

RESEARCH ARTICLE

The prevalence and demographic features of congenital cytomegalovirus infection in an urban area of East Asia: A population-based study

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Abstract

Congenital cytomegalovirus (cCMV) infection is the leading environmental cause of childhood hearing impairment. However, its significance remains largely undocumented in many regions of the world. The purpose of this study was to investigate the prevalence and clinical features of cCMV infection in East Asia. Neonates born at a municipal hospital in Taipei were prospectively recruited and underwent concurrent hearing and CMV screenings. Those who failed the hearing screening or screened positive for CMV were subjected to a focused audiological and/or virological surveillance. The characteristics of the newborns and their mothers were compared between the CMV-positive and CMV-negative groups. Of the 1,532 newborns who underwent concurrent hearing and CMV screenings, seven (0.46%) were positive for cCMV infection. All seven CMV-positive newborns were asymptomatic at birth, and none of them developed hearing or other symptoms during a follow-up period of 14.4±6.3 months. The mothers of the CMV-positive newborns demonstrated higher gravidity (2.4 ± 1.4 vs. 2.1 ± 1.2) and parity (2.0 ± 1.2 vs. 1.6 ± 0.7) than those in the CMV-negative group; however, the difference did not reach statistical significance. The prevalence of cCMV infection in Taipei newborns was 0.46%, which is slightly lower than that of other populations and that of a previous report in the Taiwanese population. The relatively low prevalence in this study might be attributed to the improved public health system and decreased fertility rate in Taiwan.

Data Availability Statement: All relevant data are within the paper and its [Supporting information files](#).

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Introduction

Sensorineural hearing loss (SNHL) is a common clinical entity in newborns [1,2] and children [3,4]. Pediatric SNHL is an etiologically heterogeneous condition caused by a plethora of genetic [5–7] and environmental factors [8–12]. Recent advances in molecular genetics have revolutionized the assessment armamentarium of pediatric SNHL, enabling us to ascertain the etiology in 40–60% of the children with SNHL [13,14]. However, the clinical significance and contribution of the environmental factors that might lead to pediatric SNHL in these children largely remains unclear [8,11,12,15,16].

Among these environmental factors, congenital cytomegalovirus (cCMV) infection is the leading cause of pediatric SNHL [17] and neurodevelopmental disability [18] in developed countries. The importance of identifying cCMV infection as the etiology of SNHL in newborns has become clinically relevant with the availability of oral antiviral agents that may prevent the progression of cCMV-related SNHL [19]. Furthermore, children with cCMV infection are at risk for progressive SNHL that may not be present until several years of age, at a time when the golden period for hearing-loss rehabilitation has passed [20–22].

The prevalence and clinical characteristics of cCMV-infected newborns have been reported in several Western series [17,23]. However, there is still a paucity of such reports in East Asia, a populated region with rapid economic development. In the present study, we aimed to investigate the prevalence of cCMV infection in newborns from an urban region of East Asia and the clinical characteristics of cCMV-positive children and their mothers.

Materials and methods

Subject recruitment

From May 2016 to Dec 2018, we prospectively enrolled neonates born at the Taipei City Hospital Fuyou Branch. All newborns underwent hearing screening using automated auditory brainstem response (AABR) testing [24], and saliva swabs were obtained simultaneously for cCMV screening.

For the newborns who screened positive for cCMV, the following variables were recorded: sex, mode of delivery, age at last follow-up, birth weight, maternal age, gestational age, mother's gravidity and parity, and presence of symptoms/signs at birth, such as newborn hearing screening (NHS) failure or neonatal jaundice, and admission status were recorded.

All infants were of Han Taiwanese ethnicity. Written informed consent was obtained from the parents of all infants. This study was approved by the Research Ethics Committees of Taipei City Hospital and the National Taiwan University Hospital.

CMV screening

CMV screening was performed using a quantitative real-time polymerase chain reaction (PCR) assay with fluorescence resonance energy transfer (FRET) hybridization probes to detect the glycoprotein B of CMV [25]. The lower limit of detection, estimated using a CMV construct, was 10 copies/ml. All positive results were replicated in a second test, and samples that tested positive in both were considered true positives. Positive CMV PCR results were then confirmed by isolating CMV from urine or saliva.

Audiologic and clinical assessments in CMV-positive infants

Infants who tested positive for CMV at birth were subjected to a focused audiologic surveillance, including repeated AABR testing at 1 month, followed by comprehensive audiologic assessments at 3 months, 6 months, and 1 year [25].

