Invasive Obstetric Procedures and Cesarean Sections in Women with Known Herpes Simplex Virus Status During Pregnancy

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INTRODUCTION

Neonatal herpes (nHSV) is a potentially devastating infection of newborns exposed to herpes simplex virus (HSV) type 1 or 2 in the maternal genital tract at the time of birth. The reported incidence of nHSV ranges from 8 to 60 cases per 100,000 live births in the US.[1-6] Although rare, nHSV may result in severe disability or death in an otherwise healthy newborn, making it as clinically significant as neonatal group B streptococcus or HIV infection. To date, prevention efforts have focused on avoiding neonatal exposure to HSV in genital secretions by performing cesarean delivery (c-section) for women with genital lesions at the time of labor. While this method likely prevents some cases of nHSV, it cannot be used to prevent infection among neonates exposed to HSV in women without signs or symptoms of genital herpes.[1] Yet epidemiologic data suggest that most cases of nHSV occur among such asymptomatic women and that women who become infected with HSV during the third trimester of pregnancy are at highest risk of transmitting HSV to their neonates.[1,7,8] Intrapartum procedures, such as assisted vaginal delivery or use of fetal scalp electrodes, can break the fetal skin and increase the risk of HSV exposure in the genital tract, thus increasing the risk of nHSV infection.[1,9] Membrane rupture also contributes to risk.[10] Avoiding intrapartum procedures in women with antibodies to HSV-2 could decrease risk of nHSV.

HSV antibody testing identifies women with HSV infection, and maternal HSV antibody testing may be helpful in identifying neonates at risk of intrapartum HSV exposure. However, routine prenatal testing for HSV antibody is not currently recommended.[11] Prenatal testing for HSV antibody status, in addition to eliciting clinical history, could inform provider decision-making at delivery and decrease the use of intrapartum procedures associated with increased nHSV risk in asymptomatic women with genital HSV infection. One concern about such a screening strategy is that it may increase the rate of c-section delivery among such women.[12,13] The actual impact of prenatal screening for maternal genital HSV infection on the use of intrapartum procedures and c-section in asymptomatic women is not known.

To our knowledge, the University of Washington Medical Center (UWMC) is the only large medical institution in the world where HSV antibody testing is routinely included in prenatal screenings. This policy provides a unique opportunity to evaluate the effect of maternal HSV testing. We hypothesized that women in labor with known HSV-2 antibody positivity or a clinical history of genital herpes but without active genital lesions were less likely than uninfected women to undergo intrapartum procedures that could increase the risk of nHSV.

We also hypothesized that infected women were no more likely than uninfected women to undergo intrapartum c-section.

METHODS

Subjects and setting

We conducted a retrospective cohort study of 750 consecutive deliveries performed in 2006 at the UWMC, a quaternary care referral center serving the Pacific Northwest that performs approximately 2,000 deliveries per year. We reviewed charts using a standardized data collection form and abstracted data on HSV antibody result, clinical history of genital herpes, use of intrapartum procedures, and final method of delivery. Data on demographics, underlying conditions and complications of pregnancy or delivery were also collected. A subset of charts was audited to confirm accuracy of data collection. Only women with available chart data on HSV antibody result or genital herpes history were included in the analysis. Women with active genital lesions suspicious for HSV during labor were excluded. Women with non-vertex fetal presentation were excluded as this was assumed, *a priori*, to be very strongly associated with c-section.

Women undergoing scheduled c-sections were also excluded from the analysis. Decisions for scheduling c-section are made, by definition, prior to labor. Women delivering by scheduled c-section are not at risk for intrapartum procedures, and the impact of genital HSV infection status on provider decisions during labor cannot be evaluated in these women. Although women with active lesions were already excluded, as noted above, we were concerned that some women may have been scheduled for c-section because of genital herpes. In our dataset, of all women with a scheduled c-section, the indication was prior c-section in 76.3%. Indications in the remaining 23.7% were largely a mix of fetal anomalies, macrosomia, and maternal anatomic abnormalities. HSV was listed as a secondary indication for scheduled c-section in two of these women: one who had a primary indication of history of fetal shoulder dystocia in a prior delivery and another who underwent a planned repeat c-section. As there was a primary indication for scheduled c-section unrelated to HSV in both of these cases, it was assumed that both women would have had scheduled c-sections regardless of HSV status and the exclusions were judged to be valid.

Exposures and outcomes

We defined the exposure of interest as HSV-2 antibody positivity or known history of genital herpes (HSV-2/GH) noted in the prenatal and delivery records. HSV serology was determined using the University of Washington Western Blot Assay. We further categorized the exposure based on use of suppressive antiviral therapy for HSV at delivery, as we assumed this could modify any effect of HSV-2/GH status on provider behavior, and thus on the outcomes of interest. Antiviral therapy typically consisted of acyclovir or valacyclovir. Since orolabial infection with HSV-1 is common in the general population, we grouped women with only HSV-1 antibody among those without any HSV antibody, in the absence of a known history of genital lesions. The primary outcome, intrapartum procedures use, was a composite of the following: use of fetal scalp electrode, artificial rupture of membranes, intrauterine pressure catheter, vacuum extraction, or forceps extraction at delivery. The secondary outcome was intrapartum c-section as the final method of delivery.

