# 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;200:196-201).*

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.

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

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## 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.[1,3] 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 $\chi^2$ 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 ± SD, y | 27.4 ± 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) |

**Table II. Characteristics of infants with CMV vs infants without CMV**

| Sites | CMV positive (n = 449), % (95% CI) | CMV negative (n = 99 883), % (95% CI) | *P* value |
|---|---|---|---|
| Infant race and ethnicity | | | |
| American Indian | 0.2 (0.01-1.2) | 0.1 (0.08-0.12) | <.0001 |
| Asian | 0.9 (0.2-2.3) | 4.2 (4.0-4.3) | |
| Black | 51.0 (46.3-55.7) | 23.9 (23.6-24.2) | |
| White, Hispanic | 21.4 (17.7-25.5) | 32.2 (32.0-32.5) | |
| White, non-Hispanic | 22.3 (18.5-26.4) | 37.2 (36.9-37.5) | |
| Multiracial | 4.2 (2.6-6.5) | 2.4 (2.3-2.5) | |
| Infant sex | | | |
| Female | 48.3 (43.6-53.1) | 49.2 (48.8-49.5) | NS |
| Male | 51.7 (46.9-56.4) | 50.8 (50.5-51.2) | |
| Insurance status | | | |
| Private | 17.2 (13.8-21.0) | 35.2 (34.9-35.5) | <.0001 |
| Public or no insurance | 82.8 (79.0-86.2) | 64.8 (64.5-65.1) | |
| Hospital nursery | | | |
| Well baby | 89.8 (86.6-92.4) | 96.6 (96.5-96.7) | <.0001 |
| Neonatal intensive care unit | 10.2 (7.6-13.4) | 3.4 (3.3-3.5) | |
| Maternal age, mean ± SD, y | 23.1 ± 5.6 | 27.4 ± 6.1 | <.0001 |

nificantly differed by race and ethnicity, insurance status, and hospital nursery from infants who were CMV negative (Table II). Also, infants who were CMV positive had significantly younger mothers than infants without cCMV.

The overall prevalence rate of cCMV was 4.5 per 1000 live births (95% CI, 4.1-4.9 per 1000 live births). The prevalence of cCMV differed by race and ethnicity (Figure 1). Black infants had the highest cCMV prevalence (9.5 per 1000 live births), followed by multiracial infants (7.8 per 1000 live births). Both black and multiracial infants had a significantly higher cCMV prevalence rate than the rate observed for non-Hispanic white infants (2.7 per 1000 live births), Hispanic white infants (3.0 per 1000 live births), and Asian infants (1.0 per 1000 live births). The unadjusted PORs for cCMV in black infants and multiracial infants were significantly higher compared with non-Hispanic white infants (Table III), whereas the unadjusted PORs for cCMV in Hispanic white infants and Asian infants did not differ from non-Hispanic white infants.

To adjust for potential confounding by socioeconomic status and maternal age on the association of race and ethnicity with cCMV, a multivariable logistic regression model that included race and ethnicity, insurance status (as a proxy for socioeconomic status), and maternal age was fit. After adjusting for socioeconomic status and maternal age, race and ethnicity were independently associated with cCMV (Table III). Black infants and multiracial infants were almost 2 times more likely to have cCMV compared with non-Hispanic white infants. However, Hispanic white infants had a lower risk of having cCMV compared with non-Hispanic white infants, although this was of borderline significance. Asian infants did not significantly differ in risk of having cCMV compared with non-Hispanic white infants.

Symptomatic cCMV was observed in 9.6% (95% CI, 7.0%-12.7%) of all the infants with cCMV. When symptomatic cCMV was stratified by race and ethnicity, no differences were observed between the groups (Figure 2, A). Sensorineural hearing