These infants also underwent additional clinical evaluations, including complete blood counts, blood biochemistry, brain transfontanelar ultrasonography, abdominal ultrasonography, neurologic assessment, and visual assessment. Virological tests, including the determination of CMV viral loads in the blood using quantitative real-time PCR and the detection of CMV from a culture of bodily fluids (either urine or a throat swab), were performed during every medical examination to monitor viral clearance [25].

Data analyses

The results of the CMV screening were compared to the NHS results. The characteristics of the newborns and their mothers were analyzed according to their sex, mode of delivery, gestational age, birth weight, maternal age at pregnancy, gravidity, and parity. The proportions between the groups were compared using Fisher's exact test. All analyses were conducted using SAS software, version 9.3 (SAS Institute, Inc., Cary, NC).

Results

During the study period, 3,273 neonates were born at the Taipei City Hospital Fuyou Branch (Fig 1). Of these, the parents of 1,532 neonates agreed to undergo a newborn CMV screening for their children. The CMV screening was positive in seven newborns (0.46%), including one girl and six boys (Table 1). CMV infection was confirmed in all seven newborns by isolation of CMV from saliva and/or urine. All seven CMV-positive newborns passed the NHS. Of the other 1,525 infants who were negative for CMV, 25 (1.6%) failed the initial NHS and three (0.2%) were subsequently confirmed to have unilateral or bilateral SNHL. Among the 1,741 infants who did not undergo CMV screening, 64 (3.7%) failed the initial NHS and 16 (0.9%) were subsequently confirmed to have SNHL. In total, the prevalence of neonatal cCMV infection was 0.46%, with 0.74% for males and 0.14% for females. There was no statistically significant difference in the prevalence between the sexes.

The characteristics of the seven CMV-positive newborns are presented in Table 2. The newborns of cases 2 and 3 were given birth by a cesarean section (2/7, 28.6%), while the other five newborns were given birth through a normal spontaneous delivery (5/7, 71.4%).

All seven newborns with cCMV infection were asymptomatic at birth, and none of them were admitted to a neonatal intensive care unit or developed hyperbilirubinemia that required a specific treatment, including phototherapy or plasmapheresis (Table 2). The newborns of cases 2 and 4 were lost to follow-up for unknown reasons. The other five newborns were followed up at the National Taiwan University Hospital for a mean duration of 14.4 ± 6.3 months. None of these five newborns developed hearing or other symptoms during the follow-up period.

Table 3 presents a comparison of the maternal/neonatal characteristics between newborns with and without cCMV infection. The mothers of the CMV-positive neonates had a slightly higher gravidity (2.4 ± 1.4 vs. 2.1 ± 1.2 , respectively) and parity (2.0 ± 1.2 vs. 1.6 ± 0.7 , respectively) than those whose newborn babies were screened negative for CMV; yet, the difference did not reach statistical significance.

Discussion

In this study, we demonstrated that the prevalence of cCMV infection is approximately 0.46% in Taipei, a typical populous city in East Asia. The rate is slightly lower than that in other populations. In developed countries, the prevalence of cCMV infection ranged from 0.58% to 0.70% [17,26,27]. In developing countries, such as Mexico, Nigeria, and Gambia, the prevalence of cCMV infection was higher than that in our study, ranging from 0.9% to 5.4% [28–32]. Several

