

# 非酒精性脂肪性肝病患者血清铁蛋白检测的意义

冯红萍, 任艳玲 (湖北医药学院附属东风医院 感染科, 湖北 十堰 442000)

**摘要:** 目的 了解非酒精性脂肪性肝病 (non-alcoholic fatty liver disease, NAFLD) 患者血清铁蛋白 (serum ferritin, SF) 的检测意义。方法 采用微粒子酶免疫分析法 (MEIA) 测定250例NAFLD患者的血清铁蛋白值, 并根据患者首诊时CT片脂肪肝分度分为轻度组 (65例)、中度组 (98例) 和重度组 (87例), 对3组患者的SF值进行比较分析。结果 250例NAFLD患者中ALT正常者135例, SF平均值为  $(320.5 \pm 167.0)$  ng/ml; ALT异常者115例, SF平均值为  $(608.5 \pm 254.4)$  ng/ml, 差异有统计学意义 ( $z = 10.38, P = 0.00$ )。轻度组、中度组和重度组患者ALT值分别为  $(87.2 \pm 52.0)$  U/L、 $(99.4 \pm 68.5)$  U/L、 $(89.4 \pm 78.0)$  U/L, 3组间差异无统计学意义 ( $z = 0.18, P = 0.43$ )。3组患者的SF值分别为  $(330.5 \pm 118.0)$  ng/ml、 $(350.2 \pm 187.5)$  ng/ml、 $(509.4 \pm 150.8)$  ng/ml, 轻度组和中度组SF无统计学差异, 重度组SF显著升高, 与轻度组和中度组差异显著 ( $z = 8.20, 6.39, P$ 值均为0.00)。结论 NAFLD患者SF的升高与肝脏脂肪变程度和肝细胞的损害程度密切相关。

**关键词:** 脂肪肝, 非酒精性; 血清铁蛋白

## Significance of serum ferritin in patients with non-alcoholic fatty liver disease

FENG Hong-ping, REN Yan-ling (Department of Infectious Diseases, Dongfeng Affiliated Hospital, Hubei University of Medicine, Shiyan 442000, Hubei Province, China)

**Abstract: Objective** To explore the significance of serum ferritin in patients with non-alcoholic fatty liver disease (NAFLD). **Methods** Serum ferritin levels among 250 patients with NAFLD were detected by microparticle enzyme immunoassay (MEIA). The patients were divided into mild group (65 cases), moderate group (98 cases) and severe group (87 cases) according to the first diagnosis of CT. The serum ferritin values were compared among the three groups. **Results** Total of 135 cases among the 250 patients with NAFLD were with normal ALT, and the mean value of SF was  $(320.5 \pm 167)$  ng/ml; 115 patients were with abnormal ALT, the mean value of SF was  $(608.5 \pm 254.4)$  ng/ml, and the difference was statistically significant ( $z = 10.38, P = 0.00$ ). The ALT values in mild group, moderate group and severe group were  $(87.2 \pm 52.0)$  U/L,  $(99.4 \pm 68.5)$  U/L and  $(89.4 \pm 78.0)$  U/L, respectively, and there were no statistical differences among the three groups ( $z = 0.18, P = 0.43$ ). The SF values in the three groups were  $(330.5 \pm 118.0)$  ng/ml,  $(350.2 \pm 187.5)$  ng/ml and  $(509.4 \pm 150.8)$  ng/ml, respectively, and there was no significant difference between mild and moderate group; SF was significantly higher in severe group than that of the mild and moderate group ( $z = 8.20, 6.39; P = 0.00$ ). **Conclusion** The increase of SF in patients with NAFLD is closely related to the degree of hepatic steatosis and hepatic cell damage.

**Key words:** Fatty liver, non-alcoholic; Serum ferritin

在我国, 成人非酒精性脂肪性肝病 (non-alcoholic fatty liver disease, NAFLD) 的发病率为15% (6.3%~27.0%) 左右, 已成为慢性肝病的重要病因<sup>[1]</sup>, 且发病率呈逐年升高的趋势, 因此, 其诊治越来越受到医生的关注。血清铁蛋白 (serum ferritin, SF) 是一种脱铁蛋白组成的具有

大分子 (450 kD) 结构的糖蛋白, 由外壳和内核组成, 外壳的24个亚单位为去核铁蛋白; 内核是一个含4500个铁原子的核心, 是体内储存铁的主要形式。铁是人体必需的微量元素之一, 但机体铁过多可引起肝脏疾病、糖尿病、脂质代谢紊乱等慢性疾病, 即使轻度铁增多也会加重包括NAFLD在内的多种慢性疾病的病情<sup>[2,3]</sup>。一些大型多中心临床研究表明, 肝细胞内铁沉积可增加肝纤维化的风险, 铁

超载在NAFLD形成中有重要的作用<sup>[4,5]</sup>；但部分学者认为肝内铁超载现象与NAFLD的发生和进展均无相关性<sup>[6,7]</sup>。为进一步了解铁超载与NAFLD的关系，对250例临床诊断为NAFLD成人患者的SF进行分析，现报道如下。