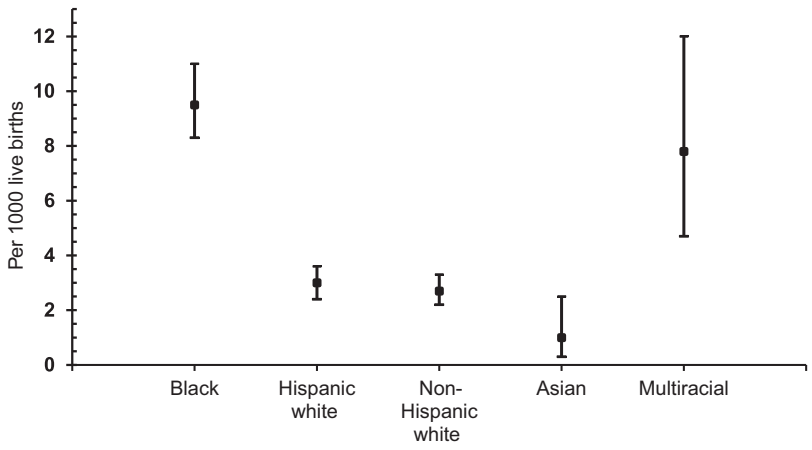


**Figure 1.** Prevalence per 1000 live births of congenital CMV infection and 95% CIs by race and ethnicity.

**Table III. Unadjusted and aPORs for cCMV infection by race and ethnicity**

| | POR (95% CI) | aPOR (95% CI)* |
|---|---|---|
| Infant race and ethnicity | | |
| Black, non-Hispanic | 3.5 (2.8-4.5) | 1.9 (1.4-2.5) |
| Multiracial | 2.9 (1.8-4.8) | 1.9 (1.1-3.0) |
| White, Hispanic | 1.1 (0.8-1.5) | 0.7 (0.5-1.0) |
| Asian | 0.4 (0.1-1.0) | 0.6 (0.2-1.2) |
| White, non-Hispanic | 1.0 | 1.0 |

*aPOR*, Adjusted prevalence OR.
*Model included race and ethnicity, insurance status, and maternal age.

loss in the neonatal period occurred in 7.8% of all the infants with cCMV (95% CI, 5.5%-10.7%). Sensorineural hearing loss at birth did not significantly differ for any of the racial and ethnic groups (**Figure 2**, B).

## Discussion

Significant racial and ethnic differences exist in the prevalence of cCMV, although once infected, the clinical manifestations and rates of hearing loss in infants are similar with respect to race and ethnicity. The overall cCMV rate of 4.5 per 1000 live births found in our cohort of more than 100 000 infants is lower than previous reported prevalence rates of 6.4 per 1000 live births and 7 per 1000 live births from 2 meta-analysis studies.[2,3] Most of the data on cCMV prevalence from these reviews are based on smaller cohorts from individual hospitals in different cities or countries. Thus, the difference in cCMV prevalence rates may be due to the selection of the underlying delivery populations in these studies.[1,3] These studies likely have overrepresented some high-risk groups of infants and may not reflect a more general population of newborns. Only 2 studies have assessed cCMV prevalence rates for a city or a region. A study in Malmö, Sweden (1977-1986), where 16 474 infants were tested for cCMV, reported a prevalence rate of 4.6 per 1000 live births.[17,18] The other study was in Hamilton, Ontario, Canada (1973-1976) where 15 212 live born infants in the city hospitals were screened for cCMV, finding a cCMV prevalence rate of 4.2 per 1000.[19]

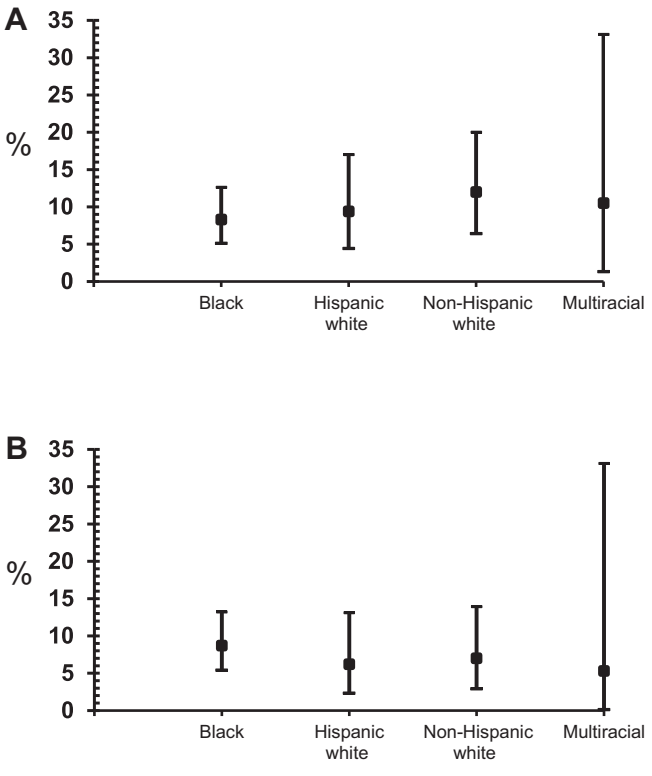


**Figure 2. A,** Symptomatic congenital CMV infection (%) and 95% CIs by race and ethnicity and **B,** sensorineural hearing loss at birth (%) and 95% CIs by race and ethnicity.

