Notes from the Field

Universal Newborn Screening and Surveillance for Congenital Cytomegalovirus — Minnesota, 2023–2024

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Summary

What is already known about this topic?

Congenital cytomegalovirus (cCMV) is the most frequent infectious cause of birth defects and the most common nongenetic cause of permanent hearing loss in U.S. children.

What is added from this report?

Universal newborn screening and population-based surveillance for cCMV, implemented in Minnesota in 2023, identified an observed cCMV prevalence of 0.3% of Minnesota live births. Nearly all cCMV cases detected through newborn screening were confirmed with diagnostic testing; most infants received comprehensive evaluations and linkage to care, leading to the detection of unapparent cCMV-specific findings among seven infants.

What are the implications for public health practice?

Universal newborn screening identified infants with neurologic abnormalities and those with or at risk for cCMV-associated permanent hearing loss and other sequelae, who might have been missed by routine care or targeted screening.

Congenital cytomegalovirus (cCMV) is the most frequent infectious cause of birth defects and the most frequent nongenetic cause of permanent hearing loss in U.S. children; cCMV affects approximately 0.5% of U.S. births. Among infants with cCMV infection, approximately 10% have clinical findings at birth (*1*). Early identification of cCMV infection could improve outcomes through the use of antiviral therapy when indicated, and audiology and developmental screenings (*1*). A recent Minnesota study found average dried blood spot sensitivity of 75% for detection of cCMV infection (*2*). In February 2023, Minnesota became the first U.S. state to implement universal newborn screening for cCMV. To evaluate performance and feasibility of newborn screening and to describe the epidemiology of cCMV, statewide surveillance was initiated. This report describes the first year of these activities.

Investigation and Outcomes

Minnesota Department of Health Newborn Screening Recommendations

Unless parents opt out, all Minnesota-born infants are screened for the presence of cytomegalovirus (CMV) using a qualitative real-time polymerase chain reaction (PCR) assay performed on a dried blood spot at the Minnesota Department of Health.* Infants whose assay detects CMV are recommended to have diagnostic PCR testing, performed on urine, within the first 21 days of life. For infants with diagnosed cCMV, recommended evaluations include complete blood count, liver function testing, neuroimaging, and audiologic and ophthalmologic assessments. In addition, infants with evidence of CMV infection† within the first 90 days of life are voluntarily reported to the Minnesota Department of Health by clinicians or through electronic laboratory reporting. The Minnesota Department of Health newborn screening program follows all identified infants with cCMV to ensure linkage to care and to evaluate long-term outcomes.

2023–2024 cCMV Surveillance Findings

During February 6, 2023–February 5, 2024, the Minnesota Department of Health screened 60,115 infants, 184 (0.31%) of whom had CMV detected; 174 detections (0.29%) occurred during the first 21 days of life, and 10 (0.02%) after age 21 days. Among the 174 infants with CMV detected during the first 21 days of life, confirmatory testing was completed for 170 (98%), including 164 (96%) before age 21 days; CMV was detected in 169 (99%) of these infants. In addition, three infants with cCMV who had a negative test result during CMV newborn screening were identified by clinician or laboratory reporting. Among all 187 infants, 176 (94%) met the confirmed case definitions (21 [12%] with cCMV disease; 155 [88%] with cCMV infection)§ (*3*); 11 (6%) infants did not meet the case definition.

Among the 176 confirmed cases of cCMV disease or cCMV infection, neuroimaging, audiology, and ophthalmology assessments were completed for 160 (91%), 157 (89%) and 141 (80%) infants, respectively; 132 (75%) completed all three

* https://www.health.state.mn.us/people/newbornscreening/program/newbornscreeningpanel.pdf

† Evidence of CMV infection includes CMV-positive culture, antigen, or nucleic acid amplification testing, from any specimen source.

§ Council of State and Territorial Epidemiologists public health surveillance case definition: confirmed cases of cCMV infection have confirmatory laboratory evidence of infection. Cases of confirmed cCMV disease meet clinical criteria and have confirmatory laboratory evidence of infection. Clinical criteria include hepatomegaly, splenomegaly, petechial rash or purpura, microcephaly, neuroimaging abnormalities consistent with cCMV, sensorineural hearing loss, seizures, cerebral palsy, chorioretinitis, and vision impairment resulting from conditions consistent with cCMV.

assessments. Fifty-nine (34%) infants had one or more clinical findings identified, most frequently nonspecific neuroimaging abnormalities; not all findings resulted in symptomatic disease (Table). cCMV-consistent findings not detected through routine newborn clinical care were observed in seven infants identified through newborn screening, including two with neuroimaging abnormalities consistent with cCMV. Overall, 29 (16%) infants received nonpassing results for newborn hearing screening. Among 11 (6.3%) infants with permanent hearing loss, four received passing results for newborn hearing screening. Fifteen (8.5%) infants received antiviral therapy. Two infant deaths, both with causes other than cCMV listed, were identified. The observed prevalence of cCMV in Minnesota was 0.29% of live births.

