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## Coagulopathy in obstetric cholestasis in Wessex Deanery



Obstetric cholestasis affects approximately 0.7% of pregnancies in England.<sup>1</sup> The condition is defined as pruritus with an onset in pregnancy, abnormal liver function in the absence of other liver disease, and resolution following delivery.<sup>2</sup> Obstetric cholestasis is of relevance to anaesthetists due to concern regarding the development of coagulopathy and the implications for regional anaesthetic and analgesic techniques. Coagulopathy is hypothesised to occur from the malabsorption of vitamin K, secondary to reduced bile acid secretion in the gastrointestinal tract. However, this concern is based upon limited evidence from small, retrospective studies.<sup>3,4</sup> Bacq et al. demonstrated an incidence of abnormal prothrombin time of 8% in 49 cases of obstetric cholestasis.<sup>3</sup> This rate has not been found in subsequent studies, and most recently DeLeon et al. found no cases of abnormal clotting in 319 parturients.<sup>2,5,6</sup> In the presence of conflicting data, and given that the consequences of an epidural haematoma secondary to coagulopathy are extreme, we sought to add to the current literature and understanding of obstetric cholestasis by conducting a multicentre observational study.

We performed a retrospective cross-sectional study across three hospital trusts in Wessex Deanery, coordinated by the local trainee-led research network. Approval for the study was obtained (South Central – Hampshire A Research Ethics Committee (14/SC/1456)). Inclusion criteria were parturients diagnosed with obstetric cholestasis, defined as at least one serum bile acid result greater than 14  $\mu\text{mol/L}$ , who delivered between January 2010 and December 2014 and had a coagulation test result during their pregnancy. Electronic maternity databases were interrogated to identify women diagnosed with obstetric cholestasis. Biochemistry departments were contacted to identify all women of reproductive age who had a bile acid assay during this time period, to mitigate against incomplete records. Patient notes were reviewed to identify obstetric cholestasis treatment initiation and the presence of co-morbidities that could account for deranged biochemistry or coagulation. The primary study outcome was the prevalence of

deranged coagulation studies within the study population (International Normalised Ratio (INR) greater than 1.4).<sup>7</sup> Sample size analysis determined that at least 113 subjects would be required to detect an 8% incidence of coagulopathy, based upon previous studies, with a 5% precision error.<sup>8</sup>

During the study period 745 parturients were diagnosed with obstetric cholestasis. With a combined number across trusts of 15 000 deliveries per year, this equates to a prevalence of 1%. Of those, 290 (39%) were excluded because they had no coagulation study result. In total, the 455 women included had 596 coagulation studies analysed. We identified no abnormal coagulation results, giving an incidence of coagulopathy of 0.0% (95% confidence interval 0.0% to 0.84%, calculated using a Poisson distribution). The mean INR (median [range]) was 0.9 (0.9 [0.8–1.2], n=303). The majority of coagulation studies were taken within 24 hours of delivery (75%, n=261). Serum bile acid and alanine aminotransferase (ALT) levels sampled at the same time as coagulation studies were severely deranged (bile acids >100  $\mu\text{mol/L}$ ; ALT >200 IU/L) in 9% and 15% of women, respectively.

None of the 455 parturients with obstetric cholestasis developed a coagulopathy. This is despite co-existing and significantly deranged serum bile acid and ALT levels, with the bile acid pathway being implicated in the mechanism for developing coagulopathy in obstetric cholestasis. As the largest sample to date, our results add, in the form of patient numbers, to the findings of similar more recent studies, such as that by DeLeon et al.<sup>6</sup> Older studies with smaller patient numbers have reported a higher incidence of coagulopathy and the reasons for this are not clear.<sup>3,4</sup> Applying the ‘rule of three’ to our sample, we can be 95% confident that fewer than 1 in 152 parturients with obstetric cholestasis will have deranged clotting, but it is impossible to quantify how many of those would go on to develop a spinal or epidural haematoma if neuraxial blockade were performed in the presence of an undiagnosed coagulopathy. Risk is a continuum and the alternative anaesthetic options are not without their own risk of serious complications.

