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Case Series

Anaesthetic management of pregnant patients with severe dengue fever for emergency caesarean section - A case series and review

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ABSTRACT

Background: Dengue, a mosquito-borne viral infection, can lead to severe complications like dengue shock syndrome and severe thrombocytopenia. Pregnant patients with dengue present unique anaesthetic challenges. In this case series, we present the anaesthetic management of four pregnant patients with dengue who required emergency caesarean delivery.

Case Illustration: All patients had severe thrombocytopenia and required platelet transfusions. Two patients developed respiratory distress and pulmonary edema in the perioperative period. One patient had severe liver function abnormalities along with thrombocytopenia, complicating the diagnosis. All patients received intensive care unit (ICU) management. None of the neonates tested positive for dengue.

Discussion: The pathophysiological changes of pregnancy and dengue infection complicate the anaesthetic management of critically ill dengue patients. Thrombocytopenia and abnormal immune response lead to acute vascular permeability, plasma leakage, circulatory insufficiency, and polyserositis. Abnormal liver function tests and thrombocytopenia must be differentiated from HELLP syndrome. Over-transfusion of fluids due to shock can lead to pulmonary edema.

Conclusion: Pregnant patients with dengue fever pose a high risk of maternal and foetal mortality and morbidity. Successful anaesthetic management requires judicious transfusion of blood products and fluids based on the disease's complications and stage of illness. General anaesthesia is safe in these patients.

1. Introduction

Dengue is a mosquito-borne viral disease caused by a virus of the Flaviviridae family and transmitted by female mosquitoes mainly of the species Aedes aegypti and, to a lesser extent, Ae. Albopictus. It has rapidly spread to all regions of WHO in recent years with 70% of the actual burden being in Asia.[1,2] Dengue is endemic in India and it had a severe outbreak of dengue infection in 2021 with data from federal health ministry suggesting more than 100,000 dengue infections.[3]

Pregnant women who develop dengue are at increased risk of severe disease i.e., increased risk of maternal haemorrhage, preterm labour, oligohydramnios and foetal deaths.[4,5] In these patients, in addition to similar COVID manifestations, the presentation can be easily confused with HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets.[4,5] The clinical suspicion including a thorough history taking and investigations may help in delineating the diagnosis of dengue from other differential diagnoses.

There have not been many studies or reports about unique anaesthesia concerns in pregnant patients with severe dengue. We report a case series of four pregnant patients with dengue who presented to a tertiary care hospital for

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emergency CD amidst the outbreak of COVID pandemic in the month of November 2021 and December 2021. These patients had varied presentations posing distinct and unique challenges in the perioperative management (Table 1). All patients were NS1positive for dengue. IgG and IgM dengue serology was positive in three of them. The COVID-19 disease was ruled out by a negative RTPCR test in all of them.

2. Case 1

A 24-year-old pregnant woman at 36 weeks of gestation was referred to the hospital with a 10-day history of high-grade fever. She had received symptomatic treatment for dengue, including 10 units of platelet transfusions. On examination, she had a pulse rate of 100/minute, SBP of 80/60mmHg, and abdominal tenderness. Investigations revealed a platelet count of 10,000, Hb of 7 gm%, and haematocrit of 21, with metabolic acidosis (pH 7.23, paCO2 32). She received 2 L of ringer lactate, oxygen therapy, one unit of SDP, and 2 units of packed red blood cells.

On day 2, she developed respiratory distress with bilateral crepitations. Further, tests showed a platelet count of 17,000, Hb% of 9gm%, haematocrit of 31%, and elevated liver enzymes (SGOT 1358, SGPT 396). A chest X-ray revealed bilateral pleural effusions and mild ascitic fluid. Despite her critical condition, she went into labour. She was managed with a propped-up position, nebulization (salbutamol and budesonide), oxygen therapy, and furosemide 0.1mg/kg. Due to severe respiratory distress, she was ventilated using BIPAP (IPAP 12, EPAP 6).

Before caesarean section, her platelet count increased to 50,000 after receiving 1 jumbo unit of SDP. The surgery was performed under GA due to foetal distress. Intraoperatively, she received 2 units of packed red blood cells. The newborn had an APGAR score of 8/10 and was transferred to the NICU. The patient was then moved to the ICU for elective ventilation due to her poor preoperative chest condition. After two days on mechanical ventilation, her platelet counts normalized, and enzyme levels decreased. She was extubated on day 3 and discharged on day 10 of admission.