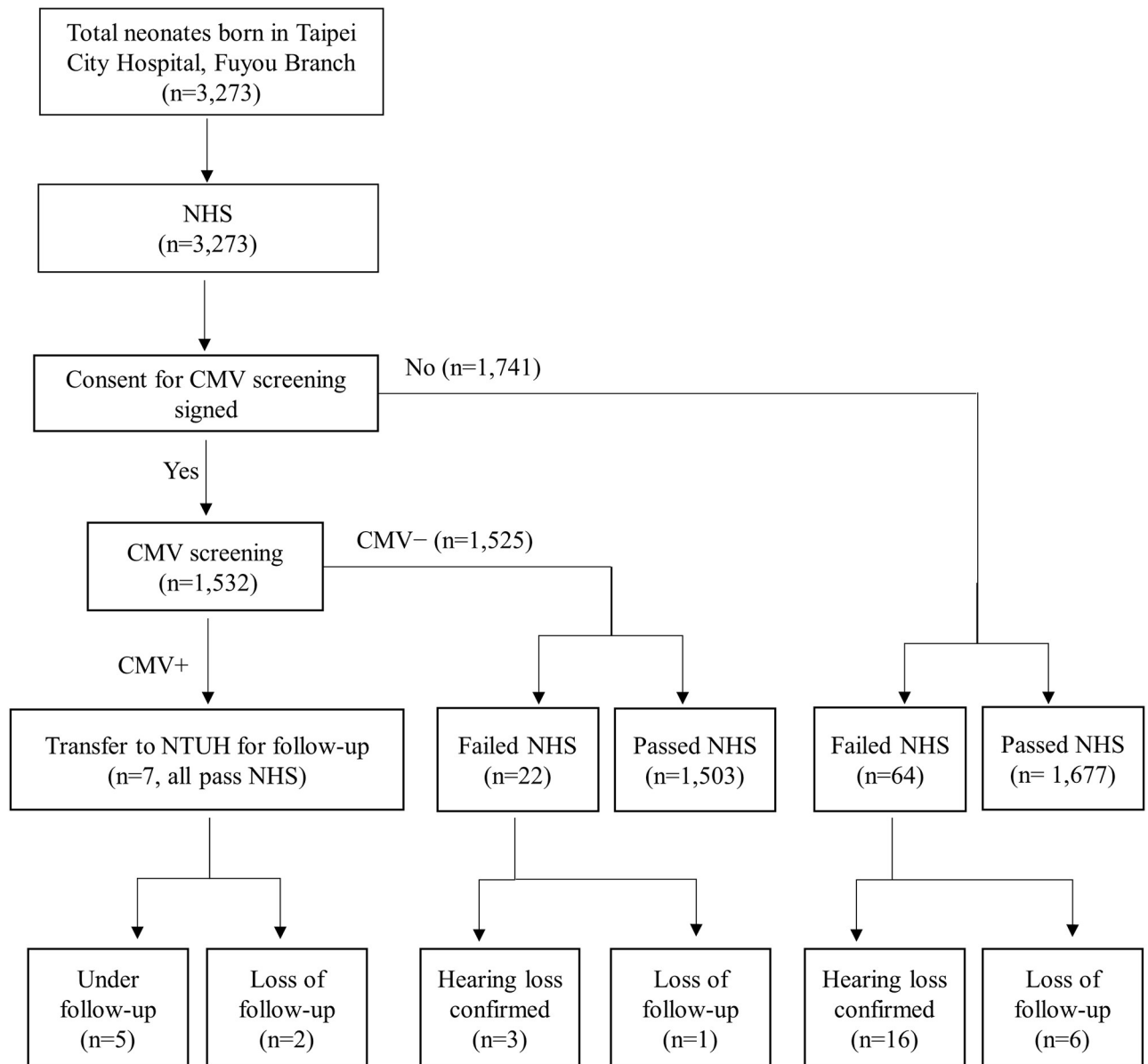


Fig 1. Flow diagram of the recruitment and the outcome of the newborn hearing screening (NHS) and cCMV screening in 3,273 newborns in Taipei, Taiwan. NTUH denotes National Taiwan University Hospital.

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Table 1. Prevalence of cCMV infection in the 1,532 newborns.

| | cCMV+ | cCMV- | Total | Prevalence | P value |
|-------------------------------|----------|-------|-------|------------|---------|
| Total number | 7 | 1,525 | 1,532 | 0.46% | |
| Sex | | | | | 0.129 |
| Male | 6 | 805 | 811 | 0.74% | |
| Female | 1 | 721 | 722 | 0.14% | |
| Mean age at last follow-up, m | 14.4±7.1 | | | | |

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Table 2. Characteristics of the 7 newborns with cCMV infection.

