

2331. Seroprevalence of Cytomegalovirus in Pregnant Women and Birth Prevalence of Congenital Cytomegalovirus Infection in Henan Province, China
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Background. Congenital cytomegalovirus infection (cCMVi) is the leading viral cause of birth defects and developmental disabilities in newborns. The epidemiology of cCMVi in settings with high cytomegalovirus (CMV) seroprevalence, such as China, is not well studied. This study sought to describe maternal CMV seroprevalence and cCMVi prevalence at birth in Henan Province, China.

Methods. A multicenter prospective cohort study was conducted in three counties of Henan Province in China from June 2015 through May 2018. Pregnant women were enrolled early in pregnancy and followed up through delivery. Serum specimens were collected at enrollment for CMV immunoglobulin G serological testing. Saliva and urine specimens were collected in newborns within 72 hours after birth and tested with real-time polymerase chain reaction for CMV DNA. cCMVi was defined as CMV DNA positive in the infants' urine or saliva specimens.

Results. A total of 6327 pregnant women underwent CMV serological testing and 6062 were CMV seropositive (95.8%). The maternal age was 26.8 ± 4.3 (mean ± SD) years. There were 49 (0.7%) newborns identified with cCMVi among 6705 newborns screened. Lower maternal education level (middle school or lower), younger maternal age (<25 years) and twin-pregnancy were associated with higher cCMVi prevalence ($P = 0.04, 0.016, \text{ and } 0.001$, respectively).

Conclusion. Despite a high maternal CMV seroprevalence in this large cohort study from China, the birth prevalence of cCMVi is similar to other studies in settings of high and medium CMV seroprevalence. In settings of high maternal CMV seroprevalence, additional research is needed to ascertain the relative contribution of non-primary CMV infections during pregnancy to congenital transmission.

Disclosures. All authors: No reported disclosures.

2332. Low Serum Vitamin D Levels Are Related to Life-Threatening Respiratory Syncytial Virus Infection in Previously Healthy Infants

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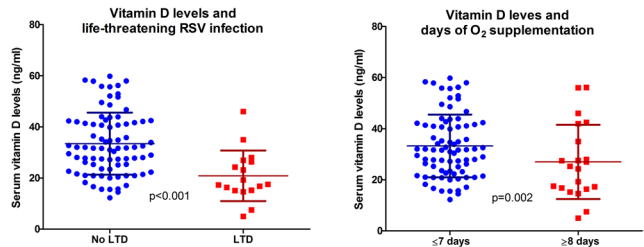
Background. Serum 25-hydroxy-vitamin D (VD) effects on lung growth and immune system modulation might affect respiratory infections outcomes. Data are controversial regarding the role of VD status in the severity of Respiratory Syncytial Virus (RSV) infection. The aim of this study was to assess serum VD levels and its association with life-threatening disease (LTD) in previously healthy infants infected with RSV.

Methods. Prospective cohort study including previously healthy infants <12 months, hospitalized with a first RSV infection in 2017–2018. Viral load (VL) was assessed by qRT-PCR in nasopharyngeal aspirates and serum VD levels measured by ECLIA, in samples obtained on admission. VD deficiency was defined as levels <20 ng/mL, VD insufficiency 20–29 ng/mL, and LTD as need of intensive care and mechanical or noninvasive ventilation

Results. 98 patients, mean age 4.5 months (±3.1), 55 (56.1%) male. VD status: 18 (18.4%) with deficiency, 32 (32.6%) with insufficiency; 14 (77.8%) patients with deficiency had not received VD supplementation. There was no relationship between VD deficiency and anemia ($P = 0.28$) or age ($P = 0.27$). LTD was observed in 17 infants, with no significant differences in socioeconomic, pregnancy and infant variables compared with other RSV cases. Patients with LTD had significantly lower levels of VD (17.5 ng/mL [IQR 15.2–26.3] vs. 31.8 ng/mL [IQR 23.5–52.1, $P < 0.001$]), Figure 1. 15 patients, 88.2% of all infants with VD levels ≤29 ng/mL developed LTD compared with a study population frequency of LTD of 17.3%. Multivariable regression analysis including breastfeeding confirmed VD deficiency as a risk factor for LTD (aOR 14.3, 95% CI 3.9–51.5, $P < 0.001$). Normal VD values conferred protection (aOR 0.1, 95% CI 0.02–0.49, $P = 0.004$). VD levels inversely correlated with days of hypoxemia ($P = 0.007$); VD deficiency increased the risk of requiring O₂ supplementation >7 days (aOR 8.5, $P < 0.001$). VL did not correlate with VD levels ($P = 0.696$), length of stay ($P = 0.378$), days of hypoxemia ($P = 0.681$). VL was not associated with LTD ($P = 0.42$).

