

# Emergency caesarean delivery in a patient with cerebral malaria-leptospira co infection: Anaesthetic and critical care considerations

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## ABSTRACT

Malaria-leptospira co-infection is rarely detected. Emergency surgery in such patients has not been reported. We describe such a case of a 24-year-old primigravida at term pregnancy posted for emergency caesarean delivery who developed pulmonary haemorrhage, acute respiratory distress syndrome, acute kidney injury, and cerebral oedema. Here, we discuss the perioperative management, pain management (with transverse abdominis plane block), intensive care management (special reference to management of pulmonary haemorrhage with intra pulmonary factor VIIa) and the role of plasmapheresis in leptospira related jaundice with renal failure.

**Key words:** Intrapulmonary factor VIIa, malaria-leptospira co-infection, plasmapheresis, transverse abdominis plane block

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## INTRODUCTION

Co-infection of malaria and leptospirosis is not common.<sup>[1]</sup> Similar clinical pictures of liver dysfunction and renal failure makes differentiation between the two diseases difficult.

Anaesthetic management for caesarean delivery in a parturient with malaria was previously reported without leptospiral co-infection.<sup>[2]</sup> We report a case of a primigravida with falciparum malaria with altered mental status and leptospiral co-infection posted for emergency caesarean delivery, which was successfully managed both perioperatively and post-operatively. To the best of our knowledge, this is the first reported case of a patient of malaria-leptospira co-infection undergoing emergency caesarean delivery and intensive care management with intrapulmonary Factor VIIa treatment. After obtaining written informed consent from the patient, we wish to report the case.

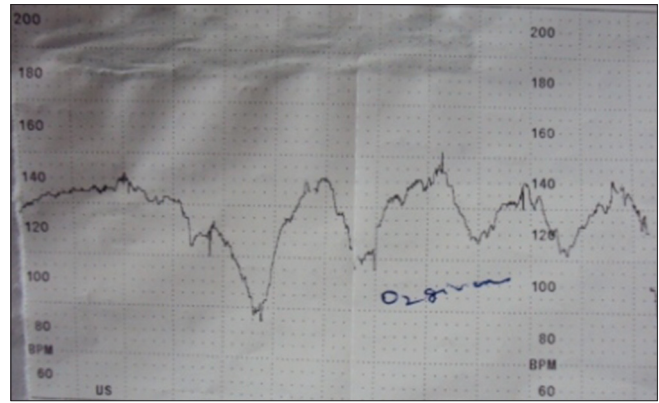
## CASE REPORT

A 24-year-old primigravida, at 37 weeks of gestation was referred to our institute for further management on supplemental oxygen (Venturi mask) after Rapid test diagnosis of *Plasmodium falciparum* (Pf) malaria (ParaSight™-F, Becton Dickinson, Sparks, MD) associated with acute icteric leptospirosis (microscopic agglutination test (MAT) titers for *Leptospira ictero-haemorrhagiae* of 1:400). Her history revealed high grade fever, decreased urine output with yellowish discoloration and altered sensorium. She was disoriented, febrile and icteric and had sub-conjunctival haemorrhages and fine basal crepitations on auscultation. She was receiving intravenous (i.v.) artesunate and ceftriaxone and doxycycline capsules. Her pre-operative investigations in referral card revealed anaemia, jaundice with deranged liver function, coagulopathy, thrombocytopenia, increased total leucocyte count, elevated blood urea nitrogen and serum creatinine. Abdominal ultrasonography showed a singleton pregnancy, adequate liquor,

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umbilical artery systolic-diastolic ratio of 2:1 and mild hepato-splenomegaly. Within 1 h of arrival she was posted for emergency caesarean delivery because of non-reassuring fetal heart rate [Figure 1].

