

## Case report

# Severe pre-eclampsia complicated by acute fatty liver disease of pregnancy, HELLP syndrome and acute kidney injury following SARS-CoV-2 infection

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## SUMMARY

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has presented many diagnostic challenges and uncertainties. Little is known about common pathologies complicating pregnancy and how their behaviour is modified by the presence of SARS-CoV-2. Pregnancy itself can alter the body's response to viral infection, which can cause more severe symptoms. We report the first case of a patient affected with sudden-onset severe pre-eclampsia complicated by acute fatty liver disease of pregnancy, HELLP (haemolysis, elevated liver enzymes and low platelet) syndrome and acute kidney injury following SARS-CoV-2 infection. Although an initial diagnostic dilemma, a multidisciplinary team approach was required to ensure a favourable outcome for both the mother and the baby. Our case report highlights the need for health professionals caring for pregnant women to be aware of the complex interplay between SARS-CoV-2 infection and hypertensive disorders of pregnancy.

## BACKGROUND

Since the start of the COVID-19 pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), patients have reported a wide spectrum of clinical presentations, including fever, respiratory symptoms as well as extrarespiratory manifestations.<sup>1</sup> Currently there is no evidence that pregnant women are more susceptible to the virus, needing admission to intensive care or dying from the illness compared with the non-pregnant population. Most of the pregnant women who needed hospitalisation for COVID-19 were in the third trimester and were from black, Asian and minority ethnic backgrounds.<sup>2</sup>

Pre-eclampsia is a common disorder of pregnancy which can lead to life-threatening complications such as acute fatty liver of pregnancy (AFLP), HELLP (haemolysis, elevated liver enzymes and low platelet) syndrome and renal failure. AFLP is a rare (1 in 13 000) variant of pre-eclampsia and potentially lethal for both the mother and the fetus. The case fatality rate is 1.8%, with a perinatal mortality rate of 104 per 100 000.<sup>3</sup>

## CASE PRESENTATION

We present a 26-year-old Asian female patient in her first pregnancy with a body mass index of 25 kg/m<sup>2</sup> and with no significant medical history.

Her antenatal booking blood, serology (syphilis, HIV and hepatitis B) and blood pressure (BP) were all unremarkable. She had been taking 75 mg aspirin from 12 weeks' gestation due to a family history of pre-eclampsia. At routine community midwife visit, her BP was 132/72 mm Hg and there was +3 protein on urine dipstick. This was 2 days prior to her attendance at our maternity unit at 37 weeks' gestation with a 7-day history of worsening nausea, vomiting, abdominal pain and anorexia, leading to a dramatic weight loss. She also reported that 2 weeks earlier she had a bout of fever with anosmia and loss of taste without any respiratory symptoms; this resolved spontaneously some days later. Her BP was 173/111 mm Hg, with significant proteinuria. She was admitted for observation and further investigations. Laboratory investigations were grossly abnormal (table 1) and indicated a diagnosis of severe pre-eclampsia complicated by AFLP and 'atypical' HELLP syndrome with acute kidney injury. A decision was made for immediate induction of labour with prostaglandin. Magnesium sulfate was administered for prevention of eclamptic seizures. She had spontaneous rupture of the amniotic membranes at 4 cm cervical dilatation which revealed significant meconium-stained liquor and abnormal fetal heart rate, leading to an uncomplicated emergency caesarean delivery under spinal anaesthesia with an estimated blood loss of 500 mL. A live baby weighing 2760 g was born in good condition. Postnatally the patient was managed in a high-dependency setting on the labour ward with supportive treatment. Her BP rapidly normalised after delivery of the baby. Magnesium sulfate was continued for 24 hours postnatally. Her liver function gradually improved, but renal function slowly deteriorated with mild metabolic acidosis. Three days later, she felt dizzy and developed tachycardia, with a significant drop in haemoglobin (68 g/L). She received a transfusion of two units of packed red blood cells and intravenous broad-spectrum antibiotics. A CT scan of the abdomen and pelvis showed a large intra-abdominal haematoma, which was evacuated via repeat laparotomy. CT scan also showed an incidental finding of bilateral basal ground glass opacifications in the lungs, suggestive of COVID-19 infection. This was confirmed by nasal and throat swab for SARS-CoV-2 using reverse transcriptase PCR. The



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## Unusual association of diseases/symptoms

**Table 1** Results of investigations on admission and 2–3 weeks postnatally

Investigations	Admission (prior to delivery of baby by CS)	Results 2–3 weeks postnatally
<b>Liver function test</b>		
ALT (0–55 IU/L)	1130	42
ALP (30–150 IU/L)	521	149
Bilirubin (<21 µmol/L)	49	9
Albumin (35–50 g/L)	21	27
<b>Test for full blood count and haemolysis</b>		
LDH (125–220 IU/L)	646	
Haptoglobin (0.63–2.73 g/L)	<0.08	
Haemoglobin (115–154 g/L)	112, 68 (3 days post-CS)	123
White cell count (3.9–10.9×10 <sup>9</sup> /L)	21.36	6.4
Platelet (150–400×10 <sup>9</sup> /L)	235	377
<b>Renal function test</b>		
Creatinine (40–90 µmol/L)	173	63
Estimated GFR (>90 mL/min/1.73 m <sup>2</sup> )	35	>90
Urate (140–360 µmol/L)	613	287
Bicarbonate (22–26 mmol/L)	15.4	
PCR (<30 mg/mmol)	394, 50 (5 days post-CS)	
<b>Clotting profile</b>		
PT (9–13 s)	15.5	
APTT (23–38 s)	47.3	
APTT ratio	1.6	
Fibrinogen (1.5–4 g/L)	2.24	
<b>Others</b>		
C reactive protein (0–5 mg/L)	22, 139 (2 days post-CS)	4
Venous glucose (4–6 mmol/L)	4.25	

