

# High serum ferritin is associated with the status of insulin resistance in subjects with non-alcoholic fatty liver disease: A community-based study

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## Background

Hyperferritinemia, expressed in an acute inflammatory phase, may independently predict the risk for non-alcoholic fatty liver disease (NAFLD).

## Aims

To assess the association between hyperferritinemia and the presence of NAFLD from a community based data.

## Methods

From August 2013 to August 2016, a community-based study was performed in the north-eastern region of Taiwan. All subjects participated in a demographic survey, physical examination, blood tests and abdominal ultrasound. The inclusion criteria of NAFLD group were non-alcohol drinking, non-viral hepatitis subjects and no other secondary disease for hepatic steatosis with or without hyperferritinemia (defined as serum ferritin values > 400 ng/ml in men and > 150 ng/ml in women) and presence of fatty liver on the abdominal ultrasound. Subjects with normal abdominal ultrasound, non-alcoholic and non-viral hepatitis were included in the control group.

**Table 1. Patient characteristics at baseline.**

Variable	Normal liver (N = 410)	NAFLD (N = 410)	P value
Age (years)	55.49 ± 13.07	56.29 ± 11.91	0.360
Male sex (%)	102 (24.9%)	106 (25.9%)	0.748
BMI (kg/m <sup>2</sup> )	22.80 ± 3.18	26.24 ± 3.67	< 0.001
Metabolic syndrome (%)	50 (12.2%)	155 (37.9%)	< 0.001
Waist circumference (cm)	75.05 ± 8.49	83.05 ± 9.78	< 0.001
SBP(mmHg)	125.91 ± 18.28	132.78 ± 18.67	< 0.001
DBP(mmHg)	75.37 ± 11.33	79.45 ± 11.04	< 0.001
Fasting glucose (mg/dl)	95.89 ± 15.99	106.62 ± 31.76	< 0.001
HDL (mg/dl)	61.54 ± 15.04	53.40 ± 13.24	< 0.001
Triglyceride (mg/dl)	90.38 ± 53.39	170.28 ± 590.81	0.007
CBC and biochemistry			
WBC (x10 <sup>9</sup> /L)	5.42 ± 1.55	6.09 ± 1.61	< 0.001
Hb (g/dl)	13.43 ± 1.39	13.51 ± 1.45	0.411
PLT (x10 <sup>9</sup> /L)	253.47 ± 56.06	265.80 ± 62.64	0.003
ALT (IU/L)	17.47 ± 5.37	27.69 ± 20.93	< 0.001
AST (IU/L)	21.38 ± 4.41	25.82 ± 13.19	< 0.001
GGT (IU/L)	15.03 ± 4.42	26.62 ± 24.96	< 0.001
Lipid profile			
Cholesterol (mg/dl)	210.02 ± 37.39	209.57 ± 54.14	0.889
LDL (mg/dl)	120.82 ± 30.50	121.08 ± 33.80	0.906
Ferritin (ng/ml)	119.64 ± 107.29	175.66 ± 158.97	< 0.001
Transferrin (mg/dl)	262.20 ± 38.99	266.46 ± 41.56	0.130
HbA1c (%)	5.61 ± 0.48	6.01 ± 1.01	< 0.001
Insulin (mIU/ml)	5.39 ± 3.12	9.85 ± 8.28	< 0.001
HOMA IR index	1.32 ± 1.00	2.79 ± 3.90	< 0.001
Insulin resistance (%) (HOMA IR > 2.5)	28 (6.8%)	151 (36.9%)	< 0.001

## Results

Finally, 410 subjects were defined as the NAFLD group and 410 subjects were control group. The mean age was 56.29 ± 11.91 years in the NAFLD group and 55.49 ± 13.07 years in the control group. Subjects in the NAFLD group had the higher percent of metabolic syndrome (MetS, by NCEP ATP III criteria) and insulin resistance (IR, by HOMA-IR > 2.5) than subjects in the control group (MetS 37.9% vs. 12.2%, *P* < 0.001; IR 36.9% vs. 6.8%, *P* < 0.001). When comparing with normal control group, subjects with hyperferritinemia increase the risk of NAFLD [odds ratio, OR = 1.633, 95% confidence interval (CI) : 1.126 - 2.367, *P* = 0.010] by logistical regression analysis, after adjusting the confounding factors of age, gender and body mass index (BMI). Moreover, hyperferritinemia in subjects with NAFLD increased the risk of IR [OR = 2.108, 95% CI : 1.297 - 3.426, *P* = 0.003].

## Conclusions

Hyperferritinemia was associated with the status of insulin resistance in subjects with NAFLD.

**Table 2. Correlation for serum ferritin and baseline characteristics**

Variable	Correlation coefficient, r	P value
BMI(kg/m <sup>2</sup> )	0.193	< 0.001
Waist circumference (cm)	0.299	< 0.001
SBP (mmHg)	0.210	< 0.001
DBP (mmHg)	0.195	< 0.001
Fasting glucose (mg/dl)	0.172	< 0.001
HbA1c (%)	0.174	< 0.001
HDL (mg/dl)	-0.224	< 0.001
Triglyceride (mg/dl)	0.083	0.018
HOMA IR index	0.161	< 0.001
Transferrin (mg/dl)	-0.316	< 0.001

**Table 3. Logistic regression analysis of the development of NAFLD**

Variable	OR	95% CI of OR	P value
Age	0.994	0.981 - 1.007	0.346
Gender	1.179	0.814 - 1.707	0.384
BMI	1.375	1.302 - 1.452	< 0.001
Ferritin	1.633	1.126 - 2.367	0.010

**Table 4. Odds ratio of insulin resistance and metabolic syndrome by logistic regression**

Variable	Adjusted for age, gender, and BMI		
	OR	95% CI of OR	P value
Normal liver			
Insulin resistance	0.788	0.280 - 2.216	0.651
Metabolic syndrome	0.713	0.300 - 1.693	0.443
NAFLD			
Insulin resistance	2.108	1.297 - 3.426	0.003
Metabolic syndrome	1.337	0.823 - 2.171	0.241