After administering aspiration prophylaxis and taking high-risk consent she was shifted to operation theatre. Basic monitors were attached and rapid sequence intubation with cricoid pressure was carried out using thiopental and succinylcholine. Right internal jugular vein and left radial artery were cannulated under ultrasonographic guidance simultaneously by two anaesthetists. Her baseline serum glucose level was normal. Anaesthesia was maintained with isoflurane in N<sub>2</sub>O-O<sub>2</sub> mixture and atracurium until delivery of a 2.25 kg baby. After cord separation, fentanyl was administered. Oxytocin (25 IU) infusion was started in titrated doses. Neonatal data recorded were an Apgar score of 6 and 8 at 1 and 5 min respectively, with cord blood pH of 7.28, base deficit of 5.4 and blood sugar level of 50 mg/dl. Hypotension started after placental separation. Blood loss was managed with packed red blood cells, fresh frozen plasma and platelets transfusion followed by noradrenaline infusion (titrated doses). At the end of the surgery, blood gases showed mild acidosis, but normal electrolytes and serum glucose. She was shifted to intensive care unit (ICU) in intubated state and on noradrenaline infusion. Post-operative analgesia was maintained by ultrasound guided bilateral transverse abdominis plane block. In ICU, on the second postoperative day, she developed pulmonary haemorrhage [Figure 2]. Considering coagulopathy, blood products were transfused, but it did not benefit. Bed side fibre-optic bronchoscopy was carried out, which revealed erythematous mucosa, blood clots, active oozing and diffuse bleeding from distal airway. Broncho alveolar lavage was performed and Factor VIIa (AryoSeven, AryoGen Biopharma Co, Tehran, Iran) was administered (50 µg/Kg of rFVIIa in 50 ml distilled water through the fibre-optic bronchoscope (25 ml in each main bronchus after lavage) because of its thrombogenic effect. Following this immediate bleeding cessation and significant reduction of inspired oxygen fraction (FiO<sub>2</sub>) was observed in the next 12 h. Her chest radiograph, which showed bilateral non-homogeneous opacities (lower and middle zones), the previous day became almost clear the next day. In view of acute kidney injury, severe hyperbilirubinemia and blood picture indicating haemolytic uremic syndrome (high serum lactate dehydrogenase, schistocytes in peripheral



**Figure 1:** Non reassuring fetal heart rate



**Figure 2:** Computed tomographic scan of thorax of the patient showing bilateral pulmonary hemorrhage

blood), nephrology opinion was obtained and based on their suggestion, plasmapheresis followed by dialysis was done (seven cycles each). Because of the altered mental status, computed tomography of the brain was carried out, which showed diffuse cerebral oedema. For which cerebroprotective measures (head elevation, not rotating neck, maintain serum sodium 145-155 Meq/L, keeping blood partial pressure of carbon dioxide 32-40 mmHg) were undertaken. Other investigations such as blood cultures, urine cultures, Weil-Felix test, typhi dot, dengue, and hepatitis viruses serology yielded negative results. Supportive therapies like stress ulcer prevention, deep vein thrombosis prophylaxis (pneumatic compression) and glycemic control were provided. By the fourth post-operative day, the intensity of fever started reducing, consciousness improved, inotropic support tapered, urine output improved and liver function test with coagulation parameters showed improving trends. Her Pao<sub>2</sub>/Fio<sub>2</sub> ratio also gradually improved. By the sixth post-operative day, she could be extubated. Subsequently, she was shifted to wards and safely discharged from the hospital.