The significantly higher cCMV prevalence observed in black infants is similar to what has been previously reported in black infants in Birmingham, Alabama.[1] An earlier study in London, UK, also found that black infants had high cCMV prevalence rates, even after adjusting for maternal age, socioeconomic status, and parity.[20] In our study, higher cCMV prevalence was observed in black infants compared with non-Hispanic white infants in all 7 hospitals located in different southern and eastern regions of the US. Multiracial infants also had a significantly higher cCMV prevalence rate similar to the black infants in our cohort. Among the multiracial infants in our cohort, 77% included black race along with 1 or more other races. All multiracial infants who were CMV positive included black race. After adjusting for the confounding effects of maternal age and socioeconomic status, both black infants and multiracial infants were almost twice as likely to be congenitally infected with CMV compared with non-Hispanic white infants.

Non-Hispanic black women have reported higher CMV seroprevalence rates compared with non-Hispanic white women.[21-23] It has been consistently shown that higher cCMV prevalence rates are found in populations with higher maternal seroprevalence; however, the exact reasons for this association are not known.[24,25] It is possible that the higher prevalence of cCMV in black and multiracial infants in our study could be due to higher maternal CMV seropositivity resulting in higher rates of nonprimary maternal CMV infections in these groups. Another explanation may be some underlying genetic influence in black infants. In a recent study of 20 fetuses and neonates with cCMV, an association between polymorphisms within the proinflammatory cytokine and Toll-like receptor genes with maternal CMV infection as well as cCMV was observed.[26-29] These findings suggest the need for a thorough evaluation of the role of genetic factors in cCMV. Our study did not have maternal CMV seroprevalence or genetic data to explore these possible hypotheses.

A surprising finding of our study was the low cCMV prevalence rate for Hispanic white infants. In fact, after adjusting for confounding by maternal age and socioeconomic status, Hispanic white women had a slightly lower risk of having an infant with cCMV compared with non-Hispanic white women. Previous National Health and Nutrition Examination Survey data in the US reported high CMV seroprevalence rates for

Mexican American women and, therefore, a higher cCMV prevalence rate similar to that in black infants was expected in Hispanic white infants.[21,22] An earlier study of 132 Hispanic infants in Houston, Texas (1980), reported a cCMV prevalence of 15 per 1000 live births.[10] In addition to the small number of infants, the higher observed rate in Hispanic infants in the Texas study might be explained by whether the mother was US born or was born outside of the US.[22] A more recent study using dried blood spots from the California Newborn Screening Program reported a cCMV prevalence rate of 9 per 1000 live births for Hispanic infants.[11] However, the sensitivity and specificity of their dried blood spots testing for detection of cCMV in that study could not be determined because the dried blood spots screening assay results were not compared with testing of urine or saliva. Also, the study did not follow-up to confirm cCMV in infants who were positive on screening. The 32 310 enrolled Hispanic white infants in our cohort comprise the largest study to date of Hispanic infants in the US for CMV screening, and 4 of 7 hospitals enrolled 500 or more Hispanic white infants in the study. It is possible that cCMV prevalence vary among the US Hispanic population based on the country of origin. We do not have study data on the country of origin for Hispanic white women nor whether they were US born. However, cCMV prevalence rates were similar across the 4 hospitals in the different regions of the US for all the Hispanic white infants in our cohort.

The lowest cCMV prevalence rate was observed in Asians in our study. These findings are similar to cCMV prevalence reports in Japan,[30,31] but are significantly lower than the reported cCMV prevalences in China,[32] Korea,[33] and India.[5] Other than the dried blood spots study by Kharrazi et al described herein that included Asian infants, no other data on the cCMV prevalence in Asian infants in the US exists previously.[11] The definition used in the CHIMES study was based on the National Institutes of Health definition of "Asian" and, because this is a very heterogeneous group in the US, cCMV prevalence may differ when country origin is considered.

Although black and multiracial infants are at increased risk for cCMV compared with non-Hispanic white infants, once infected, symptomatic infection and sensorineural hearing loss rates at birth do not differ significantly by race and ethnicity. The finding that approximately 10% of infants with cCMV were symptomatic is similar to previous meta-analysis where 12.7% of the infants with cCMV were symptomatic.[2] However, the use of differing definitions of symptomatic cCMV in different studies and in different countries has made it difficult to compare studies. Applying the same symptomatic definition to all infants in our study, we did not find significant differences in the rate of symptomatic infections between the race/ethnic groups.