We also extracted demographic characteristics of the women and other aspects of the medical and obstetric history. These included data on parity, prematurity, gestational number, failure to progress in labor, group B streptococcus culture, induction of labor, placental abruption, fetal distress, high-risk pregnancy, and other sexually transmitted diseases (STD). Prematurity was defined as delivery before 37 weeks. High-risk pregnancy was defined by the presence of any one of several maternal and fetal factors. Maternal factors included asthma, diabetes (including gestational), hypertension (including pregnancy-induced), pre-eclampsia, renal disease, and cardiac disease. Fetal factors included oligohydraminios, intrauterine growth restriction, and congenital anomalies. STD data specifically included any history of syphilis, gonorrhea, chlamydia, trichomonas, or human papilloma virus diagnosis during pregnancy.

Statistical Analysis

We used the X^2 test to compare proportions and the t-test to compare means. We calculated odds ratios (OR) and 95% confidence intervals (CI) using logistic regression and performed bivariate analyses of the associations between HSV-2/GH and the primary and secondary outcomes for women receiving and not receiving suppressive antiviral therapy at time of delivery. We also explored associations between other covariates and each outcome that may confound the association of HSV-2/GH and the outcomes. Two-sided p-values less than or equal to 0.05

were considered significant. For each outcome, we constructed an initial multivariate logistic regression model incorporating the exposure of interest, HSV-2/GH, and covariates that showed possible associations ($p \leq 0.1$) with that outcome in bivariate analysis. The final multivariate models were prepared by backwards elimination from each model of covariates lacking a strong association with the outcome ($p > 0.05$). The statistical analysis was carried out using STATA versions 9 and 10 (StataCorp, College Station, TX).

Study Power

We assumed that approximately 80% of reviewed charts would have available data on the exposure of interest, as some participants may not have undergone HSV antibody testing. From preliminary data, we also estimated a 14% overall prevalence of the exposure, HSV-2/GH, in the study population. Although the risk of undergoing several of the intrapartum procedures is less than 10%, on an individual basis, in a given delivery, the risk of a composite outcome of undergoing any intrapartum procedure is approximately 40% at our center. For an outcome with a 40% probability, we had 80% power to detect odds ratios less than 0.47 or greater than 1.96.

Human Subjects Research Review

The University of Washington Institutional Review Board approved the study. The requirement for written, informed consent was waived, as this study was a retrospective partial record review in which data were coded after abstraction, and thus the study was judged to pose minimal risk to the subjects.

RESULTS

We identified 606 women with available data on HSV-2/GH status after reviewing 750 charts. Of the women missing such data, only 39.7% had received prenatal care at UWMC, with many presenting late in pregnancy or during labor, whereas 91.7% of women with complete data had received UWMC prenatal care. After excluding women with active genital lesions (2), women with non-vertex fetal presentations (55), and women undergoing scheduled c-section (100), 449 women were included in the analysis. Of these, 97 (21.6%) had HSV-2/GH. Sixty (61.9%) were seropositive for HSV-2 without recorded clinical history of genital herpes, and 33 of these were on suppressive antiviral therapy at delivery. Thirty-seven women (38.1%) had a clinical history of genital herpes, and

24 of them were on suppressive antiviral therapy. A total of 40 women (41.2%) with HSV-2/GH were not receiving any suppressive antiviral therapy. Figure 1 summarizes the selection of the population for analysis. No cases of nHSV were detected.

The mean age of all women included in the analysis was 30.2 years. Compared to women without HSV-2/GH, a larger proportion of women with HSV-2/GH were not married at time of delivery, and there were fewer Caucasian and more African American women among those with HSV-2/GH (Table 1).

Figure 2 displays the proportions of women who underwent intrapartum procedures and c-section according to exposure group. Of the 40 women with HSV-2/GH who were not receiving antiviral therapy, 16 (40.0%) underwent intrapartum procedures. Thirty-five (61.4%) of 57 women with suppressed HSV-2/GH and 203 (57.7%) of 352 women without HSV-2/GH underwent intrapartum procedures (global p = 0.08). Comparable proportions of women underwent unplanned c-sections, regardless of risk group, as follows: 12 (30.0%) of 40 women with unsuppressed HSV-2/GH, 16 (28.1%) of 57 women with suppressed HSV-2/GH, and 88 (25.0%) of 352 without HSV-2/GH (global p = 0.73).

