OBSTETRICS

Seroprevalence of herpes simplex virus types 1 and 2 in pregnant women in the United States

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OBJECTIVE: The purpose of this study was to determine seroprevalence of herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) in a national cross-sectional sample of pregnant women.

STUDY DESIGN: Pregnancy tests (urine and serum) were performed for female patients 12-59 years of age who participated in the National Health and Nutrition Examination Survey from 1999-2002. Immunodot assays were used to detect antibodies to HSV-1 and HSV-2.

RESULTS: The mean age of the 626 pregnant women was 27 years, and the median number of lifetime sex partners was 4. Overall, HSV-1 seroprevalence was 63%; HSV-2 seroprevalance was 22%; infection with both HSV-1 and HSV-2 was 13%, and HSV seronegativity was 28%. HSV seroprevalence differed by race/ethnicity, with nonHispanic white patients more likely to be seronegative compared with other racial/ethnic groups (40% vs 11%; $P < .001$). The number of lifetime sex partners was also associated with serostatus. On the basis of serostatus-specific rates of neonatal herpes from a published study, the rate of neonatal herpes is projected to be 33/100,000 live births and is 40% higher in nonHispanic white women than in other racial/ethnic groups.

CONCLUSION: The seroprevalence of HSV-1 and HSV-2 varied by race/ethnicity; babies born to nonHispanic white mothers, whose HSV seroprevalence was the lowest, appear to be at greater risk for neonatal herpes.

Key words: herpes simplex virus, neonatal infection, seroprevalence, neonatal herpes

Cite this article as: Xu F, Markowitz LE, Gottlieb SL, Berman SM. Seroprevalence of herpes simplex virus types 1 and 2 in pregnant women in the United States. Am J Obstet Gynecol 2007;196:43.e1-43.e6.

Neonatal herpes is a potentially devastating infection caused by herpes simplex virus type 1 (HSV-1) or type 2 (HSV-2).[1,2] Because neonatal herpes is acquired usually at the time of delivery rather than early in gestation, it is a disease that should be amenable to prevention. The risk for transmission to the neonate from an infected mother is high (30-50%) among women who acquire a new HSV infection near the time of delivery.[3] Thus, the prevention of acquisition of genital HSV infection during late pregnancy is important for the prevention of neonatal herpes. Among women who acquire genital HSV before the third trimester of pregnancy, the risk of transmission to the neonate is low (< 1%).[3-5] For such mothers, prevention of neonatal herpes depends on avoiding exposure of the infant to recurrent herpetic lesions during delivery.

★ EDITORS' CHOICE ★

Most women (60-80%) who deliver infants with neonatal herpes infection have no signs, symptoms, or history of genital herpes.[4,6] Studies suggest that the risk of neonatal infection tends to be higher in pregnant women who are seronegative for both HSV-1 and -2,[3,5] which reflects the susceptibility for the acquisition of primary HSV infection in late pregnancy.[7] Some specialists recommend screening all pregnant women with type-specific serology tests to identify those women with unrecognized HSV-1 or -2 infections and those women who are still at risk for becoming infected.[8,9] Prevention efforts such as careful examination for herpetic lesions at the onset of labor, with delivery by cesarean section in women with lesions, can then be more focused. For women who are still at risk for the acquisition of HSV during pregnancy, counseling messages aimed at reducing the acquisition of HSV infection in late pregnancy are especially important. We estimated the seroprevalence of HSV-1 and -2 in a national sample of pregnant women in the United States and examined key factors that are associated with HSV-1 infection, HSV-2 infection, and HSV seronegativity. We also projected the rate of neonatal herpes by demographic characteristics of the mothers on the basis of HSV serostatus-specific rates of neonatal herpes from a recent published study.

Materials and Methods

National Health and Nutrition Examination Surveys (NHANES) are a series of cross-sectional national surveys conducted by the National Center for Health Statistics. Details of the survey methods have been published previously.[10] In brief, a nationally representative sample of the US civilian noninstitutionalized population was selected with the use of a complex, stratified, multistage probability sample design. Some populations, such as adolescents, Mexican American women, and pregnant women were oversampled. Persons who were selected

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Received March 7, 2006; accepted July 6, 2006.

