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EDITORIAL

GADD45aa as a Predictive Biomarker for *Aeromonas* Infection–Related Liver Cirrhosis

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Liver cirrhosis is recognized as the 11th leading cause of mortality in the world [1]. Cirrhosis is the last pathological outcome of different chronic liver disorders, and newer research has established that fibrosis is the starter of cirrhosis [2–4]. Many types of factors are involved in the beginning and development of liver fibrosis and cirrhosis [3]. The most common causes in the liver cirrhosis progression, especially in western countries, include alcoholism, nonalcoholic fatty liver disease, and chronic hepatitis C virus infection [5]. In addition, Gram-negative bacteria such as *Escherichia coli*, *Klebsiella* sp., and *Aeromonas* sp., can be important origins of bacteremia in patients with liver cirrhosis [6, 7].

In recent years, several effective measures have been developed in order to address the development of antifibrotic methods. Although elimination of causative factors of liver fibrosis will result in tissue scarring, it is troublous to treat advanced liver cirrhosis [8]. One approach to inhibit liver-related mortality is to detect and inhibit the progression of bacteremia [9]. It is interesting that cirrhosis patients with more acute hepatic dysfunction are mostly considered to be linked with a higher rate of inception of bacteremia and the more severe the bacteremia, the worse prognosis [10]. Some past studies provided evidence that *Aeromonas* sp. infections promote liver fibrosis and cirrhosis by the acquisition of liver tissue [7, 11]; however, few studies have been carried out in this area.

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Aeromonas sp. are oxidase-producing Gram-negative that have been implicated in a variety of human diseases. They are found overall in the natural world [12]. This genus includes 36 species that are isolated from aquatic environments, animals, foods, and diverse infectious in humans. [13]. Various species of *Aeromonas* are addressed as emerging pathogens on account of causing a broad spectrum of disease in humans, such as wound infections, gastroenteritis, and septicemia/bacteremia, infecting immunocompetent and immunocompromised [14]. Study after study has shown that 96.5% of the strains related to clinical cases were recognized as one of only four species: *Aeromonas caviae* (29.9%), *Aeromonas dhakensis* (26.3%), *Aeromonas veronii* (24.8%), and *Aeromonas hydrophila* (15.5%) [15]. *Aeromonas* bacteremia is infrequent in healthy people but is often detected in patients with hematological malignancy, hepatobiliary infection, and decompensated liver cirrhosis [13]. It has been distinguished that liver cirrhosis patients are susceptible to aggressive *Aeromonas* infections [16]. Therefore, identifying the molecular biomarkers is urgently needed to underlie the *Aeromonas* infections in liver cirrhosis and develop novel diagnostic and prognostic agents for *Aeromonas* infections that will enhance the development of therapeutic strategies for cirrhosis patients.

GADD45 (growth arrest and DNA damage-inducible 45) genes including *Gadd45aa* and Gadd45ab have been implicated in signaling responses to genotoxic stress agents, cell cycle arrest, cell survival, DNA repair, apoptosis, and innate immune [17]. The induction of *Gadd45* members occurs differentially and their functions usually overlap [18]. According to previously reported evidence, *GADD45aa* expression was downregulated in the liver but *GADD45ab* upregulated [19]. Also, in grass carp with *Aeromonas hydrophila*, the expression of both *Gadd45aa* and Gadd45ab were upregulated [19]. Therefore, the liver infected with *Aeromonas* sp. is expected to show high expression of *Gadd45aa* and *Gadd45ab*. Hence, it seems that, due to the low expression of *Gadd45aa* in the liver, this gene can be addressed as a

biomarker in *Aeromonas* infection–related liver cirrhosis. It should be noted that the study of protein and mRNA has its own importance on account of the strict control levels in both transcription and translation, and it seems that the expression of them may not be the same and need to examine both. In the current study, we hypothesized that the investigation of *GADD45aa* gene expression, as a candidate biomarker, in the prognosis of *Aeromonas* infection-related liver cirrhosis can be effective and provide the best cure choice for treatment. Indeed, if *Aeromonas* infection is the cause of liver cirrhosis, the presence of infection can be detected by *GADD45aa* expression follow-up, and it can be treated before the fibrosis reaches cirrhosis. Clearly, more direct and in vivo evaluations are needed to characterize the role of *GADD45* in *Aeromonas* sp. infection and liver cirrhosis.

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Declarations

Ethics Approval Consent to Participate Not applicable.

Consent for Publication All the authors approved the final manuscript to be published and agreed to be accountable for all aspects of the study.

Conflict of Interest The authors declare no competing interests.

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