

Factors Associated or Related to with Pathological Severity of Nonalcoholic Fatty Liver Disease

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Background : Nonalcoholic fatty liver disease (NAFLD) has been more and more often regarded as a serious disorder, because nonalcoholic steatohepatitis (NASH), a part of NAFLD, may progress to the end stage of liver disease. Though an advanced age, obesity, diabetes mellitus (DM) etc. being not infrequent conditions in Korea, are known to exacerbate the severity of this disease, there are only a few Korean reports on this subject. The purpose of this study is to identify possible factors that might add up to the pathological severity of this disorder in Korean patients.

Methods : Of 60 patients with steatosis found at liver biopsy, 43 NAFLD patients were reviewed retrospectively after exclusion of other liver diseases.

Results : The cases of steatosis were mild, moderate, and severe in 9, 10, and 24 patients, respectively. The degree of necroinflammatory activity was mild, moderate, and severe in 33, 9, and 1 patients, respectively. There were no established factors directly related to these classes. As to fibrosis, the cases were classified as none, mild, moderate, severe, and cirrhotic in 9, 11, 16, 7, and 0 patients, respectively. The stage of fibrosis correlated with the age ($p < 0.001$), BMI (body mass index) ($p = 0.032$), and the platelet count ($p = 0.009$), but the presence of NASH was associated only with BMI ($p = 0.002$) and obesity ($p = 0.001$).

Conclusion : It seems that there are no factors that are directly related to the degree of steatosis or necroinflammatory activity. BMI seems to be a unique factor directly related to both the severity of fibrosis and the presence of NASH. The age and the platelet count are factors that are directly related to the degree of fibrosis but not to the presence of NASH.

Key Words : Fatty liver, Hepatitis, Fibrosis

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is a disorder of a wide spectrum of symptoms including those of simple steatosis without any inflammation or fibrosis, steatosis with nonspecific inflammation, and steatosis accompanied by inflammation and fibrosis, namely nonalcoholic steatohepatitis (NASH)¹⁻³. NASH is a kind of hepatitis with pathologic findings similar to those of alcoholic hepatitis in nonalcoholics^{1, 2}. Since Ludwig and collea-

gues for the first time described this disease in 1980⁴, the seriousness of this disorder has been being increasingly recognized, because it may progress to cirrhosis, hepatic failure, and even hepatocellular carcinoma⁵⁻⁸. Several conditions such as an advanced age, obesity, DM or insulin resistance, hyperlipidemia, and female gender have been reported as predisposing factors in this disorder^{1, 4, 9-12}. And in several articles^{3, 6, 13-15}, a few conditions, such as an advanced age, type II DM, obesity, and increased AST/ALT ratio have been reported to be the

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conditions that can lead to the development of severe fibrosis. There have been only few Korean reports^{16, 17)} on this subject, and the results are not fully consistent with those of other reports. The aim of this study was to identify possible factors that may influence the pathological severity, such as steatosis, inflammation, and fibrosis in Korean NAFLD patients.

MATERIALS AND METHODS

1. Patient Population

Reports of 933 liver biopsies which were done between year 1998 and 2002 were analysed retrospectively. Different degrees of steatosis were found in 60 patients at microscopic examination, and, finally, 43 patients with NAFLD were reviewed after clinical exclusion of liver diseases, such as alcoholic liver disease, viral hepatitis, autoimmune hepatitis, drug-induced hepatitis, primary biliary cirrhosis, Wilson's disease, hemochromatosis, biliary obstruction, secondary nonalcoholic steatohepatitis, etc. The alcohol intake below 40 g/week was applied as a criterion for exclusion of alcoholic liver disease. Patients who had experienced gastrointestinal surgery or taken drugs^{1, 3)} which may induce hepatic steatosis, such as corticosteroids, estrogens, methotrexate, tetracycline, calcium channel blockers, or amiodarone were excluded.

