Journal of Clinical and Translational Hepatology **2021** vol. 9(2) | 274–275
DOI: 10.14218/JCTH.2021.00074

Letter to the Editor

Celiac Disease and Elevated Liver Enzymes: A Still Not Fully Defined Pathogenesis

Linda Beenet[1*] and Diego Tonesi[2]

[1]Department of Pathology & Laboratory Medicine, University of California Los Angeles (UCLA) Technology Center for Genomics & Bioinformatics, Los Angeles, CA, USA; [2]Gastroenterology and Endoscopy Unit, Ospedale Maggiore Policlinico, Milan, Italy

Received: 20 February 2021 | **Revised:** 13 March 2021 | **Accepted:** 21 March 2021 | **Published:** 7 April 2021

Citation of this article: Beenet L, Tonesi D. Celiac disease and elevated liver enzymes: A still not fully defined pathogenesis. J Clin Transl Hepatol 2021;9(2):274–275. doi: 10.14218/JCTH.2021.00074.

Dear Editor,

We read, with great interest, the comprehensive review by Villavicencio Kim J and Wu GY that systematically addressed the issue of liver enzyme elevation in celiac disease (CD) patients.[1]

The Authors reviewed, in detail, the most relevant studies reporting the frequency of liver enzyme elevation in CD patients and the possible causes, discussing the hypothesis that this elevation may be a clue to associated liver disease or an epiphenomenon, possibly secondary to the increased intestinal permeability that is known to characterize CD patients, especially at diagnosis, before starting a gluten-free diet.[2]

We would like to add some considerations that, in our opinion, could have implications in the pathogenesis of hepatic injury in CD.

As known, it has been reported that CD is frequently associated with other extraintestinal autoimmune diseases or even with the mere presence of autoantibodies without concomitant autoimmune pathology.[3–6]

Among the autoimmune diseases potentially associated with CD, autoimmune hepatitis (AIH) is worthy of mention, as previously reported.[1,3,7]

Of considerable interest, it has been reported that celiac patients frequently have anti-filamentous actin IgA antibodies that have shown reliable and significant correlation with villous atrophy.[8] These autoantibodies, although of IgG class, are also known to have very high specificity for AIH.[7,9]

This similarity between the two autoimmune diseases could be a clue that also supports possible immune-mediated pathogenesis of hypertransaminasemia in CD patients. Therefore, it would be relevant and worthy of study to analyze the presence of anti-actin antibodies in CD patients to verify whether these antibodies are markers of liver injury.

Finally, it should not be overlooked, the very remarkable issue of the potential development of hepatic steatosis, which, as appropriately mentioned by the Authors, is not uncommon in CD patients with celiac disease after starting a gluten-free diet.[10]

Funding

None to declare.

Conflict of interest

The authors have no conflict of interests related to this publication.

Author contributions

Performance of the research, collection and analysis of the data, writing of the paper, and approving the final version of the article, including the authorship list (LB, DT), guarantor of the article (LB).

Data sharing statement

All data are available upon request.

References

[1] Villavicencio Kim J, Wu GY. Celiac disease and elevated liver enzymes: A review. J Clin Transl Hepatol 2021;9(1):116–124. doi:10.14218/JCTH.2020.00089.
[2] Granito A, Zauli D, Muratori P, Muratori L, Grassi A, Bortolotti R, *et al*. Anti-Saccharomyces cerevisiae and perinuclear anti-neutrophil cytoplasmic antibodies in coeliac disease before and after gluten-free diet. Aliment Pharmacol Ther 2005;21(7):881–887. doi:10.1111/j.1365-2036.2005.02417.x.
[3] Volta U, Granito A, De Franceschi L, Petrolini N, Bianchi FB. Anti tissue transglutaminase antibodies as predictors of silent coeliac disease in patients with hypertransaminasaemia of unknown origin. Dig Liver Dis 2001;33(5):420–425. doi:10.1016/s1590-8658(01)80014-1.
[4] Cervio E, Volta U, Verri M, Boschi F, Pastoris O, Granito A, *et al*. Sera of patients with celiac disease and neurologic disorders evoke a mitochondrial-dependent apoptosis in vitro. Gastroenterology 2007;133(1):195–206. doi:10.1053/j.gastro.2007.04.070.
[5] Volta U, De Giorgio R, Granito A, Stanghellini V, Barbara G, Avoni P, *et al*. Anti-ganglioside antibodies in coeliac disease with neurological disorders. Dig Liver Dis 2006;38(3):183–187. doi:10.1016/j.dld.2005.11.013.

Abbreviations: CD, celiac disease; AIH, autoimmune hepatitis.

***Correspondence to:** Linda Beenet, Department of Pathology & Laboratory Medicine, University of California Los Angeles (UCLA) Technology Center for Genomics & Bioinformatics Los Angeles, CA 90095, USA. ORCID: https://orcid.org/0000-0002-9812-9368. Tel: +1-310-206-4520, Fax: +1-310-206-4520, E-mail: linda.beenet@gmail.com

[6] Volta U, Ravaglia G, Granito A, Forti P, Maioli F, Petrolini N, *et al*. Coeliac disease in patients with autoimmune thyroiditis. Digestion 2001;64(1):61–65. doi:10.1159/000048840.
[7] Granito A, Muratori P, Ferri S, Pappas G, Quarneti C, Lenzi M, *et al*. Diagnosis and therapy of autoimmune hepatitis. Mini Rev Med Chem 2009; 9(7):847–860. doi:10.2174/138955709788452676.
[8] Granito A, Muratori P, Cassani F, Pappas G, Muratori L, Agostinelli D, *et al*. Anti-actin IgA antibodies in severe coeliac disease. Clin Exp Immunol 2004;137(2):386–392. doi:10.1111/j.1365-2249.2004.02541.x.
[9] Granito A, Muratori L, Muratori P, Pappas G, Guidi M, Cassani F, *et al*. Antibodies to filamentous actin (F-actin) in type 1 autoimmune hepatitis. J Clin Pathol 2006;59(3):280–284. doi:10.1136/jcp.2005.027367.
[10] Tovoli F, Negrini G, Farì R, Guidetti E, Faggiano C, Napoli L, *et al*. Increased risk of nonalcoholic fatty liver disease in patients with coeliac disease on a gluten-free diet: beyond traditional metabolic factors. Aliment Pharmacol Ther 2018;48(5):538–546. doi:10.1111/apt.14910.