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CORRESPONDENCE
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HbA1c Levels as a Parameter of Glycemic Control in Patients with Liver Diseases

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Dear editor:

We read with interest the recent study by Stine, *et al.* In the article, DAA therapy for chronic hepatitis C showed no effect on glycemic control of diabetic patients as assessed by HbA1c levels.[1] Although the authors highlighted some limitations of the study in the discussion section, we would like to comment on HbA1c as a marker of glycemic control.

Several factors might result in falsely high or low HbA1c levels; some of those are common in patients with liver diseases. Falsely high HbA1c levels were related to severe hyperbilirubinemia[2] and alcoholism.[3] On the other hand, HbA1c values are decreased in patients with liver cirrhosis and are not an accurate parameter for glycemic control in those patients, especially in the setting of a more advanced liver disease.[4] Cacciatore, *et al.* when comparing cirrhotics with nondiabetic subjects with chronic hepatitis without cirrhosis and healthy controls showed that HbA1c levels were not different between groups, even though glucose intolerance and diabetes were present 15% and 27% of the cirrhotics, respectively.[5] Nomura, *et al.* also observed similar HbA1c levels between patients with cirrhosis and nondiabetic controls, even though blood glucose was significantly higher in cirrhotics as compared to controls.[6] More recently, a study included 200 patients with decompensated cirrhosis evaluated for liver transplant with HbA1c measurement and three glucose levels available for estimating HbA1c based on blood glucose.[7] In this study, a difference > 0.5% between "measured HbA1c" and "calculated HbA1c" was observed in 47% of patients and HbA1c was < 5% in 49% of the cases.[7] The reasons for that are not completely understood, but a possible explanation is the shortened erythrocyte life span and anemia frequent observed in patients with cirrhosis.[8]

In the study by Stine, *et al.*,[1] the inclusion of a limited number of patients, the majority of them cirrhotics, along with the potential impact of ribavirin use on HbA1c levels might have significantly influenced HbA1c measurement. Although HbA1c levels are known to be influenced by liver cirrhosis for decades, it continues to be used in several hepatology and liver transplant centers worldwide. One reason for that is the limited number of tools available for glycemic control in this specific group. Alternative tests such as fructosamine, glycated albumin and 1,5-Anhydroglucitol are also affected by liver cirrhosis and cannot be routinely recommended. To date, the best option for diagnosing diabetes in patients with liver cirrhosis is the oral glucose tolerance test, as fasting blood glucose and HbA1c levels may be normal despite diabetes.[5] For monitoring diabetes, self-blood glucose monitoring and continuous glucose monitoring are suitable options, especially for those with more advanced liver disease in whom HbA1c is not a reliable parameter of glycemic control.

In conclusion, clinicians should be aware of the limitations of HbA1c as a parameter of glycemic control in patients with chronic liver diseases, especially liver cirrhosis. Future studies investigating new options for glycemic monitoring in those patients are urgently required.

ABBREVIATIONS

- **DAA:** Direct antiviral agents.
- **HbA1c:** Glycated hemoglobin.

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