2. Methods

Liver biopsy was done with employment of ultrasonography in all patients, stained with hematoxylin-eosin and Masson's trichrome. All biopsy specimens were reviewed again by one pathologist. The grading and staging system proposed by Brunt and et al.¹⁸⁾ was used to classify the severity of the disease; i.e., the degree of steatosis was graded as 1 (mild), 2 (moderate), and 3 (severe), based on the percent of hepatocytes in the given biopsy specimen. The necroinflammatory activity was also graded as 1 (mild), 2 (moderate), and 3 (severe). Because there was only one patient whose necroinflammatory activity was graded 3 in this study, the comparison was done between two groups, "grade 1" and "grade 2 or more," for the purpose of the statistical processing. Fibrosis was classified into stages 0 (none), 1 (pericellular or perisinusoidal), 2 (periportal), 3 (bridging), and 4 (cirrhosis). The disease entity "NASH" was considered only when, at least, minimal fibrosis was present, and other cases were considered as "simple steatosis" regardless of the necroinflammatory activity. Presence of Mallory's hyaline was reported in all specimen. Age, gender, body mass index (BMI), presence of DM or hypertension, serum or blood tests, such as the white blood cell count (WBC), hemoglobin (Hb), platelets, total protein, albumin, total and direct bilirubin, alkaline phosphatase (ALP), aspartate

transaminase (AST), alanine transaminase (ALT), AST/ALT ratio, triglyceride (TG), cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), prothrombin time (PT) prolongation, partial thromboplastin time (PTT), type IV collagen, and hyaluronic acid level were reviewed. The patient was considered obese when BMI exceeded 25 and DM case, if there was a documented administration of oral hypoglycemic agents or insulin, with the fasting glucose level exceeding 125 mg/dL on 2 occasions, or random glucose level exceeding 200 mg/dL. Hypertension was considered when the patient had been taking antihypertensive medicine or when diastolic blood pressure exceeding 90 mmHg or systolic blood pressure exceeding 140 mmHg was noted more than on 2 separate days.

3. Statistical analysis

The SPSS statistical package 11.0 (SPSS Inc., Chicago, IL., U.S.A.) was used for the statistical analysis. All the data were summarized by mean \pm SD (standard deviation) for continuous variables and by frequency or percentage for categorical variables. The values of the variables were compared among each grades of steatosis and the necroinflammatory activity. The comparison was also done in respect of each stage of fibrosis and between the groups of simple steatosis and NASH. The univariate analysis was performed using Mann-Whitney test for comparison of two groups and Kruskal-Wallis test for more than two groups. Chi-square test was used for comparison of the frequency data. Values of p less than 0.05 were considered as "significant" and values of p between 0.05 to 0.1 were considered as "tending to significant" statistically. The multiple regression analysis was used to identify the independent effects of significant variables on steatosis, the necroinflammatory activity, and fibrosis.

RESULTS

1. Patients' demographic and basic laboratory data

The main clinical and laboratory data of the patients of the study are summarized in Table 1. Thirty four (79.1%) patients were male. The mean age was 32.9 years. Mean BMI was 26.8, and the obese patients, whose BMI exceed 25.0, were thirty (69.8%). Three (7.0%) patients had DM and six (14.0%) patients had hypertension. Only three (7.0%) patients had AST/ALT ratio above 1.

2. Histologic findings

The biopsy findings are summarized in Table 2. The grades of steatosis were 1 in 9 (20.9%), 2 in 10 (23.3%), and 3 in 24 (55.8%) patients, respectively. The grades of the necroinflammatory activity were 1, 2, and 3 in 33 (76.8%), 9 (20.9%),

