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Prevalence of Congenital Cytomegalovirus Infection in Nigeria: a Pilot Study

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Abstract

Dried saliva specimens from 263 neonates in Lagos, Nigeria were tested for CMV using real-time PCR and 10 infants (3.8%; 95%CI, 2.1-6.8) were positive. Congenital CMV infection was not associated with any of the demographic or maternal factors including HIV. These data demonstrate high prevalence of congenital CMV infection and the feasibility of CMV screening by testing real-time PCR.

Keywords

congenital CMV; saliva PCR; newborn screening; developing country

Cytomegalovirus (CMV) is a frequent cause of congenital infection and a leading non-genetic cause of permanent congenital or early-onset hearing loss (PCEHL) in children [1,2]. Although limited data suggests high prevalence of congenital CMV infection (cCMV) in developing countries with high maternal CMV seroprevalence, the burden of disease and natural history of congenital CMV infection (cCMV), especially sub-Saharan Africa, have not been well defined [1,3-5]. Additionally, the role of cCMV in PCEHL in the African continent has not been examined although infants with microcephaly have been reported to be significantly at-risk for PCEHL in Nigeria [6]. Early identification of infants with cCMV allows for prompt detection of children at risk for PCEHL requiring appropriate intervention during critical stages of language development [1,2]. Real-time polymerase chain reaction (PCR) testing of newborn saliva has been shown to be highly specific and sensitive for detecting CMV-infected infants [7,8]. We therefore conducted a pilot study to determine the prevalence of cCMV in an inner-city community in Lagos, Nigeria with a previously reported high occurrence of PCEHL [9].

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Methods

Infants were enrolled in the study by convenient sampling of neonates on admission between November 2012 and April 2013 at Island Maternity Hospital (IMH) and Massey Children's Hospital (MCH) in Lagos, Nigeria whose mothers gave consent to participate in the study. Demographic data and medical history were obtained from hospital records and ethical approval from the Lagos State Government Health Service Commission. Dried saliva swabs were collected, labeled with a unique ID number, and transported to the University of Alabama at Birmingham (UAB), for testing by real-time PCR for CMV without the DNA extraction step as described [7,8]. A sample was considered positive if one or more International Units (IU) per reaction was detected. The detection limit of this PCR assay was determined to be 116 IU per mL of the sample ($1.72\text{ge/mL}=1\text{IU/mL}$) using the Acrometrix® CMV international standards (Life Technologies, Grand Island, NY). No follow-up visits were included but parents were informed of the infant's CMV status for further medical attention. HIV 1 and 2 testing were routinely conducted during pregnancy using two rapid immunochromatographic screening test kits [9]. Two negative or positive results are confirmatory for HIV-status. Discordant results were resolved with ELISA. Data was analyzed using SPSS statistical package version 21 (IBM Corp, Armonk, New York). To determine differences between infants with or without cCMV, we used a case-control sample in which infants with CMV were matched on the basis of gender to infants without CMV in the ratio of 1:10. Gender was selected as the matching criterion because of the potential confounding effect of the high frequency of G6PD deficiency in male infants in the study population. The controls were selected from infants with the closest dates of birth from the same hospital. Maternal age, ethnicity, gravidity, parity, mode of delivery, HIV status, multiple gestation, gestational age, birth weight, presence of neonatal jaundice and admission status were compared between CMV-infected and uninfected infants. Statistical significance was determined by Pearson chi-square test or Fisher exact for categorical variables and student-t test for continuous variables.

Results

Of the 263 infants tested, 10 (6 females, 4 males) were CMV positive, a prevalence rate of 3.8% (95% CI: 2.1% – 6.9%). The prevalence of cCMV was not significantly different between the two hospitals: 3.4% (5/149) vs 4.4% (5/114). The characteristics of CMV-infected newborns are shown in Table 1. Mean age of mothers with CMV-infected babies was 29.7 ± 6.1 years (IMH: 30.2 ± 8.04 ; MCH: 29.2 ± 4.38 years). Mean gestational age for CMV-infected infants was 35.9 ± 4.0 weeks (IMH: 35.0 ± 3.74 ; MCH: 37.0 ± 3.94 weeks) with a mean birth weight of 2.2 ± 1.3 kg (IMH: 2.39 ± 1.30 ; MCH: 3.23 ± 1.06 kg). Of the infected children, two infants were symptomatic. Both infants had hepatosplenomegaly and bronchopneumonia and one baby also had neonatal jaundice. Maternal HIV status was known for 162 infants including 8 congenitally infected children. The prevalence of maternal HIV infection was 4.9% (6/162) and none of the CMV-infected babies were born to a HIV-positive mother. There were no statistically significant differences between CMV-infected infants and their matched controls with respect to maternal age, ethnicity, gravidity, parity, gestational age, maternal HIV status, and birth weight (Supplemental Digital Content 1).