## 1 资料与方法

**1.1 病例选择** 选择2010年1月至2014年6月在本院感染科、综合内科门诊和住院的临床诊断为NAFLD的患者250例，年龄在20~65岁，平均44.6岁。根据患者首诊时CT片脂肪肝分度分为轻度组、中度组和重度组，其中轻度组65例、中度组98例、重度组87例，3组患者间的性别、年龄等无差异。诊断标准符合2010年1月修订的《非酒精性脂肪性肝病诊疗指南》<sup>[8]</sup>中的诊断标准，并排除有以下情况：酒精性脂肪肝，病毒性肝炎，药物诱导性/中毒性肝病、全胃肠外营养、肝豆状核变性等可导致脂肪肝的特定疾病；合并严重器质性疾病（心、肝、脑、肾、肺、恶性肿瘤等）患者；NAFLD患者已进展至肝硬化阶段或肝功能障碍已进入终末期，或准备肝移植手术者；自身免疫性肝炎患者。

**1.2 检测方法** 250例患者首诊时均采取清晨空腹血3 ml进行肝功能生物化学指标和SF的相关检测，并行肝脏CT探查。SF采用微粒子酶免分析法（MEIA）测定，仪器为美国雅培AXSYM免疫发光分析仪，试剂为该仪器配套试剂盒，严格按说明书操作。正常参考值范围为21.80~274.66 ng/ml。CT片由CT室专人统一阅片。

**1.3 统计学处理** 采用SPSS 17.0软件进行数据分析，计量资料的比较采用 $z$ 检验，计数资料的比较采用 $\chi^2$ 检验，以 $P < 0.05$ 为差异有统计学意义。

## 2 结果

250例NAFLD患者中ALT正常者135例，SF平均值为 $(320.5 \pm 167.0)$  ng/ml；ALT异常者115例，SF平均值为 $(608.5 \pm 254.4)$  ng/ml，ALT异常者的SF值显著高于正常者，差异有统计学意义（ $z = 10.38$ ， $P = 0.00$ ）。3组间ALT值无统计学差异；轻度组和中度组SF差异无统计学意义（ $z = 0.82$ ， $P =$

0.21），重度组SF显著升高，与轻度组、中度组比较差异有统计学意义（ $z$ 值分别是8.20、6.39， $P = 0.00$ ），见表1。

## 3 讨论

NAFLD是以肝实质细胞脂肪变性和脂肪贮积为特征的，且无过量饮酒史的临床病理综合征，是一种与遗传、环境、代谢等相关的疾病。其疾病谱包括单纯性脂肪肝、非酒精性脂肪性肝炎及其相关肝硬化甚至肝细胞癌<sup>[9,10]</sup>。目前研究认为NAFLD并非单一肝脏器官的疾病，而是代谢综合征在肝脏的表现，涉及全身多个器官，不仅存在肝功能异常，血糖、血脂的代谢也异常紊乱，并与心血管疾病的发生密切相关<sup>[11-13]</sup>，严重危害公众健康。

到目前为止，尚无一个学说能很好地解释NAFLD疾病进展的过程。最为广泛接受的是“二次打击”学说，即在胰岛素抵抗引起肝脏脂肪变性的基础上，发生以线粒体反应氧体系为核心的氧应激和脂质过氧化为主的二次损伤<sup>[14]</sup>。铁是脂质氧化的促进剂，参与NAFLD的发病，尤其是在二次打击中参与肝细胞损伤及肝纤维化的过程<sup>[15]</sup>。临床上NAFLD患者多存在不同程度的铁超载现象<sup>[4,16]</sup>，NAFLD相关的铁超载主要发生在肝网状内皮系统中，肝网状内皮系统细胞内的铁沉积或是NAFLD病情进展的独立危险因素<sup>[17,18]</sup>。SF可反应体内铁储存水平，被广泛用于机体及组织中铁过载的评估<sup>[19]</sup>。本研究观察250例临床诊断为NAFLD患者的SF值，显示随肝细胞脂肪变程度的加重SF呈升高趋势，特别是重度脂肪肝患者的SF升高更显著，与轻度和中度脂肪肝有统计学差异。在病毒性肝炎患者中，血清铁代谢指标与肝脏炎症活动有显著相关性，肝功能与SF呈正相关，ALT和AST越高，SF越高<sup>[20]</sup>。本组250例NAFLD患者中ALT正常者135例，SF平均值为 $(320.5 \pm 167.0)$  ng/ml；ALT异常者115例，SF平均值为 $(608.5 \pm 254.4)$  ng/ml，差异有统计学意义，提示NAFLD患者SF的升高与肝细胞的损害关系同病毒性肝炎一致，而且SF在轻度脂肪肝时即可较早地反映出肝功能损害，较ALT、AST更灵敏<sup>[21]</sup>。

表1 3组NAFLD患者间ALT、SF的比较（ $\bar{x} \pm s$ ）

组别	例数	ALT (U/L)	SF (ng/ml)
轻度组	65	87.2 ± 52.0	330.5 ± 118.0
中度组	98	99.4 ± 68.5	350.2 ± 187.5
重度组	87	89.4 ± 78.0*	509.4 ± 150.8*
$z$ 值	-	0.18	8.20
$P$ 值	-	0.43	0.00