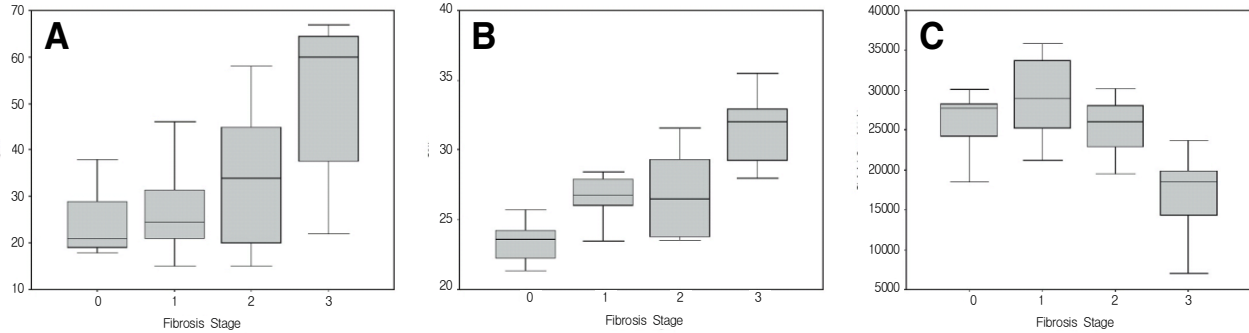


Figure 1. The distribution of age (A), BMI (B), and platelet count (C) according to the stage of fibrosis. In all three above variables, the statistically significant differences were taken from radically different values of the stage 3 group.

Table 1. Patient demographics and basic laboratory data (n=43)

Variables	Value/Number
Age (years)	32.9±15.8
Gender (Male)	34 (79.1%)
BMI	26.8±3.5
Obesity (BMI>25)	30 (69.8%)
Diabetes mellitus (+)	3 (7.0%)
Hypertension (+)	6 (14.0%)
WBC (/mm ³)	7206±1437
Hb (g/dL)	14.7±1.4
Platelet (X1000/mm ³)	255±63
Protein (g/dL)	7.5±0.6
Albumin (g/dL)	4.7±0.4
T-Bilirubin (mg/dL)	0.9±0.4
D-Bilirubin (mg/dL)	0.3±0.2
ALP (IU/L)	93.8±51.8
AST (IU/L)	72.6±39.4
ALT (IU/L)	133.8±71.4
AST/ALT ratio (>1)	3 (7.0%)
TG (mg/dL)	190.8±93.7
Chol (mg/dL)	189.3±31.6
HDL (mg/dL)	41.4±8.1
LDL (mg/dL)	134.6±34.7
Type IV collagen (ng/mL)*	4.3±1.6
Hyaluronic acid (ng/mL)*	25.6±5.2

All values are described as mean±SD. BMI, body mass index; WBC, white blood cell; Hb, hemoglobin; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TG, triglyceride; Chol, cholesterol; HDL, high density lipoprotein; LDL, low density lipoprotein

*Total number of subject is 18.

and 1 (2.3%) patients, respectively. There were 9 (20.9%) simple steatosis and 34 (79.1%) NASH patients. The stages of fibrosis were 0 in 9 (20.9%), 1 in 11 (25.6%), 2 in 16 (37.2%), and 3 in 7 (16.3%) patients, respectively. There were no patients with fibrosis stage 4. Mallory bodies were found in 7 (16.3%) patients.

3. Factors associated with the degree of steatosis, necroinflammatory activity, and fibrosis

ROC Curve

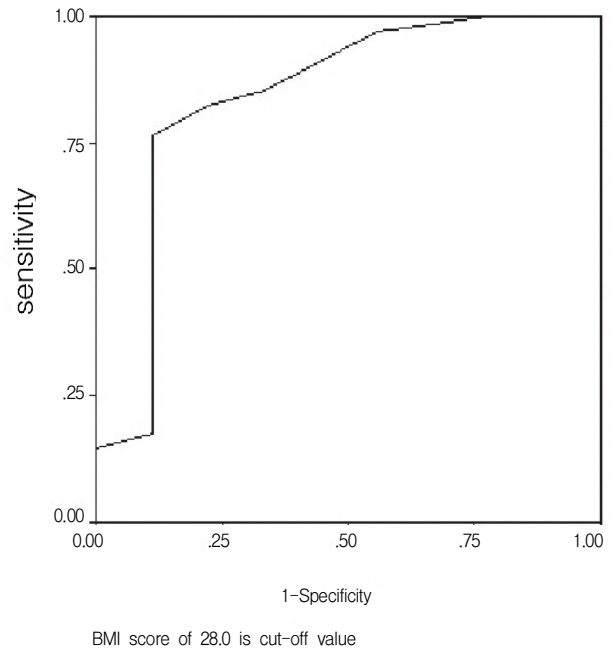


Figure 2. ROC curve for diagnosis of NASH with BMI. Cut-off BMI value of 26.0 was relevant for the diagnosis of NASH, with sensitivity and specificity of 76% and 89%, respectively (BMI : body mass index).

