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The importance of analytical methodology in accurate diagnosis and monitoring of intrahepatic cholestasis of pregnancy

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Intrahepatic cholestasis of pregnancy (ICP) is a liver disease with deleterious consequences for the fetus [1]. As soon as ICP is diagnosed, the mother should be considered a high-risk patient. Ursodeoxycholic acid (UDCA) treatment, coupled with close maternal–fetal monitoring, is indicated to optimize fetal outcome.

Usually, diagnosis of ICP is based on pruritus, altered liver tests, and/or raised serum total bile acid (TBA) levels evaluated via enzymatic method [2]. Serum bile acid profile, particularly lithocholic acid (LCA), determined by capillary electrophoresis provides more information than serum TBA alone [3,4].

An 18-year-old primigravida with severe pruritus was admitted to Hospital de Clínicas "Jose de San Martin," Buenos Aires, Argentina, at 33 + 2 weeks. She was on no medication and had no family history of ICP. Liver laboratory tests were slightly altered. Enzymatically determined serum TBA levels were within the normal range, although bile acid profile and serum TBA values determined via capillary electrophoresis were altered, with high levels of LCA (Table 1). On the basis of the symptoms and capillary electrophoresis results, ICP was diagnosed and UDCA treatment started (900 mg per day).

Weekly patient evaluation revealed that, as expected [3,4], treatment with UDCA relieved pruritus, improved liver test results, and promoted a shift toward a more hydrophilic bile acid profile with a decrease in LCA levels (Table 1).

Evaluation 21 days after treatment revealed recurrence of intense pruritus, indicating treatment failure. Enzymatically determined serum TBA profile and liver tests showed values within reference ranges. However, bile acid profile determined via capillary electrophoresis showed increased LCA and serum TBA (Table 1, Fig. 1). On the basis of these results, pregnancy was immediately interrupted at 37 weeks. A 3110-g infant was delivered via cesarean. The 1- and 5-minute Apgar scores were 9 and 10, respectively. The neonate experienced 2 days of respiratory distress requiring oxygen therapy but no other complications.

The present case demonstrates the problematic results associated with routine liver tests and enzymatically determined serum TBA. The optimal way to diagnose ICP accurately and follow its progression is through evaluation of bile acid profile and serum TBA. In the present case, the determination of these parameters via capillary electrophoresis optimized management. Regular monitoring of this disease with adequate analytical methodology is important.

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Conflict of interest

The authors have no conflicts of interest.

References

- [1] Brites D, Rodrigues CM, Oliveira N, Cardoso M, Graça LM. Correction of maternal serum bile acid profile during ursodeoxycholic acid therapy in cholestasis of pregnancy. *J Hepatol* 1998;28(1):91–8.
- [2] Reyes H, Simon FR. Intrahepatic cholestasis of pregnancy: an estrogen-related disease. *Semin Liver Dis* 1993;13(3):289–301.

Table 1
Biochemical parameters at diagnosis and during UDCA treatment.

Parameter	Before treatment	Days of treatment		
		7	15	21
Total bilirubin, mg/dL ^a	0.2	0.2	0.2	0.2
AST, U/L ^b	57	17	18	18
ALT, U/L ^c	24	9	7	5
ALP, U/L ^d	372	373	394	499
γGT, U/L ^e	18	16	5	7
Bile acids				
Enzymatic method				
Serum TBA, μM ^f	5.0	4.6	2.7	9.1
Capillary electrophoresis				
Serum TBA, μM ^f	56.8	12.3	6.4	51.0
LCA, μM ^g	21.3	0.23	0.23	15.2
DCA, μM ^h	6.2	0.6	0.29	8.9
UDCA, μM ⁱ	—	2.2	3.6	8.4

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; DCA, deoxycholic acid; GT, glutamyltranspeptidase; LCA, lithocholic acid; TBA, total bile acid; UDCA, ursodeoxycholic acid.

^a Normal range is up to 1.0 mg/dL. For direct bilirubin, normal range is up to 0.3 mg/dL.

^b Normal range is up to 31 U/L.

^c Normal range is up to 31 U/L.

^d Normal range is up to 104 U/L.

^e Normal range is 5–36 U/L.

^f Normal range is up to 11 μM.

^g Normal range is up to 0.3 μM.

^h Normal range is up to 1.3 μM.

ⁱ Normal range is up to 4.5 μM.