| Case | Sex | Mode of delivery | Age at last follow-up, m | Age of mother | Gestational age (weeks) | Gravidity | Parity | Birth weight in kg (%) | Head girth at birth in cm (%) | Hearing level | Other symptoms |
|------|-----|------------------|--------------------------|---------------|-------------------------|-----------|--------|------------------------|-------------------------------|---------------|----------------|
| 1 | F | NSD | 19 | 19 | 39 | 1 | 1 | 3.50 (50–85) | 36 (50–85) | normal | none |
| 2 | M | CS | lost to follow-up | 39 | 38 | 2 | 2 | 3.14 (15–85) | 35 (50–85) | NA | NA |
| 3 | M | CS | 18 | 41 | 38 | 5 | 4 | 3.70 (50–85) | 36 (50–85) | normal | none |
| 4 | M | NSD | lost to follow-up | 37 | 39 | 2 | 2 | 3.90 (50–85) | 35.5 (50–85) | NA | NA |
| 5 | M | NSD | 18 | 26 | 34 | 3 | 3 | 3.36 (50–85) | 34 (15–50) | normal | none |
| 6 | M | NSD | 15 | 51 | 39 | 3 | 1 | 3.58 (50–85) | 36 (50–85) | normal | none |
| 7 | M | NSD | 2 | 27 | 37 | 1 | 1 | 2.78 (3–15) | 33 (15–50) | normal | none |

CS, cesarean section; NA, not available; NSD, normal spontaneous delivery.

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factors have been proposed to account for the differences in the prevalence of cCMV infections in newborns between the developed and developing countries, including the testing methods [26], sampling methodology [26], selection bias [26], and seroprevalence rate in the general population [31,33–35], and ethnicity [26,36,37].

Noticeably, in a prior study in 1996, the prevalence of cCMV infection in Taiwanese newborns was found to be 1.8% [38]. The significantly lower prevalence in the present study might reflect the improved public health conditions, including better prenatal care in Taiwan over the past two decades. Interestingly, a recent study in China also reported a low cCMV infection prevalence (0.7%, $n = 10,933$) [33] as compared to that in three other large-scale studies in Portuguese (1.05%, $n = 3,600$) [34], Brazilian (1.1%, $n = 8,047$) [35], and Turkish (1.9%, $n = 944$) [31] populations, although the seroprevalence of CMV is commensurately high among the four populations. The authors attributed the lower cCMV infection in the Chinese population to the lower exposure of pregnant women to young children than in the other populations as a result of China's unique one-child policy [33]. In our study, we also observed a higher parity number in the mothers with CMV-positive newborns (2.0 ± 1.2) than in those with CMV-negative newborns (1.6 ± 0.7). It is thus likely that the low fertility rate, that is, the number of children a woman is expected to have during her childbearing years, might also contribute to the low cCMV infection rate in the Taiwanese newborns in the present study. Since 2008, one of the lowest fertility rates (0.895–1.27) among any territory in the world has been recorded in the Taiwanese population (https://eng.stat.gov.tw/public/data/dgbas03/bs2/yearbook_eng/y005.pdf).

Table 3. Comparison of maternal/neonatal characteristics between subjects with and those without cCMV infection.

| Characteristics | CMV+($n = 7$) | CMV-($n = 1,525$) | P value |
|-------------------------|-----------------|---------------------|---------|
| Gender (male) | 6 (85.7%) | 804 (52.7%) | .083 |
| Mode of delivery (NSD) | 5 (71.4%) | 1041 (68.3%) | .608 |
| Birth weight (kg) | 3.3 ± 0.3 | 3.1 ± 0.4 | .088 |
| Age of mother (y) | 34.4 ± 10.9 | 33.2 ± 4.7 | .768 |
| Gestational age (weeks) | 38.3 ± 0.8 | 38.5 ± 1.2 | .643 |
| Gravidity | 2.4 ± 1.4 | 2.1 ± 1.2 | .509 |
| Parity | 2.0 ± 1.2 | 1.6 ± 0.7 | .154 |
| Failed NHS | 3 (0.5%) | 0 (0%) | .986 |

NHS: Newborn hearing screen; NSD: Normal spontaneous delivery.

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The screening tool for cCMV infection is also crucial when the prevalence of cCMV infection is determined and compared across populations. It has been demonstrated that real-time PCR assays on saliva samples collected from live-born newborns performed within 2 days from birth, as performed in the present study, enables high sensitivity and specificity for identifying a cCMV infection in newborns [39,40]. In contrast, real-time PCR assay on dry blood-spot samples had a low sensitivity, restraining its value as a screening test for cCMV infection [41]. Our earlier work also showed a lower rate of cCMV infection (0.17%, 3/1,716) in a similar population when PCR on dried blood spot (DBS) specimens was used as a screening method [25].

Of note, although all seven newborns who screened positive for cCMV infection passed the hearing screening at birth and none of them developed a hearing impairment during the follow-up period, a regular and continual check-up on the hearing level and viral status is necessary in these infants, as it has been documented that a certain proportion of infants with asymptomatic cCMV infection might develop a hearing impairment or other sequelae later on, even as late as at the adolescent age [22].

