PDECs; and (3) ATP_i depletion by itself can be responsible for the impaired fluid and HCO_3^- secretion. The relationship between mitochondrial function and HCO_3^- secretion and the differences between the effects of conjugated and non-conjugated bile acids needs further investigation.

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How accurate are the Swansea criteria to diagnose acute fatty liver of pregnancy in predicting hepatic microvesicular steatosis?

We noted that in two recent reports in *Gut*, none of 62 patients diagnosed by the Swansea criteria to have acute fatty liver of pregnancy (AFLP) underwent liver biopsy.[1 2] We retrospectively assessed the accuracy of the Swansea criteria to predict hepatic microvesicular steatosis in 34 patients with suspected pregnancy-related liver disease who underwent liver biopsy at our centre between 1998 and 2006. These patients tested negative for other causes of acute liver dysfunction such as hepatitis viruses (hepatitis B virus surface antigen (HBsAg), hepatitis C virus (HCV) antibody, immunoglobulin (Ig) M hepatitis A virus (HAV) antibody, IgM hepatitis E virus (HEV) antibody), malarial parasite and sepsis (blood culture). No patient gave a history of ingestion of a potentially hepatotoxic drug. We excluded 10 patients (details in figure 1).

The remaining 24 patients included in this study were at 36 (21–40) weeks gestation (median (range)), 23 (17–29) years old and 71% were primigravida. The interval from the first symptom to presentation to our centre was 5 (1–14) days.

Abnormal variables in Swansea criteria for AFLP at presentation in the 24 study patients were: vomiting (11/21 patients), abdominal pain (3/14), polydipsia/polyuria (1/1), encephalopathy (9/24), hyperbilirubinaemia (24/24), hypoglycaemia (8/24), hyperuricaemia (8/10), leucocytosis (20/23), ascites/bright liver on ultrasonogram (16/22), elevated transaminases (23/24), hyperammonaemia (2/2), renal impairment (17/24), coagulopathy (23/24) and hepatic microvesicular steatosis (17/24). Some variables were not recorded/not tested in all 24 patients (eg, vomiting recorded in only 21; uric acid tested in only 10). Baseline laboratory results in study patients were: serum total bilirubin, 12.7±6.2 mg/dl (mean±SD); alanine aminotransferase (ALT), 119±6.2 IU/l; prothrombin time, 39±30 s; serum creatinine, 1.7±0.9 mg/dl; and MELD (Model for End-Stage Liver Disease) score, 30 (range 13–46).

Liver biopsy was done either immediately postmortem (5/24) or postnatally via the transjugular route (19/24). Biopsies were fixed in formalin and routinely stained for H&E and

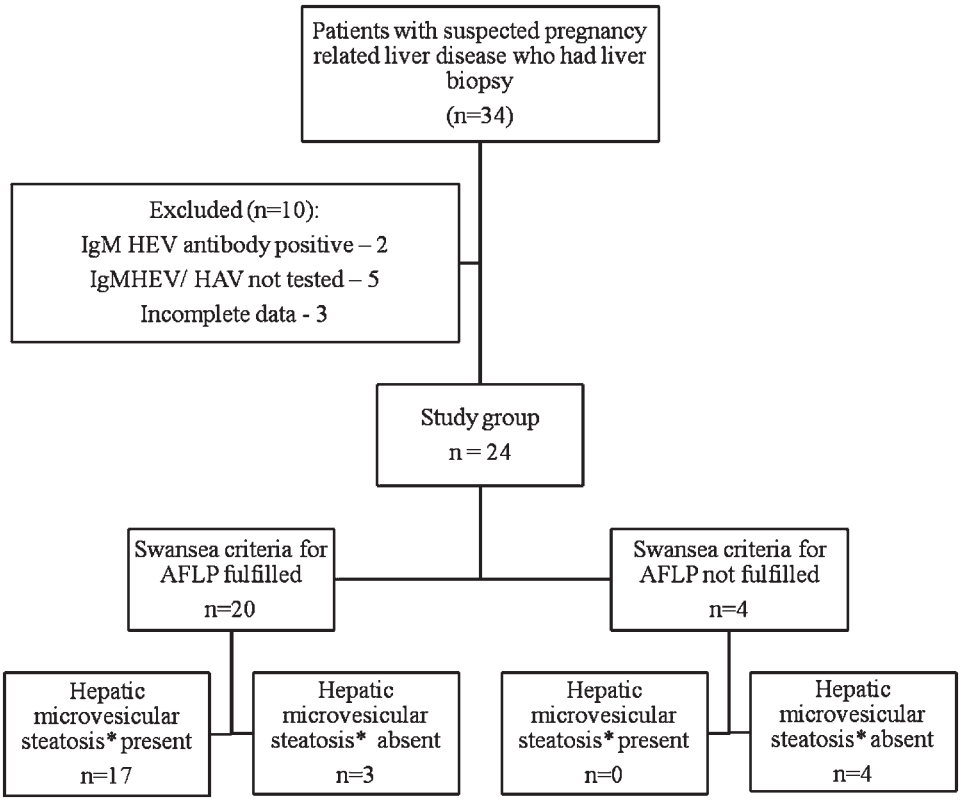

Figure 1 Flowchart of patients with suspected pregnancy-related liver disease who underwent liver biopsy. *Refers to diffuse/perivenular hepatic microvesicular steatosis.