Conclusion. Vitamin D deficiency was a risk factor for LTD in previously healthy infants with RSV infection. Viral titers did not correlate with VD levels. These findings provide additional evidence for the development of low-cost preventive and therapeutic strategies.

Figure 1. Serum vitamin D levels according to severity outcomes: life-threatening disease and prolonged oxygen supplementation.



Disclosures. All authors: No reported disclosures.

2333. Influenza-Related Neurologic Complications in Hospitalized Children with Underlying Neurologic Disorders

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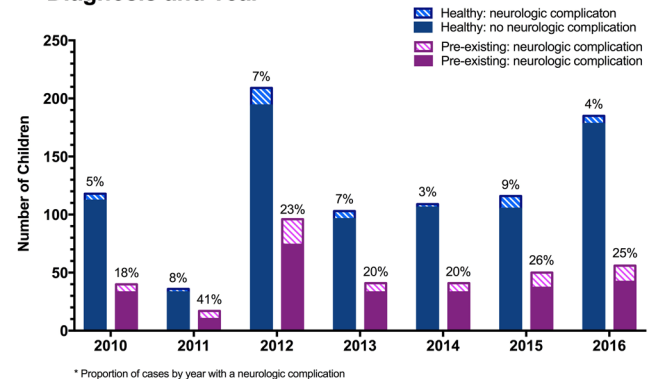
Background. Children with underlying neurological and neuromuscular conditions are considered "high risk" for developing severe infection due to influenza. Prior reports highlighted this population's increased risk for respiratory failure. Little is known about neurological complications experienced by children with pre-existing neurologic disorders (PNDs) when infected with influenza.

Methods. Retrospective cohort study of children 0.5–18.0 years old hospitalized at a tertiary care pediatric hospital between August 2010 and June 2017 with laboratory-confirmed influenza. Eligible children were identified by electronic medical record query for influenza assay CPT codes with positive results during an admission; cases were confirmed by chart review. Demographics and clinical data were abstracted.

Results. A total of 1217 immune competent children (median age 5.5 [IQR 2.2–9.8] years) were hospitalized with laboratory-confirmed influenza during the study period. About 28% (341/1217) had at least one PND, including epilepsy ($n = 105$), developmental delay or intellectual disability ($n = 234$), neurogenetic or metabolic disorders ($n = 77$), neuromuscular disorders ($n = 22$) and others ($n = 253$). Compared with previously healthy peers, these children were more often admitted to the intensive care unit (31% vs. 16%, $P < 0.001$), had a longer length of stay (3 vs. 2 days, $P < 0.001$), and had a higher incidence of neurologic complications (23% vs. 6%, $P < 0.001$). Seizures (18% vs. 4%, $P < 0.001$) and encephalopathy (8% vs. 2%, $P < 0.001$) in particular were more common in children with PNDs, but other neurologic complications occurred in comparable proportions (3% vs. 1%, $P = 0.088$). Only 49% of the overall cohort had documented annual influenza vaccine; coverage was slightly better for children with PNDs than those without (55% vs. 48%, $P = 0.017$). The odds of having a neurologic complication in children with documented vaccination was nearly half that of other children when adjusted for age, influenza strain, and any PND (adjusted OR 0.64, 95% CI 0.44–0.94, $P = 0.021$).

Conclusion. The excess risk of neurological complications in children with PNDs highlights the importance of vaccinating this population. Additional consideration should be given to post-exposure prophylaxis for children with PNDs who have not received vaccine.

Neurologic Complications by Pre-Existing Neurologic Diagnosis and Year



Disclosures. All authors: No reported disclosures.