## DISCUSSION

Multisystem involvement of Pf-malaria results in its severe and fatal complications. The prevalence and parasite density of Pf is higher in primigravida, compared to multigravida or non-pregnant patients.<sup>[2]</sup> Infected erythrocytes aggregate, causing microcirculatory obstruction, thrombosis and local ischaemia,<sup>[3]</sup> compromising cerebral, hepatic, renal, intestinal and pulmonary circulations leading to raised intracranial pressure (ICP), liver dysfunction, acute kidney injury, gastrointestinal bleeding and haemorrhagic pulmonary oedema. Pf's placental sequestration reduces their standard smear visibility, producing false-negative results and therefore, Rapid diagnostic tests are preferred.<sup>[4]</sup> Leptospirosis is common in low socioeconomic class with poor sanitation and hygiene and is under-diagnosed. In a patient with febrile illness with hepato-renal involvement malaria, leptospirosis, typhoid fever, viral hepatitis (specially hepatitis E in pregnancy) and scrub typhus.<sup>[5]</sup> should be considered in the differential diagnosis. Our decision to administer general anaesthesia was influenced by the presence of thrombocytopenia, coagulopathy, suspected raised ICP, and impaired mental status. Moreover, concerns of introducing malarial parasites into the cerebrospinal fluid, with regional anaesthesia exist.<sup>[6]</sup> Intraoperatively, thiopental and propofol are better suited in increased ICP with cerebral malaria,<sup>[6]</sup> whereas ketamine should be avoided. Isoflurane in sub-MAC concentration is appropriate as lesser cerebral vasodilatation causes less increase in ICP. Atracurium or cis-atracurium is the relaxants of choice in the presence of hepatic and renal dysfunction. Hyperpyrexia, anorexia, impaired gluconeogenesis, and quinine therapy predispose to severe hypoglycaemia. Cautious use of glucose infusion is advised.<sup>[7]</sup> Endothelial clogging, vasospasm, microthrombosis, local ischaemia, and organ hypo-perfusion leads to lactic acidosis. Hormonal imbalances because renal failure and fluid shift predisposing to fluid overload, which associated with parasite injured pulmonary capillaries can precipitate pulmonary oedema. Fluid management should be meticulous obligating the use of a central venous pressure catheter.<sup>[8]</sup> Haematological abnormalities include anaemia, thrombocytopenia and coagulation system dysregulation. Anaemia occurs due to bone marrow depression, splenic uptake, erythrophagocytosis and autoimmune haemolysis. Pregnancy itself causes thrombocytopenia, which further accentuates by platelet activation, splenic

pooling and a decreased platelet life span (2-3 days).<sup>[9]</sup> Invasive procedures preferably should be performed under real-time ultrasound guidance. Non-steroidal anti-inflammatory drugs should be avoided.

Similar clinical features make a diagnosis of acute leptospirosis co-infection difficult and lead to delay in therapy initiation. microscopic agglutination test (MAT) is the preferred diagnostic modality. IgM enzyme linked immunosorbent assay antibodies have more false positive results. A 21% higher mortality exist in falciparum infection associated with acute respiratory distress syndrome.<sup>[10]</sup> High secondary bacterial infection also increases mortality. Pulmonary haemorrhage is common in leptospirosis. Plasma exchange is an option in patients with severe icteric leptospirosis (severe hyperbilirubinaemia) complicated by renal failure who do not show rapid clinical response to conventional treatment.<sup>[11]</sup>

Other than disseminated intravascular coagulation there are many off license use of FVIIa such as severe perioperative blood loss, traumatic massive bleeding and obstetric haemorrhage. Application of intrapulmonary FVIIa has been reported in diffuse alveolar haemorrhage.<sup>[12]</sup> We used it in our patient as Pf leptospira infection with superimposed sepsis is associated with endothelial dysfunction and propensity for systemic vascular thrombosis (venous and arterial) and received favourable results.

In conclusion, Pf-leptospira co infection adversely affects the majority of the organ systems mainly through endothelial dysfunction. Proper understanding of the pathophysiology helps anesthesiologist during the conduct of anaesthesia as well as ICU management. Intrapulmonary Factor VIIa is a useful modality in pulmonary haemorrhage of malaria-leptospira co-infection. Plasmapheresis can be considered in acute kidney injury with hepatorenal syndrome.

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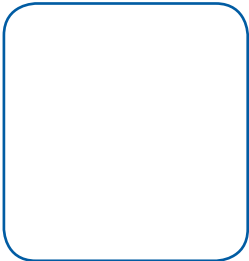
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