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Letter to Editor

The Complex Role of Autophagy in Cirrhosis Progression; A Call for Comprehensive Research: Letter to the Editor

Dear Editor

We recently have read with great interest an article entitled “The Potential Role of Autophagy in Progression of Liver Fibrosis in Chronic Hepatitis B Patients Receiving Antiviral Treatment: A Brief Report”, by Lankarani and others, which was published in your esteemed journal (IJMS Volume 49, Issue 3, March 2024).[1] The authors should be commended for their efforts to investigate the potential role of autophagy in the progression of liver fibrosis in chronic hepatitis B (CHB) patients receiving antiviral treatment. Their findings, which suggested an association between elevated serum Beclin-1 levels and cirrhosis progression, provided valuable insights into the complex pathogenesis of liver fibrosis and cirrhosis. However, we respectfully recommend that some important considerations should be taken into account when interpreting these findings and planning future studies.

First and foremost, it is crucial to recognize that serum Beclin-1 levels might not be the only indicator of autophagic activity in the liver. While Beclin-1 is indeed a key regulator of autophagy initiation, it also has non-autophagy functions, such as regulating apoptosis.[2] Apoptosis, a form of programmed cell death, has been extensively documented to be increased in liver cirrhosis.[3] Therefore, the elevated Beclin-1 levels, observed in cirrhotic patients, might be due to increased apoptotic signaling rather than a specific upregulation of autophagy. To conclusively demonstrate the role of autophagy in cirrhosis progression, future studies should employ a combination of autophagy markers and assess autophagic flux in liver tissues.

Secondly, the small sample size and single-center design of the study limit the generalizability of its findings. To validate these findings and account for potential confounding variables, such as disease severity, comorbidities, and medication use, larger and multi-center studies are warranted. Moreover, the case-control design of the study makes it difficult to establish a causal relationship between autophagy and cirrhosis progression. More conclusive evidence could be obtained from prospective studies that track patients from the initiation of treatment and incorporate data from liver biopsies.

Furthermore, it is important to consider the complex interplay of multiple pathogenic mechanisms in the development and progression of liver cirrhosis. Chronic inflammation, oxidative stress, and tissue remodeling are well-established hallmarks of cirrhosis.[4] These processes were shown to regulate Beclin-1 expression and autophagy. As a result, higher Beclin-1 levels in cirrhotic patients might reflect the cumulative effect of these various pathogenic mechanisms rather than a specific upregulation of autophagy. To completely understand the function of autophagy in cirrhosis progression, future studies should investigate the intricate relationships between autophagy, apoptosis, inflammation, and fibrogenesis in the context of liver disease.

In conclusion, the study by Lankarani and others provided valuable insights into the potential role of autophagy in the progression of liver fibrosis and cirrhosis in CHB patients receiving antiviral treatment.[1] However, we respectfully suggest that further comprehensive research is required to determine the specific contribution of autophagy in this context. Future studies should employ a multi-faceted approach, including various autophagy markers, assessing autophagic flux in liver tissues, and controlling the potential confounding variables. Additionally, mechanistic studies investigating the complex interplay between autophagy and other pathogenic mechanisms in cirrhosis progression would assist in understanding the precise role of autophagy in this process and guide the development of targeted therapeutic strategies. We believe that a deeper understanding of the role of autophagy in liver fibrosis and cirrhosis will not only advance our understanding of the underlying pathogenesis but

will also pave the way for novel interventions to prevent or reverse liver damage in patients with chronic liver diseases.

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Statement from IJMS: The response letter from Dr. Lankarani and colleagues will be published whenever received by the Journal.

Conflict of Interest: None declared.

Keywords ● Autophagy ● Liver cirrhosis ● Beclin-1

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