Women with HSV-2/GH who were not on suppressive antiviral therapy for HSV were less likely to undergo intrapartum procedures than women without HSV-2/GH (OR 0.49; 95%CI: 0.25, 0.95; p = 0.036). However, we did not detect a difference in the rate of intrapartum procedures for women with HSV-2/GH on suppressive therapy as compared with women without HSV-2/GH (OR 1.17; 95%CI: 0.66, 2.07; p = 0.60). Women ages 39 and older were much less likely to undergo intrapartum procedures than women 20 years and younger (OR 0.11; 95%CI: 0.04, 0.35; p = <0.001). Intrapartum procedures were used less frequently in multiparous women than in primiparous women (OR 0.62; 95%CI: 0.42, 0.90; p = 0.01) and in women with multiple gestation pregnancies compared with women with singleton pregnancies (OR 0.23; 95%CI: 0.09, 0.60; p = 0.003). Prematurity was associated with a decreased likelihood of intrapartum procedures use (OR 0.46; 95%CI: 0.29, 0.73; p = 0.001), but failure to progress in labor was associated with an increased likelihood (OR 2.22; 95%CI: 1.21, 4.08; p = 0.01). Covariates examined for associations with intrapartum procedures that were not significant on bivariate analysis included Hispanic ethnicity, marital status, high-risk pregnancy, obesity, infection with another STD during pregnancy, group B streptococcus culture-positive, fetal distress, placental abruption, and induction of labor.

Compared with Caucasian woman, African American women were as likely (OR 1.02; 95%CI: 0.59, 1.77; p = 0.95) and Asian women were more likely (OR 1.88; 95%CI: 1.09, 3.26; p = 0.02) to undergo intrapartum procedures. Women categorized as biracial or of other racial backgrounds were examined as a single category; these women appeared much more likely to undergo intrapartum procedures (OR 14.74; 95%CI 1.93, 112.58; p = 0.01). Of the 17 women coded as "biracial/other," 16 had an intrapartum procedure.

On multivariate analysis, after adjusting for age, race, prematurity and failure to progress in labor, the association between HSV-2/GH status and intrapartum procedures in women was attenuated and no long statistically significant. The adjusted odds of intrapartum procedures in women with unsuppressed HSV-2/GH were 31% lower than those of women without HSV-2/GH (OR 0.69; 95%CI: 0.34, 1.41; p = 0.31), and the adjusted odds of intrapartum procedures in women with suppressed HSV-2/GH were 45% higher than those of women without HSV-2/GH (OR 1.45; 95%CI: 0.77, 2.72; p = 0.26), but neither of these findings reached statistical significance. Results of bivariate and multivariate analyses of intrapartum procedures are presented in Table 2. To examine the effect of race on the model, the analysis was repeated excluding the "biracial/other" category and again excluding the entire race covariate, but these had only a minor impact on the adjusted OR.

Potential predictors of intrapartum c-section were also explored. On bivariate analysis, we were unable to detect any significant increase in likelihood of intrapartum c-section for women with unsuppressed (OR 1.29; 95%CI: 0.63, 2.64; p = 0.49) or suppressed HSV-2/GH (OR 1.17; 95%CI: 0.63, 2.19; p = 0.62) relative to women without HSV-2/GH. Multiparity was associated with a decreased likelihood of undergoing intrapartum c-section (OR 0.53; 95%CI: 0.35, 0.82; p = 0.004), but high-risk pregnancy was associated with an increased likelihood (OR 1.89; 95%CI: 1.22, 2.92; p = 0.004). Multiple gestation (OR 4.51; 95%CI: 1.94, 10.47; p < 0.001), prematurity (OR 1.81; 95%CI: 1.10, 2.97; p = 0.02), and chorioamnionitis (OR 3.38; 95%CI: 1.58, 7.25; p = 0.002) were all associated with an increased likelihood of intrapartum c-section. Covariates not found to have a significant association with intrapartum c-section on bivariate analysis included age, race, Hispanic ethnicity, marital status, obesity, other sexually transmitted disease during pregnancy, group B streptococcus culture positive, preterm rupture of membranes, placental abruption, and induction of labor.

After adjusting for parity, high-risk pregnancy, and multiple gestation pregnancy in a multivariate model, we did not detect a significant increase in the likelihood of intrapartum c-section in women with HSV-2/GH. This was true regardless of whether they were receiving (OR 1.21; 95%CI: 0.63, 2.33; p = 0.57) or not receiving suppressive antiviral therapy (OR 1.13; 95%CI: 0.51, 2.50; p = 0.76). Results of the bivariate and multivariate analyses of intrapartum c-section are presented in Table 3.

DISCUSSION

Strategies to identify pregnant women at risk of transmitting HSV during delivery are controversial.[12-14] No prior studies have evaluated the role of prenatal HSV screening programs in nHSV prevention efforts. We explored the impact of a prenatal HSV testing program at the University of Washington on the use of intrapartum procedures that increase risk of nHSV. In our study, fewer asymptomatic pregnant women with antibodies to HSV-2 or a clinical history of genital herpes underwent intrapartum procedures if they were not receiving antiviral suppression, when compared with women who lacked HSV-2 antibodies or a history of genital herpes. In contrast, women with antibodies to HSV-2 or a clinical history of genital herpes who received suppressive therapy were as likely to undergo intrapartum procedures as women without the exposure. The decreased risk of undergoing intrapartum procedures observed in women not on suppressive therapy was attenuated after adjusting for age, race, multiparity, prematurity, and failure to progress in labor. In particular, older women and women categorized as "biracial/other" were more likely to have HSV-2 antibodies or a clinical history of genital herpes and were less likely to undergo intrapartum procedures than younger women, although this may be explained in part by differences in parity.

