

Racial and Ethnic Differences in the Prevalence of Congenital Cytomegalovirus Infection

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Objective To evaluate the impact of race and ethnicity upon the prevalence and clinical spectrum of congenital cytomegalovirus infection (cCMV).

Study design From 2007 to 2012, 100 332 infants from 7 medical centers were screened for cCMV while in the hospital. Ethnicity and race were collected and cCMV prevalence rates were calculated.

Results The overall prevalence of cCMV in the cohort was 4.5 per 1000 live births (95% CI, 4.1-4.9). Black infants had the highest cCMV prevalence (9.5 per 1000 live births; 95% CI, 8.3-11.0), followed by multiracial infants (7.8 per 1000 live births; 95% CI, 4.7-12.0). Significantly lower prevalence rates were observed in non-Hispanic white infants (2.7 per 1000 live births; 95% CI, 2.2-3.3), Hispanic white infants (3.0 per 1000 live births; 95% CI, 2.4-3.6), and Asian infants (1.0 per 1000 live births; 95% CI, 0.3-2.5). After adjusting for socioeconomic status and maternal age, black infants were significantly more likely to have cCMV compared with non-Hispanic white infants (adjusted prevalence OR, 1.9; 95% CI, 1.4-2.5). Hispanic white infants had a slightly lower risk of having cCMV compared with non-Hispanic white infants (adjusted prevalence OR, 0.7; 95% CI, 0.5-1.0). However, no significant differences in symptomatic cCMV (9.6%) and sensorineural hearing loss (7.8%) were observed between the race/ethnic groups.

Conclusions Significant racial and ethnic differences exist in the prevalence of cCMV, even after adjusting for socioeconomic status and maternal age. Although once infected, the newborn disease and rates of hearing loss in infants are similar with respect to race and ethnicity. (*J Pediatr* 2018;■■■:■■■-■■■).

Congenital cytomegalovirus (CMV) infection (cCMV) occurs worldwide and contributes to permanent disabilities including hearing loss, vision loss, cerebral palsy, and/or cognitive impairment in thousands of children born each year. In the US, Canada, Western Europe, and Australia, cCMV is estimated to occur in about 5-7 per 1000 live births.¹⁻³ Higher cCMV rates of 10-20 per 1000 live births have been reported in South America, Africa, and most countries in Asia.⁴⁻⁸ The vast majority of the infants born with cCMV (approximately 90%) are asymptomatic during the newborn period.⁹ However, asymptomatic infants along with symptomatic infants are at risk for CMV-related disabilities.

Few data are available on the prevalence and the clinical spectrum of cCMV according to race and ethnicity. Previous studies in Birmingham, Alabama, reported that cCMV rates were higher in black infants than white infants.¹ Although higher cCMV rates have been reported in Hispanic white infants in the US, the number of Hispanic infants studied is small and the differences did not attain statistical significance.^{10,11} The lack of accurate prevalence estimates in the US could contribute to the underrecognition of cCMV as a common cause of disabilities in infants and young children. Therefore, regional and national estimates of the prevalence and clinical spectrum of cCMV in the US according to race and ethnicity are needed. As part of a multicenter study, more than 100 000 infants were tested for CMV while in the hospital nursery, allowing us to determine the impact of race and ethnicity on the prevalence and clinical spectrum of cCMV in newborns.

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cCMV	Congenital CMV infection
CHIMES	CMV and Hearing Multicenter Screening Study
CMV	Cytomegalovirus
PCR	Polymerase chain reaction
POR	Prevalence OR

Methods

From March 2007 to March 2012, infants born at 7 US medical centers were enrolled in the CMV and Hearing Multicenter Screening (CHIMES) Study.¹² Saliva specimens were collected from the newborn and additional dried blood spots were obtained at the time of newborn metabolic screening and tested for CMV, as previously described.¹³⁻¹⁵ Infants with positive saliva or dried blood spots screening specimens were enrolled in the follow-up component of the study within the first 3 to 6 weeks of life to confirm cCMV.¹⁴ CMV infection was confirmed by a follow-up saliva or urine sample which was positive using the rapid culture and/or polymerase chain reaction (PCR) methods.¹⁶

Race and ethnicity data were self-reported by the mothers for their infants at time of consent.¹³ National Institutes of Health definitions were used to categorize ethnicity and race. The 2 categories for ethnicity were Hispanic or non-Hispanic. The 5 individual categories for race were American Indian or Alaska Native, Asian, black or African American, Native Hawaiian or other Pacific Islander, and white. In addition, infants with reported multiple races were categorized as multiracial. All infants who were either black, multiracial, Asian, or American Indian race were non-Hispanic.

