SMFM Update on Oropouche Virus Disease in Pregnancy
August 23, 2024

This guidance was developed by the Society for Maternal-Fetal Medicine Committee on Infectious Diseases and Emerging Threats with the assistance of Naima Joseph MD, MPH and Brenna Hughes MD, MSc.

On August 16, 2024, the Centers for Disease Control and Prevention issued a Health Alert Network (HAN) Health Advisory to notify clinicians and public health authorities of an increase in Oropouche virus (OROV) disease, originating from endemic areas and in new areas in South America and the Caribbean.[1] OROV is usually transmitted through insect bites and causes a mild, self-limiting illness in most people. Vertical transmission of OROV is possible, and reported cases of OROV disease during pregnancy have been associated with pregnancy loss or congenital anomalies.[1] There are no currently available vaccines or curative treatments for OROV.[1] Due to the risk of perinatal transmission and possible adverse pregnancy outcomes, pregnant people are advised to avoid nonessential travel to high transmission and endemic areas or to deploy personal protective strategies if travel is warranted.[1]

The Society for Maternal-Fetal Medicine (SMFM) continues to monitor the outbreak closely and will provide updated guidance as necessary. The following are interim clinical considerations.

Key Highlights

- Outbreaks of OROV have been reported in endemic areas and new regions in South America and the Caribbean.
    - The CDC has issued a Level 1 Travel Health Notice for Bolivia, Brazil, Colombia, and Peru.
    - The CDC has issued a Level 2 Travel Health Notice for Cuba.
- OROV is spread through bites of infected midges and possibly mosquitos.
- OROV disease is usually symptomatic and recurrent and presents with fever, arthralgia, and myalgia. It rarely progresses to hemorrhagic or neuroinvasive disease. Treatment is supportive.
- Infection during pregnancy may be associated with vertical transmission, miscarriage, stillbirth, or congenital anomalies, such as microcephaly.
- Health providers must contact their state or local health departments to submit blood or other samples for OROV testing.

Summary of Recommendations

- In the setting of confirmed maternal infection during pregnancy, an early fetal anatomical survey and serial fetal growth surveillance should be considered when feasible.
- Pregnant people should be counseled to avoid nonessential travel to endemic areas or areas experiencing outbreaks.

- Pregnant people traveling to high-risk areas should be advised to use personal protection such as long sleeves, pants, DEET-containing insect repellent registered by the Environmental Protection Agency, window and door screens, and outdoor fans.

Introduction

Arboviral infections have re-emerged in South America in the past decade, initially with the large Zika outbreaks in 2015 and 2016 and recurrent outbreaks of chikungunya and dengue.[1] Most recently, OROV has re-emerged at an unprecedented scale.

Between January 1 – August 1, 2024, more than 8,000 cases of OROV disease have been reported in Bolivia, Brazil, Columbia, and Peru, as well as for the first time in Cuba and Haiti.[1, 2]

OROV is a member of the Orthobunyavirus genus and was first identified in 1955. Since then, the virus has had limited circulation in parts of South America, with cases reported in settings close to forested areas. However, the current OROV outbreak has infected people living in regions far from forested areas. It is transmitted primarily through bites from small midges (*Culicoides paraensis*) as well as possibly some mosquitoes, including the *Culex* and *Aedes* species (which also transmit West Nile virus).[1,2]

Clinical Presentation

Approximately 60% of persons infected with OROV become symptomatic. The incubation period is 3 to 10 days. Most cases of Oropouche disease are mild, with symptoms similar to dengue, including abrupt-onset fever, severe headache, myalgia, arthralgia, chills, rash, and nausea. Initial symptoms resolve within a few days; however, as many as 70% of patients will experience recurrent symptoms within days to weeks after resolution of their initial illness.[1]

Most people infected with OROV will have a mild illness. Up to 5% develop a hemorrhagic illness, characterized by gingival bleeding and petechial rash, or a neuroinvasive disease, such as meningitis or meningoencephalitis. Fatality is rare; the first two reported deaths were in young, nonpregnant women without medical comorbidities or risk factors.[1,2] It is unknown how the clinical presentation or severity of the disease differs during pregnancy or how the timing of infection during pregnancy impacts OROV disease outcomes.

Risk of Vertical Transmission

In July 2024, Brazilian authorities alerted the Pan American Health Organization regarding suspected vertical transmission and adverse pregnancy outcomes, specifically the risk of pregnancy loss and congenital anomalies in six pregnancies.[3]

In one case, a patient at 30 weeks of gestation developed symptoms and tested positive for OROV by real-time polymerase chain reaction (RT-PCR). The patient re-presented two weeks later with decreased fetal movement, and fetal demise was confirmed. Placental and fetal tissue samples were RT-PCR positive for OROV and negative for other arboviruses (ie, dengue, chikungunya). In a second case, a patient presented in the early first trimester with symptoms, and serum RT-PCR testing confirmed OROV disease. Spontaneous miscarriage occurred two weeks later, in the eighth week of gestation.[3] Pregnancy tissue was not available for testing.[3]

Also reported were four cases of infants with microcephaly who underwent testing after cerebrospinal fluid (CSF) returned negative for Zika, dengue, and chikungunya but positive for OROV immunoglobulin (IgM).

