

AperTO - Archivio Istituzionale Open Access dell'Università di Torino

## The role of hepatic enzymes in Crohn's disease

**This is a pre print version of the following article:**

*Original Citation:*

*Availability:*

This version is available <http://hdl.handle.net/2318/1632784> since 2018-10-31T17:20:28Z

*Published version:*

DOI:10.1007/s00384-017-2829-1

*Terms of use:*

Open Access

Anyone can freely access the full text of works made available as "Open Access". Works made available under a Creative Commons license can be used according to the terms and conditions of said license. Use of all other works requires consent of the right holder (author or publisher) if not exempted from copyright protection by the applicable law.

(Article begins on next page)

1 Davide Giuseppe Ribaldone,<sup>1</sup> Marco Astegiano,<sup>1</sup> Rinaldo Pellicano<sup>2</sup>

2

3 The role of hepatic enzymes in Crohn's disease

4

5 Department(s) and institution(s)

6 <sup>1</sup>MD, Gastroenterology - U, General and Specialist Medicine Department, Città della

7 Salute e della Scienza of Turin, C.so Bramante 88, 10126 Turin, Italy, <sup>2</sup>MD,

8 Department of Gastroenterology, Molinette Hospital, Turin, Italy

9

10 Corresponding Author: Dr. Davide Giuseppe Ribaldone, General and Specialist  
11 Medicine Department, Città della Salute e della Scienza of Turin, C.so Bramante 88,  
12 10126 Turin, tel 00390116335208, fax 00390116336752, Italy. E-mail:  
13 davrib\_1998@yahoo.com

14

15 Davide Giuseppe Ribaldone ORCID iD 0000-0002-9421-3087

16 Marco Astegiano ORCID iD 0000-0003-0916-1188

17 Rinaldo Pellicano ORCID iD 0000-0003-3438-0649

18

19

20

21

22

23

24

25

26

27

28

29

30

31

32 Abstract

33 N/A

34

35

36

37

38

39

40

41

42

43

44

45

46

47

48

49

50

51

52

53

54

55

56

57

58

59

60

61

62

63

64 Keywords: biopsy, Crohn disease, elastography, histology, inflammatory bowel

65 diseases, liver

66 Sir,  
67 a systematic review has reported that, in Crohns' disease (CD) patients, the prevalence of cholelithiasis ranged  
68 from 11% to 34%, that of primary sclerosing cholangitis (PSC) from 1.2% to 3.4%, that of fatty liver  
69 disease 23% and hepatic amyloidosis occurred in <1% [1]. In a prospective, single-blind study we evaluated the  
70 prevalence of histological changes in the liver of patients with CD, without alterations of both liver biochemical  
71 tests and ultrasound, and their prognostic significance. The patients underwent liver biopsy at the time of  
72 intestinal resection. Exclusion criteria were a known liver disease. Thereafter, patients were clinically monitored  
73 every 6 months, upper abdomen ultrasound was performed at least every 12 months. Finally, after a mean  
74 interval of 14 years from liver biopsy, these patients were assessed using the Fibroscan® (Echosens®, Paris,  
75 France). Ultrasound examination in the pre-operative step showed steatosis in 10 (29%) patients. At biopsy  
76 specimens alterations in 60% of patients, without serious liver injuries, were found. No evidence of a significant  
77 liver damage progression after a mean period of 14 years were found. The average result ( $5.2 \pm 1.2$  kPa)  
78 obtained performing Fibroscan® was comparable to that ( $5.30 \pm 1.45$  kPa,  $p = 0.63$ ) reported in healthy subjects  
79 [2].

80 A recent interesting retrospective study was performed in 383 CD patients newly diagnosed (not treated). One  
81 patient with chronic liver disease (small duct PSC) was excluded. Of the 383 patients included in this study, 131  
82 had liver test abnormalities (34.1%), but liver diseases were not found, apart from liver steatosis in 6% of  
83 patients [3] (*versus* 29% in the previous study [2]).

84 The two studies [2, 3] agree that, considering the cost/benefit ratio, patients with CD should be considered as  
85 healthy from the liver perspective, without the need for additional biochemical and instrumental examinations  
86 than the general population, unless the presence of clinical or biochemical suspicion of liver disease.

87 In the more recent study [3], however, the authors found that, patients with liver test abnormalities, without an  
88 hepatic disease, more often developed complicated CD behaviour and more often needed hospitalization or  
89 surgery within 5 years of diagnosis than patients without liver test abnormalities. Patients with a C-reactive  
90 protein (CRP) <16 mg/L but with liver test abnormalities had a higher risk of developing complicated disease  
91 compared to those without liver test abnormalities. This demonstrates that the presence of liver test abnormalities  
92 does not merely reflect a higher CRP concentration, but may be a more sensitive indicator of an increased risk of  
93 complicated disease behaviour than CRP. At multivariate analysis, the presence of liver test abnormalities was  
94 independent risk factors for complicated disease behaviour; additionally, the presence of liver test abnormalities

95 was independently associated with an increased risk of hospitalizations (HR 1.7,  $p = 0.023$ ) as well as surgery  
96 (HR 2.3,  $p = 0.015$ ) [3].

97 In conclusion, in the absence of a known liver disease or of a risk factor for hepatic injury (e.g., a potentially  
98 hepatotoxic drugs), liver enzymes in CD do not need to be routinely measured. However, when increased, liver  
99 enzymes could predict a more aggressive CD behaviour.

100

101 **Compliance with ethical standards**

102

103 **Funding** None to declare.

104

105 **Conflict of Interest** None to declare.

106

107 **Ethical approval** The study was conducted in accordance with ICH Good Clinical Practice  
108 guidelines, the Declaration of Helsinki, and local laws and regulations.

109

110 **Informed consent** Informed consent due to the observational study has been obtained in the  
111 cited studies.

112

113

114

115

116

117

118

119

120 **References**

- 121 1. Gizard E, Ford AC, Bronowicki JP, Peyrin-Biroulet L (2014) Systematic review: The  
122 epidemiology of the hepatobiliary manifestations in patients with inflammatory bowel  
123 disease. *Aliment Pharmacol Ther* 40:3–15.
- 124 2. Ribaldone DG, Garavagno M, Pellicano R, Bresso F, Fagoonee S, David E, Sapone N,  
125 Bonagura AG, Resegotti A, Astegiano M (2015) Prevalence and prognostic value of  
126 hepatic histological alterations in patients with Crohn's disease. *Scand J Gastroenterol*  
127 50:1463-1468.
- 128 3. Barendregt J, de Jong M, Haans JJ, van Hoek B, Hardwick J, Veenendaal R, van der  
129 Meulen A, Srivastava N, Stuyt R, Maljaars J (2017) Liver test abnormalities predict  
130 complicated disease behaviour in patients with newly diagnosed Crohn's disease. *Int J*  
131 *Colorectal Dis* 32:459-467.