A limitation of our study is that it does not include the total population of newborns in the regions where the hospitals were located; therefore, our estimate of the overall prevalence of cCMV may not be representative for the region or the US. However, because the cCMV prevalence differs by race and ethnicity, the use of an overall cCMV prevalence could be obscuring the burden of cCMV in certain populations, such as blacks. The consistency of the race- and ethnicity-specific cCMV prevalence rates across the 7 hospitals in this study, and the fact that more than 96% of the infants were in the well-baby nurseries and not a selected population, would argue that our race/ethnicity-specific cCMV prevalence rates could be used to estimate prevalence in specific race/ethnic groups.

CMV is the most frequent cause of congenital infection, and hospital or regional cCMV prevalence rates reflect the underlying racial and ethnic groups of the delivery populations. Although CMV affects infants from all race and ethnic groups, black infants and multiracial infants are at significantly increased risk for cCMV. Our findings highlight the need for developing strategies to increase awareness of cCMV and prevention messages for all women, including culturally relevant messages for black and multiracial women whose offspring bear a disproportionately higher burden of cCMV. ■

*A list of additional members of the CHIMES study is available at www.jpeds.com (**Appendix**).*

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## References

1. Fowler KB, Stagno S, Pass RF. Maternal age and congenital cytomegalovirus infection: screening of two diverse newborn populations, 1980-1990. J Infect Dis 1993;168:552-6.
2. Dollard SC, Grosse SD, Ross DS. New estimates of the prevalence of neurological and sensory sequelae and mortality associated with congenital cytomegalovirus infection. Rev Med Virol 2007;17:355-63.
3. Kenneson A, Cannon MJ. Review and meta-analysis of the epidemiology of congenital cytomegalovirus (CMV) infection. Rev Med Virol 2007;17:253-76.
4. Britt WJ. Cytomegalovirus. In: Remington J, Klein J, Wilson C, Nizet V, Maldonado Y, eds. Infectious diseases of the fetus and newborn infant. 7th ed. Philadelphia (PA): Elsevier Saunders; 2011. p. 706-55.
5. Dar L, Pati SK, Patro AR, Deorari AK, Rai S, Kant S, et al. Congenital cytomegalovirus infection in a highly seropositive semi-urban population in India. Pediatr Infect Dis J 2008;27:841-3.
6. Kaye S, Miles D, Antoine P, Burny W, Ojuola B, Kaye P, et al. Virological and immunological correlates of mother-to-child transmission of cytomegalovirus in The Gambia. J Infect Dis 2008;197:1307-14.
7. van der Sande MA, Kaye S, Miles DJ, Waight P, Jeffries DJ, Ojuola OO, et al. Risk factors for and clinical outcome of congenital cytomegalovirus infection in a peri-urban West-African birth cohort. PLoS ONE 2007;2:e492.
8. Yamamoto AY, Mussi-Pinhata MM, Cristina P, Pinto G, Moraes Figueiredo LT, Jorge SM. Congenital cytomegalovirus infection in preterm and full-term newborn infants from a population with a high seroprevalence rate. Pediatr Infect Dis J 2001;20:188-92.
9. Pass RF, Fowler KB, Boppana S. Clinical importance of cytomegalovirus infection: an overview. In: Landini MP, ed. Progress in cytomegalovirus research. New York: Elsevier Science Publishers; 1991. p. 3-10.
10. Montgomery JR, Mason EO, Williamson AP, Desmond MM, South MA. Prospective study of congenital cytomegalovirus infection. South Med J 1980;73:590.
11. Kharrazi M, Hyde T, Young S, Amin MM, Cannon MJ, Dollard SC. Use of screening dried blood spots for estimation of prevalence, risk factors, and birth outcomes of congenital cytomegalovirus infection. J Pediatr 2010;157:191-7.