3. Case 2

A 28-year-old G1P1 patient at 37 weeks of gestation presented with a 10-day fever and 3 days of labour. On admission, she was afebrile, with a platelet count of 25,000, Hb of 9 gm%, haematocrit of 30%, SGOT/SGPT of 108/78. She received 1 unit of SDP and underwent caesarean section at a platelet count of 80,000 under GA. Intraoperatively, she received 2 L of ringer lactate. The surgery and anaesthesia were uneventful, and the baby had an APGAR of 9/10. Postoperatively, she developed respiratory distress along with bilateral basal crepitation's and 88% saturation on 0.4 FiO2, revealing mild pulmonary edema. Managed with fluid restriction, oxygen therapy, and propped up position, her condition improved, and she was discharged from ICU to the ward on postoperative day 3.

4. Case 3

A 27-year-old woman at 37 weeks of gestation was referred to our hospital with a 4-day history of high-grade fever, headache, nausea, and vomiting. On examination, she had a temperature of 39 °C, blood pressure of 100/60 mmHg, pulse rate of 88/min, and respiratory rate of 18/min. Blood tests revealed a haemoglobin level of 12 g/dL, white blood count of 3780/mm3, and platelet count of 22,000/μL. Liver enzymes (SGOT/SGPT) were elevated (47/86 U/L). She underwent emergency LSCS under GA for decreased foetal movements after receiving 1 unit of SDP at a platelet count of 60,000. The surgery and anaesthesia were uneventful. The baby had an APGAR score of 9/10 and was sent to the NICU. The patient was observed and treated in the ICU for three days without requiring mechanical ventilation. She recovered and was discharged on day 9 of fever.

5. Case 4

A 27-year-old G2, P1, L1 patient at 34 weeks gestation was referred to our hospital with a 5-day history of fever, non-bilious vomiting, and right hypochondrial tenderness. She also experienced decreased foetal movements for 3 days. On examination, she had a high-grade fever, low blood pressure (85/58 mm Hg), and a pulse rate of 78/minute. Ultrasound revealed intrauterine growth retardation, mild ascites, and mild pleural effusion. Investigations showed a platelet count of 70,000, haemoglobin of 10.2, TLC of 6600, SGOT of 1649, and SGPT of 1581. The patient was managed with intravenous paracetamol, antibiotics, and fluid resuscitation with Normal Saline and lactated Ringer's solution. An emergency caesarean delivery (CD) under GA was performed due to cephalopelvic disproportion and foetal distress. The baby had an APGAR score of 7/10 and was sent to the NICU. The mother was shifted to the ICU for elective ventilation. In the ICU, her condition worsened with spontaneous petechial patches all over her body, low blood pressure (80/45 mm Hg), platelet count of 12,000, elevated liver enzymes, and evidence of serositis with pleural effusions. She received fluid resuscitation with 4 units of FFP and 6 units of platelet concentrates, and noradrenaline infusion was started. Ultrasonography showed mild ascites, mild hepatomegaly, and splenomegaly. With supportive therapy, her platelet counts and liver function tests gradually improved. After 3 days of mechanical ventilation, she was extubated. Her liver function tests improved within 10 days of hospital admission, and she was subsequently discharged.

Table 1: Patient characteristics

Patient	Case 1	Case 2	Case 3	Case 4
Age (yrs.)	24	28	27	27
Gestational age (Weeks)	36 weeks	37	37	34
NS1	+	+	+	+
IgG/IgM	++/+	++/+	-	++/+
Haematocrit (highest)	31%	30%	36	
Platelet Count (lowest)	17,000	25,000	22000	12000
Platelet transfusion	+++	++	++	+++
SGOT/SGPT (highest)	373/1358	108/78	47/86	2562/2300
Presenting complaints	fever, shock, altered mental status	fever	Fever, Headache, Nausea vomiting	Fever, pain abdomen
Respiratory distress	+ preoperatively	+ in post operative period	-nt	++ preoperatively
Mechanical Ventilation/oxygen therapy	Mechanical ventilation × 2 days	oxygen therapy +	Oxygen therapy +	Mechanical ventilation×3 days
Anaesthesia technique used	GA	GA	GA	GA
APGAR Score	7/10	9/10	9/10	7/10
Dengue serology of baby	Negative	Negative	Negative	Negative

