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Analysis of additional risk factors for liver fibrosis in diabetic patients with end-stage chronic kidney disease

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Dear Editor,

I would like to provide a contrast to the article by Ismael Yepes-Barreto and colleagues, *Risk Factors for Liver Fibrosis in Diabetic Patients with End-Stage Chronic Kidney Disease*, published in your journal. In their article, they stated that "several associated factors were identified, such as a history of cerebrovascular disease, peripheral vascular disease, body mass index (BMI), total cholesterol, glycosylated hemoglobin, sodium, and aspartate aminotransferase (AST). However, no significant relationship was found between the NAFLD score and the APRI index with the presence of hepatic fibrosis, "suggesting the influence of other factors". The statistical analysis of the data did not include risk factors such as smoking and alcoholism, which are associated with the development of hepatic fibrosis in patients with end-stage chronic kidney disease. Therefore, it would be necessary to include these variables in the study.

It is important to understand these risk factors due to their influence on the development of these diseases, as these habits are not only closely related to the onset of these pathologies but can also exacerbate their effects on health. For example, concerning the influence on the development of diabetes, Rebekka Aarsand and colleagues, in *Tobacco and Diabetes*, indicate that nicotine, a highly toxic component of tobacco smoke, alters the function and quantity of β-cells. This impacts insulin production and glucose regulation, significantly contributing to the development of type 2 diabetes[(1)].

According to Kenji Ito and colleagues, in *The Role of Smoking in the New Onset of Chronic Kidney Disease in a Japanese Population without Previous Chronic Kidney Disease: The Iki Epidemiological Study on Atherosclerosis and Chronic Kidney Disease (ISSA-CKD)*, it was noted that smoking increases the risk of new onset chronic kidney disease. The analysis shows that smokers under 50 years of age had a significantly higher risk ratio than non-smokers, with a ratio of 2.55 and a 95% confidence interval (CI)[(2)]. Similarly, Ayako Matsumoto and colleagues, in their article *Smoking and Progression of Renal Dysfunction: A Longitudinal Cohort Study*, indicate that smoking has a negative effect on the progression of chronic kidney disease and is considered the second most relevant factor for deterioration[(3)]. Additionally, Mahitha Lampimukhi and colleagues, in *A Review of the Incidence and Risk Factors Associated with the Development of Hepatocellular Carcinoma*, state that "heavy smoking causes hepatic accumulation of excess iron, which is the cause of fibrosis and HCC", particularly in Asian countries[(4)].

Regarding the factor of alcoholism, Pietro Vairo and colleagues, in their article *Nutritional Support for Alcoholic Liver Disease*, point out that metabolic syndromes,

including diabetes, significantly contribute to the development of hepatic fibrosis. Alcohol increases hepatic gluconeogenesis and glycogenolysis and inhibits insulin secretion, which promotes diabetes *mellitus*. Studies on metabolic-associated fatty liver disease (MAFLD) show that alcohol and metabolic abnormalities are independent factors that worsen hepatic fibrosis. Continuous alcohol consumption and high levels of inflammatory cytokines activate stellate cells, leading to progressive fibrosis[5].

Furthermore, Marija Dukic and her colleagues, in their article *Alcohol, Inflammation, and Microbiota in Alcoholic Liver Disease*, state that excessive alcohol consumption is a significant socioeconomic and health risk factor in today's population. Alcoholic liver disease (ALD) is a multimodal spectrum that includes alcoholic fatty liver disease (AFL) and alcoholic steatohepatitis (ASH), which can lead to hepatic fibrosis and cirrhosis. They conclude that ALD may represent a chronic condition that slowly progresses toward terminal liver damage[6].

Therefore, it is crucial to address this modifiable factor, as alcohol consumption may have played an important role not only in the development of chronic kidney disease but also in the onset of hepatic fibrosis, exacerbating both conditions.

Finally, we sincerely thank the authors for their valuable contributions to medical research. Their work in identifying risk factors for hepatic fibrosis in diabetic patients with end-stage chronic kidney disease is essential for improving knowledge and clinical outcomes. We believe that this study will inspire further research and promote more effective clinical interventions.

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Reply to the letter to the editor

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Dear Editor,

Regarding the letter to the editor about our article, *Risk Factors for Liver Fibrosis in Diabetic Patients with End-Stage Chronic Kidney Disease*[(1)], we would like to make the following points:

As highlighted in your letter, alcohol and tobacco are potential contributors to the progression of both chronic liver and kidney diseases. Our study collected data cross-sectionally from a group of patients enrolled in a chronic dialysis program, who were under multidisciplinary medical care. At the time of data collection, reported alcohol and tobacco use among these patients was nil. This finding may be attributed to the continuous healthcare provided, which emphasizes healthy lifestyle habits and highlights the potentially deleterious effects of these habits on their underlying health conditions. As a result, the patients may have ceased alcohol and tobacco use well before their inclusion in the study.

We did not consider it appropriate to gather this information retrospectively due to the challenge of accurately measuring exposure levels and the additional risk of reporting bias if patients felt they might be judged by healthcare personnel for disclosing substance use. The absence of this information in our study does not reflect a disregard for the potential impact of alcohol and tobacco on the progression of liver disease. Instead, it is due to the study's methodological design, which precluded a precise examination of this association.

We appreciate your comments and will take them into consideration for future research in this area.

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