There are limitations to our data. It is a retrospective study, and there were challenges collating complete data sets and identifying treatment initiation. Determination of the true incidence of coagulopathy in obstetric cholestasis, and the subsequent demonstration of an acceptably low level of risk for a complication, would require a large prospective study. However, we believe that our results strengthen those of recent studies and that this information will add to the clinician’s decision-making when weighing-up the risks and benefits

of different anaesthetic techniques for the individual patient in front of them.

J. Lees

Wessex Deanery, UK

E-mail address: jessmakey@doctors.org.uk

S. Al-Rawi

University Hospital Southampton NHS Foundation Trust, UK

H. McPhee

Poole Hospital NHS Foundation Trust, UK

on behalf of The Southcoast Perioperative Audit and Research Collaboration <sup>†1</sup>

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<sup>†</sup> Dr P. McGlone, Dr J. Gray, Dr A. Sinha, Dr R. Bolton, Dr S. Allen, Dr K. Blethyn, Dr F. Riccio and Dr M. Simpson.

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## Umbilical artery flow monitoring with transesophageal echocardiography during maternal cardiac surgery



Pregnancy in women with mechanical prosthetic valves is associated with a high risk of maternal mortality

due to valve thrombosis if anticoagulant use is irregular.<sup>1</sup> While cardiac surgical maternal risks are approximately the same as those in non-pregnant women, fetal mortality associated with cardiopulmonary bypass (CPB) can be up to 19%.<sup>2,3</sup> Fetal heart rate (FHR) monitoring using transesophageal echocardiography (TEE) has been reported in our institution, and end-diastolic velocity (EDV) is a more sensitive peri-operative fetal monitor than FHR.<sup>4</sup>

A 27-year-old patient (G<sub>5</sub>P<sub>0</sub>) at 30 weeks-of-gestation presented with severe aortic stenosis. She had undergone aortic valve replacement and ventricular septal defect (VSD) repair 15 years previously. She took warfarin irregularly, and had stopped taking all medications 10 months previously to conceive. She refused termination of pregnancy and was scheduled for aortic valve replacement.

Baseline blood pressure was 102/57 mmHg, heart rate was 84 beats/min. After positioning supine with left-lateral tilt of 30 degrees, general anesthesia was induced with 150 mg propofol, 70 mg rocuronium and 50 µg sufentanil. Anesthesia was maintained by continuous intravenous infusion of 4 mg/kg/h propofol, 3 µg/kg/min of cisatracurium, 0.4 µg/kg/min remifentanyl and intermittent sufentanil when anesthesia depth decreased. A TEE probe was inserted, positioned at the deep gastric level and rotated until the placenta was seen and the umbilical artery was identified using color Doppler (Fig. 1a). Fetal heart rate was calculated and positive EDV could be observed by using the pulsed-wave Doppler signal (Fig. 1b).

Heparin was administered to achieve an active clotting time >480 s and normothermic CPB was established, at which point maternal blood pressure was 92/56 mmHg, heart rate was 85 beats/min while FHR was 120 beats/min with a positive EDV. As pump flow increased, EDV gradually disappeared, FHR remained unchanged, while maternal blood pressure was 79/45 mmHg and heart rate was 91 beats/min (Fig. 2a).

The fetal heart rate (FHR) significantly decreased following aortic-cross clamping since the pump flow was temporarily decreased (Fig. 2b). As mean arterial pressure (MAP) increased (from 54 to 74 mmHg), FHR also increased but with absence of end-diastolic velocity (AEDV) that persisted throughout the rest of the operation.

The operation continued without incident. As CPB was terminated, the patient's blood pressure was 100/60 mmHg and heart rate was 98 beats/min, the FHR had increased to 133 beats/min. The hemodynamic changes are summarized in Fig. 3.

The patient was then transferred to the cardiac intensive care unit where she stayed for one night with continuous cardiotocography monitoring and intermittent transabdominal ultrasound examination. Fetal heart rate was sustained at 140–150 beats/min and the EDV