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LETTER TO THE EDITOR

Serum $7\alpha C4$ as a pragmatic diagnostic tool for bile acid malabsorption in Mexico: Implications and future directions

El 7αC4 sérico como herramienta diagnóstica práctica para la mala absorción de ácido biliar en México: implicaciones y direcciones futuras

Dear Editors,

We read with great interest the recent article by Mendoza-Domínguez et al.¹ titled "Real-world experience with the diagnosis of bile acid malabsorption (BAM) using serum 7-alpha-C4 and 48-h stool bile acids." Their work offers crucial insights into diagnostic alternatives for BAM in Mexico, where 75SeHCAT testing remains unavailable.

The authors demonstrate that serum $7\alpha C4$ levels correlate moderately with total fecal bile acids (TBA) and can identify BAM even when primary (PBA) and TBA levels are normal. This is clinically significant, as it suggests serum $7\alpha C4$ is a reliable and cost-saving biomarker, with their data indicating an approximate 49% reduction in diagnostic costs compared with combined stool and serum testing.

However, we wish to highlight three key considerations for clinical translation and future research.

First, although serum $7\alpha C4$ offers logistical and economic advantages over 48-h stool collection, its current utility remains limited by the necessity of shipping samples abroad for analysis, leading to delays and higher systemic costs. As the authors note, establishing local tandem mass spectrometry facilities for $7\alpha C4$ quantification would accelerate diagnosis and enhance equitable access for public sector patients. Indeed, Camilleri et al.² previously emphasized that widespread clinical use of serum $7\alpha C4$ requires standardized protocols and availability of high-throughput assays, which remain limited in low- and middle-income settings.

Second, the low prevalence of BAM among patients with functional diarrhea or IBS-D in their cohort contrasts with meta-analytic data indicating a prevalence of $\sim\!30\%$ in IBS-D³ and up to 63.5% following cholecystectomy.⁴ This discrepancy may reflect underdiagnosis due to limited clinician awareness or referral bias toward patients

with structural causes of diarrhea. Recent guidelines recommend consideration of BAM in all cases of chronic unexplained diarrhea, given its responsiveness to bile acid sequestrants.⁵

Third, while cholestyramine remains the primary treatment option in Mexico, tolerability issues and poor palatability often lead to non-adherence. Emerging therapies such as colesevelam, which have demonstrated better gastrointestinal tolerability profiles, warrant evaluation in Mexican populations.

Furthermore, while Mendoza-Domínguez et al. found serum $7\alpha C4$ to be elevated in patients with BAM despite normal fecal BA levels, combining serum $7\alpha C4$ with single stool bile acid measurements may offer a pragmatic diagnostic approach to avoid the logistical difficulties of 48-h stool collection while maintaining diagnostic accuracy.

In sum, this timely study by Mendoza-Domínguez et al. advances our understanding of BAM diagnosis in Mexico and underscores the need to integrate serum $7\alpha C4$ testing into routine clinical practice, supported by local laboratory capacity and clinician education. Further research should establish national reference values for serum $7\alpha C4$, validate combined serum-stool diagnostic algorithms, and evaluate newer sequestrants to optimize treatment outcomes.

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Declaration of competing interest

The authors declare there is no conflict of interest.

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