Total bilirubin (mg/dl)	Normal	0.79±0.33
	fatty liver	0.75±0.29
ALP (u/l)	Normal	77.83±38.09
	fatty liver	71.24±29.15
AST (u/l)	Normal	29.61±17.36
	fatty liver	39.23±33.98
ALT (u/l)	Normal	28.00±26.31
	fatty liver	40.89±26.15
GGT (u/l)	Normal	51.10±85.28
	fatty liver	68.17±95.85
Creatinine (mg/dl)	Normal	0.98±0.55
	fatty liver	0.98±0.35
Hemoglobin (g/dl)	Normal	13.81±1.61
	fatty liver	14.14±2.00
Total cholesterol (mg/dl)	Normal	177.92±35.40
	fatty liver	181.67±35.22
HDL (mg/dl)	Normal	51.09±11.48
	fatty liver	43.13±12.88
LDL (mg/dl)	Normal	105.00±35.63
	fatty liver	106.75±32.53
Trigyceride (u/l)	Normal	99.75±43.95
	fatty liver	199.31±111.95

BUN: blood urea nitrogen; ALP: alkaline phosphatase; AST: aspartate aminotransferase; ALT: alanine aminotransferase; GGT: gamma-glutamyl transferase; HDL: high density lipoprotein-cholesterol; LDL: low density lipoprotein-cholesterol

DISCUSSION

Fatty liver disease is the most common chronic liver disease in Western society. It is not caused by alcohol or hepatitis virus, but by the accumulation of fatty acid in liver parenchymal cells in the form of triglyceride[13]. Espe-

Table 2. Risk analysis of general characteristics based on the presence or absence of fatty liver

(n=118)

Division		Presence of fatty liver		Total	Odds ratio (95% CI)
		Normal	Fatty liver		
Smoking	Non smoking	75 (63.6%)	73 (58.9%)	148 (61.2%)	1.129 (0.726–2.046)
	Smoking	43 (36.4%)	51 (41.1%)	94 (38.8%)	
Blood pressure	Normal	67 (56.8%)	43 (34.7%)	110 (45.5%)	2.475 (1.473–4.159)
	High	51 (43.2%)	81 (65.3%)	132 (54.5%)	
Drinking	Non drinking	73 (61.9%)	87 (70.2%)	160 (66.1%)	0.690 (0.404–1.178)
	Drinking	45 (38.41%)	37 (29.8%)	82 (33.9%)	
Diabetes	Normal	79 (66.9%)	62 (50.0%)	141 (58.3%)	2.026 (1.204–3.409)
	Diabetes	39 (33.1%)	62 (50.0%)	101 (41.7%)	

Table 3. Correlation analysis based on the presence or absence of fatty liver, individual characteristics and biochemical markers

		Presence of fatty liver			Presence of fatty liver
Sex	Correlation coefficient	−0.076	GGT	Correlation coefficient	0.092
Glucose	Correlation coefficient	0.250	Creatinine	Correlation coefficient	0.017
Total protein	Correlation coefficient	0.195	Hemoglobin	Correlation coefficient	0.085
Presence of fatty liver	Correlation coefficient	1.000	Total cholesterol	Correlation coefficient	0.051
Albumin	Correlation coefficient	0.080	HDL	Correlation coefficient	−0.308
Total bilirubin	Correlation coefficient	−0.061	LDL	Correlation coefficient	0.016
ALP	Correlation coefficient	−0.094	Triglyceride	Correlation coefficient	0.505
AST	Correlation coefficient	0.175	Smoking	Correlation coefficient	0.045
ALT	Correlation coefficient	0.234	Blood pressure	Correlation coefficient	0.237
Drinking	Correlation coefficient	−0.088	Diabetes	Correlation coefficient	0.187

BUN: blood urea nitrogen; ALP: alkaline phosphatase; AST: aspartate aminotransferase; ALT: alanine aminotransferase; GGT: gamma-glutamyl transferase; HDL: high density lipoprotein-cholesterol; LDL: low density lipoprotein-cholesterol

Table 4. Logistic regression analysis based on the presence or absence of fatty liver, individual characteristics and biochemical markers

Division	B	Standard Error (SE)	Odds ratio (95% CI)
Glucose	0.003	0.005	1.003 (0.994–1.013)
Total protein	0.590	0.303	1.804 (0.996–3.269)
AST	0.016	0.012	1.015 (0.993–1.040)
ALT	0.014	0.010	1.014 (0.994–1.035)
HDL	−0.036	0.016	0.964 (0.935–0.995)
Triglyceride	0.024	0.004	1.024 (1.016–1.033)
Blood pressure	1.047	0.370	2.848 (1.379–5.887)
Diabetes	−0.115	0.461	0.891 (0.361–2.203)
Coefficient	−7.430	2.253	0.00059 (0.361–2.203)

AST: aspartate aminotransferase; ALT: alanine aminotransferase; HDL: high density lipoprotein-cholesterol

cially, histological fat accumulation in the liver is a feature of non-alcoholic fatty liver disease and manifests as various symptoms including simple steatosis, steatohepatitis and cirrhosis[14]. Also, fatty liver disease increases insulin resistance[15], which promotes decomposition of adipose tissue. The resulting increased fatty acid supply to the liver promotes fat oxidation that induces fat accumulation in the liver cells.

A significant correlation between the severity of fatty liver and insulin resistance has been observed in normal subjects and those with diabetes[4, 16]. Consistent with this, in the present study diabetic subjects were 2.026 times more

likely to have onset of fatty liver than normal subjects. We believe this to be an outcome of increased insulin resistance.

AST and ALT levels in fatty liver were higher than normal. In general, AST and ALT increases are closely related to fatty liver[17]. In a study of obese children, a 92% increase of ALT was reported in subjects by fatty liver diagnosed with ultrasound[18]. Another study of obese children reported a significant correlation between the increase of ALT and the severity of fatty liver diagnosed by abdominal ultrasound[19]. In the present study, the ALT level had a stronger positive linear relationship with fatty liver than the AST level. This is understandable, given that in general, ALT mostly exists in the cytoplasm while only 20% of AST exists in cytoplasm with the remainder found in mitochondria. Also, when the infiltration of fat in liver cells with fat causes damage, the secretion of enzymes will be mainly from the cytoplasm[17].

In this study, the possibility of onset of fatty liver was increased if total protein, triglyceride and HDL levels were high. In general, fat accumulation in the liver is related to triglyceride, and HDL levels, and insulin resistance. An abnormal triglyceride, which reflects insulin resistance in the liver, is induced by partial insulin resistance in the liver and muscle[13, 20]. In the present study, increased hypertension was associated with an increased risk of onset of fatty liver. Regarding metabolic syndrome, in general, due to insulin resistance, metabolic diseases such hypertension, obesity and diabetes, as well as non-alcoholic fatty liver disease can occur. As a result, there is a correlation between fatty liver and hypertension, and hypertension also occurs in fatty liver patients.

This study had several limitations. Only adults who visited a university hospital were selected and the number of participants was small. The present rate of fatty liver cases (49%) was considerably higher than that of another study (14–27%)[21], since we included many patients in their 50's and older. This age group is prone to onset of fatty liver. Thus it was difficult to obtain objective age-related data. More studies with larger numbers of adults should be conducted. Finally, although abdominal ultrasound, which has relatively high sensitivity and specificity for the diagnosis of fatty liver, was used for our study, liver biopsy, which is the most accurate test method, was not used. Fatty liver is a representative disease of obese people and more attention should be paid to its prevention and treatment. A direct cause of fatty liver was not identified in this study. Large-scale prospective studies will be necessary.

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