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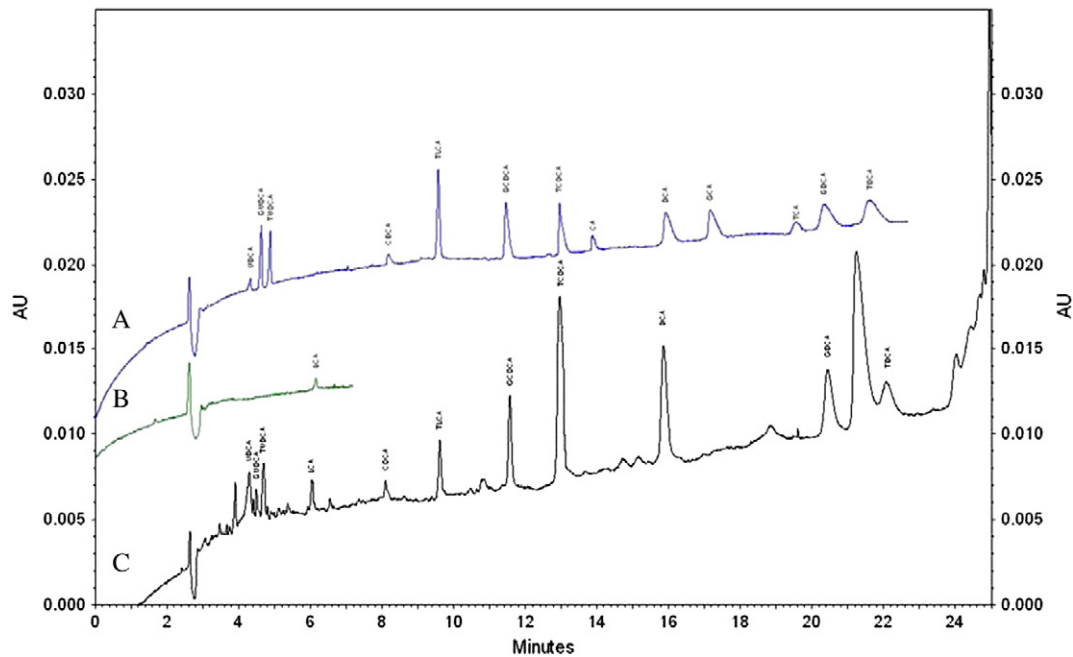


Fig. 1. Patient evaluation. Line A shows level of 13 bile acids in standard solution. Line B shows level of lithocholic acid in standard solution. Line C shows patient at day 21 of treatment.

[3] Castaño G, Lucangioli S, Sookoian S, Mesquida M, Lemberg A, Di Scala M, et al. Bile acid profiles by capillary electrophoresis in intrahepatic cholestasis of pregnancy. *Clin Sci (Lond)* 2006;110(4):459–65.

[4] Lucangioli SE, Castaño G, Contin MD, Tripodi VP. Lithocholic acid as a biomarker of intrahepatic cholestasis of pregnancy during ursodeoxycholic acid treatment. *Ann Clin Biochem* 2009;46(Pt 1):44–9.

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Use of institutional delivery services in Kassala, eastern Sudan

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The number of deliveries assisted by a skilled birth attendant is an important indicator in meeting Millennium Development Goal 5 [1]. Different rates of institutional delivery and various barriers to

institutional delivery (e.g. distance, higher cost, illiteracy of the mother, higher parity, and fewer prenatal care visits) have been reported in many settings [2–6]. The aim of the present study was to investigate the prevalence of and predictors for institutional delivery in Kassala, eastern Sudan.

A community-based cross-sectional household survey was conducted in Kassala between May 1 and September 30, 2012. The study population comprised women who had delivered in the previous 12 months in Kassala (where there are 28 health centers and 3 hospitals). A total sample size of 680 women was calculated using a formula for a single population proportion that would provide 80% power to detect a 5% difference at $\alpha = 0.05$ and which assumed that 10% of women would not respond. Multistage sampling was used to select the study population. After eligible women had signed an informed consent form, structured questionnaires were used to gather data. Ethics approval was received from the Health Research Board of the Ministry of Health in Kassala state. Women were asked about their delivery experience and their sociodemographic characteristics (age, parity, prenatal care in index pregnancy, education, and working status). Questions regarding barriers to hospital delivery (e.g. cost, lack of privacy, lack of approval of husband, and perceived low quality of service provided in hospitals) were included.

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