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CLINICAL ARTICLE

Influence of parity and sexual history on cytomegalovirus seroprevalence among women aged 20–49 years in the USA

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ABSTRACT

Objective: To assess the influence of parity, as a proxy for exposure to children, and sexual history on cytomegalovirus (CMV) seroprevalence. *Methods:* Data were retrospectively analyzed from women aged 20–49 years who were tested for CMV immunoglobulin G antibodies in the 1999–2004 National Health and Nutrition Examination Survey, a nationally representative survey of the US population. Logistic regression was used to determine independent variables associated with CMV seroprevalence. *Results:* Among 3710 women, the age-adjusted CMV seroprevalence was 61.3% (95% CI 58.9%–63.6%). In age-adjusted univariate analysis, women who had given birth at least once had higher overall CMV seroprevalence (66.0%, 95% CI 63.1%–68.9%) than did those who had not given birth (49.0%, 95% CI 44.4%–53.7%; $P < 0.001$). In multivariate logistic analysis, higher CMV seroprevalence was independently associated with number of live births (each additional birth: adjusted odds ratio [aOR] 1.2, 95% CI 1.1–1.3), age at first sexual intercourse (<18 vs ≥18 years: aOR 1.3, 95% CI 1.1–1.6), lifetime sexual partners (≥10 vs <10: aOR 1.4, 95% CI 1.1–1.9), and herpes type 2 seropositivity (aOR 1.9, 95% CI 1.5–2.6) after controlling for age, race/Hispanic origin, place of birth, poverty index, and education. *Conclusion:* Among US women of reproductive age, parity and sexual exposures were independently associated with increased CMV seroprevalence.

1. Introduction

Every year in the USA, an estimated 28 000 neonates—0.7%—are born with congenital cytomegalovirus (CMV) infection [1]. Mother-to-fetus transmission, congenital CMV disease at birth, and permanent disabilities due to congenital CMV infection are more likely when CMV infection occurs during pregnancy among CMV-seronegative women, but can result from non-primary infections (reinfection or reactivation) in CMV-seropositive women [2]. In the USA, the overall CMV immunoglobulin G (IgG) seroprevalence among women aged 12–49 years was 57.9% in 1988–1994 [3]. The estimated annual seroconversion rate is 2.3% among the general population of pregnant women, but is approximately 10-fold higher among parents with a child shedding CMV [4].

Previous studies [5,6] have shown that women caring for young children and those with recent onset of sexual activity are at greatest risk of having a neonate with congenital CMV infection, and that adolescent mothers are likely to be disproportionally affected by the disease burden caused by congenital CMV infection. In the USA, however, the highest birth rates are observed among women aged 20–34 years [7]. The extent to which these women remain susceptible to primary CMV infections throughout successive pregnancies is not well understood. The aim of the present study was to assess the influence of parity, as a proxy for exposure to children, and sexual history on CMV seroprevalence among women aged 20–49 years in the USA.

2. Materials and methods

Data on CMV seroprevalence among US women were obtained from the National Health and Nutrition Examination Survey (NHANES), a nationally representative, cross-sectional survey of the non-institutionalized US population conducted by the Centers for Disease Control and Prevention, between 1999 and 2004. The National Center for Health Statistics Research Ethics Review Board, Centers for Disease Control and Prevention, reviewed and approved all protocols for the conduct of NHANES 1999–2004. All participants provided written informed consent, including consent to storage of blood, urine, and saliva specimens for use in future studies [8].

Data collection in NHANES consisted of: a household screen to determine the eligibility of any household members for interview or examination; an interview of each eligible sample individual to collect individual-level data on demographics, health, and nutrition, and

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household information; and a physical examination including the collection of specimens for laboratory testing. NHANES methods have been reported elsewhere [8]. CMV-specific IgG in stored sera from NHANES 1999–2004 was measured by an enzyme-linked immunosorbent assay (Quest International, Miami, FL, USA) [9], and added to the NHANES database, which is publicly available [10].

A previous analysis [11] of the 1999–2004 NHANES showed that CMV seroprevalence was independently associated with older age, female sex, low household income, high h2ousehold crowding, low education, and foreign country of birth. The present analysis focused on women aged 20–49 years because complete risk factor data were not available for women younger than 20 years. Seroprevalence for CMV IgG was calculated for women overall, and by age group (20–29, 30–39, or 40–49 years), race/Hispanic origin, country of birth, family income to poverty ratio, insurance status, education level, household crowding, age at first live birth, parity (number of live births), and sexual history variables.

Race/Hispanic origin was based on the respondents' self-assessment and was categorized as non-Hispanic white, non-Hispanic black, Mexican American, or other (including non-Hispanic Asians, other Hispanic races, and multiracial women). Country of birth was categorized as USA or non-USA. The family income-to-poverty ratio was calculated by dividing family income by a poverty threshold specific for family size obtained from the US Department of Health and Human Services' poverty guidelines, and was categorized as below (<1.0) or at or above (≥1.0) the poverty threshold [12]. The household crowding index was calculated by dividing the household size by the number of rooms in the household, excluding bathrooms, and categorized as low (<0.5 individuals per room), average (0.5–0.99 individuals per room), or high (≥1 individuals per room). Sexual history variables included age at first intercourse, number of lifetime sexual partners, herpes type 2 seropositivity, self-report of ever being diagnosed with any of four sexually transmitted infections (chlamydia, gonorrhea, genital herpes, or genital warts), and any oral contraceptive use.