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0002-9378/$32.00
Published by Mosby Inc.
doi: 10.1016/j.ajog.2006.07.051

TABLE 1
The distribution by demographic factors in the sample of pregnant women in our analyses (n = 626) and in all women who gave birth in the United States in 2000 (n = 4,058,814)

Demographic variable	Pregnant women in our analyses (%)	All births in the United States in 2000: mothers' characteristics (%)*
Race/ethnicity		
NonHispanic white	57.9	58.2
NonHispanic black	15.3	14.9
Mexican American	13.5	14.3
Other	13.3	12.6
Age ≤ 20 y	13.2	11.8
Education > high school	77.1	78.3

* Data on all births were from the report published by Martin JA, Hamilton BE, Ventura SJ, Menacker F, Park MM. Births: final data for 2000. National vital statistics reports; vol 50, no. 5. Hyattsville (MD): National Center for Health Statistics; 2002.

for the surveys were interviewed and underwent a health examination in mobile examination centers.

In the NHANES conducted from 1999-2002, all persons 14-59 years of age were interviewed about sexual behavior. The questionnaire was administered with audio computer-assisted self-interview in a private room. As part of the survey examination, pregnancy tests (urine and serum) were performed for female participants 12-59 years of age and menstruating girls aged 8-11 years. Only persons aged 14-49 years were tested for HSV antibodies. Of participants aged 14-49 years who were originally selected for the survey, 83% were interviewed, 79% were examined, and 72% were tested for HSV-1 and -2.

Laboratory methods

A rapid chromatographic immunoassay (Icon 25 human chorionic gonadotropin [urine/serum] test kit; Beckman Coulter Inc, Fullerton, CA) was used for qualitative detection of human chorionic gonadotropin in urine and serum. The test uses a combination of monoclonal and polyclonal antibodies to detect selectively elevated levels of human chorionic gonadotropin in urine or serum.

We used purified glycoprotein specific for HSV-1 (gG-1) and HSV-2 (gG-2) antigens to detect type-specific antibodies using the solid-phase enzymatic immunodot assays.[11,12] The performance of the immunodot assays is high, with respect to sensitivity and ability to discriminate between HSV-1 and HSV-2.[11-13]

Statistical analyses

SUDAAN software (release 9.0; Research Triangle Institute, Cary, NC) was used for statistical analyses to account for the complex survey design. All prevalence or seroprevalence estimates were weighted to represent the noninstitutionalized civilian US population and to account for oversampling and nonresponse to the interview and the examination.[14] The standard weights for survey examination published by the National Center for Health Statistics were used for all analyses. Confidence intervals (CIs) for the seroprevalence estimates were calculated based on a log transformation, with the standard error (SE) calculated by the delta method.[15] In NHANES 1999-2002, race/ethnicity categories were defined by self-report as nonHispanic black (NH-black), nonHispanic white (NH-white), and Mexican American. Persons who did not fit into these categories were classified as "Other" and were included in the total population.

RESULTS

In NHANES 1999-2002, a total of 704 women had a positive pregnancy test or reported being pregnant. Of these, 700 women were between 14-49 years of age; HSV serology results were available for 626 women (89%). The reasons for missing HSV serology test results included refusal or unsuccessful venipuncture or the need to use serum for other tests. Pregnant women with and without HSV test results were not statistically different with respect to age, race/ethnicity, or education level.

Among the 626 women with HSV serology results available, the mean age was 27 years (range, 15-41 years). The median number of lifetime sex partners was 4 (mean, 7). The distributions by age, race/ethnicity, and education level in this sample of pregnant women were similar to those in all births in the United States in 2000 (Table 1). Overall, HSV-1 seroprevalence was 63%, HSV-2 seroprevalence was 22%, infection with both HSV-1 and HSV-2 was 13%; and HSV seronegativity was 28%.

In Table 2, we present the seroprevalence of HSV-1 only, HSV-2 (with and without HSV-1), and HSV seronegativity by selected demographic and behavioral factors. Both HSV-1 and HSV-2 seroprevalence varied by race/ethnicity. As a result, NH-white mothers were more likely to be seronegative compared with other racial/ethnic groups (40% vs 11%; $P < .001$). A regression model was fit to find demographic and behavioral factors that were associated independently with HSV-2 infection. All 7 variables in Table 2 were considered in the initial model, and only age, race/ethnicity, and the lifetime number of sex partners were associated independently with HSV-2 infection (all $P < .05$). Marital status, education level, poverty status, and age at first sex were not associated statistically with HSV-2 infection after adjustment for other variables in the model. Similar approaches were used to find factors that were associated with HSV seronegativity, and only race/ethnicity, education level, and the lifetime number of sex partners were associated independently with being HSV-seronegative. On the basis of these analyses, we conclude that race/ethnicity and the lifetime number of sex partners are the best 2 predictors of HSV serostatus in pregnant women in the United States.