

# Oral Herpes Simplex Virus Infection in Pregnancy: What Are the Concerns?

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## ABSTRACT

Although epidemiologic data and the potentially serious effects of transmission of *genital* herpes from mother to infant during birth have been widely reported, published reports on *oral* herpes disease in pregnancy remain scarce and no clear management guidelines exist. Thus, questions remain about acquisition, transmission and outcome of infection, especially with respect to acute gingivostomatitis in pregnancy. In response to these questions, we summarize previous reports on herpes simplex virus 1 (HSV-1) oral disease in pregnancy and, briefly, present 2 cases of primary gingivostomatitis in the first trimester of pregnancy, resulting in a favourable outcome for both mother and infant. We also point out the most recent data on rare, potentially severe in outcome, but treatable, primary central nervous system HSV-1 infection in later stages of pregnancy. Finally, we emphasize a multidisciplinary approach to oral HSV disease in pregnancy, with dentist participation in the diagnosis and treatment.

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Herpes simplex virus (HSV) types 1 and 2 are among the most ubiquitous viruses in the adult population, in the form of overt or latent infections. In immunocompetent people, the most common manifestations of HSV infections are uncomplicated and localized to the oral<sup>1</sup> or genital<sup>2</sup> area. HSV-2 is known as the primary cause of genital herpes, while HSV-1 is the main cause of oral herpes, including acute herpetic gingivostomatitis (mostly as primary infection) and herpes labialis (recurrent or secondary infection). However, HSV-1 has emerged increasingly frequently as an agent in genital herpes in some populations, and this may have an impact on acquisition of HSV infection in pregnancy.<sup>3-5</sup>

Both primary and secondary genital HSV infections may develop during pregnancy, with potentially severe consequences to the

fetus or neonate. If transmitted to the embryo or fetus, these infectious agents may cause, albeit rarely, early embryonic or fetal damage, with or without miscarriage, or major congenital or developmental anomalies.<sup>6</sup> If acquired intrapartum (during the passage through the birth canal), neonatal HSV infection often develops, usually between the first and fourth weeks of age. Without prompt effective treatment, the infected neonate progresses to potentially fatal disseminated multi-organ involvement, often with central nervous system (CNS) involvement, such as fulminant encephalitis.<sup>7,8</sup>

Literature on the subject of oral HSV infections is particularly scarce, probably not because of a lack of interest in the problem, but more likely because of the relative rarity of overt oral HSV infection in pregnancy.



**Figure 1:** Multiple oral ulcers on gingiva and palate, as seen in primary herpetic gingivostomatitis in a woman in the eighth week of pregnancy.



**Figure 2:** Lip lesions in primary herpetic gingivostomatitis in a woman in the 13th week of pregnancy.

All the cases described in an earlier series<sup>9-12</sup> indicate that HSV-1 gingivostomatitis in the first, second and third trimester of pregnancy is not associated with adverse fetal effects. With respect to recurrent herpes labialis (RHL) before and during pregnancy, one study even showed a lower than average proportion of preterm births among affected mothers,<sup>13</sup> and another allowed the conclusion that pregnant women with a history of RHL report a reduced incidence of RHL during pregnancy.<sup>14</sup> Further, according to a recently published large, population-based study, self-reported maternal herpes labialis during pregnancy is not associated with a substantially increased risk of neural tube defects in infants.<sup>15</sup>

### HSV Gingivostomatitis in the First Trimester of Pregnancy

Below we describe 2 previously unpublished cases of HSV-induced primary herpetic gingivostomatitis in women who acquired the disease during the first trimester of gestation. The documentation, oral clinical presentation, laboratory results and outcome were similar in the 2 cases. Observations support the assertion that with primary HSV-1 gingivostomatitis, at least during the first trimester, it is reasonable to expect a normal gestational course with a normal delivery and a good neonatal outcome.

To identify other cases of primary herpetic gingivostomatitis associated with pregnancy, we reviewed the files of the Reference Centre for the Study of Oral Diseases in Florence, Italy. The wide range of oral diseases seen at this centre includes oral cancer and precancer, infections and related conditions including those of HIV-associated immunosuppression, as well as salivary gland dysfunction, autoimmune dermatoses and bone diseases. Each year 2,300–2,500 new patients are seen. For the current study, we had access to records for 8 years, from 1988 to 2006. In spite of the knowledge that herpes virus infections are extremely contagious, among all the files of this busy urban reference centre for oral diseases within this

time span, we were able to find only 2 cases of acute herpetic gingivostomatitis during pregnancy. This would be consistent with an assumed low incidence of HSV-1 infection in pregnancy.

The diagnosis of herpetic gingivostomatitis was based on clinical manifestations (typical ulcerations on any oral mucosal surface, accompanied by lymphadenopathy and systemic symptoms) and laboratory findings.