ALP, alkaline phosphatase; ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; CS, caesarean section; GFR, glomerular filtration rate; LDH, lactate dehydrogenase; PCR, urine protein to creatinine ratio; PT, prothrombin time.

following day, she developed sudden-onset confusion with retrograde amnesia, restlessness, sighing and inability to recall the date or her current location. An urgent CT scan of the head was arranged, which was normal. Her confusion spontaneously resolved a few days later, with rapidly improving creatinine and liver function tests. She was discharged home on the seventh postnatal day with low molecular weight heparin, oral labetalol and antibiotics. Her baby was asymptomatic for COVID-19 and was not tested as per local protocol. Two weeks later, her liver and renal function tests returned to normal (table 1).

### OUTCOME AND FOLLOW-UP

This patient made a remarkable recovery and was discharged a week later with improving serum liver function tests, renal function tests, clotting profile and inflammatory markers. She was followed up in the outpatient postnatal clinic a week later with complete resolution of both liver function and renal tests. Her BP was well controlled with labetalol 200 mg two times per day. She was advised that in her future pregnancy she will be under consultant care as the risk of recurrence of pre-eclampsia is high and that she will receive 150 mg aspirin daily from 12 weeks of pregnancy to reduce the risk of pre-eclampsia. Furthermore, her BP will be checked weekly from the second trimester of pregnancy, with serial fetal growth scans in the third trimester to detect fetal intrauterine growth restriction.

### DISCUSSION

We have described the case of a pregnant patient who was affected simultaneously by severe pre-eclampsia and COVID-19 in late pregnancy. AFLP is part of the spectrum of hypertensive disorders of pregnancy, which includes pre-eclampsia and HELLP syndrome. It is often associated with mild-to-moderate disease. The Swansea criteria for the diagnosis of AFLP are relevant in this patient as she satisfied more than six (vomiting, abdominal pain, elevated bilirubin, leucocytosis, elevated transaminase, renal impairment, raised urate).<sup>4</sup> The degree of liver enzyme derangement is characteristically more severe with AFLP than with HELLP, and there is a greater degree of synthetic liver damage (characterised by abnormal clotting or hypoglycaemia). Thrombocytopenia is usually mild or absent. Confusion is not a feature of pre-eclampsia unless it is related to encephalopathy caused by AFLP. However, it is a common extrapulmonary manifestation of COVID-19. It is highly likely that COVID-19 may have contributed to her confusion. However, other causes such as postsurgery, sepsis and acute insult to liver and kidney can also lead to confusion.

Both pre-eclampsia and COVID-19 infection are examples of microvascular disease causing endothelial injury. They both cause a high prothrombotic tendency leading to multiorgan failure. The presence of both diseases likely had either a synergistic or an opportunistic effect, which may have led to severe clinical manifestations via the interplay of the renin-angiotensinogen-aldosterone system in their pathogenesis.

There are case reports in the literature of influenza A hepatitis infections causing AFLP by activation of Kupffer cells in the foci of apoptosis leading to release of inflammatory cytokines, hepatic oxidative stress and hepatocyte injury.<sup>5</sup> It is plausible that SARS-CoV-2 has triggered a similar response in this patient. There is now emerging evidence that pregnant women

### Patient's perspective

The patient was followed up in the postnatal clinic where she was debriefed about the management of her intrapartum care. She said: 'I am grateful to the both medical and midwifery staff about the care I received and did not realize how ill I was. Although I was very confused and scared but medical staff took very good care of me and made a frightening situation very comfortable.'

### Learning points

- ▶ Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in pregnant patients may be considered a risk factor for hypertensive diseases of pregnancy, including acute fatty liver of pregnancy and severe pre-eclampsia, particularly in women who have risk factors for pre-eclampsia such as nulliparity, family history of pre-eclampsia in first-degree relatives and so on; further research with larger patient numbers is needed to confirm this.
- ▶ We would recommend that pregnant patients who have been tested positive for SARS-CoV-2 are followed up with regular blood pressure checks.
- ▶ Pregnant women presenting with severe forms of pre-eclampsia with abnormal biochemical results should be tested for SARS-CoV-2 and a chest radiograph performed as part of the investigations.

with severe COVID-19 infection can develop a pre-eclampsia-like syndrome.<sup>6</sup> Healthcare providers should be aware of its existence and monitor pregnancies with suspected pre-eclampsia with caution.

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