**Name of Journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 72642

**Manuscript Type:** LETTER TO THE EDITOR

**Intestinal virome: An important research direction for alcoholic and nonalcoholic liver diseases**

Li Y *et al*. Intestinal virome in FLD

Yan Li, Wen-Cheng Liu, Bing Chang

**Yan Li, Wen-Cheng Liu, Bing Chang,** Department of Gastroenterology, The First Affiliated Hospital of China Medical University, Shenyang 110001, Liaoning Province, China

**Author contributions:** Li Y and Liu WC wrote this manuscript; Li Y and Chang B revised this manuscript; and all the authors contributed to the writing of this manuscript.

**Corresponding author: Bing Chang, MD, Associate Professor,** Department of Gastroenterology, The First Affiliated Hospital of China Medical University, No. 155 Nanjing North Street, Heping District, Shenyang 110001, Liaoning Province, China. cb000216@163.com

**Received:** November 3, 2021

**Revised:** December 7, 2021

**Accepted:** June 13, 2022

**Published online:** July 14, 2022

**Abstract**

In recent years, the interaction between the gut microflora and liver diseases has attracted much attention. The intestinal microflora is composed of bacteria, archaea, fungi and viruses. There are few studies on the intestinal virome, and whether it has a causal relationship with bacterial changes in the gut is still unclear. However, it is undeniable that the intestinal virome is also a very important portion of the blueprint for the development of liver diseases and the diagnosis and therapeutic modalities in the future.

**Key Words:** Alcoholic fatty liver disease; Nonalcoholic fatty liver disease; Fatty liver disease; Gut microbiome; Intestinal virome

**©The** **Author(s) 2022.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Citation:** Li Y, Liu WC, Chang B. Intestinal virome: An important research direction for alcoholic and nonalcoholic liver diseases. *World J Gastroenterol* 2022; 28(26): 3279-3281

**URL:** <https://www.wjgnet.com/1007-9327/full/v28/i26/3279.htm>

**DOI:** https://dx.doi.org/10.3748/wjg.v28.i26.3279

**Core Tip:** As of the study of the gut microflora expands, the interaction between the intestinal virome and liver diseases has been gradually revealed. In this letter to the editor, we discuss the changes in the intestinal virome in patients with alcoholic liver disease and nonalcoholic liver disease, and provide suggestions for developing future diagnosis and treatment methods.

**TO THE EDITOR**

We have carefully studied the reviews recently written by Sharma *et al*[1], titled “Significance of gut microbiota in alcoholic and nonalcoholic fatty liver diseases”. The authors elaborated the intestinal microecological changes in both alcoholic and nonalcoholic liver diseases, and the important effects of intestinal microorganisms on the development of fatty liver diseases. These findings could provide new ideas for the future diagnosis and treatment of fatty liver disease.

In addition to bacteria, archaea and a small amount of fungi, viruses are also an indispensable part of the intestinal microflora in human[2] . In 2020, a multicenter observational study on the enteroviruses from 89 patients with alcoholic hepatitis, 36 patients with alcohol use disorder and 17 patients without alcohol use disorder was concluded[3]. The results showed that in stool samples from patients with alcoholic liver disease, bacterial and fungal diversity decreased and virus diversity increased, which mainly manifested as a large increase in the number of *Myoviridae*, *Lactobacillus* phages, *Streptococcus* phages, *Podoviridae*, *Geobacillus* phages, *Escherichia* phages, and *Herpesviridae*[3]. This trend was positively correlated with the severity of the disease. The changes in the intestinal microecology of people with alcohol use disorder are mainly characterized by an increase in *Parvoviridae* and *Lactococcus* phages[3]. Another study of the intestinal virome in patients with nonalcoholic fatty liver disease (NAFLD) showed that the average relative abundance and viral diversity of phages in patients with NAFLD and severe hepatic fibrosis were significantly lower than those in patients with NAFLD and no or mild hepatic fibrosis[4]. Hence viruses also have positive implications in the diagnosis, severity classification, treatment and prognosis of alcoholic and nonalcoholic liver diseases. However, as an easily neglected part of gut microecology, the impact of viruses was not mentioned in Sharma *et al*[1]’s article.

Bacteria and fungi in the gut microflora have large individual variability and are susceptible to various factors such as age, drugs[5], environment[6], and diet[7]. Likewise, the same is true for viruses. A shotgun metagenome sequencing analysis of DNA viruses in fecal samples from cynomolgus monkeys of different ages showed that the abundance of DNA viruses was inversely proportional to age; that is, the DNA virus group in fecal samples of elderly individuals decreased significantly[8]. However, Lang *et al*[4] found that after the use of proton pump inhibitors, enteroviruses in the feces of patients with nonalcoholic liver disease were also changed. In addition, in high-fat diet-fed mice, the structural composition and β-diversity of enteroviruses were changed. There was a significant decrease in the expression of *Siphoviridae* and a significant increase in the expression of the eukaryotic viruses *Phycodnavridae* and *Mimivirdae*, and these changes were accompanied by changes in intestinal bacteria[9]. Therefore, considering the original proposal that gut microorganisms should be included in future liver disease diagnosis and treatment, we suggest that in addition to performing a horizontal comparison and finding representative biological markers, it is indispensable to have a methodological design and vertical comparison. However, the effects of confounding factors should also be considered, and individualized diagnosis and treatment plans should be developed for different patients.