Newborn medical records were reviewed for infants with cCMV to determine if the infants had symptomatic infection. The a priori definition of symptomatic cCMV included generalized petechial rash, purpuric rash, hepatomegaly, splenomegaly, jaundice with direct bilirubin of 3 mg/dL or greater, unexplained neurologic/central nervous system abnormalities (eg, microcephaly, seizures, focal or generalized neurologic deficits), or chorioretinitis diagnosed by eye examination.¹² The physicians at each study site made clinical decisions about further evaluations and possible treatment of the infants with CMV as part of the infant's standard medical care. Infants with cCMV enrolled in the follow-up component of the CHIMES study received an initial diagnostic audiologic assessment at 3-8 weeks of age. Local institutional review board approval was obtained at each site.

Statistical Analyses

All statistical analyses were performed using SAS software, version 9.4 (SAS Institute, Cary, North Carolina). To determine statistical significance, routine methods for calculating χ^2 or Fisher exact test, and the 2-tailed *t* test were used where appropriate. For prevalence, the unit of measure was the total number of cCMV infection per 1000 live births. CIs for prevalence rates were based on the Binomial distribution. Also, univariate prevalence ORs (PORs) and 95% CIs using the exact method were calculated to evaluate the association of race and ethnicity with cCMV. Because socioeconomic status and maternal age have been previously reported to be associated with cCMV and might confound the association of race and ethnicity and cCMV, multivariable logistic regression analysis was used to adjust for the effect of insurance status (as a proxy for socioeconomic status) and maternal age on the race/ethnicity-specific adjusted PORs for cCMV. Adjusted PORs and 95% CIs

were calculated by exponentiating the regression coefficients and the standard errors of the respective coefficients.

Results

Of the 108 925 mothers approached for participation in the CHIMES Study, 100 607 mothers consented and 8318 (7.6%) mothers declined to participate in the study. Adequate enrollment specimens were available for 100 332 of the infants and 497 infants screened positive for CMV. In 391 infants, cCMV was confirmed by a follow-up positive saliva or urine sample using the rapid culture or PCR methods.¹⁶ Thirty-five infants were considered uninfected because the follow-up saliva and urine samples were negative. Another 13 infants had indeterminate positive screening results by saliva PCR and did not enroll in follow-up to obtain confirmation samples.^{13,14,16} None of these infants had clinical findings consistent with cCMV on medical record review. These 13 infants were not included as cCMV cases. An additional 58 infants did not enroll in follow up owing to death (*n* = 3), refusal (*n* = 17), loss to follow-up (*n* = 33), or migration (*n* = 5), but had positive screening saliva rapid culture and/or PCR.^{14,16} Five of these infants had symptomatic CMV. These 58 infants are included in the estimates of cCMV prevalence for a total to 449 cCMV cases.

Most of the 100 332 enrolled infants were from the well-baby nurseries with 6 of the 7 sites having more than 10 000 infants who underwent CMV screening (Table I). Non-Hispanic white infants, Hispanic white infants, and black infants were the largest racial/ethnic groups in the cohort with most infants having public or no insurance. Infants with cCMV sig-

Table I. Study characteristics for the 100 332 newborns who underwent newborn CMV screening at the 7 sites

Characteristics	No. (%)
Hospital site	
Birmingham, Alabama	12 193 (12.1)
Jackson, Mississippi	6360 (6.3)
New Brunswick, New Jersey	10 715 (10.7)
Charlotte, North Carolina	15 093 (15.0)
Cincinnati, Ohio	14 126 (14.1)
Pittsburgh, Pennsylvania	19 200 (19.1)
Dallas, Texas	22 645 (22.6)
Maternal age, mean \pm SD, y	27.4 \pm 6.1
Infant sex	
Female	49 320 (49.2)
Male	51 012 (50.8)
Infant race/ethnicity	
American Indian	101 (0.1)
Asian	4166 (4.1)
Black	24 100 (24.0)
White, Hispanic	32 310 (32.2)
White, non-Hispanic	37 219 (37.1)
Multiracial	2436 (2.4)
Insurance status for hospital stay	
Private	35 270 (35.2)
Public or no insurance	65 062 (64.8)
Hospital nursery	
Well-baby	96 873 (96.6)
Neonatal intensive care	3459 (3.4)

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