

Medical Guidelines

Dengue Guidelines in Pregnancy

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Dengue is the most common viral mosquito-borne disease. It is a major public health problem, especially in tropical and sub-tropical areas. Dengue is now extending into areas with previously lower transmission areas making it a global issue and has been labelled among top ten global health emergencies by WHO. In many parts of the world, dengue affects the adult population. Adults and particularly females of childbearing age are at risk of catching dengue infection and this may impact ongoing and future pregnancies. The effects of dengue during and on pregnancy are unclear, moreover there is a lack of a cohesive reference to inform women of reproductive age who live in or travel to endemic areas and are at risk of contracting dengue. Pregnant women with dengue need early identification and their clinical management requires a multi-disciplinary approach. Timely and precise interventions in dengue infected pregnant women are needed for optimal outcome. Early detection and access to proper medical care in this specific group can reduce complications and mortality.

Clinical Manifestations: Spectrum of Dengue virus infection ranges from asymptomatic to symptomatic forms. Clinically it can manifest as undifferentiated febrile illness, dengue fever (DF), or dengue hemorrhagic fever (DHF) including dengue shock syndrome (DSS). Symptomatic dengue infection can present as either of two clinical entities DF and DHF or are collectively considered as Dengue Illness. Dengue fever (DF) and DHF are distinct from each other as DHF is characterized by plasma leakage due to increased capillary permeability. This plasma leakage is mostly seen in secondary infection due to cytokine storm and is specifically noted in the pleural and peritoneal cavities.¹ When this plasma leakage is massive and not compensated it leads to decreased intravascular volume and may lead to a state of circulatory failure and shock known as Dengue Shock Syndrome (DSS). The duration of leak, known as the 'critical phase' ranges from 24-48 hours. Majority of the dengue illness presents as DF, but the risk of

developing DHF is higher in individuals who have secondary infection with a different serotype. Hemorrhage, though more likely in DHF, is common to both DF and DHF.

Dengue fever (DF) is generally an acute febrile illness with severe headache, retro orbital pain, myalgia, arthralgia and rashes. It is characterized by leucopenia and thrombocytopenia. Although DF is usually benign, it could be incapacitating with severe headache, retro orbital pain, muscle, joint and bone pain, particularly in adults. Occasionally DF patients have unusual hemorrhage such as epistaxis, gastrointestinal bleeding and menorrhagia or occult bleeding. Dengue hemorrhagic fever (DHF) is associated with repeated dengue infection (secondary infection) with a different virus serotype. Unlike in DF where usually patients will have a brief febrile phase followed by convalescent phase, in DHF, patients will have intermediate critical phase where plasma leaks out of vessels into serosal spaces. This leads to decreased intravascular volume and has a tendency to develop hypovolemic shock (DSS). Preceding warning signs such as persistent vomiting, severe abdominal pain, lethargy or restlessness, or irritability and oliguria are important for early detection of impending shock and warrant intervention to prevent shock. Bleeding is more frequently seen in DHF than DF. More recently, there have been reports of DF and DHF with unusual or atypical manifestations.¹

Gestation and Dengue: Dengue illness has been increasingly reported in pregnant women in the last few years. A higher percentage of more severe form of dengue known as Dengue Hemorrhagic Fever (DHF) has been seen among pregnant women compared to non-pregnant women suffering from dengue illness. The overall severity of DHF is also higher in pregnant women as compared to non-pregnant women.²

Dengue has many implications during pregnancy: Acute dengue illness during third trimester can increase the

risk of fetal compromise. This is largely attributed to maternal hemodynamic decompensation which may lead to increased need of surgical intervention for delivery.

In pregnancy with Dengue there is more likelihood of early overt or occult bleeding specially in DHF. Traumatic procedures during delivery, such as instrumentation or surgery will further increase the risk of bleeding. Labour during dengue illness can be associated with worse maternal outcomes as a result of massive bleeding due to surgical interventions such as caesarean section and operative vaginal delivery. Both mother and the newborn with dengue infection, if progress to DSS undetected, may be at an increased risk of severe hemorrhage due to coagulopathy.

Delayed or misdiagnosed DHF/DSS in the early stage can lead to complication and may even cause death. Common causes of death in pregnant women with dengue can be prolonged shock with multi-organ failure, massive bleeding, fluid overload or due to a combination of the above conditions. Vertical transmission among women with dengue during the late pregnancy period is a well-established fact. All babies born to such mothers should be closely observed during perinatal period.