In the univariate analysis (Table 3), there was a significant difference in the direct bilirubin concentration among the 3 grades groups of steatosis ($p=0.025$), but the mean levels were within the normal range. The degree of steatosis by DM ($p=0.076$), total bilirubin concentration ($p=0.055$), AST ($p=0.057$), and serum cholesterol level ($p=0.064$). None of these variables were significant independently in the multivariate analysis.

Though the patients of the advanced age ($p=0.082$) and low hemoglobin concentration ($p=0.056$) showed a tendency to have

Table 2. Histologic data of the study group (n=43)

	Number of Patients
Grade of steatosis	
1	9 (20.9%)
2	10 (23.3%)
3	24 (55.8%)
Grade of necroinflammatory activity	
1	33 (76.8%)
2	9 (20.9%)
3	1 (2.3%)
Stage of fibrosis	
0	9 (20.9%)
1	16 (37.2%)
2	11 (25.6%)
3	7 (16.3%)
4	0 (0.0%)
Mallory bodies	7 (16.3%)

a more severe activity, there were no independent factors which could be regarded as directly associated with the degree of the necroinflammatory activity (Table 4).

Table 3. Univariate comparison among groups according to the degree of steatosis

	Grade of steatosis			<i>p</i> value
	1	2	3	
N	9	10	24	
Age (years)	42.7±18.7	31.7±16.8	29.7±13.2	0.176
Gender (Male)	7 (77.8%)	8 (80.0%)	19 (79.2%)	0.993
BMI	25.7±2.7	27.1±5.2	27.1±2.9	0.668
Obesity (BMI>25)	5 (55.6%)	6 (60.0%)	19 (79.2%)	0.314
Diabetes mellitus (+)	2 (22.2%)	1 (10.0%)	0 (14.3%)	0.076
Hypertension (+)	1 (11.1%)	0 (0%)	5 (20.8%)	0.269
WBC (/mm ³)	7054±1799	7397±1345	7184±1382	0.838
Hb (g/dL)	14.1±1.2	14.8±1.5	14.9±1.4	0.317
Platelet (X1000/mm ³)	243±77.4	244±68.1	264±55.3	0.822
Protein (g/dL)	7.8±0.8	7.5±0.7	7.5±0.5	0.555
Albumin (g/dL)	4.5±0.4	4.6±0.4	4.7±0.4	0.145
T-Bilirubin (mg/dL)	0.9±0.4	1.1±0.5	0.8±0.2	0.056
D-Bilirubin (mg/dL)	0.3±0.2	0.4±0.2	0.3±0.1	0.025
ALP (IU/L)	86.8±30.6	107.6±90.9	90.6±35.0	0.555
AST (IU/L)	72.6±49.0	57.0±37.7	92.1±51.3	0.057
ALT (IU/L)	126.2±71.1	125.1±85.3	140.3±67.8	0.760
AST/ALT ratio (>1)	0 (0%)	0 (0%)	3 (12.5%)	0.279
TG (mg/dL)	169.2±73.8	168.2±100.9	205.6±97.0	0.460
Chol (mg/dL)	192.2±38.5	169.6±28.5	196.5±27.6	0.064
HDL (mg/dL)	42.2±2.9	40.1±7.4	41.8±9.5	0.901
LDL (mg/dL)	135.9±44.3	117.2±34.2	141.2±31.2	0.361
Type IV collagen (ng/mL)*	3.4±0.8	4.4±1.1	4.6±2.1	0.262
Hyaluronic acid (ng/mL)*	28.3±5.7	26.8±1.8	24.0±6.4	0.588
Necroinflammatory grade	1.33±0.71	1.20±0.42	1.25±0.44	0.952
Fibrosis stage	1.44±1.13	1.40±1.08	1.33±0.96	0.972
Mallory body (+)	4 (25%)	1 (9.1%)	2 (28.6%)	0.769

All values are described as mean±SD. BMI, body mass index; WBC, white blood cell; Hb, hemoglobin; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TG, triglyceride; Chol, cholesterol; HDL, high density lipoprotein; LDL, low density lipoprotein

*Total number of subject is 18.