2334. Saliva Screening for Congenital Cytomegalovirus Infection in the Neonatal Intensive Care Unit: Beware!

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Background. Congenital cytomegalovirus (cCMV) infection is the most common cause of non-genetic sensorineural hearing loss in infancy. Screening of newborns for cCMV infection has been performed utilizing saliva due to ease of collection and high sensitivity. Positive saliva screens for CMV DNA by polymerase chain reaction (PCR) testing has been reported to occur secondary to breast milk feeding without signifying congenital infection. The NICUs of Nationwide Children's Hospital recently began universal saliva screening of all admissions. We report 3 neonates whose saliva CMV screen was positive yet the urine CMV PCR test was negative in order to inform CMV screening strategies.

Methods. Retrospective review of the electronic health records of neonates admitted to the neonatal intensive unit (NICU) at Nationwide Children's Hospital, Columbus, OH who had CMV detected by PCR from saliva specimens but not from urine. Pertinent demographic and clinical data were obtained.

Results. Three female neonates had a positive saliva CMV DNA PCR test but urine CMV PCR was negative. The first infant (gestational age [GA] 34 weeks, birth weight [BW] 1790 Grams) was a monochorionic diamniotic twin gestation and born vaginally with unknown duration of rupture of membranes (ROM). At 16 days of age, the infant had a positive saliva CMV PCR but a negative urine CMV PCR test. The infant received maternal milk. The twin's CMV PCR tests of saliva and urine were negative. The second infant (GA 38 weeks, BW 2952 grams) was born vaginally after 9 hours of ROM. On the first day of age, the infant had a positive saliva CMV PCR test that was followed by a negative urine CMV PCR on the third day of age. The infant had not been breastfed. The third infant (GA 33 weeks, BW 1762 grams) was born by C-section delivery with ROM at delivery. Saliva CMV PCR screen was positive on the second day of age but urine PCR was negative twice (days 5 and 7). All 3 infants had no signs/symptoms of cCMV infection and passed the newborn hearing screen.

Conclusion. Testing of saliva for CMV DNA by PCR is not always confirmatory for cCMV infection as contamination of saliva specimens with CMV could result from exposure to maternal milk and possibly vaginal secretions. Definitive diagnosis of cCMV infection requires additional confirmatory testing preferably with urine.

Disclosures. All authors: No reported disclosures.

2335. Newborn Dried Blood Spot for Retrospective Diagnosis of Congenital Cytomegalovirus (CMV) Infection: It's Time for Universal Screening!

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Background. The diagnosis of congenital cytomegalovirus (cCMV) infection requires that CMV be detected in a body fluid before 3 weeks of age. After 3 weeks, a diagnosis of cCMV infection is difficult since one cannot differentiate between prenatal, natal, and postnatal CMV acquisition. Infants who refer on the newborn hearing screen often are diagnosed with hearing loss after 3 weeks of age. Our objective was to describe the use of the newborn dried blood spot (DBS) for detection of CMV DNA in infants who are evaluated for sensorineural hearing loss (SNHL).

Methods. Retrospective review of the electronic health records of infants who were referred to the Neonatal Infectious Disease (NEO-ID) Clinic at Nationwide Children's Hospital, Columbus, OH since 2015 for evaluation of SNHL. Demographic, clinical, laboratory, and radiographic data were reviewed. With maternal informed consent, the newborn DBS was obtained from the Ohio Department of Health for detection of CMV DNA by polymerase chain reaction (PCR) testing as previously described (Boppana et al. *JAMA*, 2010).

Results. Eighteen infants (gestational age [mean ± SD], 38 ± 4 weeks; birth weight, 3,094 ± 705 g) with SNHL were referred by Otolaryngology for evaluation of possible cCMV infection; 17 (94%) had referred on the newborn hearing screen. The 18 infants were first tested for CMV at 151 ± 124 days of age (mean ±SD; range, 21–521 days), and 3 (17%) had a positive CMV DBS. Fourteen (78%) of the 18 infants had a positive serum CMV IgG antibody while 5 (63%) of 8 infants had CMV DNA detected in urine by PCR. Of the 3 infants with a positive CMV DBS, 2 were tested for CMV DNA PCR in urine and both were positive. Of the 3 infants, 1 had a negative serum CMV IgG antibody test at 174 days of age but the urine CMV PCR test was positive. In comparison, of 54 infants with cCMV infection confirmed by a positive urine CMV PCR in the first 3 weeks of age, 37 (68%) had a positive CMV DBS.