Shedding of HSV in the maternal genital tract during labor, by itself, poses substantial risk of nHSV, but prolonged amniotic membrane disruption, vacuum-assisted delivery, and fetal scalp monitors have also been shown to increase the risk to the neonate.[1,9,10] Collectively, these studies strongly suggest that any intrapartum instrumentation that can breach the infant skin should be avoided in the setting of possible maternal mucosal HSV shedding. Currently, practice guidelines suggest using suppressive antiviral therapy for women with a history of recurrent genital HSV lesions in pregnancy.[11] Antiviral therapy for HSV from week 36 to delivery has been shown to reduce viral shedding, genital herpes recurrences and the rate of c-section use, but evidence that this strategy prevents nHSV is lacking.[15-20] Furthermore, in the last 2 decades, a period in which this approach has been increasingly popular, there has been no change in the incidence of nHSV in the US.[1-6] This is consistent with the observation in non-pregnant women with genital HSV infection that antiviral therapy reduces but does not eliminate subclinical HSV shedding from genital mucosa.[21,22] A recent series reported 8 cases of nHSV in infants whose mothers received antiviral suppression at the end of pregnancy.[23] Thus management of women with genital herpes with antiviral therapy does not abrogate the risk of nHSV. The findings from our study suggest that providers modify their use of intrapartum procedures that increase risk of nHSV in asymptomatic women with known, unsuppressed genital HSV infection, but that women who are receiving suppressive antiviral therapy are considered to be at low risk and are managed similarly to women without genital HSV infection. Improved provider education about the risks of intrapartum procedures and breakthrough nHSV despite suppressive therapy is warranted.

We also investigated the impact of prenatal HSV testing on the use of intrapartum c-sections. Pregnant women with HSV-2 antibodies or a clinical history of genital herpes but without active lesions underwent intrapartum c-sections with the same frequency as other women. Use of antiviral suppressive therapy did not affect this outcome. Not surprisingly, women with multiple gestation pregnancies and high-risk pregnancies were more likely to undergo intrapartum c-section, whereas the outcome was less likely in multiparous women. This finding provides important evidence to inform debates about prenatal HSV testing. C-section delivery is recommended for women who have active genital herpes lesions at term.[11] However, one feared potential consequence of prenatal HSV testing is increased use of c-section in women with asymptomatic genital HSV infection.[12,13] There is no evidence to support the use of c-section in asymptomatic women to prevent nHSV, thus such an increase could consist of unnecessary operative interventions. We did not observe such an increase in intrapartum c-sections in our cohort of women undergoing prenatal HSV testing.

This study offers the first evidence that routine prenatal HSV testing does not result in harm by increasing c-sections and that such testing may benefit women who are identified as HSV-2 antibody positive. Specifically, our data suggest that providers may be more wary of use of intrapartum procedures that could increase the risk of HSV transmission to neonates delivered by asymptomatic women with known genital HSV infection. Although most obstetricians believe nHSV merits systematic prevention strategies, few report performing regular prenatal HSV antibody testing outside of academic settings.[24] In addition to c-section use, costs and psychosocial burdens of prenatal HSV testing have been put forth as concerns.[12-14] Cost-effectiveness models of nHSV prevention strategies that include prenatal HSV-2 antibody testing are conflicting, although the most recent models are more favorable.[14,25-28] With regard to the psychosocial burden, in a recent systematic review of studies exploring the impact of HSV-2 antibody testing in asymptomatic persons, most participants testing positive did not suffer sustained emotional harm.[29] In pregnancy, the motivation to be tested may be higher as there is a desire to protect the fetus. Of note, studies assessing the acceptability such programs suggest pregnant women are amenable to prenatal HSV testing.[30-32] More targeted prenatal HSV screening would likely miss a substantial proportion of cases.[2] However, routine prenatal screening alone is unlikely to impact the incidence of nHSV, because the greatest risk occurs in women who acquire genital herpes late in pregnancy and lack detectable HSV antibodies at delivery.[1] Further strategies need to be developed to identify women who are infected near the time of delivery and are asymptomatic.

Our study has several limitations. Observational data are subject to the effects of unmeasured confounding, and a randomized trial of prenatal HSV testing would be necessary to address this problem. The size of the study population also limited our approach to the analysis in several ways. We could not assess nHSV as an outcome. A much larger study would be needed for this, as it is uncommon to have many nHSV cases in a single center in a single year. In addition, in order to provide more statistical power, we combined all women with evidence of genital HSV infection regardless of prior symptom history, as long as they were asymptomatic at delivery. It is possible that providers treat women with a clinical history of genital herpes differently from HSV-2 antibody positive women without any such history, but we were unable to explore that possibility with this analysis. Of note, in our population, suppressive antiviral therapy was administered to some HSV-2 antibody positive women without a clinical history of genital herpes. The other consequence of the study population size was that we lacked the power to assess the effect of the exposure on individual intrapartum procedures. Combining these outcomes may have masked differing associations between the exposure and individual procedure use. There are also inherent limitations to using chart data to assess provider behavior. We were unable to measure provider decision-making directly using this approach. Also, although the charts likely reflect the majority of intrapartum procedures used, it is possible that some interventions were not recorded. Lastly, this study was conducted at an academic medical center with strong institutional knowledge of nHSV disease and risk factors. The impact of prenatal HSV testing programs, in the absence of clear guidelines for management of asymptomatic women with genital HSV infection, could differ substantially by setting.