Age ($p=0.034$), BMI ($p<0.001$), obesity ($p=0.011$), and the platelet count ($p=0.001$) showed a significant correlation with the stage of fibrosis in the univariate analysis (Table 5). Of them, age ($p=0.032$), BMI ($p<0.001$), and the platelet count ($p=0.009$) also showed a significant correlation with the stage of fibrosis in the multivariate analysis (Table 6). The significant difference results from the different values of the stage 3 group by the different values of the stage 3 group (Figure 1).

4. Factors associated with NASH

When compared by the presence of NASH, BMI ($p=0.002$) and obesity ($p=0.001$) were related to the presence of it in the univariate analysis (Table 7). With the cut-off BMI value of 26.0 in diagnosing NASH, the sensitivity and specificity was 76% and 89%, respectively (Figure 2).

DISCUSSION

The pathologic findings of NASH are similar to those in alcoholic hepatitis¹, but there are some inconsistencies in the diagnosis of this disease due to different diagnostic criteria applied in the studies, on which the reports have been published. Although some studies used expanded criteria, which require only nonspecific inflammation combined with steatosis, to diagnose NASH^{3, 5, 11, 19, 20}, other studies used criteria which impose strictly specific conditions, such as hepatocyte ballooning degeneration, fibrosis, and neutrophilic infiltration with or without Mallory hyaline^{2, 4, 6, 9, 10}. In previously published two Korean studies^{16, 17}, the expanded criteria were used to diagnose NASH. In this study, we used only strictly specific criteria to diagnose NASH, because recent studies report that the prognosis of NAFLD patients differs considerably in respect to the presence of fibrosis¹⁻³. We considered three factors proposed by the Brunt et al.¹⁸ to describe the histology of NAFLD as variables representing the severity of this disease. They are the grades of steatosis, the grades of the necroin-

flammatory activity, and the stage of fibrosis. Then several clinical and laboratory factors which effect the degree of each variable were analyzed.

In general, several conditions, such as obesity, DM or insulin resistance, hyperlipidemia, hypertension, and other metabolic disorders have been known as causes of steatosis^{1, 4, 9-12, 22, 23}. But in this retrospective study, the influence of the above factors on the development of steatosis couldn't be analyzed, because there was no control group.

Although in many published articles²³⁻²⁵, the serum transaminase level, such as AST or ALT, has been reported to strongly correlate with the degree of the necroinflammatory activity in liver diseases, but report with different also exist²⁶. In several reports, the correlation between the serum transaminase level and the necroinflammatory activity was poor or absent^{18, 27}. Our study also shows no statistically significant factors, which effect the degree of the necroinflammatory activity.

Several conditions, such as obesity, type 2 DM or insulin resistance, an advanced age, and an increased AST/ALT ratio have been identified as risk factors of the development and pro-

Table 4. Univariate comparison among groups according to the degree of necroinflammatory activity

	Grade of necroinflammatory activity		p value
	1	Above 2	
N	33	10	
Age (years)	30.1±13.8	42.0±19.0	0.082
Gender (Male)	28 (84.8%)	5 (15.2%)	0.177
BMI	26.6±3.6	27.7±3.0	0.249
Obesity (BMI>25)	22 (66.7%)	8 (80.0%)	0.696
Diabetes mellitus (+)	1 (3.0%)	2 (20.0%)	0.130
Hypertension (+)	4 (12.1%)	2 (20.0%)	0.611
WBC (/mm ³)	7110±1309	7523±1842	0.561
Hb (g/dL)	14.9±1.4	14.0±1.4	0.056
Platelet (X1000/mm ³)	257±57.6	247±80.0	0.561
Protein (g/dL)	7.6±0.6	7.3±0.5	0.286
Albumin (g/dL)	4.7±0.4	4.6±0.3	0.944
T-Bilirubin (mg/dL)	0.9±0.4	0.8±0.2	0.452
ALP (IU/L)	87.6±37.6	114.2±82.9	0.341
AST (IU/L)	69.3±38.2	83.3±43.5	0.273
ALT (IU/L)	137.5±75.6	121.6±56.9	0.640
AST/ALT ratio (>1)	2 (6.1%)	1 (10.0%)	0.558
TG (mg/dL)	194.8±98.1	177.3±81.0	0.862
Chol (mg/dL)	189.5±30.4	188.6±36.9	0.854
HDL (mg/dL)	40.1±7.2	45.9±9.5	0.120
LDL (mg/dL)	137.0±32.7	126.8±42.2	0.307
Type IV collagen (ng/mL)*	4.6±1.4	3.4±2.4	0.382
Hyaluronic acid (ng/mL)*	26.5±2.6	22.6±10.4	0.645
Steatosis grade	2.33±0.82	2.40±0.84	0.832
Fibrosis stage	1.21±0.99	1.90±0.88	0.072
Mallory body (+)	4 (12.1%)	3 (30.0%)	0.325