Table 2: Differential diagnoses of dengue in pregnancy

Signs/Symptoms	Normal pregnancy	Dengue	HELLP
Fever	Blunted response	+	-
Bleeding	Bleeding due to obstetric cause	+ mild/severe	Severe DIC
Abdominal pain	±	±	±
Ascites, pleural effusion	-	±	-
Liver enzymes	Mild ↑	Moderate to severe ↑	Mild to moderate↑
WBC	Elevated	Leucopenia	No specific changes
Thrombocytopenia	+	+	+
Haematocrit	↓	↑ in plasma leakage phase/↓ in active bleeding	↓
Homolysis	-	±	+

6. Discussion

Symptomatic dengue infection is a systemic and dynamic disease with a clinical course of three phases i.e., febrile, critical and recovery.[6,7] Most of the serious complications of dengue are seen during the defervescence phase i.e., during transition from febrile to afebrile phase.[6,7] In this case series, two patients were afebrile at presentation to the hospital.

Three of our patients exhibited high levels of IgG and low levels of IgM antibodies, indicating secondary dengue infection.[8] This places them at an increased risk of an exaggerated cytokine cascade response, potentially leading to severe Dengue Haemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS).

The main pathophysiological change observed in dengue is an acute increase in vascular permeability caused by an abnormal immune response and the release of inflammatory cytokines. This leads to plasma leakage and circulatory insufficiency.[9,10] Clinically, our patients presented with shock and polyserositis, resulting in pulmonary effusion and elevated liver enzymes. However, it is important to note that this vascular change appears to be a short and transient functional alteration, as no destructive or inflammatory vascular lesions were observed also in our patients.[10]

The recommended treatment of plasma leakage and shock is fluid and blood resuscitation given to our patient was as recommended by WHO i.e., 8-10 ml/kg for first hour and then 5-7ml/kg for next 1-2 hours and then 3-5 ml/kg for 2-4 hours and 2-3 ml/kg for next 24-48 hours using pre pregnant eight for calculation.[6,7]

In a pregnant patient with Dengue Shock Syndrome (DSS), the physiological changes of pregnancy, such as low haematocrit, tachycardia, and hypotension, complicate fluid management. These changes mask the typical rise in haematocrit and haemoconcentration seen during the defervescence phase of Dengue haemorrhagic Fever (DHF).[11–13]

Patients in critical phases of dengue infection, like those in case 1, 2, and 4, may present with normal haematocrit despite being in a state of shock with reduced perfusion and altered mental status. It is essential not to solely target a normal heart rate and blood pressure or a specific haematocrit level, as this could lead to fluid overload.

If fluid overload occurs, crystalloid transfusion should be stopped, and colloids may be started. In cases of late-stage fluid overload or those with evident pulmonary edema, furosemide 1mg/kg can be administered if the patient's vital signs are stable.[6,7] According to the WHO protocol, patients who receive excessive transfusion during the critical phase with signs of both shock and haemorrhage should be managed with the transfusion of fresh whole blood or packed red blood cells. If significant bleeding occurs, fresh whole blood or fresh packed red cells should be administered as soon as possible, with blood loss limited to 500 ml.[6]

Severe dengue can lead to pulmonary manifestations like pleural effusion, pneumonia and haemoptysis.[14] Dengue haemorrhagic fever and DSS are reported to be third leading cause of ARDS in endemic areas.[14] Cases 1 and 2 involved full-term pregnant patients with positive dengue serology presenting in the critical phase of the illness. Unfortunately, during treatment, both patients experienced fluid overload, leading to pulmonary edema. This can be attributed to the failure to recognize the unique characteristics of dengue in pregnancy, exacerbated by the restricted tolerance for fluid accumulation in the peritoneal and pleural cavities due to the gravid uterus.[4–6] The management approach included fluid overload management, administration of furosemide, and oxygen therapy. While one patient required mechanical ventilation for two days, the other showed improvement with fluid restriction and oxygen therapy. In the case of our third patient, she presented with thrombocytopenia, oligohydramnios, and reduced foetal movements, which could potentially be attributed to dengue infection. This necessitated an emergency Lower Segment Caesarean Section (LSCS) for delivery.

