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LETTER TO THE EDITOR

Response to Rattanapitoon et al., ''Serum 7αC4 as a pragmatic diagnostic tool for bile acid malabsorption in Mexico: Implications and future directions''

Respuesta a Rattanapitoon et al., ''El 7αC4 sérico como herramienta diagnóstica pragmática para la malabsorción de ácidos biliares en México: implicaciones y perspectivas futuras''

To the Editors,

We are grateful to Dr. Rattanapitoon et al. for their thoughtful letter and interest in our study: ''Real-world experience with the diagnosis of bile acid malabsorption (BAM) using serum 7-alpha-C4 and 48 -h stool bile acids''.[1] Their remarks highlight several important considerations for the clinical implementation and future research of BAM diagnosis in patients with functional diarrhea in Mexico.

First, we fully agree with the need to standardize serum 7αC4 quantification at the local level to overcome the logistical and economic limitations associated with sending samples abroad. As noted by Camilleri and Vijayvargiyah, the clinical utility of this biomarker depends not only on its diagnostic performance but also on the availability of standardized, high-throughput mass spectrometry assays, which remains a challenge in many middle or low-income countries.[2]

Second, while our study reported a lower prevalence of BAM among patients with functional diarrhea compared with prior reports,[3,4] we coincide that BAM must be actively investigated in all patients with chronic diarrhea of unknown origin. However, the cost of this approach remains a limitation in our setting. As outlined in our recently presented abstract during the 2025 Digestive Disease Week (DDW), we support a broader diagnostic strategy that includes evaluating other potential etiologies of chronic diarrhea, such as accelerated intestinal transit and post-infectious disorders, BAM/bile acid diarrhea (BAD), as well as obtaining small bowel and colonic biopsies to rule out celiac disease and microscopic colitis, respectively.[5] In our view, the next step is to explore the overlap between BAM and these conditions, which may be underestimated and requires individualized assessment of each patient.

Third, we share the authors' concern regarding the tolerability of cholestyramine when used as a treatment for BAM. Nevertheless, this is the only currently available bile acid binding agent in Mexico. Although both cholestyramine and colesevelam are effective in controlling diarrhea, there is a higher incidence of nausea with cholestyramine.[6] However, the unavailability of colesevelam in our country is a barrier that should be addressed to enable its clinical implementation.

Finally, we support the pragmatic recommendation of combining serum 7αC4 with a single stool bile acid sample, as discussed in our article discussion,[1] which aligns with the proposal by Lupianez-Merly et al. to simplify BAM workup with an adequate diagnostic performance when 48-h stool collection is impractical.[7] In fact, a recent abstract, also presented at the 2025 DDW, about an audit of the diagnosis of BAD, showed that the combination of single stool primary bile acids >10% and a fasting serum 7αC4 > 52.5 ng/mL was feasible for diagnosing BAD.[8] This combined strategy should be further evaluated in future studies, as it may enhance diagnostic accuracy while maintaining feasibility in clinical practice.

We appreciate the authors' interest in our work and their emphasis on advancing BAM research in clinical settings. Collaborative efforts will be essential to improve diagnostic accuracy and accessibility, establish local reference values, and optimize therapeutic outcomes for this underrecognized condition.

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Declaration of competing interest

GMD, ZMGS, and ADS: nothing to declare.

CL and RB: worked at *Biomédica de Referencia*, the clinical lab that collected the samples to be shipped to the US for analysis.

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MSW: is on the Advisory Council of Daewoong South Korea, Gemelli Biotech Inc, Moksha 8 Mexico, and Pro.Med.CS. Praha A.S.; he is a speaker for Alfa Sigma Mexico, Armstrong Mexico, Carnot, Daewoong South Korea, Ferrer Mexico/Central America, Medix Mexico, Megalabs Ecuador, Tecnofarma Colombia/Bolivia; he provides educational materials for Moksha 8.

References

1. Mendoza-Domínguez G, Garrido-Santos ZM, Lau C, et al. Real-world experience with the diagnosis of bile acid malabsorption (BAM) using serum 7-alpha-C4 and 48-hour stool bile acids. Rev Gastroenterol Méx. 2025;90:169–75, http://dx.doi.org/10.1016/j.rgmxen.2025.05.002.
2. Camilleri M, Vijayvargiya P. The role of bile acids in chronic diarrhea. Am J Gastroenterol. 2020;115:1596–603, http://dx.doi.org/10.14309/ajg.0000000000000696.
3. Ruiz-Campos L, Gisbert JP, Ysamat M, et al. Systematic review with meta-analysis: the prevalence of bile acid malabsorption and response to colestyramine in patients with chronic watery diarrhoea and previous cholecystectomy. Aliment Pharmacol Ther. 2019;49:242–50, http://dx.doi.org/10.1111/apt.15099.
4. Slattery SA, Niaz O, Aziz Q, et al. Systematic review with meta-analysis: the prevalence of bile acid malabsorption in the irritable bowel syndrome with diarrhoea. Aliment Pharmacol Ther. 2015;42:3–11, http://dx.doi.org/10.1111/apt.13227.
5. Zaragoza-Galicia SA, Morales-Guzmán AS, Hernández-Hernández A, Schmulson-Wasserman MJ. Work-up for chronic diarrhea with a focus on clinical modifiers and biomarkers for functional diarrhea. Gastroenterology. 2025;169 Suppl:S-1129, http://dx.doi.org/10.1016/S0016-5085(25)03497-3.
6. Soares GAR, Godoi A, Marcolin P, et al. Efficacy of bile acid sequestrants in the treatment of bile acid diarrhea: a meta-analysis of randomized controlled trials. J Clin Pharmacol. 2025;65:478–85, http://dx.doi.org/10.1002/jcph.6154.
7. Lupianez-Merly C, Dilmaghani S, Busciglio I, et al. Single stool bile acid measurements in bile acid diarrhea and irritable bowel syndrome with diarrhea: relationship to serum measurements of C4 and FGF-19. Gastroenterology. 2024;166:S–1371, http://dx.doi.org/10.1016/S0016-5085(24)03603-5.
8. Matar A, Camilleri M, Eckert D, et al. Single center audit of the diagnosis of bile acid diarrhea based on fasting serum 7αC4 and stool primary bile acid content. Clin Gastroenterol Hepatol. 2025;S1542-3565(25):00534–8. Ahead of print.

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