All values are described as mean±SD. BMI, body mass index; WBC, white blood cell; Hb, hemoglobin; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TG, triglyceride; Chol, cholesterol; HDL, high density lipoprotein; LDL, low density lipoprotein

*Total number of subject is 18.

Table 5. Univariate comparison among groups according to the degree of fibrosis

	Stage of Fibrosis				<i>p</i> value
	0	1	2	3	
N	9	16	11	7	
Age (years)	27.1±12.6	27.5±9.9	34.2±16.0	50.4±19.2	0.034
Gender (Male)	8 (88.9%)	14 (87.5%)	8 (72.7%)	4 (57.1%)	0.087
BMI	23.5±3.3	26.6±1.6	26.9±3.0	31.4±2.7	0.000
Obesity (BMI>25)	2 (22.2%)	14 (87.5%)	7 (63.6%)	7 (100%)	0.011
DM (+)	0 (0%)	1 (6.3%)	1 (9.1%)	1 (14.3%)	0.263
Hypertension (+)	1 (11.1%)	2 (12.5%)	0 (0%)	3 (42.9%)	0.306
WBC (/mm ³)	7775±876	6966±1164	7719±1586	6219±1892	0.102
Hb (g/dL)	15.3±1.0	14.9±1.5	14.3±1.4	14.2±1.7	0.170
Platelet (X1000/mm ³)	263±55.7	290±46.5	252±37.5	168±57.3	0.001
Protein (g/dL)	7.6±0.6	7.5±0.7	7.4±0.7	7.5±0.6	0.901
Albumin (g/dL)	4.7±0.3	4.6±0.4	4.7±0.4	4.6±0.4	0.603
T-Bilirubin (mg/dL)	0.9±0.5	1.0±0.4	0.8±0.1	0.9±0.3	0.787
ALP (IU/L)	99.0±41.1	91.2±67.1	95.5±51.1	90.3±28.3	0.526
AST (IU/L)	54.8±14.4	72.5±44.0	74.8±36.3	92.1±51.3	0.559
ALT (IU/L)	136±73	125±67	142±65	137±101	0.867
AST/ALT ratio (>1)	1 (11.1%)	2 (12.5%)	0 (0%)	0 (0%)	0.196
TG (mg/dL)	218±116	158±80	210±96	192±93	0.485
Chol (mg/dL)	193±36	180±30	207±28	179±29	0.122
HDL (mg/dL)	41.0±6.4	39.1±7.7	45.6±9.8	40.4±7.1	0.385
LDL (mg/dL)	142±42	132±36	146±27	113±30	0.178
Type IV collagen (ng/mL)*	3.9±1.8	3.9±2.0	5.0±0.5	5.2	0.566
Hyaluronic acid (ng/mL)*	26.6±2.1	25.0±6.9	25.6±1.1	30.1	0.420
Steatosis grade	2.33±0.87	2.37±0.81	2.45±0.82	2.14±0.90	0.872
Necroinflammatory grade	1.00±0.00	1.25±0.45	1.27±0.47	1.57±0.79	0.207
Mallory body (+)	0 (0%)	4 (25%)	1 (9.1%)	2 (28.6%)	0.354

All values are described as mean±SD. BMI, body mass index; WBC, white blood cell; Hb, hemoglobin; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TG, triglyceride; Chol, cholesterol; HDL, high density lipoprotein; LDL, low density lipoprotein

*Total number of subject is 18.