**ACKNOWLEDGEMENTS**

We would like to thank the Department of Gastroenterology of the First Affiliated Hospital of China Medical University for technical assistance.

**REFERENCES**

1 **Sharma SP**, Suk KT, Kim DJ. Significance of gut microbiota in alcoholic and non-alcoholic fatty liver diseases. *World J Gastroenterol* 2021; **27**: 6161-6179 [PMID: 34712025 DOI: 10.3748/wjg.v27.i37.6161]

2 **Whon TW**, Shin NR, Kim JY, Roh SW. Omics in gut microbiome analysis. *J Microbiol* 2021; **59**: 292-297 [PMID: 33624266 DOI: 10.1007/s12275-021-1004-0]

3 **Jiang L**, Lang S, Duan Y, Zhang X, Gao B, Chopyk J, Schwanemann LK, Ventura-Cots M, Bataller R, Bosques-Padilla F, Verna EC, Abraldes JG, Brown RS Jr, Vargas V, Altamirano J, Caballería J, Shawcross DL, Ho SB, Louvet A, Lucey MR, Mathurin P, Garcia-Tsao G, Kisseleva T, Brenner DA, Tu XM, Stärkel P, Pride D, Fouts DE, Schnabl B. Intestinal Virome in Patients With Alcoholic Hepatitis. *Hepatology* 2020; **72**: 2182-2196 [PMID: 32654263 DOI: 10.1002/hep.31459]

4 **Lang S**, Demir M, Martin A, Jiang L, Zhang X, Duan Y, Gao B, Wisplinghoff H, Kasper P, Roderburg C, Tacke F, Steffen HM, Goeser T, Abraldes JG, Tu XM, Loomba R, Stärkel P, Pride D, Fouts DE, Schnabl B. Intestinal Virome Signature Associated With Severity of Nonalcoholic Fatty Liver Disease. *Gastroenterology* 2020; **159**: 1839-1852 [PMID: 32652145 DOI: 10.1053/j.gastro.2020.07.005]

5 **Fasullo M**, Rau P, Liu DQ, Holzwanger E, Mathew JP, Guilarte-Walker Y, Szabo G. Proton pump inhibitors increase the severity of hepatic encephalopathy in cirrhotic patients. *World J Hepatol* 2019; **11**: 522-530 [PMID: 31293720 DOI: 10.4254/wjh.v11.i6.522]

6 **Ng KM**, Aranda-Díaz A, Tropini C, Frankel MR, Van Treuren W, O'Loughlin CT, Merrill BD, Yu FB, Pruss KM, Oliveira RA, Higginbottom SK, Neff NF, Fischbach MA, Xavier KB, Sonnenburg JL, Huang KC. Recovery of the Gut Microbiota after Antibiotics Depends on Host Diet, Community Context, and Environmental Reservoirs. *Cell Host Microbe* 2019; **26**: 650-665.e4 [PMID: 31726029 DOI: 10.1016/j.chom.2019.10.011]

7 **González Olmo BM**, Butler MJ, Barrientos RM. Evolution of the Human Diet and Its Impact on Gut Microbiota, Immune Responses, and Brain Health. *Nutrients* 2021; **13** [PMID: 33435203 DOI: 10.3390/nu13010196]

8 **Tan X**, Chai T, Duan J, Wu J, Zhang H, Li Y, Huang Y, Hu X, Zheng P, Song J, Ji P, Jin X, Zhang H, Xie P. Dynamic changes occur in the DNA gut virome of female cynomolgus macaques during aging. *Microbiologyopen* 2021; **10**: e1186 [PMID: 33970533 DOI: 10.1002/mbo3.1186]

9 **Schulfer A**, Santiago-Rodriguez TM, Ly M, Borin JM, Chopyk J, Blaser MJ, Pride DT. Fecal Viral Community Responses to High-Fat Diet in Mice. *mSphere* 2020; **5** [PMID: 32102942 DOI: 10.1128/msphere.00833-19]

**Footnotes**

**Conflict-of-interest statement:** All the authors report no relevant conflicts of interest for this article.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

**Provenance and peer review:** Unsolicited article; Externally peer reviewed

**Peer-review model:** Single blind

**Peer-review started:** November 3, 2021

**First decision:** November 29, 2021

**Article in press:** June 13, 2022

**Specialty type:** Gastroenterology and hepatology

**Country/Territory of origin:** China

**Peer-review report’s scientific quality classification**

Grade A (Excellent): A

Grade B (Very good): B

Grade C (Good): 0

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** AbdEl-Wahab EW, Ghoneim S **S-Editor:** Antwi SO, United States **S-Editor:** Wang JJ **L-Editor:** A **P-Editor:** Wang JJ



Published by **Baishideng Publishing Group Inc**

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

**Telephone:** +1-925-3991568

**E-mail:** bpgoffice@wjgnet.com

**Help Desk:** https://www.f6publishing.com/helpdesk

https://www.wjgnet.com



**© 2022 Baishideng Publishing Group Inc. All rights reserved.**