The strength of this study is that all subjects were recruited from a community-based hospital, which offered an unbiased estimation of the representative prevalence of cCMV infection among newborns in Taipei. All the CMV PCR and confirmatory CMV isolation tests were fully supported by research grants and were hence free to parents. This further prevented selection biases brought about by socioeconomic status. The composition of newborns in the present study is different from that recruited from medical centers [26], where the recruitment of subjects could be biased to a study population with a higher risk of disease propensity.

However, some limitations of this study deserve discussion. First, the current study included a sample size of 1,532 newborns and an average follow-up period of 14.4 months. A larger series with a longer follow-up period will possibly disclose the prevalence and clinical outcomes of cCMV infection with greater precision. Second, the notion that low cCMV infection prevalence is associated with low fertility rates needs to be tested in other populations with low fertility rates. Further investigations in other East Asian populations with a low fertility rate, such as the Korean and Japanese populations, are highly expected.

Conclusion

The prevalence of cCMV infection in newborns of Taipei, Taiwan is 0.46%, which is slightly lower than that in other populations and that previously reported in the Taiwanese population. The relatively low prevalence in this study might be attributed to the improved public health and prenatal care system and the decreased fertility rate in Taiwan.

Supporting information

S1 File.
(XLSX)

Author Contributions

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References

1. Kennedy CR, McCann DC, Campbell MJ, et al. Language ability after early detection of permanent childhood hearing impairment. *N Engl J Med* 2006; 354(20): 2131–41. <https://doi.org/10.1056/NEJMoa054915> PMID: 16707750
2. Thompson DC, McPhillips H, Davis RL, Lieu TL, Homer CJ, Helfand M. Universal newborn hearing screening: summary of evidence. *Jama* 2001; 286(16): 2000–10. <https://doi.org/10.1001/jama.286.16.2000> PMID: 11667937
3. Yang TH, Wu CS, Liao WH, Yeh KC, Chou P. Mean hearing thresholds among school children in Taiwan. *Ear Hear* 2011; 32(2): 258–65. <https://doi.org/10.1097/AUD.0b013e3181f46a17> PMID: 20938342
4. Wake M, Tobin S, Cone-Wesson B, et al. Slight/mild sensorineural hearing loss in children. *Pediatrics* 2006; 118(5): 1842–51. <https://doi.org/10.1542/peds.2005-3168> PMID: 17079553
5. Smith RJ, Bale JF Jr., White KR. Sensorineural hearing loss in children. *Lancet* 2005; 365(9462): 879–90. [https://doi.org/10.1016/S0140-6736\(05\)71047-3](https://doi.org/10.1016/S0140-6736(05)71047-3) PMID: 15752533
6. Morton CC, Nance WE. Newborn hearing screening—a silent revolution. *N Engl J Med* 2006; 354(20): 2151–64. <https://doi.org/10.1056/NEJMra050700> PMID: 16707752
7. Hilgert N, Smith RJ, Van Camp G. Forty-six genes causing nonsyndromic hearing impairment: Which ones should be analyzed in DNA diagnostics? *Mutat Res* 2009. <https://doi.org/10.1016/j.mrrev.2008.08.002> PMID: 18804553
8. Kenna MA. Acquired Hearing Loss in Children. *Otolaryngol Clin North Am* 2015; 48(6): 933–53. <https://doi.org/10.1016/j.otc.2015.07.011> PMID: 26452421
9. Leal MC, Muniz LF, Ferreira TS, et al. Hearing Loss in Infants with Microcephaly and Evidence of Congenital Zika Virus Infection—Brazil, November 2015–May 2016. *MMWR Morb Mortal Wkly Rep* 2016; 65(34): 917–9. <https://doi.org/10.15585/mmwr.mm6534e3> PMID: 27585248
10. Correa CC, Maximino LP, Weber SAT. Hearing Disorders in Congenital Toxoplasmosis: A Literature Review. *Int Arch Otorhinolaryngol* 2018; 22(3): 330–3. <https://doi.org/10.1055/s-0037-1605377> PMID: 29983776
11. Cohen BE, Durstenfeld A, Roehm PC. Viral causes of hearing loss: a review for hearing health professionals. *Trends Hear* 2014; 18. <https://doi.org/10.1177/2331216514541361> PMID: 25080364
12. Longnecker MP, Hoffman HJ, Klebanoff MA, et al. In utero exposure to polychlorinated biphenyls and sensorineural hearing loss in 8-year-old children. *Neurotoxicol Teratol* 2004; 26(5): 629–37. <https://doi.org/10.1016/j.ntt.2004.04.007> PMID: 15315812
13. Sloan-Heggen CM, Bierer AO, Shearer AE, et al. Comprehensive genetic testing in the clinical evaluation of 1119 patients with hearing loss. *Hum Genet* 2016; 135(4): 441–50. <https://doi.org/10.1007/s00439-016-1648-8> PMID: 26969326
14. Yokota Y, Moteki H, Nishio SY, et al. Frequency and clinical features of hearing loss caused by STRC deletions. *Sci Rep* 2019; 9(1): 4408. <https://doi.org/10.1038/s41598-019-40586-7> PMID: 30867468
15. Li MC, Wu HP, Yang CY, Chen PC, Lambert GH, Leon Guo Y. Gestational exposure to polychlorinated biphenyls and dibenzofurans induced asymmetric hearing loss: Yucheng children study. *Environ Res* 2015; 137: 65–71. <https://doi.org/10.1016/j.envres.2014.12.002> PMID: 25490244