12. Fowler KB, McCollister FP, Sabo DL, Shoup AG, Owen KE, Woodruff JL, et al. A targeted approach for congenital cytomegalovirus screening within newborn hearing screening. Pediatrics 2017; 139.
13. Boppana SB, Ross SA, Novak Z, Shimamura M, Tolan RW Jr, Palmer AL, et al. Dried blood spot real-time polymerase chain reaction assays to screen newborns for congenital cytomegalovirus infection. JAMA 2010;303:1375-82.
14. Boppana SB, Ross SA, Shimamura M, Palmer AL, Ahmed A, Michaels MG, et al. Saliva polymerase-chain-reaction assay for cytomegalovirus screening in newborns. N Engl J Med 2011;364:2111-8.
15. Ross SA, Ahmed A, Palmer AL, Michaels MG, Sanchez PJ, Stewart A, et al. Newborn dried blood spot polymerase chain reaction to identify infants with congenital cytomegalovirus-associated sensorineural hearing Loss. J Pediatr 2017;184.
16. Balcarek KB, Warren W, Smith RJ, Lyon MD, Pass RF. Neonatal screening for congenital cytomegalovirus infection by detection of virus in saliva. J Infect Dis 1993;167:1433-6.
17. Ahlfors K, Ivarsson SA, Harris S, Svanberg L, Holmqvist R, Lernmark B, et al. Congenital cytomegalovirus infection and disease in Sweden and the relative importance of primary and secondary maternal infections. Scand J Infect Dis 1984;16:129-37.
18. Ahlfors K, Ivarsson S, Harris S. Report on a long-term study of maternal and congenital cytomegalovirus infection in Sweden. Review of prospective studies available in the literature. Scand J Infect Dis 1999;31:443-57.
19. Larke RBP, Wheatley E, Saigal S, Chernesky MA. Congenital cytomegalovirus infection in an urban Canadian community. J Infect Dis 1980;142:647-53.
20. Preece PM, Tookey P, Ades A, Peckham CS. Congenital cytomegalovirus infection: predisposing maternal factors. J Epidemiol Community Health 1986;40:205-9.
21. Colugnati FA, Staras SA, Dollard SC, Cannon MJ. Incidence of cytomegalovirus infection among the general population and pregnant women in the United States. BMC Infect Dis 2007;7:71.
22. Bate SL, Dollard SC, Cannon MJ. Cytomegalovirus seroprevalence in the United States: the national health and nutrition examination surveys, 1988-2004. Clin Infect Dis 2010;50:1439-47.
23. Wang C, Zhang X, Bialek S, Cannon MJ. Attribution of congenital cytomegalovirus infection to primary versus non-primary maternal infection. Clin Infect Dis 2011;52:e11-3.
24. Manicklal S, Emery VC, Lazzarotto T, Boppana SB, Gupta RK. The "silent" global burden of congenital cytomegalovirus. Clin Microbiol Rev 2013;26:86-102.
25. de Vries JJ, van Zwet EW, Dekker FW, Kroes AC, Verkerk PH, Vossen AC. The apparent paradox of maternal seropositivity as a risk factor for congenital cytomegalovirus infection: a population-based prediction model. Rev Med Virol 2013;23:241-9.
26. Wujcicka W, Wilczynski J, Paradowska E, Studzinska M, Nowakowska D. The role of single nucleotide polymorphisms, contained in proinflammatory cytokine genes, in the development of congenital infection with human cytomegalovirus in fetuses and neonates. Microb Pathog 2017;105:106-16.
27. Wujcicka W, Paradowska E, Studzinska M, Wilczynski J, Nowakowska D. Toll-like receptors genes polymorphisms and the occurrence of HCMV infection among pregnant women. Virol J 2017;14:64.
28. Wujcicka W, Paradowska E, Studzinska M, Wilczynski J, Nowakowska D. TLR2 2258 G>A single nucleotide polymorphism and the risk of congenital infection with human cytomegalovirus. Virol J 2017;14:12.
29. Wujcicka WI, Wilczynski JS, Nowakowska DE. Association of SNPs from IL1A, IL1B, and IL6 genes with human cytomegalovirus infection among pregnant women. Viral Immunol 2017;30:288-97.
30. Numazaki K, Fujikawa T. Chronological changes of incidence and prognosis of children with asymptomatic congenital cytomegalovirus infection in Sapporo, Japan. BMC Infect Dis 2004;4:22.
31. Koyano S, Inoue N, Oka A, Moriuchi H, Asano K, Ito Y, et al. Screening for congenital cytomegalovirus infection using newborn urine samples collected on filter paper: feasibility and outcomes from a multicentre study. BMJ Open 2011;1:e000118.
32. Wang S, Wang T, Zhang W, Liu X, Wang X, Wang H, et al. Cohort study on maternal cytomegalovirus seroprevalence and prevalence and clinical manifestations of congenital infection in China. Medicine (Baltimore) 2017;96:e6007.
33. Sohn YM, Park KI, Lee C, Han DG, Lee WY. Congenital cytomegalovirus infection in Korean population with very high prevalence of maternal immunity. J Korean Med Sci 1992;7:47-51.

## Appendix

### Additional members of the CHIMES Study Group

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