other special stains. Liver histology, reviewed by a single hepatopathologist, showed diffuse microvesicular steatosis (15 patients), perivenular microvesicular steatosis (2), hepatocanalicular cholestasis (4), marked centrizonal congestion (1), bridging necrosis (1) and non-specific changes (1). The interval between delivery and liver biopsy was <3 days (8 patients), 3–7 days (13 patients) and 8–11 days (3 patients). There was a trend, albeit non-significant, to find diffuse/perivenular microvesicular steatosis in patients who underwent liver biopsy earlier after delivery (seen in 10/12 patients biopsied ≤4 days after delivery and in 7/12 patients biopsied >4 days after delivery (p=0.19)). Three patients who did not have hepatic microvesicular steatosis despite fulfilling Swansea criteria underwent liver biopsy 2, 5 and 8 days after delivery.

The sensitivity and specificity of Swansea criteria vis-à-vis diffuse or perivenular microvesicular steatosis was 100% (95% CI 77% to 100%) and 57% (95% CI 20% to 88%), with positive and negative predictive value of 85% and 100%, respectively. Of four patients not fulfilling the Swansea criteria, none had diffuse or perivenular microvesicular steatosis (figure 1). A median of 8 (range: 7–11) variables were abnormal in 20 patients fulfilling the Swansea criteria. All 20 patients who fulfilled the Swansea criteria (ie, had ≥6 abnormal variables), met these criteria, despite excluding histology. We found that by fulfilling the Swansea criteria, no patient with hepatic microvesicular steatosis would have been missed, even if liver biopsy was not done (negative predictive value of 100%). Only four patients did not fulfil the Swansea criteria—this is a limitation of our report.

Based on the described criteria,[1] some of the 20 patients who met the Swansea criteria for AFLP also fulfilled the criteria for HELLP (haemolysis, elevated liver enzymes, low platelets) syndrome (8 patients), partial HELLP syndrome (5 patients) and pre-eclamptic liver dysfunction (2 patients).

The urgent need in a patient with suspected AFLP is early diagnosis, since early termination of pregnancy dramatically improves maternal survival. In this clinical scenario, the Swansea criteria (without liver biopsy) are a good screening tool with 100% negative predictive value for hepatic microvesicular steatosis, thus obviating the need for liver biopsy in clinical management. Studies with larger numbers of patients are warranted to validate our findings.

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Authors' response

We thank Drs Goel *et al* for their interest[1] in our manuscript.[2] The authors present a very interesting exploratory analysis which helps inform the debate about the use of liver biopsy in the diagnosis of cases of acute fatty liver of pregnancy (AFLP). Liver biopsy is recognised as a useful tool in the diagnosis of the condition, but it is also recognised to have potential risks,[3] particularly in the presence of coagulopathy. Almost 90% of the women in our series had a coagulopathy and thus a liver biopsy would be contraindicated. We demonstrated in our study a high agreement between clinical assessment and the Swansea criteria (κ statistic 0.78), and Drs Goel *et al* have demonstrated similarly high agreement between the Swansea criteria and a liver biopsy diagnosis of hepatic microvesicular steatosis (κ statistic 0.65, indicating substantial agreement) (table 1).

The data reported by Goel *et al* thus help to demonstrate further that the use of the Swansea criteria without liver biopsy is a valid diagnostic option and suggest that the infrequent use of liver biopsy reported in the two recent studies may be appropriate.[2 4] The authors correctly state that their analysis is limited by small numbers, and as such can only be interpreted as an interesting exploratory analysis to stimulate further research and debate. It would be extremely useful to investigate whether these results could be replicated in studies using larger data sets, and we would urge any researchers with access to such data to undertake these analyses.

Table 1 Comparison of liver biopsy diagnosis of microvesicular steatosis with use of the Swansea criteria in cases reported by Goel *et al* (n, %)

	Swansea criteria	
	AFLP	**Not AFLP**
Liver biopsy		
AFLP	17 (71)	0 (0)
Not AFLP	3 (13)	4 (17)

Acute fatty liver of pregnancy.

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Author's response

The report by Goel *et al*[1] from Vellore is interesting and valuable. The authors identified 34 patients who had undergone liver biopsy for suspected pregnancy-related liver disease in their institution over a 9-year period. Twenty-four of those cases were deemed suitable for retrospective study. They applied the Swansea criteria for acute fatty liver of pregnancy (AFLP) and found that of the 20 cases fulfilling those criteria, in only 17 could they detect histological evidence of microvesicular steatosis (positive predictive value 85%), whereas none of the four cases not fulfilling Swansea criteria had microvesicular fat (negative predictive value 100%). This could imply that the Swansea criteria, although having good sensitivity, may lack specificity. However, such a conclusion can be made only if there is complete confidence about the histological processing of the liver tissue of the three Vellore cases, which had clinical evidence of