Conclusion. DBS testing for CMV DNA by PCR testing identified a small minority of infants with SNHL and thus confirming congenital infection. However, the overall sensitivity of CMV DBS testing in our cohort was 68%, suggesting that some infants with SNHL due to congenital CMV infection are missed.

Disclosures. All authors: No reported disclosures.

2336. Adherence to Follow-up and CMV Testing in Infants Who Failed Newborn Hearing Screens: Evaluation of New Protocol to Ensure Follow-up and Testing

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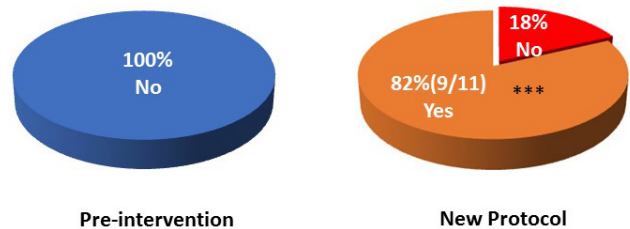
Background. CMV is the most common non-hereditary cause of sensorineural hearing loss (SNHL) in children in the United States. SNHL may be the only presenting symptom in otherwise asymptomatic infants. Several states are making CMV testing mandatory for newborn infants who have a hearing deficit. Testing should be performed before 21 days of life to diagnose congenital CMV infection and provide effective therapy. However, the results of a retrospective 1 year audit of all newborn patients in the nursery of University Hospital of Brooklyn (UHB) who failed their hearing screen found that none were tested for CMV and approximately half failed to follow-up with audiology. Therefore we developed a new protocol to ensure testing and follow-up.

Methods. Under the new protocol, newborns who fail an initial and repeat hearing screen are tested for CMV in urine by culture and the audiology appointment is scheduled before discharge. Patients are tracked by a pediatric infectious disease fellow to ensure adherence to protocol.

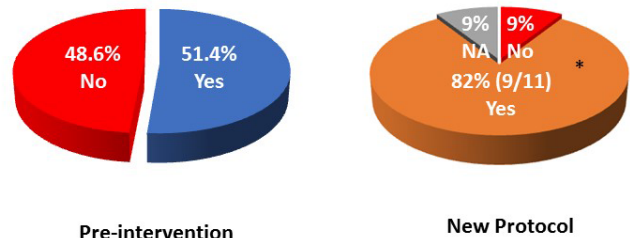
Results. The pre-intervention audit conducted from November 1, 2017 to October 31, 2018 found 37/923 (4%) infants failed their hearing screening tests. Although 34/37 (92%) of these children had audiology appointments made before discharge, only 19 (56%) actually attended. Two (11%) children failed an otoacoustic emissions hearing test. One infant also went on to fail an auditory brainstem response test; both were lost to follow-up. None of these infants was tested for CMV. The new protocol was initiated November 1, 2018, 11/372 (3%) infants failed initial and repeat hearing screening tests. All 11 (100%) of these children had audiology appointments made before discharge, of which 9 (82%) attended. 2 (18%) of these children failed the otoacoustic emissions hearing test at that visit, 1 infant was lost to follow-up; 9 infants who failed hearing test were tested for CMV; 1 (9%) was positive.

Conclusion. Although it has only been in place for 5 months, the new protocol has increased adherence to audiology appointments. CMV testing has increased from 0% to 82% and 1 patient has tested positive for congenital CMV infection. The ongoing success of this protocol could facilitate timely and appropriate treatment of CMV with valgancyclovir.

CMV Testing Performed



Adherence to Audiology Appointment



Disclosures. All authors: No reported disclosures.

2337. Health Outcomes in Congenital Cytomegalovirus, a Systematized and Unbiased Approach in the Electronic Medical Record Era

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