Discussion

This study utilized a virologic assay that is reliable and convenient to identify CMV-infected newborns. By eliminating the requirement for DNA extraction, this PCR assay also has significant cost savings. The results from this population with near-universal seroimmunity demonstrated a high prevalence of cCMV and the feasibility of screening newborns with real-time PCR of dried-saliva swabs in resource-poor settings.

The prevalence of cCMV in this study falls within the reported range of 0.9% (Mexico) and 5.4% (Gambia) for developing countries but well over 0.5% to 0.7% reported in developed countries [1,3-5]. Our findings are consistent with a recent study from Zambia in which cCMV based on the detection of CMV DNA in saliva, urine or sera, or the detection of serum CMV IgM antibodies, was detected in 3.8% (15/395) of neonatal admissions in the first 3 weeks in a population with high maternal HIV prevalence [3]. A study from the Gambia reported significantly higher prevalence of cCMV (5.4%, 40/741) and was associated with active placental malarial infection [4]. Although CMV seroprevalence was not determined as part of this study, a previous study among pregnant women in Lagos, Nigeria showed that 97.2% were CMV-IgG positive [10]. It is therefore likely that most women in our study were seroimmune before pregnancy.

High prevalence (2.9%, 22/748) of cCMV in HIV-exposed infants was also documented in a recent study from South Africa [5]. Compared with findings from Zambia and South Africa, none of the HIV-exposed infants were CMV-infected in our study [3,5]. In the Zambian study, the prevalence of cCMV was 11.4% and 2.1% among neonates born to HIV-infected and uninfected mothers, respectively [3]. In Western Cape, South Africa, 2.9% of infants born to 748 HIV-infected mothers had cCMV [5]. The prevalence of maternal HIV infection of 4.9% in our study population is consistent with previous data from this inner-city community [8]. HIV infection status was known for 162 mothers including 8 mothers with CMV-infected newborns and none of the babies with cCMV were born to HIV-infected mothers. However, the number of women with HIV infection in this study is too small to determine the role of maternal HIV infection on intrauterine CMV transmission and therefore, the association between cCMV and maternal HIV in this population merits further research.

There were no associations between congenital CMV and maternal age, parity, mode of delivery, gestational age, birth weight, gender and jaundice. A major limitation of this study is the small sample size and the use of convenience sampling. Thus, it is not clear whether this data is representative of cCMV prevalence in the population in Nigeria. Additionally, infected children were not followed, to document long-term outcomes. Although the real-time PCR assay has been shown to be highly specific in previous studies in the United States, it is possible that the rate of false positive PCR results could be higher in populations with concurrent maternal infections [7,8]. Nevertheless, the findings of this study underscore the need for prospective newborn CMV screening study with long-term follow-up to document the natural history and disease burden of cCMV in this population. In addition, the utility of the real-time PCR assay should be evaluated in larger studies in such populations. It is crucial to examine the role of cCMV among infants with congenital, early/