Thrombocytopenia is a common characteristic of dengue and can be caused by various factors, including bone marrow hypo-cellularity, immune complex-mediated platelet destruction, and platelet dysfunction.[15] Surgery during the critical phase of dengue can be complicated by severe thrombocytopenia, coagulopathy, and vasculopathy, increasing the risk of significant bleeding.[16–18] The American College of Obstetrics and Gynaecology (ACOG) recommends platelet transfusion to raise maternal platelet counts above 50,000/μL before major surgery. Epidural and spinal anaesthesia can be considered with a platelet count of 70,000/μL to reduce the risk of epidural hematoma.[19] The Directorate of the national vector-borne diseases control program, Government of India, recommends a transfusion trigger of a platelet count of 10,000/μL, but prophylactic platelet transfusions are not necessary for stable patients with platelet counts below 20,000/μL.[20,21] Studies have shown that prophylactic platelet transfusions in patients with Dengue Shock Syndrome (DSS) may only provide a temporary increase in platelet count, returning to pre-transfusion levels within a few hours.[22,23] In the described cases, the patients' platelet counts were increased to more than 50,000 by transfusion just before surgery and continued during the intra and postoperative period. This approach aimed to manage the thrombocytopenia effectively during the critical phase of dengue.

Hepatitis is a common occurrence in dengue-infected patients, affecting around 60%-70% of cases. While transaminase levels are usually moderately elevated in most patients, about 3%-11% may experience a significant increase of more than 10 times the normal value.[24,25] Case 4 in our study demonstrated a rapid and substantial rise in liver enzymes within just one week from the onset of infection, which has been reported in literature as well.[24,25]

The exact mechanism behind dengue-associated liver injury is not fully understood but could be attributed to the direct effect of the virus or an abnormal immune response.[24,25] Drug-induced injury from medications like acetaminophen or paracetamol, commonly used for fever and myalgia in dengue, could also be a contributing factor. Other potential diagnoses include pregnancy-related conditions like HELPP syndrome, cholestasis of pregnancy, or normal physiological changes during pregnancy (Table 2).

The treatment of dengue-associated liver disorders primarily involves supportive care, including cautious volume replacement, ventilator support, if necessary, antibiotic coverage to prevent bacterial sepsis, and continuous monitoring of coagulation and neurological status.[24,25]

Dengue infection in a pregnant patient is associated with adverse foetal and neonatal effects like vertical transmission of infection to the neonate, low birth weight, oligohydramnios, IUGR and foetal distress.[4,5,26] In our case series, none of the neonates born to dengue-infected mothers showed evidence of dengue infection, with all having negative NS1 reports. However, most of the patients experienced foetal distress and required emergency caesarean delivery, resulting in NICU admission for a day or two.

The literature on anaesthesia management in pregnant patients with dengue is mainly in the form of case reports, and there are no specific guidelines for their anaesthetic management.[16–18] One of the key concerns in these patients is the risk of haemorrhage, so preventing perioperative bleeding is essential, and platelet transfusions should be administered closer to the surgery.[27] Due to the high risk of spinal hematoma in pregnant patients with dengue, general anaesthesia is a safer choice compared to regional anaesthesia.[23]

Understanding the pathophysiology of dengue fever and its critical phases is crucial, as patients may be afebrile but still at risk of progressing from Dengue Haemorrhagic Fever (DHF) to Dengue Shock Syndrome (DSS). The physiologic changes of pregnancy can lead to significant

volume loss, shock, and pulmonary edema without a rise in haematocrit, which requires careful fluid management. Pregnant patients with dengue may experience a marked rise in liver enzymes and thrombocytopenia, which should be differentiated from HELLP syndrome, a pregnancy-related condition. Consequently, fluid and drug dosages should be adjusted accordingly.[28]

Thus, clinicians need to maintain a high index of suspicion when dealing with a pregnant patient presenting with or after a febrile illness, increased liver enzymes, and thrombocytopenia, even in the absence of evidence of Pregnancy-Induced Hypertension (PIH).

7. Conclusion

The key to successful anaesthetic management of a critically ill pregnant patient with dengue or DHF lies in early recognition of the stage of the illness and possible complications. Conservative fluid therapy should be employed, and timely transfusion of blood products should be administered during the perioperative period as needed. Vigilant monitoring and a thorough understanding of the unique characteristics of dengue in pregnancy are essential to ensure optimal outcomes for both the mother and the baby.

Written consent from all patients was taken.

8. Conflict of Interest

There are no conflicts of interest and no sources of funding for this article,

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