National estimates of CMV seroprevalence were calculated using weights developed for NHANES to represent the total civilian non-institutionalized US household population and to account for oversampling and non-response to the household interview and physical examination [13]. Because the percentage of women tested for CMV seroprevalence among those examined in NHANES varied by less than 5% across the categories of each variable analyzed, the original NHANES examination weights were used without adjustment for non-response.

All data were analyzed by SUDAAN version 9.0 (Research Triangle Institute, Research Triangle Park, NC, USA). Standard errors were estimated by Taylor series linearization, a design-based method that incorporates sample weights and accounts for stratification and clustering of the NHANES sample design [13]. Estimates were considered unstable if the relative standard error (defined as the estimate divided by its standard error expressed as a percentage) around the proportion of participants who were seropositive or seronegative was more than 30%, or if the estimate was based on less than 10 seropositive or seronegative women. The exact binomial method was used to calculate 95% confidence intervals (CIs). Pairwise differences between seroprevalence estimates and trends were evaluated using a t statistic from an orthogonal linear contrast procedure. $P < 0.05$ was considered to be significant with no adjustments for multiple comparisons.

The association between CMV seroprevalence and sociodemographic variables, parity, and sexual history variables was assessed by univariate analysis. Because the age distribution varied by many of these variables and age was strongly associated with CMV seroprevalence, the estimates were adjusted to the 2000 US population age structure using the direct method to remove the confounding effect of age.

Logistic regression was used to calculate the adjusted odds ratio (aOR) and 95% CIs, and to determine independent variables associated with CMV seroprevalence. The initial model included all variables that were significant in the univariate analysis. Variables that were no longer significantly associated with CMV seroprevalence were subsequently excluded by using backward stepwise elimination. Variables that remained in the final model were those with a P value of less than 0.05 based on the Satterthwaite-adjusted F statistic.

3. Results

In NHANES 1999–2004, 5291 women aged 20–49 years were surveyed, of whom 4264 (80.6%) were interviewed. Among the 4264 women interviewed, 4042 (94.8%) were examined, of whom 3710 (91.8%) were tested for CMV IgG.

The overall age-adjusted CMV seroprevalence among women aged 20–49 years was 61.3% (95% CI 58.9%–63.6%). In univariate analysis, CMV seroprevalence was higher among women aged 30–39 years and 40–49 years than among those aged 20–29 years ($P < 0.001$ for both comparisons) (Table 1). CMV seroprevalence was higher among non-Hispanic black and Mexican American women than among non-Hispanic white women ($P < 0.001$ for both) (Table 1). Additionally, it was higher among women born outside the USA, those living below the poverty threshold, and those with less education, no health insurance, or high household crowding ($P < 0.05$ for all) (Table 1).

Overall age-adjusted CMV seroprevalence was higher among women who had given birth at least once than among women who had not ($P < 0.001$) (Table 2). CMV seroprevalence was significantly higher among women who had given birth at least once than among women who had not given birth across all age and race/Hispanic origin groups (Table 2).

The multivariate logistic model included 2643 women who had complete risk factor data. Higher CMV seroprevalence was independently associated with increasing number of live births, younger age at first sexual intercourse, 10 or more lifetime sexual partners, and herpes type 2 seropositivity, after controlling for age group, race/Hispanic origin, country of birth, living below poverty, and education level (Table 1). Considering the number of live births as a continuous variable in the same multivariate logistic model, the aOR for each additional live birth was 1.2 (95% CI 1.1–1.3; $P < 0.001$).

4. Discussion

In the present population-based sample of US women, an increasing number of live births, early sexual debut, 10 or more lifetime sexual partners, and herpes type 2 seropositivity were independently associated with higher CMV seroprevalence, after controlling for age and other sociodemographic risk factors. A previous study using data from the 1988–1994 NHANES [14] found that number of sexual exposures was associated with higher CMV seroprevalence, but it did not assess the effect of parity. Two studies among pregnant women [15,16] found that increasing parity was independently associated with higher CMV seroprevalence after controlling for age and sociodemographic risk factors, but sexual exposures were not assessed. In the present study, higher CMV seroprevalence was associated with having at least one live birth, both overall and across all age and race/Hispanic groups. Approximately half the women who had not given birth remained susceptible to primary CMV infection, decreasing to approximately one-third of women with at least one live birth.

Parents with a child shedding CMV and childcare workers have an annual CMV seroconversion rate that is much higher (3- to 12-fold) than do parents with a child not shedding CMV [4]. CMV infection early in life can result from mother-to-neonate transmission either through exposure to CMV in genital secretions during labor or in breastmilk or saliva. Additionally, close contact among children in the household or a daycare setting can result in horizontal transmission from child to child. Because young CMV-seropositive children can shed the virus in body fluids for months after primary infection [17], the risk period for CMV transmission from child to mother might coincide with a subsequent pregnancy. The risk of CMV seroconversion among women has been shown to increase

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