

Herpes Simplex Virus Infection During Pregnancy



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KEYWORDS

- Genital herpes • Pregnancy • Antiviral therapy • Prevention • Neonatal herpes
- Serologic screening

KEY POINTS

- Genital herpes is common, with 22% of pregnant women seropositive for herpes simplex virus (HSV)-2.
- An increasing number of genital herpes infections are due to oral-labial transmission of HSV-1.
- Women with a primary infection of HSV-1 or HSV-2 at the time of delivery have a 57% risk of neonatal herpes infection.
- Neonatal herpes is rare, occurring in less than 1 in 3000 live births, but has high mortality and poor neurologic outcome for disseminated disease.
- Antiviral prophylaxis is recommended to suppress recurrent herpes infection in women from 36 weeks until delivery.
- Cesarean section should be performed if an active primary or recurrent herpes outbreak is suspected at delivery, to prevent neonatal transmission.
- There is an unclear role of routine serologic screening for HSV-1 and HSV-2 during pregnancy.

BACKGROUND

The herpesviruses are double-stranded DNA viruses that include several clinically important viruses during pregnancy: herpes simplex virus (HSV), varicella zoster virus, and cytomegalovirus. Herpesviruses encode most of the enzymes required for

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replication and, can establish latency by replicating in slowly or nondividing cells such as neurons. Herpes simplex virus types 1 (HSV-1) and 2 (HSV-2) glycoproteins mediate cellular infection, and glycoprotein G on the viral envelope provides the antigenic specificity that allows for detection of distinct antibodies for HSV-1 and HSV-2. HSV is transmitted via direct mucosal contact, and results in replication in the dermis and epidermis. The primary infection may include painful vesicles or ulcers in the genital tract, fever, lymphadenopathy, dysuria or other nonspecific genitourinary symptoms, or may lack symptoms entirely. Eventually the virus infects the sensory ganglia and persists in a latent form. Reactivation of viral replication may occur periodically for life. Recurrent infections may have a more mild presentation, ulcerative lesions, subtle genitourinary symptoms, asymptomatic lesions, or viral shedding without clinically apparent lesions.

PREVALENCE OF GENITAL HERPES

Genital herpes is one of the most common sexually transmitted diseases. HSV-1 causes gingivostomatitis and keratoconjunctivitis, whereas both HSV-1 and HSV-2 can cause genital herpes. The National Health and Nutrition Examination Survey (NHANES) serologic data from 1988 to 2004 estimated that 22% of pregnant women were seropositive for HSV-2, 63% for HSV-1, and 13% for both HSV-1 and HSV-2¹; this was the first time that the prevalence of HSV-2 had decreased since the inception of NHANES in 1976. Of the women seronegative for HSV-2 during pregnancy, 10% will have an HSV-2 seropositive partner, putting them at risk for acquisition during pregnancy.²

The most recent NHANES data from 2005 to 2010 continue to show a decline in the seroprevalence of HSV-1 (53.9%) and HSV-2 (15.7%) in adults aged 14 to 49 years.³ HSV-1 continues to be more common in women (33.2%) and minority populations such as Mexicans (58.3%) and non-Hispanic blacks (39.6%).³ From the 2007-2010 NHANES data, 20.3% of women versus 10.6% in men have HSV-2. Non-Hispanic black women have the highest rates of HSV-2 (49.9%).⁴ There is no clear explanation for the racial disparity in HSV-2 infection, which has persisted over time.

The declining seroprevalence of HSV-1 with fewer infections in childhood in developed countries and the increase in oral-labial sexual contact has resulted in an increase in HSV-1 genital infections in young women and adolescents, which accounts for up to 80% of new genital herpes infections in college students.⁵ The declining seroprevalence of HSV-1 and HSV-2 increases the risk of primary HSV infection among seronegative pregnant women, the primary risk factor for neonatal herpes transmission.

Poor Correlation Between Symptoms and Infection

Because of the heterogeneous and often asymptomatic nature of primary or recurrent genital herpes infections, up to 90% of persons with serologic evidence of HSV-2 do not report a clinical history of the infection.⁶ Neither a basic nor detailed clinical history correlates with HSV-2 infection by serology.⁷ Signs and symptoms are not able to accurately predict primary herpes infections.⁸ The presence of lesions has a poor correlation with detection of genital tract HSV by culture or polymerase chain reaction (PCR).⁹ These issues create a major diagnostic dilemma for obstetric providers caring for pregnant women who are at risk for primary or recurrent genital herpes infections. While genital herpes is an ongoing cause of maternal morbidity during pregnancy, the real dilemma is how to effectively prevent peripartum herpes transmission. This aspect has been made more complicated by the changing epidemiology of maternal herpes infections (HSV-1 vs HSV-2)¹⁰ and challenges with clinical diagnosis.

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