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Introduction

Cytomegalovirus (CMV) is a herpesvirus. It is a common infection that is usually harmless and generally passed from infected people to others through direct contact with body fluids, such as urine, saliva, blood, breast milk, and semen. Among every 100 adults in the United States, 50–80 are infected with CMV by the time they are 40 years old.

Pregnant women who are infected can transmit CMV to their fetuses, referred to as a congenital CMV (cCMV) infection. This can cause serious disease in babies with prenatal infection. About 1 in 150 children is born with a cCMV infection. About 1 of every 5 children born with cCMV infection will develop permanent problems (such as hearing loss or developmental disabilities) due to the infection. Congenital CMV is the most frequently identified viral cause of mental retardation and is the leading nongenetic cause of neurosensory hearing loss.

In the United States, the estimated birth prevalence of cCMV infection is 0.7%, with approximately 12.7% of infants symptomatic at birth, and a 0.5% mortality rate. Congenital CMV is a reportable condition to the Michigan Birth Defects Registry (MBDR). In addition, it may be recorded in the Michigan Inpatient Database. As estimated from these sources (2004-2011), the prevalence of cCMV was about 0.9 confirmed cases per 10,000 live births in Michigan. The mortality rate was 0.1 confirmed cases per 10,000 live births, whereas the fatality rate was 56.8 deaths per 1,000 confirmed cases.



Objective

- To assess the accuracy of cCMV cases: 1) reported to the Michigan Birth Defects Registry (MBDR) and 2) ascertained from the Michigan Inpatient Database (MIDB) linked with birth files and death records.
- To provide baseline information on possible approaches to cCMV surveillance.

Methods

Population:

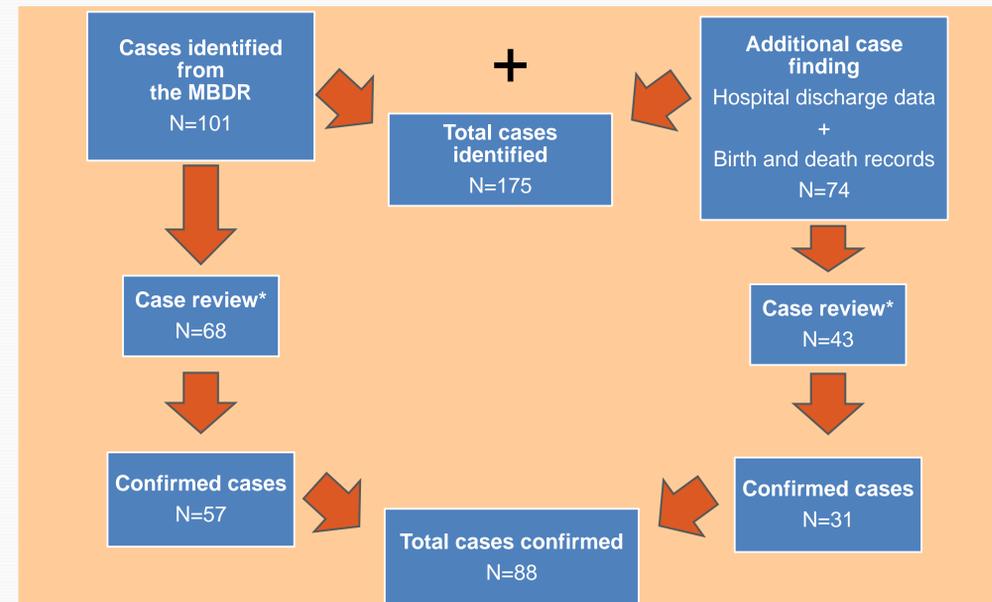
- Michigan resident children born from 2004 through 2011 who were under one year of age when treated for cCMV.
- Birth, death and hospital discharge data was used to enhance case finding and review efforts.
- Exclusion criteria:** Children diagnosed with HIV and/or Heart Transplant patients were excluded from this study.

Analysis:

- A comprehensive, retrospective review of health records was performed at treating facilities for cases with a diagnosis of cCMV.
- Hospital admissions data related to the diagnosis and treatment of cCMV, including complications and comorbidities related to this diagnosis were compiled.
- Data variables were extracted directly into a table of cases and a field map was developed for reference.
- Results were analyzed using Statistical Analysis Software (SAS) version 9.2.