#### Case 1

In September 1998, a 33-year-old woman was referred to our centre in week 8 of her first pregnancy because of multiple oral ulcers associated with fever of 3 days duration, nausea and anorexia. Oral examination revealed multiple ulcerations on the fixed gingiva, dorsum of tongue, vestibular and palatal mucosa (**Fig. 1**) in addition to cervical lymphadenopathy. HSV was isolated from the oral ulcers by viral culture. Microscopic examination of the cytological smears showed features typically seen in herpes infection, such as ballooning degeneration, margination of chromatin and multinucleation. The patient had no previous history of oral or genital herpes infection.

In consultation with the obstetrician, oral acyclovir (400 mg 5 times a day for 7 days) was offered to the patient. After 7–8 days, her oral condition returned to normal, and she was able to eat and drink without pain. The patient underwent a program of fetal monitoring until term and gave birth to a healthy boy in week 39 of pregnancy. At a follow-up interview in June 2007, she reported that the child was in perfect physical and mental health.

#### Case 2

In December 2005, a 26-year-old woman in week 13 of her pregnancy presented to our hospital with complaints of high fever, sore throat and eating and drinking difficulties that had started 4 days earlier. Oral examination showed multiple ulcerations on the attached gingiva, palatal mucosa and vermilion border of both lips (**Fig. 2**) in addition to enlarged cervical and submandibular lymph nodes. HSV-1, but not HSV-2, was isolated from the oral ulcers by polymerase chain reaction (PCR) investigation. Cytology revealed typical features of herpes infection, although the patient had no previous history of oral or genital herpes infection. She was treated with oral acyclovir, 800 mg 5 times a day for 7 days. The oral ulcers healed completely after 6–7 days of treatment. The patient was placed on a strict follow-up schedule by her obstetrician with periodic ultrasound evaluation. There was no ultrasonographic evidence of fetal abnormalities.

At gestational week 38, the patient gave birth to a healthy boy. At follow-up in June 2007, the child was in excellent physical and mental health.

### Herpetic Encephalitis in Late Pregnancy

In a recent case study and review, Sellner and colleagues<sup>16</sup> point out that the most common infectious agent of acute, sporadic encephalitis is HSV-1 (10%–20% of all cases in the United States) as either primary infection or reactivation of the virus. Although herpetic encephalitis in pregnancy is rare, it is most likely to occur in the late second and early third trimester of pregnancy. The triad signs of viral encephalitis have been described as fever, headache and altered mental state. Other common manifestations are seizures, hemiparesis and aphasia. Empirical treatment with antibacterial and antiviral agents is often required before a specific diagnosis is made by viral culture and PCR from cerebrospinal fluid. Before the era of antiviral therapies, the prognosis for the mother and fetus was poor, but intravenous acyclovir therapy improved diagnosis and critical care have reduced mortality significantly. However, even with treatment, the long-term neurological sequelae of CNS disease in survivors remain a problem.<sup>16,17</sup>

### Conclusions

In spite of the probably favourable outcome of oral HSV-1 infection, at least in the first trimester, and the rarity of potentially severe CNS HSV-1 infection, the following concerns should be kept in mind in relation to pregnancy:

- the risk of acquisition and development of fulminant HSV-1 disease, which is higher than in the general population, because of physiological immunosuppression in pregnancy<sup>16,18</sup>
- the risk of misdiagnosis, without prompt recognition of symptoms as those of HSV infection, and immediate initiation of treatment
- the possibility of non-peripartum modes of HSV-1 transmission to the infant, from oral lesions by direct contact with health personnel<sup>19</sup>

In view of these issues, understanding the significance of maternal oral herpes infection during pregnancy remains critically important. The primary responsibilities of the dentist with respect to oral HSV infection in general and HSV infection in pregnancy in particular, remain as follows:

- maintain strict infection control in the dental office
- be familiar with and promptly recognize manifestations
- be prepared to collect samples of oral lesions promptly for viral culture and type-specific laboratory diagnosis

- be prepared to refer the patient and participate in the treatment, management and monitoring of oral manifestations, in close consultation with the family physician, infectious disease specialist and obstetrician
- make patient education (as reviewed earlier)<sup>1</sup> an integral part of prevention as well as management

Although reactivation of oral HSV infection with routine dental treatment is common, previous research by Miller and colleagues<sup>20</sup> has shown that human herpes viruses, including HSV-1, are present in the saliva of healthy adults at levels that could facilitate transmission. Their data indicate that prophylactic treatment with valacyclovir (2 g taken twice on the day of dental treatment and 1 g taken twice the next day) significantly reduces the percentage of patients who develop recurrences and shed HSV-1 in saliva 72 hours after dental procedures and reduces the mean time to pain cessation.<sup>21</sup> Based on these findings, the authors recommend that clinicians consider prophylactic antiviral therapy for patients at risk, to minimize recurrences as well transmission of the disease.

With respect to efficacy and safety of antiviral prophylaxis for preventing HSV primary infection or recurrence in the third trimester, the concerns of clinical trials to date have been limited largely to the problem of genital herpes,<sup>3,22,23</sup> but it appears that treatment with acyclovir and valacyclovir is reasonably safe and effective. In view of this, it would be reasonable to extend the recommendations of Miller and colleagues to pregnant women with a history of oral recurrent HSV infections. Clearly, postponing dental treatment should be considered first. ♦

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