CONCLUSION

Improved interventions are needed to reduce or eliminate nHSV in neonates delivered by asymptomatic women with genital HSV infection. In our study, identification of these women with a routine prenatal testing program reduced the use of procedures known to increase nHSV risk in women not on antiviral suppression. We envision prenatal HSV testing as one component of any successful combination nHSV prevention strategy. Fortunately, we have shown that prenatal HSV testing does not increase the use of intrapartum c-section, and concerns about this appear to be unwarranted. While a vaccine or new antiviral medication that more effectively suppresses genital HSV shedding may eventually become available, immediate strategies for nHSV prevention are required, such as use of rapid polymerase chain reaction to detect HSV shedding at delivery.[33] Prenatal HSV screening should be a part of such strategies.

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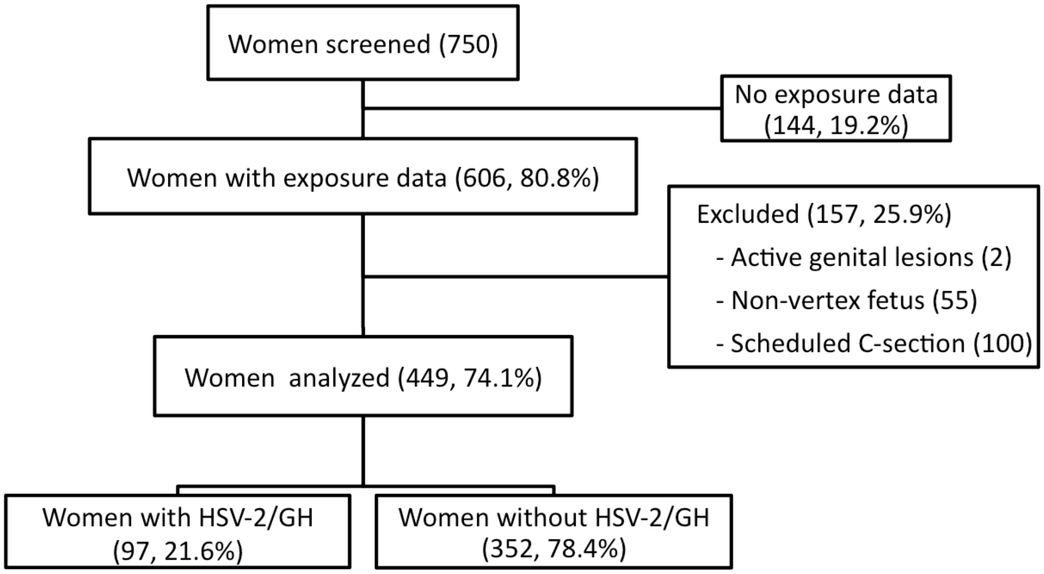
A.



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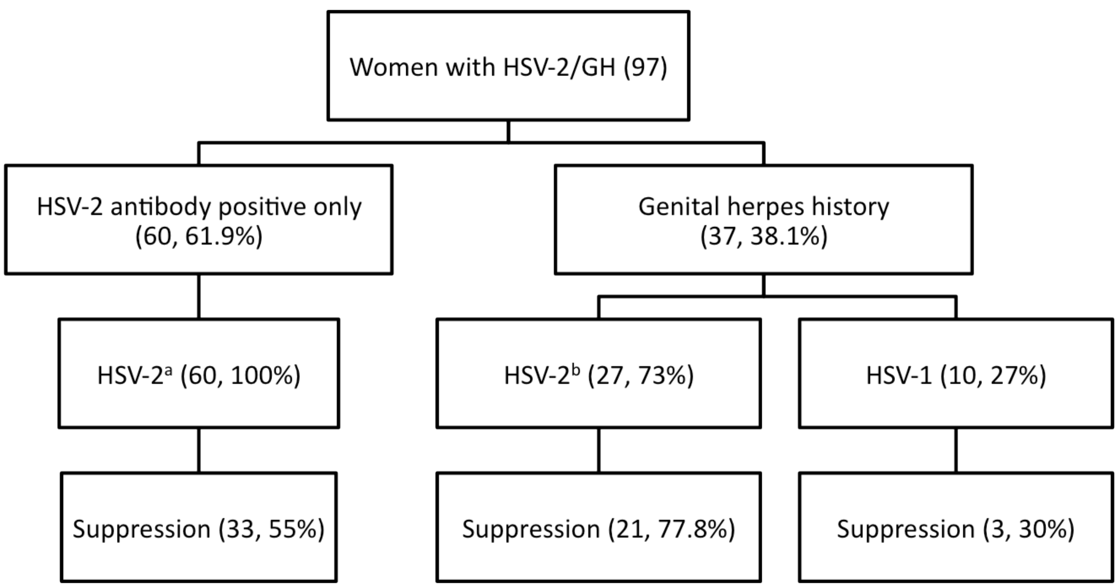

Figure 1. Part A shows a flow diagram of study participant selection. Charts were reviewed from 750 women with consecutive deliveries at UWMC in 2006, of which 606 had exposure data. After excluding women with active genital lesions, non-vertex fetal presentation, and scheduled c-sections, 449 women were included in the analysis. Of these, 97 (21.6%) had HSV-2/GH. Part B shows the distribution of HSV-2 antibody positivity and clinical history of genital herpes in the 97 women with HSV-2/GH. Women with a clinical history are further divided into those who were HSV-2 antibody positive and those positive for antibodies to HSV-1 only. The distribution of the 57 women (58.8%) on suppressive anti-HSV therapy is also shown. Abbreviations: C-section, cesarean section; HSV, herpes simplex virus; HSV-2/GH, HSV-2 antibody positive or with a history of genital herpes.