Table 6. Multiple regression analysis about the association between the degree of fibrosis and related variables

value	Regression Coefficient	SE of Regression Coefficient	F value	Significance
BMI	0.536	0.030	26.978	0.000
Age	0.241	0.007	4.920	0.032
Platlet	-0.300	0.000	7.640	0.009
R ²	0.583			

gression of fibrosis in a number of previous reports^{3, 6, 13-15, 28, 29}. In Korea, BMI was reported as a unique factor, which was associated with the development of fibrosis in both two previous reports,^{16, 17} and a low ALT level, besides BMI, was reported to add up to the severity of fibrosis in one report¹⁶. Our results are consistent with those of previous Korean reports in the stipulation that BMI is a unique factor, which influences the development of fibrosis. The cut-off BMI value of 26.0 was relevant for the diagnosis of NASH with the sensitivity and specificity of 76% and 89%, respectively. In terms of the severity of fibrosis, our results are not consistent with previous Korean reports in respect of age, platelet count, and ALT level.

Though a low platelet count appeared to be related to the severity of fibrosis, only one patient with severe fibrosis showed thrombocytopenia in our study. As the disease progresses from mild fibrosis to cirrhosis, the platelet count is known to decrease due to the disturbed thrombopoietin synthesis in viral hepatitis³⁰. Further studies seems to be needed to assess the application of this phenomenon in NAFLD or NASH. The two laboratory variables, which are known to strongly correlate with the degree of fibrosis, type IV collagen and hyaluronic acid, were examined only in 18 patients. Being not statistically significant as they are, the values of these variables tend to be high in the fibrosis stage 3 group.

Table 7. Univariate comparison between groups according to the presence of fibrosis

	Presence of fibrosis		p value
	-	+	
N	9	34	
Age (years)	27.1±12.6	34.4±16.3	0.164
Gender (Male)	8 (88.9%)	26 (76.5%)	0.657
BMI	23.5±3.3	27.7±3.0	0.001
Obesity (BMI>25)	2 (22.2%)	28 (82.4%)	0.001
Diabetes mellitus (+)	0 (0.0%)	3 (8.8%)	1.000
Hypertension (+)	1 (11.1%)	5 (14.7%)	1.000
WBC (/mm ³)	7775±876	7056±1526	0.114
Hb (g/dL)	15.3±1.0	14.6±1.5	0.066
Platelet (X1000/mm ³)	263±55.7	253±64.9	0.687
Protein (g/dL)	7.6±0.6	7.5±0.6	0.491
Albumin (g/dL)	4.7±0.3	4.6±0.4	0.641
T-Bilirubin (mg/dL)	0.9±0.5	0.9±0.3	0.751
ALP (IU/L)	99.0±41.1	92.4±54.7	0.269
AST (IU/L)	54.8±14.4	77.3±42.6	0.256
ALT (IU/L)	135.8±72.8	133.3±72.1	0.731
AST/ALT ratio (>1)	1 (11.1%)	2 (5.9%)	0.515
TG (mg/dL)	217.7±116.5	184.1±88.3	0.509
Chol (mg/dL)	192.9±35.6	188.4±31.0	0.698
HDL (mg/dL)	41.0±6.4	41.5±8.6	0.983
LDL (mg/dL)	142.7±42.2	132.5±33.2	0.537
Type IV collagen (ng/mL)*	3.9±1.8	4.4±1.7	0.778
Hyaluronic acid (ng/mL)*	26.6±2.1	25.5±5.5	0.779
Steatosis grade	2.33±0.87	2.35±0.81	0.960
Necroinflammatory activity	1.00±0.00	1.32±0.54	0.067
Mallory body (+)	0 (0.0%)	7 (16.3%)	0.314

All values are described as mean±SD. BMI, body mass index; WBC, white blood cell; Hb, hemoglobin; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TG, triglyceride; Chol, cholesterol; HDL, high density lipoprotein; LDL, low density lipoprotein

*Total number of subject is 18.

CONCLUSION

No significant factors related to the severity of steatosis and the necroinflammatory activity seem to have been found, but BMI, age, and platelet count may have a certain value for the prognosis of the development and progress of fibrosis.

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