Although these data are insufficient to establish a causal relationship between OROV infection and congenital anomalies, data suggest that perinatal transmission occurs. SMFM supports the CDC recommendation that pregnant people reconsider nonessential travel to areas with an Oropouche Level 2 Travel Health Notice. If travel must occur to areas with Level 1 or Level 2 Travel Health Notices, pregnant travelers should deploy personal protective strategies (See CDC Travel Health Notices).[1,4]

Diagnostic Testing

A case definition of OROV infection in regions also experiencing endemic circulation of other highly prevalent arboviruses (ie, dengue, chikungunya) is only possible with the use of OROV-specific serological or molecular laboratory tests, which are not currently commercially available in the US. Preliminary diagnosis is based on the patient's clinical symptoms and epidemiologic risk factors, such as recent travel to or from an endemic country. As was initially the case with the diagnosis of Zika virus infection, plaque reduction neutralization tests (PRNT) can be performed to detect virus-specific neutralization antibodies that are usually present after the first week of infection. Currently, confirmatory testing can be obtained through PRNT testing of both acute and convalescent samples (serum, CSF, or both).

CDC and other public health laboratories are currently working to validate additional diagnostic assays. Health providers must contact their state or local health departments to submit blood or other samples for OROV testing.[5] Notably, any initially positive testing requires confirmatory evaluation, and final test reports may take three weeks.

In many countries, outbreaks of dengue are also occurring in areas with reported OROV transmission.[1] For patients with suspected OROV disease, it is important to evaluate concomitantly for dengue virus infection because proper clinical management of dengue, which has a case-fatality rate as high as 10%, can improve health outcomes.[1] Other diagnostic considerations include chikungunya, Zika, leptospirosis, malaria, or infections caused by various other bacterial or viral pathogens native to OROV-endemic regions.[1]

Treatment

Currently, there are no available curative OROV treatments.[1,6] Supportive treatment includes rest, fluids, analgesia, and antipyretic medications. Clinicians should be on high alert for patients who develop obstetric symptoms, neurologic symptoms, or a new rash and consider inpatient observation in these cases or patients at high risk for adverse outcomes (eg, medical comorbidity such as hypertension, diabetes, chronic pulmonary disease, immunosuppressed state, hemoglobinopathy).[1]

Fetal Surveillance

Currently, there is no role for prenatal diagnostic testing. The data to guide fetal surveillance are currently insufficient. The potential risks to the fetus and appropriate follow-up should inform

the timing of infection during pregnancy and co-existing risks for adverse outcomes. In the setting of confirmed maternal infection during pregnancy, an early fetal anatomic ultrasound and serial fetal growth surveillance should be considered when feasible.[1,7] Evaluation of fetal neuroanatomy should be performed during sonographic surveillance.[1,7]

To facilitate postnatal care and treatment, obstetric care clinicians should alert the appropriate neonatal care team with clinical concerns. Delivery at an institution capable of providing advanced neonatal resuscitation should be considered. SMFM will continue to monitor cases of vertical transmission and update its recommendations for fetal surveillance as indicated.

Prevention

There are no vaccines available to prevent OROV disease.[1,6] Pregnant people are advised to avoid nonessential travel to areas with an OROV Level 2 Travel Alert.[1,4] Personal protective strategies are advised for those who must travel, including wearing long-sleeved pants and shirts and using EPA-registered DEET-containing insect repellant, window and door screens, and outdoor fans. [1,6] Pregnant persons can be counseled that DEET is safe to use during pregnancy.[8]

References

1. Centers for Disease Control and Prevention. Health Alert Network Notice. *Increased Oropouche Virus Activity and Associated Risk to Travelers*. August 16, 2024. https://emergency.cdc.gov/han/2024/han00515.asp. Accessed August 23, 2024.
2. The Lancet Infectious Diseases. Oropouche fever, the mysterious threat. Lancet Infect Dis. 2024 Aug 8:S1473-3099(24)00516-4. doi: 10.1016/S1473-3099(24)00516-4.
3. Pan Health American Organization. World Health Organization. Epidemiological Alert Oropouche in the Region of the Americas: vertical transmission event under investigation in Brazil. July 17, 2024. https://www.paho.org/en/documents/epidemiological-alert-oropouche-region-americas-vertical-transmission-event-under Accessed August 23, 2024.
4. Centers for Disease Control and Prevention. Travel Health Notices. https://wwwnc.cdc.gov/travel/notices Accessed August 23, 2024.
5. Centers for Disease Control and Prevention. Interim Guidance for Health Departments on Testing and Reporting for Oropouche Virus Disease. August 16, 2024. https://www.cdc.gov/oropouche/php/reporting/index.html, Accessed August 23, 2024.
6. Centers for Disease Control and Prevention. Preventing Oropouche. August 2, 2024. https://www.cdc.gov/oropouche/prevention/index.html Accessed August 23, 2024.
7. Centers for Disease Control and Prevention. Interim Clinical Considerations for Pregnant People with Confirmed or Probable Oropouche Virus Disease. August 16, 2024. https://www.cdc.gov/oropouche/hcp/clinical-care-pregnancy/index.html Accessed August 23, 2024.
8. Wylie BJ, Hauptman M, Woolf AD, Goldman RH. Insect Repellants During Pregnancy in the Era of the Zika Virus. Obstet Gynecol. 2016 Nov;128(5):1111-1115. doi: 10.1097/AOG.0000000000001685.

Suggested Citation: Society for Maternal-Fetal Medicine (SMFM). SMFM Update on Oropouche Virus Disease in Pregnancy. Washington, DC: SMFM; 2024. Available at: https://www.smfm.org/oropouche-fever. Retrieved [enter date].