

# Histological steatosis is not associated with liver fibrosis severity in chronic hepatitis B patients

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## Backgrounds

- Hepatic steatosis is associated with body mass index (BMI) and metabolic syndrome.
- Co-existence of hepatic steatosis is present in 30-40% of chronic hepatitis B (CHB) patients.
- Metabolic syndrome has been reported to increase the risk of liver fibrosis progression in CHB patients.
- A lower BMI has found to be an associated factor for liver fibrosis regression.
- However, the knowledge of relationship between hepatic steatosis and severity of liver fibrosis in CHB patients is limited and controversial.

## Aims

- We conducted a large-scale, retrospective cohort study to explore the relationship between the hepatic steatosis and severity of liver fibrosis assessed by histology.

## Patients and Methods

- A cohort of consecutive CHB patients who have been regularly followed up and received liver biopsy were reviewed.
- Patients with co-infection of hepatitis C virus (HCV), hepatitis D virus (HDV) or human immunodeficiency virus (HIV) and autoimmune, alcoholic or drug-induced liver disease and a history of hepatocellular carcinoma (HCC) at biopsy were excluded.
- The liver fibrosis score was graded by Ishak scoring system and advanced fibrosis was defined as scores 4-6.
- Hepatic steatosis was defined as the presence of steatosis in >5% of hepatocytes according to histological analysis.
- The clinical characteristics were compared between patients with and without hepatic steatosis. Univariate and stepwise multivariate logistic regression analysis was performed to determine the associated factors for advanced liver fibrosis.

## Results

- A total of 712 CHB patients were included from 2003 May to 2017 December.
- Three hundred and four (42.7%) were of hepatic steatosis and were significantly older than those without steatosis (mean age 47.4 vs 45.7 years,  $p=0.033$ ).

- The mean BMI was 26.0 and 23.5 kg/m<sup>2</sup> in patients with and without steatosis, respectively ( $p<0.001$ ).
- The mean levels of serum AST, ALT and HBV DNA were significantly lower in patients with hepatic steatosis, as compared to those without steatosis (68.5 vs 105.9 U/L,  $p<0.001$ ; 121.2 vs 179.1 U/L,  $p<0.001$ ; 5.5 vs 5.9 log IU/mL,  $p=0.004$ , respectively).
- Among the 304 patients with hepatic steatosis, 140 (46.1%) had advanced liver fibrosis and the rate was significantly higher than that of non-steatotic patients (156/408, 38.2%,  $p=0.044$ ).
- With stepwise multivariate logistic regression analysis, genotype [C vs B, odds ratio (OR) 2.735, 95% confidence interval (CI) 1.694-4.416,  $p<0.001$ ], BMI (OR 1.158, 95% CI 1.085-1.236,  $p<0.001$ ), AST (OR 1.016, 95% CI 1.006-1.026,  $p=0.002$ ), ALT (OR 0.993, 95% CI 0.989-0.998,  $p=0.0070$  and platelet (OR 0.984, 95% CI 0.978-0.989,  $p<0.001$ ) were significantly factors associated with advanced liver fibrosis.
- Patients with old age had a trend to have advanced fibrosis (OR 1.021, 95% CI 0.999-1.044,  $p=0.062$ ).
- Hepatic steatosis was not an associated parameter for advanced liver fibrosis.

	Overall	Fat ≤5%	Fat >5%	p
No	712	408	304	
Age, years	46.4±11.0	45.7±11.3	47.4±10.5	0.033
Male, No (%)	568 (79.8)	318 (77.9)	250 (82.2)	0.188
Genotype				0.844
B	429 (73.3)	256 (73.8)	173 (72.7)	
C	156 (26.7)	91 (26.2)	65 (27.3)	
HBeAg(+)	240 (33.7)	139 (34.1)	101 (33.2)	0.876
BMI, kg/m <sup>2</sup>	24.7±3.6	23.5±3.2	26.0±3.6	<0.001
AST, U/L	89.4±91.6	105.9±110.6	68.5±52.5	<0.001
ALT, U/L	153.6±163.5	179.1±188.8	121.2±116.8	<0.001
PLT, 10 <sup>9</sup> /L	182.0±51.6	179.7±50.3	185.0±53.2	0.192
DNA, log IU/ml	5.7±2.0	5.9±1.9	5.5±2.2	0.004
Fibrosis score	3.5±1.5	3.4±1.4	3.6±1.5	0.043
Cirrhosis	214 (30.1)	106 (26.0)	108 (35.5)	0.008
Fibrosis 0-3	416 (58.4)	252 (61.8)	164 (53.9)	0.044
Fibrosis 4-6	296 (41.6)	156 (38.2)	140 (46.1)	

## Conclusions

- Hepatic steatosis accounted for 42.7% of CHB patients.
- Genotype, BMI, levels of AST, ALT and platelet were significantly associated factors for advanced liver fibrosis.
- The proportion of advanced liver fibrosis was significantly higher in patients with hepatic steatosis, whereas the association between histological steatosis and advanced liver fibrosis was not statistically significant.