16. Lai DC, Tseng YC, Lin CY, Guo HR. Screening, rubella vaccination, and childhood hearing impairment in Taiwan. *Res Dev Disabil* 2014; 35(11): 3182–90. <https://doi.org/10.1016/j.ridd.2014.07.051> PMID: 25151608
17. Goderis J, De Leenheer E, Smets K, Van Hoecke H, Keymeulen A, Dhooge I. Hearing loss and congenital CMV infection: a systematic review. *Pediatrics* 2014; 134(5): 972–82. <https://doi.org/10.1542/peds.2014-1173> PMID: 25349318
18. Britt W. Cytomegalovirus. In: Remington Jack S. K JO, Wilson C.B., Baker C.J., ed. *Infectious Diseases of the Fetus and Newborn*. 7th ed. Philadelphia: W.B. Saunders; 2011: 706–55.
19. Kimberlin DW, Jester PM, Sanchez PJ, et al. Valganciclovir for symptomatic congenital cytomegalovirus disease. *N Engl J Med* 2015; 372(10): 933–43. <https://doi.org/10.1056/NEJMoa1404599> PMID: 25738669
20. Fowler KB, McCollister FP, Dahle AJ, Boppana S, Britt WJ, Pass RF. Progressive and fluctuating sensorineural hearing loss in children with asymptomatic congenital cytomegalovirus infection. *J Pediatr* 1997; 130(4): 624–30. [https://doi.org/10.1016/s0022-3476\(97\)70248-8](https://doi.org/10.1016/s0022-3476(97)70248-8) PMID: 9108862
21. Fowler KB, Dahle AJ, Boppana SB, Pass RF. Newborn hearing screening: will children with hearing loss caused by congenital cytomegalovirus infection be missed? *J Pediatr* 1999; 135(1): 60–4. [https://doi.org/10.1016/s0022-3476\(99\)70328-8](https://doi.org/10.1016/s0022-3476(99)70328-8) PMID: 10393605
22. Lanzieri TM, Chung W, Flores M, et al. Hearing Loss in Children With Asymptomatic Congenital Cytomegalovirus Infection. *Pediatrics* 2017; 139(3).
23. Mestas E. Congenital Cytomegalovirus. *Adv Neonatal Care* 2016; 16(1): 60–5. <https://doi.org/10.1097/ANC.000000000000242> PMID: 26752783
24. Huang HM, Chiang SH, Shiau YS, et al. The universal newborn hearing screening program of Taipei City. *Int J Pediatr Otorhinolaryngol* 2013; 77(10): 1734–7. <https://doi.org/10.1016/j.ijporl.2013.08.004> PMID: 24012220
25. Lu CY, Tsao PN, Ke YY, et al. Concurrent Hearing, Genetic, and Cytomegalovirus Screening in Newborns, Taiwan. *J Pediatr* 2018; 199: 144–50 e1. <https://doi.org/10.1016/j.jpeds.2018.02.064> PMID: 29681450
26. Kenneson A, Cannon MJ. Review and meta-analysis of the epidemiology of congenital cytomegalovirus (CMV) infection. *Rev Med Virol* 2007; 17(4): 253–76. <https://doi.org/10.1002/rmv.535> PMID: 17579921
27. 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(5): 355–63. <https://doi.org/10.1002/rmv.544> PMID: 17542052
28. Mwaanza N, Chilukutu L, Tembo J, et al. High rates of congenital cytomegalovirus infection linked with maternal HIV infection among neonatal admissions at a large referral center in sub-Saharan Africa. *Clin Infect Dis* 2014; 58(5): 728–35. <https://doi.org/10.1093/cid/cit766> PMID: 24265360
29. Noyola DE, Mejia-Elizondo AR, Canseco-Lima JM, Allende-Carrera R, Hernansez-Salinas AE, Ramirez-Zacarias JL. Congenital cytomegalovirus infection in San Luis Potosi, Mexico. *Pediatr Infect Dis J* 2003; 22(1): 89–90. <https://doi.org/10.1097/00006454-200301000-00022> PMID: 12553301
30. Olusanya BO, Slusher TM, Boppana SB. Prevalence of congenital cytomegalovirus infection in Nigeria: a pilot study. *Pediatr Infect Dis J* 2015; 34(3): 322–4. <https://doi.org/10.1097/INF.0000000000000555> PMID: 25742080
31. Sahiner F, Cekmez F, Cetinkaya M. Congenital cytomegalovirus infections and glycoprotein b genotypes in live-born infants: a prevalence study in turkey. *Infect Dis* 2015; 47: 6.
32. van der Sande MA, Kaye S, Miles DJ, et al. Risk factors for and clinical outcome of congenital cytomegalovirus infection in a peri-urban West-African birth cohort. *PLoS One* 2007; 2(6): e492. <https://doi.org/10.1371/journal.pone.0000492> PMID: 17551573
33. Wang S, Wang T, Zhang W, et al. Cohort study on maternal cytomegalovirus seroprevalence and prevalence and clinical manifestations of congenital infection in China. *Medicine (Baltimore)* 2017; 96(5): e6007. <https://doi.org/10.1097/MD.0000000000006007> PMID: 28151899
34. Paixao P, Almeida S, Gouveia P, Vilarinho L, Vaz Osorio R. Prevalence of human cytomegalovirus congenital infection in Portuguese newborns. *Euro Surveill* 2009; 14(9): 13–5. PMID: 19317972
35. Mussi-Pinhata MM, Yamamoto AY, Moura Brito RM, et al. Birth prevalence and natural history of congenital cytomegalovirus infection in a highly seroimmune population. *Clin Infect Dis* 2009; 49(4): 522–8. <https://doi.org/10.1086/600882> PMID: 19583520
36. Cannon MJ, Schmid DS, Hyde TB. Review of cytomegalovirus seroprevalence and demographic characteristics associated with infection. *Rev Med Virol* 2010; 20(4): 202–13. <https://doi.org/10.1002/rmv.655> PMID: 20564615
37. Cannon MJ. Congenital cytomegalovirus (CMV) epidemiology and awareness. *J Clin Virol* 2009; 46 Suppl 4: S6–10. <https://doi.org/10.1016/j.jcv.2009.09.002> PMID: 19800841