late-onset, fluctuating and progressive sensorineural hearing loss to develop evidence-based guidelines for intervention advocacy for at-risk infants. Overall, this pilot study and the follow-up research should fill an important epidemiologic gap on cCMV in sub-Saharan Africa.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Manicklal S, Emery VC, Lazzarotto T, Boppana SB, Gupta RK. The “silent” global burden of congenital cytomegalovirus. *Clin Microbiol Rev.* 2013; 26:86–102. [PubMed: 23297260]
2. Dahle AJ, Fowler KB, Wright JD, Boppana SB, Britt WJ, Pass RF. Longitudinal investigation of hearing disorders in children with congenital cytomegalovirus infection. *J Am Acad Audiol.* 2000; 11:283–290. [PubMed: 10821506]
3. Mwaanza N, Chilukutu L, Tembo J, Kabwe M, Musonda K, Kapasa M, Chabala C, Sinyangwe S, Mwaba P, Zumla A, Bates M. 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; 58:728–35. [PubMed: 24265360]
4. van der Sande MA, Kaye S, Miles DJ, Waight P, Jeffries DJ, Ojuola OO, Palmero M, Pinder M, Ismaili J, Flanagan KL, Aveika AA, Zaman A, Rowland-Jones S, McConkey SJ, Whittle HC, Marchant A. Risk factors for and clinical outcome of congenital cytomegalovirus infection in a peri-urban West-African birth cohort. *PLoS One.* 2007; 2:e492. [PubMed: 17551573]
5. Manicklal S, van Niekerk AM, Kroon SM, Hutto C, Novak Z, Pati SK, Chowdhury N, Hsiao NY, Boppana SB. Birth Prevalence of Congenital Cytomegalovirus Among Infants of HIV-Infected Women on Prenatal Antiretroviral Prophylaxis in South Africa. *Clin Infect Dis.* 2014; 58:1467–72. [PubMed: 24567248]
6. Olusanya BO. Risk of sensorineural hearing loss in infants with abnormal head size. *Ann Afr Med.* 2013; 12:98–104. [PubMed: 23713016]
7. Boppana SB, Ross SA, Shimamura M, Palmer AL, Ahmed A, Michaels MG, Sánchez PJ, Bernstein DI, Tolan RW Jr, Novak Z, Chowdhury N, Britt WJ, Fowler KB. National Institute on Deafness and Other Communication Disorders CHIMES Study. Saliva polymerase-chain-reaction assay for cytomegalovirus screening in newborns. *N Engl J Med.* 2011; 364:2111–8. [PubMed: 21631323]
8. Ross SA, Ahmed A, Palmer AL, Michaels MG, Sanchez PJ, Bernstein DI, Tolan RW Jr, Novak Z, Chowdhury N, Fowler KB, Boppana SB, for the National Institute on Deafness and Other Communication Disorders CHIMES Study. Detection of congenital cytomegalovirus infection by real-time polymerase chain reaction analysis of saliva or urine specimens. *J Infect Dis.* May 5.2014 (Epub ahead of print).
9. Olusanya BO, Afe AJ, Onyia NO. Infants with HIV-infected mothers in a universal newborn hearing screening programme in Lagos, Nigeria. *Acta Paediatr.* 2009; 98:1288–93. [PubMed: 19519758]
10. Akinbami AA, Rabiou KA, Adewunmi AA, Wright KO, Dosunmu AO, Adeyemo TA, Adediran A, Osunkalu VO. Seroprevalence of cytomegalovirus antibodies amongst normal pregnant women in Nigeria. *Int J Womens Health.* 2011; 3:423–8. [PubMed: 22247628]

Table 1

Characteristics of infants with congenital CMV infection

	Status at screening	Mother's age (years)	Mode of delivery	Gestation	Gestational age (weeks)	Birth weight (kg)	Clinical features
1	Out-born	30	SVD	Singleton	39	Missing	Symptomatic: hepatosplenomegaly and bronchopneumonia
2	Out-born	30	SVD	Singleton	39	Missing	Asymptomatic
3	Inborn	38	SVD	First Twin	31	1.0	Asymptomatic, NNJ
4	Inborn	38	BREECH	Second Twin	31	1.0	Asymptomatic, NNJ
5	Out-born	30	EMCS	One of Triplet	38	Missing	Asymptomatic
6	Out-born	22	SVD	Singleton	39	N	Asymptomatic
7	Inborn	31	EMCS	Singleton	37	3.30	Asymptomatic, NNJ
8	Out-born	34	EMCS	Singleton	30	1.25	Symptomatic: hepatosplenomegaly and bronchopneumonia, and NNJ
9	Inborn	21	EMCS	Singleton	39	3.75	Asymptomatic
10	Inborn	23	EMCS	Singleton	37	2.90	Asymptomatic

SVD: spontaneous vertex delivery, EMCS: emergency caesarean delivery, NNJ: treated for jaundice