[a] HSV-1 antibodies detected in 39 (65%)

[b] HSV-1 antibodies detected in 14 (51.9%)

Table 1. Demographic and clinical factors of women included in analysis. N = 449 except as noted.

Factor	HSV-2/GH: Yes, n (%)[a]	HSV-2/GH: No, n (%)[a]	Total	p[b]
All subjects	97 (21.6)	352 (78.4)	449	
Antiviral suppression	57 (58.8)			
No antiviral suppression	40 (41.2)			
Mean Age (n = 448)	31.1	30.0	30.2	0.126[c]
Race (n = 440)				< 0.001
African American	27 (28.1)	34 (9.9)	61 (13.9)	
Asian	10 (10.4)	60 (17.4)	70 (15.9)	
Caucasian	55 (57.3)	237 (68.9)	292 (66.4)	
Biracial/other	4 (4.2)	13 (3.8)	17 (3.9)	
Hispanic Ethnicity (n = 434)	7 (7.5)	37 (10.9)	44 (10.1)	0.347
Non-Hispanic	86 (92.5)	304 (89.2)	390 (89.9)	
Married (n = 446)	53 (55.2)	272 (77.7)	325 (72.9)	< 0.0001
Not married	43 (44.8)	78 (22.3)	121 (27.1)	
Multiparous	55 (56.7)	163 (46.3)	218 (48.6)	0.070
Primiparous	41 (43.3)	189 (53.7)	231 (51.5)	
Premature	25 (25.8)	65 (18.5)	90 (20.0)	0.111
Not premature	72 (74.2)	287 (81.5)	359 (80.0)	
Multiple gestation (n=442)	7 (7.4)	17 (4.9)	24 (5.4)	0.347
Singleton	88 (92.6)	330 (95.1)	418 (94.6)	
High-risk condition[d]	58 (59.8)	181 (51.4)	239 (53.2)	0.143
No high-risk condition	39 (40.2)	171 (48.6)	210 (46.8)	
HSV-1 antibody positive (n=441)	62 (66.7)	223 (64.1)	285 (64.6)	0.643
HSV-1 antibody negative	31 (33.3)	125 (35.9)	156 (35.4)	
Any intrapartum procedure	51 (52.6)	203 (57.7)	254 (56.6)	0.370
No intrapartum procedure	46 (47.4)	149 (42.3)	195 (43.4)	
Intrapartum procedure by type				
Fetal scalp electrodes	10 (10.3)	51 (14.5)	61 (13.6)	
AROM	35 (36.1)	144 (40.9)	179 (39.9)	
IUPC	27 (27.8)	89 (25.3)	116 (25.8)	
Vacuum extraction	4 (4.1)	11 (3.1)	15 (3.3)	
Forceps extraction	4 (4.1)	6 (1.7)	10 (2.2)	
Intrapartum cesarean section	28 (28.9)	88 (25.0)	116 (25.8)	0.441
Vaginal delivery	69 (71.1)	264 (75.0)	333 (74.2)	

Abbreviations: HSV, herpes simplex virus; HSV-2/GH, HSV-2 antibody positive or clinical history of genital herpes; AROM, artificial rupture of membranes; IUPC, intrauterine pressure catheter.

[a] Column percents as a subset of the total for each covariate presented; percents may not sum to 100% due to rounding.

[b] Calculated with X^2 test except as noted

[c] Two-sided t-test

[d] Asthma, diabetes, hypertension, pre-eclampsia, renal or cardiac disease, intrauterine growth restriction, oligohydramnios, congenital anomaly