38. Tsai CH, Tsai FJ, Shih YT, Wu SF, Liu SC, Tseng YH. Detection of congenital cytomegalovirus infection in Chinese newborn infants using polymerase chain reaction. *Acta Paediatr* 1996; 85(10): 1241–3. <https://doi.org/10.1111/j.1651-2227.1996.tb18237.x> PMID: 8922092
39. Boppana SB, Ross SA, Shimamura M, et al. Saliva polymerase-chain-reaction assay for cytomegalovirus screening in newborns. *N Engl J Med* 2011; 364(22): 2111–8. <https://doi.org/10.1056/NEJMoa1006561> PMID: 21631323
40. Yamamoto AY, Mussi-Pinhata MM, Marin LJ, Brito RM, Oliveira PF, Coelho TB. Is saliva as reliable as urine for detection of cytomegalovirus DNA for neonatal screening of congenital CMV infection? *J Clin Virol* 2006; 36(3): 228–30. <https://doi.org/10.1016/j.jcv.2006.03.011> PMID: 16750653
41. Boppana SB, Ross SA, Novak Z, et al. Dried blood spot real-time polymerase chain reaction assays to screen newborns for congenital cytomegalovirus infection. *JAMA* 2010; 303(14): 1375–82. <https://doi.org/10.1001/jama.2010.423> PMID: 20388893