Signs and Symptoms of Dengue Fever³

- Acute onset of high-grade fever (lasting 2-10 days) with headache, retro orbital pain, myalgia, arthralgia, rash, abdominal pain, or bleeding manifestation. Some patients may have anorexia, diarrhea, flu like illness and conjunctival infection.
- Rash looks like flushed skin on day 1 to 2, which may mimic as pregnancy rash.
- Minor bleeding can manifest as petechial hemorrhages, mucosal bleeding or epistaxis. However, bleeding may be heavy in some patients if they are on medications such as Aspirin, NSAIDs, steroids or long-term anti-platelet drugs.
- Occasionally, unusual hemorrhage such as gastrointestinal bleeding, menorrhagia and epistaxis may occur, especially GI bleeding is seen in those having an underlying peptic ulcer disease.
- Physical examination may reveal no focus of infection except facial and skin flushing and positive tourniquet test.
- All suspected patients should be subjected to Complete blood count (CBC) which in dengue infection typically shows leucopenia and thrombocytopenia.
- While NS1 Antigen/IgM Antibody tests will provide an aetiological diagnosis, a negative

result should not exclude dengue if high clinical suspicion is there.

- Dengue viraemia in a patient is short, typically occurring a day or two before the onset of fever and lasts for up to four to seven days of illness. During this period the dengue virus, its nucleic acid and circulating viral antigen can be detected. Viral antigen detection (NS1) has become the most common early diagnostic tool to confirm dengue infection.

NS1 Antigen and IgM/IgG Antibodies: Results depend on the tested day of fever; Ns1 antigen is usually diagnostic on first 3-4 days. Anti-dengue IgM antibody is usually detectable by day 5 of the illness or later. In most patients IgM may persist up to 60 days. In primary infection IgG is usually detectable few days after IgM antibodies and in secondary infection IgG will become positive early. Therefore, IgG might be useful to differentiate primary and secondary dengue infections. If IgG is positive by day 3 it would indicate a secondary infection and may have some use in predicting DHF. If patient is clinically suggestive of dengue, even if NS1 antigen is negative, consider dengue as a possibility and manage accordingly.

Dengue in Pregnancy

The clinical manifestations, treatment and outcome of dengue in pregnant women can be different from those of nonpregnant women. Misdiagnosis or delayed diagnosis are due to some of the overlapping clinical and/or laboratory features with the better recognized conditions of pregnancy like HELLP syndrome, pulmonary embolism, various obstetric causes of per-vaginal bleeding and other infectious diseases.

Early Management and Admission

Suspect Dengue in every pregnant lady coming with high grade fever (specially in endemic countries around monsoon and in tropical countries all year round)

Symptoms of dengue in pregnancy are similar to that in non-pregnant population and include³

- High grade fever
- Headache
- Retro orbital pain
- Bone, Muscle and Joint pains
- Bleeding (epistaxis, gum bleed, hematemesis, hematuria etc)
- Rash (flushed skin or petechiae)
- Nausea, Vomiting and Abdominal pain
- If a patient comes with these symptoms, she is labeled a Suspected case of Dengue infection

- Do baseline CBC on Day 1 and day 2 of fever
- If WBC count $<4000/\text{mm}^3$ along with thrombocytopenia ($<100,000/\mu\text{l}$) it becomes a Probable dengue case
- If first CBC is normal but there is clinical suspicion of Dengue, repeat CBC after 24 hours.
- Label Probable if there is falling trend in WBC or platelet count.

Admission Criteria

- All pregnant patients with probable dengue fever are advised admission⁴

Assessment of Admitted Patients

Febrile Phase: Monitor;

- Temperature charting , Pulse, BP and Pulse pressure 4-6 hourly
- Ensure urine output at least 4-6 hours. (minimum 100 cc every 4 hours)
- Intake Output record.
- Labs: Daily CBC, USG abdomen and for fetal wellbeing and other investigations if necessary.

Treatment of febrile phase

Paracetamol 500-1000mg 6 hourly. Warn the patient that fever may not settle with this dose but NOT to exceed 4 grams paracetamol in 24 hours.^{5,6} NSAID like ibuprofen and diclofenac Sodium should NOT be used.

