Table 1. Prevalence of clinical, histological and laboratory items in relation to the diagnostic score.

	BA (n = 16)	Non-BA (n = 11)
Clay stool	8 (50%)	1 (9%)
Triangular cord	2 (12.5%)	0
Contractile gallbladder	2 (12.5%)	5 (45.4%)
GL >20.5 mm	0	3 (27 %)
HAD >2.05 mm	4 (25%)	2 (18.2%)
HAD/PVD >0.445 mm	8 (50%)	5 (45.4%)
Hepatic subcapsular flow	1 (6%)	0
gGT >286	14 (87.5%)	6 (54.5 %)
PLT >349,000	11 (68.7%)	5 (45.4%)
DP	16 (100%)	6 (54.5 %)
BP	13 (81.2%)	3 (27 %)
GC	8 (50%)	3 (27 %)

GL, gallbladder length; HAD, hepatic artery diameter; PVD, portal vein diameter; gGT, gamma glutamyl transpeptidase; PLT, platelets; DP, ductular proliferation; BP, bile plugs; GC, giant cells.

(5/16), specificity 90.9% (10/11), positive predictive values was 0.81 and negative predictive values 0.47. Overall diagnostic accuracy resulted 0.55.

Reasons for such disappointing results might be numerous. First, the retrospective nature of this study is a major confounding factor. A large, multicentric, prospectic study is needed to validate this score. On the other hand, we believe that our group of patients is quite different than the one used by authors to validate the score. Our patients belong to a highly selected subset of cholestatic infants, addressed even from reference centers for invasive investigation. This new scoring system seems to work poorly in this clinical setting, but the paradox is that an effective score is typically needed in such kind of patients.

Children with a various combination of cholic stools, mild cholestasis, known risk factors for transient cholestasis, normal GGT activity and other features not suggestive of BA might be, in most cases, effectively managed without the need of liver histology as our results suggest. The overall performance of our current protocol (3 diagnostic errors out of 64 cases), indeed, is similar to that of this new scoring system, as claimed in the paper. However, 48 liver biopsies were spared. Moreover, even a large, prospective, collaborative study must include some kind of selection criteria because it might not be ethical to propose a liver biopsy to all children with "direct hyperbilirubinemia", as stated in the paper, without further details.

In conclusion, waiting for results of prospective studies, we believe that we are still waiting for an efficacious and practical clinical score for BA.

Conflict of interest

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

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Reply to: "A scoring system for biliary atresia: Is this the right one?"

To the Editor:

We appreciate the interest of Sciveres and colleagues in our recent study [1] and we would like to respond to their letter and help them answer the question they raised. Looking thoroughly into their retrospective study, many limitations can be easily pointed out and may account for their disappointment and poor results. First, the retrospective nature of the study was not the optimal approach for the validation of the biliary atresia (BA) score. Second, the small number of patients (n = 27) in their study carries a very low statistical power of 28.2% at an alpha of 0.05, 2-tailed with 95% CI. This intensifies the need for validation of the BA score on a sample size larger than the one in the original article (n = 75) by El-Guindi *et al.*, as we already suggested. Third, the historical data they collected were not pre-designed to evaluate the score parameters beforehand. For example, the gallbladder length before and after

feeding was assessed using two timely-spaced ultrasound reports, which may carry a high fallacy related to different operators with different judgments.

Another critical point is the evaluation of hepatic subcapsular flow (HSF), which has the highest value in the BA score (6.735). Sciveres *et al.* could detect HSF in only one patient among their 27 patients. In our earlier report [2], we detected HSF in 96.3% (26/27) of cases in the BA group and in one patient in the non-BA group. In addition, Lee *et al.* [3] detected HSF in 100% (29/29) of cases in the BA group and in 14% (5/35) of the non-BA group. This raises a doubt about HSF results by Sciveres and colleagues. Apart from the minimum level of experience needed for such technique, as we elaborated in our article, this raises the question of whether the Doppler machine parameters were set as reported by Lee *et al.* [3] or El-Guindi *et al.* [2] for the detection of HSF. This is not clear in their study.

A further point of concern, although the radiology records were reviewed by a single radiologist, this does not obviate the fact that the procedures were performed by different operators and that the pre-set parameters might have been different or the machine itself used in evaluating the patients over this long period might have varied from one patient to another. All of these may be a source of biased results and interpretation. For that, we advice Sciveres and his colleagues to validate the BA score in a prospective well-designed cohort with pre-set parameters, as reported in the original report [1]. Furthermore, the use of an appropriate sample size with acceptable statistical power is essential.

Sciveres *et al.* suggested that children with a various combination of normal-colored stool, mild cholestasis, known risk factors for transient cholestasis, normal gamma glutamyl transpeptidase activity, and other features not suggestive of BA might be, in most cases, effectively managed without the need of liver histology. Here, a question enforces itself. Why would patients with such criteria of known risk factors and other features not suggestive of BA be included in a study like ours in the first place?

Sciveres and colleagues debated the indication for liver biopsy in the patients in our study. They mentioned that liver biopsy was proposed to all children with "direct hyperbilirubinemia" in our article. This statement can be found nowhere in our article. Therefore, the allegation is not a true one. Herein, we invite Sciveres and his colleagues to review our article with special focus on the different diagnoses of patients in the non-BA group (in all of whom liver biopsy was strongly indicated and justified).

It is well understood that liver biopsy is not indicted for all cases of neonatal cholestasis, as some etiologies can be managed without its need. However, the high rate of neonatal cholestasis patients (200–300 case/year) in our center, including BA patients (25–35 case/year) [4], makes the number of candidate cases for liver biopsy relatively high, when compared with other centers with lower rates [1].

In this concern, we need to emphasize, again, that liver biopsy is considered as an integral part of the diagnostic workup of neonatal cholestasis patients and is strongly encouraged according to "The Cholestasis Guideline Committee of NASPGN" [5], unless there is a contraindication or when the parents refuse the procedure. Furthermore, liver biopsy can be performed safely, even in the smallest infants, with sedation and local anesthesia [6]. The aim of liver biopsy in neonatal cholestasis is, not only to evaluate the features of biliary outflow obstruction, but also essential to reveal the etiology of the liver disease, and assess fibrosis stage, which affects the treatment policy.

Conflict of interest

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