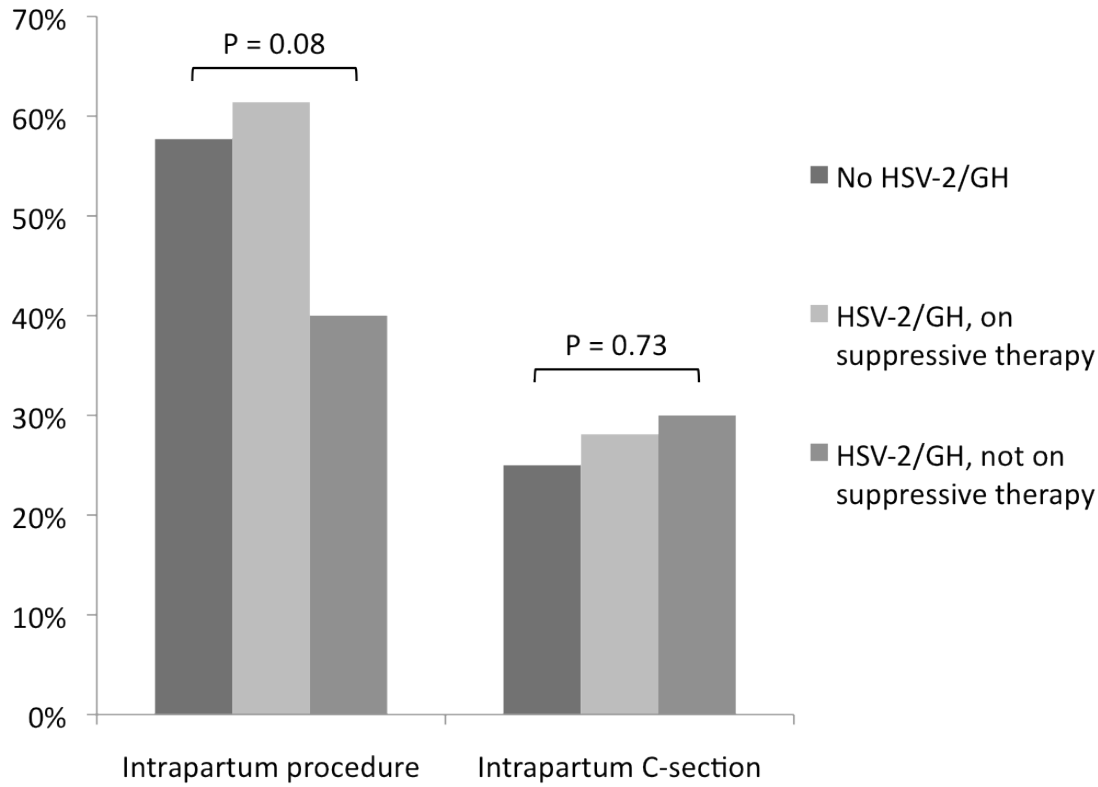

Figure 2. Proportions of women undergoing intrapartum procedures and intrapartum c-section, by risk group, are shown. Risk groups include asymptomatic women with and without HSV-2 antibody positivity or a clinical history of genital herpes (HSV-2/GH). Women with HSV-2/GH are further stratified by whether or not they were receiving suppressive antiviral therapy at delivery. Global p values for differences between groups are shown. Abbreviations: C-section, cesarean section; HSV, herpes simplex virus; HSV-2/GH, HSV-2 antibody positive or with a clinical history of genital herpes.

Table 2. Predictors of invasive obstetric procedure[a] use at delivery

N=449[b]	Invasive procedure: Yes, n (%)[c]	No, n (%)[c]	OR (95% CI)	p	aOR (95% CI)	p
HSV-2/GH status						
Uninfected	149 (76.4)	203 (79.9)	Ref	0.08[d]	Ref	0.25[d]
Antiviral suppression	35 (13.8)	22 (11.3)	1.17 (0.66, 2.07)	0.60	1.45 (0.77, 2.72)	0.26
No suppression	16 (6.3)	24 (12.3)	0.49 (0.25, 0.95)	0.04	0.69 (0.34, 1.41)	0.31
Age (years)						
≤ 20	24 (9.5)	8 (4.1)	Ref	<0.001[d]	Ref	0.01[d]
21 to 38	222 (87.4)	163 (83.6)	0.45 (0.20, 1.04)	0.06	0.51 (0.21, 1.25)	0.14
≥ 39	8 (3.2)	24 (12.3)	0.11 (0.04, 0.35)	<0.001	0.15 (0.05, 0.50)	0.002
Race (N=440)						
Caucasian	152 (61.5)	140 (72.5)	Ref	0.01[d]	Ref	0.03[d]
Asian	47 (19)	23 (11.9)	1.88 (1.09, 3.26)	0.02	1.84 (1.04, 3.25)	0.04
African American	32 (13)	29 (15)	1.02 (0.59, 1.77)	0.95	1.17 (0.64, 2.14)	0.62
Biracial/Other	16 (6.5)	1 (0.5)	14.74 (1.93, 112.6)	0.01	11.35 (1.46, 88.5)	0.02
Hispanic (N=434)	25 (10.2)	19 (10.1)	1.02 (0.54, 1.91)	0.96		
Married (N=446)	186 (73.8)	139 (71.7)	1.11 (0.73, 1.70)	0.61		
Multiparous	110 (43.3)	108 (55.4)	0.62 (0.422, 0.90)	0.01	0.65 (0.42, 0.99)	0.05
High-risk[e]	134 (52.8)	105 (53.9)	0.96 (0.66, 1.39)	0.82		
Obesity	30 (11.8)	24 (12.3)	0.95 (0.54, 1.69)	0.87		
Multiple gest. (N=442)	6 (2.4)	18 (9.5)	0.23 (0.09, 0.60)	0.003		
Other STD[f]	21 (8.3)	23 (11.8)	0.67 (0.36, 1.26)	0.22		
GBS positive (N=421)	69 (28.8)	57 (31.5)	0.88 (0.58, 1.34)	0.54		
Premature	37 (14.6)	53 (27.2)	0.46 (0.29, 0.73)	0.001	0.43 (0.26, 0.72)	0.001
Failure to progress	42 (16.5)	16 (8.2)	2.22 (1.21, 4.08)	0.01	1.98 (1.03, 3.82)	0.04
Fetal distress	22 (8.7)	25 (12.8)	0.65 (0.35, 1.18)	0.16		
Placental abruption	2 (0.8)	5 (2.6)	0.30 (0.06, 1.57)	0.16		
Induction of Labor	58 (22.8)	42 (21.5)	1.08 (0.69, 1.69)	0.74		

