Furthermore, while Mendoza-Domínguez et al.[1] found serum 7αC4 to be elevated in patients with BAM despite normal fecal BA levels, combining serum 7αC4 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.[1] advances our understanding of BAM diagnosis in Mexico and underscores the need to integrate serum 7αC4 testing into routine clinical practice, supported by local laboratory capacity and clinician education. Further research should establish national reference values for serum 7αC4, 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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N.K. Rattanapitoon[a,*], K. Punnasirimangmee[b], P. Pholyiam[a], S.K. Rattanapitoon[a]

[a] *Centro Médico de Tailandia FMC, Nakhon Ratchasima, Thailand*

[b] *Hospital Ta Phraya, Sa Kaeo, Thailand*

[*] Corresponding author at: Centro Médico de Tailandia FMC, Nakhon Ratchasima 30000, Thailand.
E-mail address: nathkapach.ratt@gmail.com (N.K. Rattanapitoon).

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.

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.

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G. Mendoza-Domínguez[a,b], Z.M. Garrido-Santos[a,b], C. Lau[c], R. Balbuena[c], A.D. Santana-Vargas[d], M. Schmulson-Wasserman[a,e,*]

[a] *Laboratorio de Hígado, Páncreas y Motilidad (HIPAM), Unidad de Investigación en Medicina Experimental (UME) Dr. Ruy Pérez Tamayo, Facultad de Medicina, Universidad Nacional Autónoma de México (UNAM), Mexico City, Mexico*
[b] *Programa de Estudios Combinados en Medicina (PECEM), Facultad de Medicina, Universidad Nacional Autónoma de México (UNAM), Mexico City, Mexico*
[c] *Laboratorios Biomédica de Referencia, Mexico City, Mexico*
[d] *Departamento de Investigación, Hospital General de México Dr. Eduardo Liceaga, Mexico City, Mexico*
[e] *Gastroenterología y Motilidad Gastrointestinal, Clínica Lomas Altas, Mexico City, Mexico*

* Corresponding author at: Laboratorio de Hígado, Páncreas y Motilidad (HIPAM), Unidad de Investigación en Medicina Experimental Dr. Ruy Pérez Tamayo, Facultad de Medicina, Universidad Nacional Autónoma de México (UNAM). Dr. Balmis #148, Col. Doctores, Mexico City, C.P. 06726, Mexico.

E-mail address: mschmulson@gmail.com (M. Schmulson-Wasserman).

Considerations about the balanced crystalloid solution recommendation in acute variceal bleeding

Consideraciones sobre la recomendación de soluciones balanceadas en hemorragia variceal aguda

Dear Editors,

We read with great interest the ''Mexican consensus on the approach to and treatment of acute variceal bleeding'', by Higuera de la Tijera et al.,[1] whom we congratulate for their valuable work. We would like to make a comment on statement 3, related to fluid management.

The authors recommend replacing intravascular volume with balanced crystalloid solutions, arguing that there is a lower association with adverse events and mortality, based on a single randomized clinical trial (RCT) by Semler et al. in 2018 (n = 7,942). However, better evidence is currently available.

The largest RCT at present was recently published that compared the use of lactated Ringer's solution versus saline solution 0.9% in intravenous fluid administration (n = 43,626).[2] The primary outcome was a composite of death or hospital readmission within 90 days of the index admission. Incidence of the composite was 20.3% in the lactated Ringer's solution group and 21.4% in the saline solution group, with no statistically significant difference (adjusted difference: −0.53 percentage points; 95% CI: −1.85—0.79; p = 0.35). No serious adverse events were reported. The conclusion was that a hospital-wide policy of preferential use of lactated Ringer's solution, compared with saline solution, did not significantly reduce mortality or hospital readmission.

In addition, a systematic review and meta-analysis of individual patient data[3] that included 6 RCTs (n = 34,685) evaluated whether the use of balanced crystalloid solutions, compared with saline solution 0.9%, reduced in-hospital mortality in critically ill adults admitted to the intensive care unit. Mortality was 16.8% in the balanced crystalloid group and 17.3% in the saline group (OR: 0.962; 95% CI: 0.909–1.019; absolute difference: −0.4 percentage points). The posterior probability that balanced crystalloids would reduce mortality was 89.5%. Nevertheless, in patients with traumatic brain injury, mortality was higher in the balanced crystalloid group (19.1% vs. 14.7%; OR: 1.424; 95% CI: 1.100–1.818; absolute difference: 3.2 percentage points), with a 97.5% probability that balanced crystalloids would increase mortality in that subgroup.

That finding could be explained by the higher risk of cerebral edema when using intravenous solutions with a lower sodium concentration (130 mEq/L in Hartmann's solution and 140 mEq/L in Plasma-Lyte), compared with normal saline solution (154 mEq/L). Considering that patients with acute variceal bleeding are at high risk for developing hepatic encephalopathy,[4] we believe that the routine use of balanced crystalloid solutions could result in more risks than benefits in that context, but this must be confirmed through RCTs, given that none of the previous studies are specific for acute variceal bleeding.

Another point to be taken into account is that the acquisition and administration of large quantities of different types of solutions has an ecologic and economic impact. The approximate cost of 100 mL of sodium chloride solution 0.9% is $0.60 USD, whereas the cost of balanced crystalloid solutions is higher, with Plasma-Lyte being the most expensive, at between $3.00 and $3.80 USD.

In conclusion, we consider that, at present, the available evidence does not justify recommending one intravenous solution over another, in a generalized manner, for patients with variceal bleeding.

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Declaration of competing interest

The authors declare that there is no conflict of interest.

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