注：\* 为与轻度组比较，“-”表示无相关数据

因此认为NAFLD患者SF的升高与肝脏脂肪变程度和肝细胞的损害密切相关, SF可作为NAFLD病情进展程度的独立预测指标<sup>[22]</sup>。

#### 参考文献

- [1] Fan JG. Epidemiology of alcoholic and nonalcoholic fatty liver disease in china[J]. *Gastroenterol Hepatol*,2013,28:11-17.
- [2] Ahmed U, Latham PS, Oates PS. Interactions between hepatic iron and lipid metabolism with possible relevance to steatohepatitis[J]. *World J Gastroenterol*,2012,18:4651-4658.
- [3] Dongiovanni P, Fracanzani AL, Fargion S, et al. Iron in fatty liver and in the metabolic syndrome:a promising therapeutic target[J]. *Hepatology*,2011,55:920-932.
- [4] Sumida Y, Nakashima T, Yoh T, et al. Serum thioredoxin levels as a predictor of steatohepatitis in patients with nonalcoholic fatty liver disease[J]. *Hepatology*,2003,38:32-38.
- [5] Valenti L, Fracanzani AL, Bugianesi E, et al. HFE genotype, parenchymal iron accumulation, and liver fibrosis in patients with nonalcoholic fatty liver disease[J]. *Gastroenterology*,2010,138:905-912.
- [6] Bugianesi E, Manzini P, D'Antico S, et al. Relative contribution of iron burden, HFE mutations, and insulin resistance to fibrosis in nonalcoholic fatty liver[J]. *Hepatology*,2004,39:179-187.
- [7] Chitturi S, Weltman M, Farrell GC, et al. HFE mutations, hepatic iron, and fibrosis:ethnic-specific association of NASH with C282Y but not with fibrotic severity[J]. *Hepatology*,2002,36:142-149.
- [8] 中华医学会肝病学会脂肪肝和酒精性肝病学组[J]. 非酒精性脂肪性肝病诊疗指南(2010年修订版)[J]. *中华肝病杂志*,2010,18:163-166.
- [9] Krawczyk M, Bonfrate L, Portincasa P. Nonalcoholic fatty liver disease[J]. *Best Pract Res Clin Gastroenterol*,2010,24:695-708.
- [10] Farrell Geoffrey C, Larter Claire Z. Non-alcoholic fatty liver disease:from steatosis to cirrhosis[J]. *Hepatology*,2006,43:99-112.
- [11] 刘宗英. 非酒精性脂肪肝患者肝功能酶学指标与血脂检测结果相关分析[J/CD]. *中国肝脏病杂志(电子版)*,2014,6:50-52.
- [12] 丁晴,唐静,方芳,等. 脂肪肝相关因素临床分析[J/CD]. *中国肝脏病杂志(电子版)*,2015,7:65-67.
- [13] 王军,魏艳玲,范丽玲,等. 非酒精性脂肪性肝病与心血管疾病的相关性分析[J]. *实用肝病杂志*,2013,16:499-501.
- [14] Day CP, James OF. Steatohepatitis:a tale of two "hits"?[J]. *Gastroenterology*,1998,114:842-845.
- [15] Kandle KV, Belt P, Wilson LA, et al. Serum ferritin is an independent predictor of histologic severity and advanced fibrosis in patients with nonalcoholic fatty liver disease[J]. *Hepatology*,2012,55:77-85.
- [16] Fargion S, Mattioli M, Fracanzani AL, et al. Hyperferritinemia, iron overload, and multiple metabolic alterations identify patients at risk for nonalcoholic steatohepatitis[J]. *Am J Gastroenterol*,2001,96:2448-2455.
- [17] Nelson JE, Klintworth H, Kowdley KV. Iron metabolism in nonalcoholic fatty liver disease[J]. *Gastroenterology*,2012,14:8-16.
- [18] Nelson JE, Wilson L, Brunt EM, et al. Relationship between pattern of hepatic iron deposition and histologic severity in nonalcoholic fatty liver disease[J]. *Hepatology*,2011,53:448-457.
- [19] Moyer TP, Highsmith WE, Smyrk TC, et al. Hereditary hemochromatosis:laboratory evaluation[J]. *Clin Chim Acta*,2011,412:1485-1492.
- [20] 韩梅丽,于浩,江宇泳. 病毒性肝炎患者的血清铁代谢指标分析[J]. *天津医药*,2014,42:896-899.
- [21] 刘玉霞,尹石华,史健,等. 脂肪肝与铁蛋白、血脂及转氨酶的相关性分析[J]. *国际检验医学杂志*,2011,31:1001-1003.
- [22] Kowdley KV, Belt P, Wilson LA, et al. Serum ferritin is an independent predictor of histologic severity and advanced fibrosis in patients with nonalcoholic fatty liver disease[J]. *Hepatology*,2012,55:77-85

收稿日期: 2015-08-25