- Tepid sponging for fever.
- Withhold Aspirin if she is taking it.
- Oral intake is encouraged.
- ORS, fluids, juice all are encouraged apart from routine food.
- If nausea/vomiting of pregnancy, restrict oral intake, give IV fluid (NS) 100 cc/ hour.
- Keep on maintenance fluid around 2 liters/day.
- Platelet count should be kept $>75000/\text{mm}^3$.
- If the patient is in first or second trimester and <37 weeks of gestation, continue the pregnancy with close monitoring
- If the patient is 37 weeks of gestation, patient can be delivered by vaginal delivery or caesarean section depending on the obstetrical indications.
- Arrange platelet concentrate if platelet count is $<75000/\text{mm}^3$.

Critical Phase

It is characterized by warning signs of⁷

- Abdominal pain and tenderness

- Persistent vomiting
- Lethargy
- Restlessness
- Tender hepatomegaly (Liver >2 cm enlarged)
- Capillary Refill Time >2 sec.
- Decreased urine output.
- Mucosal Bleed: epistaxis, gum bleed petichae.
- Rise in HCT (20% of baseline) (If baseline is not known consider 36 as baseline).
- If any of these signs develop, label the patient in critical phase and shift to High Dependency Unit (HDU).

Monitor

- Vitals(BP /Pulse/Pulse pressure, Capillary Refill) hourly
- Ultrasound abdomen for any fluid leak and obstetric ultrasound to document fetal wellbeing. Ultrasound can also be used to measure size of IVC and its collapsibility, sign of hypovolemic shock or fluid overload.
- Catheterize to know precise UOP hourly (Aim 0.5ml/kg/hour).

Treatment⁶

- Start fluid therapy.
- Bolus of 5-10ml/kg/hour X 2 hours given followed by 3-5ml/kg/hr as a maintenance.
- This is monitored by UOP and Pulse pressure
- Avoid induction of labour/ planned surgery in this phase.

Dengue Shock Syndrome⁸

- These patients should be managed in ICU setting.
- Timely appropriate fluid management can save life.

Timing and Mode of Delivery

- Pregnant women with symptomatic dengue infection have a slightly higher risk of maternal death as compared to pregnant women without dengue, and this risk is considerably higher with DHF.
- If possible elective delivery should be postponed till patient is out of critical phase of disease.
- If delivery is inevitable, bleeding should be anticipated and closely monitored.
- Mode of delivery must be decided according to obstetrical indications.

- Normal vaginal delivery is preferred method over operative delivery.
- Tocolytic agents and measures to postpone labor to a suitable time may be considered during the critical phase of dengue illness.

Preparation for Delivery⁹

- Blood and blood products should be cross-matched and saved in preparation for delivery.
- Transfusion of platelet concentrates should be initiated during or at delivery but not too far ahead of delivery, as the platelet count is sustained by platelet transfusion for only a few hours during the critical phase.
- Fresh whole blood/fresh packed red cells transfusion should be administered as soon as possible if significant bleeding occurs.
- Do not wait for blood loss to exceed 500ml before replacement, as in postpartum hemorrhage. Do not wait for the hematocrit to decrease to low levels
- Fetal monitoring must be done by continuous electronic FHR monitoring.
- Progress of labour must be evaluated by partogram.
- Operative delivery should be avoided during critical phase.
- If delivery is unavailable platelet count must be above $50,000 \times 10^3/\text{mm}^3$.
- Consultant obstetrician must conduct operative or instrumental delivery to keep the trauma or injury to the minimum.
- It is essential to check for complete removal of the placenta after delivery.
- Oxytocin infusion should be commenced to contract the uterus after delivery to prevent postpartum hemorrhage. Misoprostol may be given for PPH prophylaxis/treatment.
- Intramuscular injections are to be avoided.
- No steroids should be given.

Post Delivery Care¹⁰

- Keep under strict observation.
- Strict monitoring for BP, Pulse, pulse pressure and urine output.
- Observation regarding Post-Partum Hemorrhage.
- Prophylactic use of uterotonic drugs like Oxy-

tocin and Misoprostol is indicated.

- If delivery occur in less than seven days from appearance of symptoms of dengue fever, then risk of vertical transmission is high.
- Baby should be evaluated for congenital Dengue.
- Breast feeding is not contraindicated in Dengue fever.

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