Abbreviations: OR, odds ratio; aOR, odds ratio adjusted for age, race, multiparity, prematurity, failure to progress in labor; Ref, reference category; HSV-2/GH, herpes simplex virus type 2 seropositive or clinical history of genital herpes; STD, sexually transmitted disease; GBS, group B streptococcus culture.

[a] Fetal scalp electrode, artificial rupture of membranes, intrauterine pressure catheter, vacuum extraction or forceps extraction
[b] Except where noted otherwise
[c] Percentages may not sum to 100% because of rounding
[d] Global P value for all categories
[e] Asthma, diabetes, hypertension, pre-eclampsia, renal or cardiac disease, intrauterine growth restriction, oligohydramnios, congenital anomaly
[f] Syphilis, gonorrhea, Chlamydia, trichomonas, or human papilloma virus diagnosed during pregnancy

Table 3. Predictors of intrapartum cesarean section use at delivery

N=449[a]	Unplanned c-section: Yes, n (%)[b]	No, n (%)[b]	OR (95% CI)	p	aOR (95% CI)	p
HSV-2/GH status						
Uninfected	88 (75.9)	264 (79.3)	Ref	0.73[c]	Ref	0.83[c]
Antiviral suppression	16 (13.8)	41 (12.3)	1.17 (0.63, 2.19)	0.62	1.21(0.63, 2.33)	0.57
No suppression	12 (10.3)	28 (8.4)	1.29 (0.63, 2.64)	0.49	1.13 (0.51, 2.50)	0.76
Age (years)						
≤ 20	6 (5.2)	26 (7.8)	Ref	0.36[c]		
21 to 38	99 (85.3)	286 (85.9)	1.50 (0.60, 3.75)	0.39		
≥ 39	11 (9.5)	21 (6.3)	2.27 (0.72, 7.16)	0.16		
Race (N=440)						
Caucasian	84 (72.4)	208 (64.2)	Ref	0.38[c]		
Asian	14 (12.1)	56 (17.3)	0.62 (0.33, 1.17)	0.14		
African American	15 (12.9)	46 (14.2)	0.81 (0.43, 1.52)	0.51		
Biracial/Other	3 (2.6)	14 (4.3)	0.53 (0.15, 1.89)	0.33		
Hispanic (N=434)	11 (9.6)	33 (10.3)	0.92 (0.45, 1.9)	0.81		
Married (N=446)	85 (73.3)	240 (72.7)	1.03 (0.64, 1.66)	0.91		
Multiparous	43 (37.1)	175 (52.6)	0.53 (0.35, 0.82)	0.004	0.51 (0.32, 0.80)	0.003
High-risk[d]	75 (64.7)	164 (49.3)	1.89 (1.22, 2.92)	0.004	1.95 (1.23, 3.08)	0.003
Obesity	17 (14.7)	37 (11.1)	1.37 (0.74, 2.55)	0.31		
Multiple gest. (N=442)	14 (12.4)	10 (3.0)	4.51 (1.94, 10.47)	<0.001	4.56 (1.92, 10.81)	0.001
Other STD[e]	9 (7.8)	35 (10.5)	0.72 (0.33, 1.54)	0.39		
GBS positive (N=421)	31 (29.0)	95 (30.3)	0.94 (0.58, 1.52)	0.80		
Premature	32 (27.6)	58 (17.4)	1.81 (1.10, 2.97)	0.02		
PPROM	6 (5.2)	11 (3.3)	1.60 (0.58, 4.42)	0.37		
Placental abruption	2 (1.7)	5 (1.5)	1.15 (0.22, 6.01)	0.87		
Chorioamnionitis	15 (12.9)	14 (4.2)	3.38 (1.58, 7.25)	0.002		
Induction of Labor	25 (21.6)	75 (22.5)	0.95 (0.57, 1.58)	0.83		

Abbreviations: OR, odds ratio; aOR, odds ratio adjusted for multiparity, high-risk pregnancy, multiple gestation; Ref, reference category; HSV-2/GH, herpes simplex virus type 2 seropositive or clinical history of genital herpes; STD, sexually transmitted disease; GBS, group B streptococcus culture; PPROM, preterm premature rupture of membranes.

[a] Except where otherwise noted
[b] Percentages may not sum to 100% because of rounding
[c] Global P value for all categories
[d] Asthma, diabetes, hypertension, pre-eclampsia, renal or cardiac disease, intrauterine growth restriction, oligohydramnios, congenital anomaly
[e] Syphilis, gonorrhea, Chlamydia, trichomonas or human papilloma virus diagnosed during pregnancy