Results

Figure 1: Congenital CMV Case Validation Process and Outcome



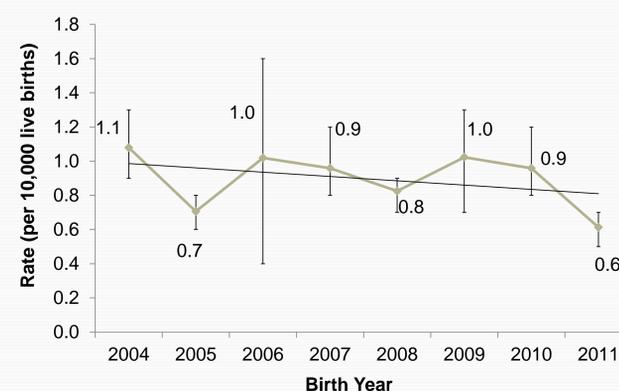
*Reviewed cases are less than the identified number as facilities did not submit health records for all cases identified.

Table 1: Validity of cCMV cases in Michigan, 2004-2011

Source and Case (cCMV)	Health Record Review			Positive Predictive Value (PPV)*
	Case (cCMV)	Non Case (No cCMV)	Total	
MBDR	57 (TP)	11 (FP)	68	84%
MIDB	31 (TP)	12 (FP)	43	72%
All sources	88 (TP)	23 (FP)	111	79%

*The probability that a reported positive is a true case. Cases with insufficient information to either confirm or exclude cCMV infection were included in the denominator.

Figure 2: Congenital CMV Prevalence Rate Trend, 2004-2011



- Although prevalence rates varied throughout the years, there was a slight decreasing trend for cCMV prevalence overall from 2004-2011. However, this decrease did not reach statistical significance (Poisson Regression: $p=0.5550$).
- In 2004, the prevalence of cCMV was about 1.1 confirmed cases per 10,000 live births and 0.6 cases per 10,000 live births in 2011.

Table 2: Delivery Type and Case Status for all reviewed cases

Delivery Type	Case Status			
	Positive (Case)	Negative (Non Case)	Unknown	Total
Vaginal	45 (91.8%)	2 (4.1%)	2 (4.1%)	49 (100%)
C-section	32 (91.4%)	3 (8.6%)	0 (0%)	35 (100%)
Unknown	8 (53.3%)	1 (1.0%)	6 (40.0%)	15 (100%)
Total	85	6	8	99

The type of delivery and case status were significantly associated (Fisher's exact test: $p<.0001$).

Table 3: Clinical presentation of positive cases, 2004-2011

Clinical Presentation	Number	Percent
Hematologic Symptoms¹	62	70.5
Petechiae or purpura	21	23.9
Hemolytic anemia	27	30.7
Direct bilirubin >3 mb/dl	41	46.6
Platelet count <75,000/mm	40	45.5
Elevated alanine aminotransferase (ALT) levels (> 100 IU)	16	18.8
Jaundice at birth	34	38.6
Neurologic Deficits^{1,2}	47	53.4
Intracranial calcifications	24	27.3
Microcephaly	14	15.9
Seizures	8	9.1
Neurologic abnormality	10	11.4
Chorioretinitis	2	2.3
Hearing impairment	17	19.3
Hepatosplenomegaly³	17	19.3
Hepatomegaly	19	21.6
Splenomegaly	18	20.5
Pneumonia	10	13.0
Other congenital complications	12	13.6

¹Encompasses infants with any of the sequelae. Symptom totals will not equal individual totals because symptom totals includes individuals that have any of the listed complications.

²Structural or functional abnormality of the brain, spinal cord, muscles, or nerves.

³Encompasses infants that have both hepatomegaly and splenomegaly.

Discussion

- Of 175 cCMV cases identified from both sources, 111 cases were investigated. A comprehensive health record review of these cases found 88 cases (79.2%) to be true positives (Table 1). Thus among Michigan infants under 1 year of age identified with a diagnosis of cCMV, 79% actually had the disease (PPV). Reporting to the MBDR (PPV=84%) had a higher predictive value than presence in the MIDB (PPV=72%). However, there was no overlap between cases; both were important for case-finding.
- Analysis of data for cCMV confirmed cases from 2004-2011 indicated a slight decrease in trend for cCMV prevalence in Michigan for this time period (Figure 1).
- A statistically significant relationship between delivery type and case status was observed (p -value $<.0001$). Analysis showed that infants born by vaginal delivery (4.1%) were less likely to have a negative status compared to infants born through C-section (8.6%; Table 2).
- Over two-thirds of the infants (70.5%) presented with hematologic symptoms. Approximately half (53.4%) had neurologic deficits, and about 14% had individual cases of other congenital infections as well as cCMV (Table 3).

Public Health Impact

- Congenital CMV presents medical complications and serious consequences for affected children, including lasting disabilities or even death.
- Potential future direction includes intersecting with other systems such as the Early Hearing Detection and Intervention (EHDI) system due to the high proportion of children with hearing loss (19%).
- Pregnant women may want to take steps to reduce their risk of exposure to CMV and so reduce the risk of CMV infection of their fetus by washing their hands often with soap and water for 15-20 seconds.



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