Preliminary Conclusions and Actions

Universal cCMV newborn screening was implemented in Minnesota in 2023; nearly all cases (99%) in infants with positive newborn screening results during February 2023–February 2024 were confirmed by diagnostic testing, and most infants (75%) had comprehensive evaluations and linkage to care. The observed cCMV prevalence was lower than the 0.45% estimated in an earlier Minnesota study performed during 2016–2019 (*2*). Three cases of cCMV in infants who had negative newborn screening test results for CMV were voluntarily reported to the Minnesota Department of Health. Further evaluation of the newborn screening using dried blood spot sensitivity is warranted inclusive of improving case reporting

TABLE. Characteristics of confirmed cases of congenital cytomegalovirus, by case classification* — Minnesota, 2023–2024

Characteristic	No. (%) Confirmed cCMV disease* n = 21	Confirmed cCMV infection* n = 155	Total N = 176
Ascertainment method			
cCMV detected on newborn screen	21 (100.0)	152 (98.1)	**173 (98.3)**
Clinician or laboratory reporting	0 (—)	3 (1.9)	**3 (1.7)**
Newborn hearing screen			
Referred/Did not pass	9 (42.9)	20 (12.9)	**29 (16.5)**
Recommended evaluation completed			
Audiology	21 (100.0)	136 (87.7)	**157 (89.2)**
Neuroimaging	20 (95.2)	140 (90.3)	**160 (90.9)**
Ophthalmology	18 (85.7)	123 (79.4)	**141 (80.1)**
All three evaluations	18 (85.7)	114 (73.5)	**132 (75.0)**
Clinical findings			
Anemia	2 (9.5)	3 (1.9)	**5 (2.8)**
Cerebral palsy†	0 (—)	—	**0 (—)**
Chorioretinitis†	0 (—)	—	**0 (—)**
Elevated liver enzymes	2 (9.5)	8 (5.2)	**10 (5.7)**
Hepatomegaly†	2 (9.5)	—	**2 (1.1)**
Hydrops	0 (—)	0 (—)	**0 (—)**
Intrauterine growth restriction	3 (14.3)	8 (5.2)	**11 (6.3)**
Jaundice	2 (9.5)	8 (5.2)	**10 (5.7)**
Microcephaly†	7 (33.3)	—	**7 (4.0)**
Neuroimaging abnormality, consistent with cCMV†,§	5 (23.8)	—	**5 (2.8)**
Neuroimaging abnormality, nonspecific¶	8 (38.1)	19 (12.3)	**27 (15.3)**
Permanent hearing loss†,**	11 (52.4)	—	**11 (6.3)**
Petechial rash or purpura†	2 (9.5)	—	**2 (1.1)**
Seizures†	0 (—)	—	**0 (—)**
Small for gestational age	3 (14.3)	8 (5.2)	**11 (6.3)**
Splenomegaly†	1 (4.8)	—	**1 (0.6)**
Thrombocytopenia	2 (9.5)	2 (1.3)	**4 (2.3)**
Vision impairment†	0 (—)	—	**0 (—)**
Antiviral therapy initiated	8 (38.1)	7 (4.5)	**15 (8.5)**
Infant death	0 (—)	2 (1.3)	**2 (1.1)**

Abbreviation: cCMV = congenital cytomegalovirus.

* Confirmed cases of cCMV infection have confirmatory laboratory evidence of infection. Cases of confirmed cCMV disease meet clinical criteria and have confirmatory laboratory evidence of infection. https://ndc.services.cdc.gov/case-definitions/congenital-cytomegalovirus-ccmv-infection-and-disease

† Denotes clinical findings listed in clinical criteria for national cCMV disease case definition.

§ Neuroimaging abnormality, consistent with cCMV, is defined as presence of calcifications, cerebellar or cortical malformations, periventricular echogenicity or leukomalacia, ventriculomegaly, or migrational abnormalities.

¶ Includes other neuroimaging findings that are not considered consistent with cCMV (e.g., cerebral cysts, vasculopathy, and white matter changes). https://pubmed.ncbi.nlm.nih.gov/28291720/

** Permanent hearing loss as documented at the most recent audiologic diagnostic assessment.

through a disease reporting mandate, which is presently underway in Minnesota. The inclusion of statewide population-based surveillance for cCMV complemented and helped the evaluation of case ascertainment by newborn screening. This comprehensive approach, along with long-term follow-up, will guide development and implementation of cCMV screening policy and facilitate understanding of the incidence of cCMV and identification of groups at increased risk.

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