STATE OF MICHIGAN

MBDR MICHIGAN BIRTH DEFECTS REGISTRY

The Michigan Monitor

Following trends, promoting prevention and linking families to resources

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Prenatal Infection and Birth Defects: Congenital Cytomegalovirus

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Points of Interest

- CMV is generally transmitted through body fluids.[2]
- Pregnant women who are infected can transmit CMV to their fetuses.[1]
- Children with cCMV infection are more likely to have permanent disabilities if they had symptoms of the infection at birth.[3]

Background

Women of childbearing age may not know that certain prenatal infections may have life-long effects on fetal development. Health professionals use the acronym TORCH to identify these infections as: toxoplasmosis, other, rubella, cytomegalovirus and herpes simplex virus.

Cytomegalovirus (CMV) is a herpes virus. CMV infection is common and usually harmless. Once CMV is in a person's body, it is there for life. Among every 100 adults in the United States, 50–80 are infected with CMV by the time they are 40 years old.[1] The virus is generally passed from person to person through direct contact with body fluids, such as urine, saliva, blood, breast milk, and semen.[2]

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 who were infected before birth. About 1 in 150 children is born with cCMV infection.[1] Most (90 of every 100) infants with cCMV infection appear healthy at birth. Children are more likely to have permanent disabilities if they had symptoms of cCMV infection at birth.[3] Congenital CMV is the most frequently identified viral cause of cognitive impairment and the leading non-genetic cause of neurosensory hearing loss.[4,5]

We assessed the accuracy of cCMV data in Michigan through a comprehensive health record review at hospitals where infants were treated for cCMV. A summary of the findings are highlighted in the following pages.

Occurrence and Effects

In the United States, the estimated birth prevalence of cCMV infection is 0.7%, with about 12.7% of infected infants symptomatic at birth, and a 0.5% mortality rate.[6] Congenital CMV is reportable to the Michigan Birth Defects Registry (MBDR). In addition, it may be recorded in the Michigan Inpatient Database (MIDB). From 2004 to 2011, a total of 101 infants under one year of age were reported to the MBDR with a diagnosis of cCMV infection. In searching Michigan resident hospital discharge files and linking with birth and death files, 74 additional cCMV cases were identified. As estimated from these sources, from 2004 to 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 1,000 live births, whereas the fatality rate was 56.8 deaths per 1,000 confirmed cases.

TORCH Infections

Toxoplasma
Other
Rubella
Cytomegalovirus
Herpes Simplex Virus

Treatment

There is no drug licensed to treat cCMV infection. There are limited data on the use of antiviral medications in symptomatic infants with central nervous system involvement.[1]

Case-Finding and Validation of Congenital Cytomegalovirus (cCMV) Related Hospital Admissions in Michigan Infants under One Year of Age

Purpose

The purpose of this study was to assess the validity of cCMV cases reported to the MBDR, and ascertained from the MIDB linked with birth files and death records. Providing a baseline incidence and better understanding of effective approaches to cCMV surveillance were additional objectives. Findings were used to describe infants with a diagnosis of cCMV by socio-demographic and clinical characteristics and to assess the completeness of reporting of cCMV cases and related deaths using hospital death records, MBDR data, and MIDB data.

Methods

The MDHHS Institutional Review Board approved this study as exempt. Data from the MBDR, MIDB, and death records were utilized to identify hospital admissions for Michigan resident infants born from 2004 through 2011 who were less than one year of age when treated for cCMV. Michigan resident hospital discharge data was linked to birth and death records as an additional avenue to identify cCMV cases for review. Approximately 175 infected infants were identified from all sources. Children diagnosed with HIV and/or Heart Transplant patients were excluded from this study. A comprehensive, retrospective review of health records was performed at facilities where infants were treated to validate the diagnosis, document the typical course of treatment and verify congenital versus perinatally acquired infection. 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 (SAS Institute, Cary, North Carolina).

Results

Validation of cCMV cases

A total of 175 cCMV cases were identified from the data sources. From a comprehensive health record review of 111 cases, 88 (79.3%) were identified as true positives, 8 cases (7.2%) as false positives or not having cCMV and 15 cases (13.5%) without enough documentation to confirm diagnosis of cCMV (Table 1). The Positive Predictive Value (PPV) of all cCMV cases identified was 79% [88/ (88+23) = 0.79 = 79%]. Thus, among Michigan infants under one year of age identified with a diagnosis of cCMV from all sources, 79% actually had the disease. Reporting to the MBDR (PPV=84%) had a higher predictive value than presence in the MIDB (PPV=72%). However, there was no overlap between case sources; both were important for case-finding.

Table 1: Validity of cCMV Cases in Michigan: cCMV Case Review, 2004-2011

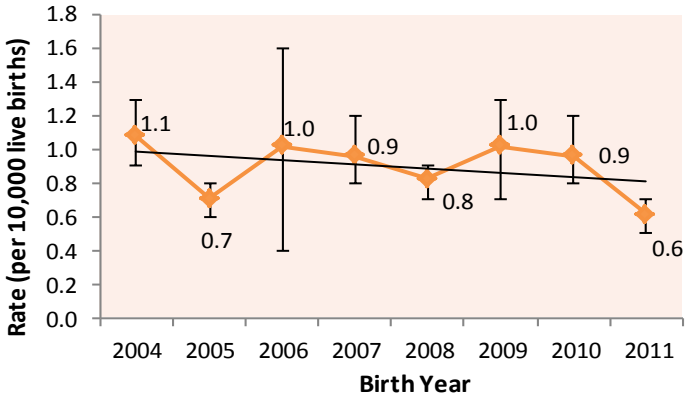
Source and case (cCMV)	Health Record Review			Positive Predictive Value (PPV)*
	Case (cCMV)	Non Case (No cCMV)	Total	
MBDR	57 (TP)	11 (FP)	68	84%
MIDB	31 (TP)	12 (FP)	43	72%
Total	88 (TP)	23 (FP)	111	79%

* 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.

cCMV Prevalence Trend

Analysis of data for cCMV confirmed cases from 2004-2011 indicated that although the prevalence rates varied throughout the years, there was a slight decreasing trend for cCMV prevalence overall (Figure 1). In 2004, the prevalence of cCMV was about 1.1 confirmed cases per 10,000 live births and about 0.6 confirmed cases per 10,000 live births in 2011 (Figure 1). However, this decrease did not reach statistical significance (p=0.5550).

Figure 1: Congenital CMV Confirmed Cases Reported by One Year of Age: cCMV Case Review, 2004-2011



Maternal Demographics for MBDR Cases

Confirmed cCMV cases from the MBDR were analyzed by selected maternal demographic variables. About a quarter (25.5%) of the infants with confirmed cCMV were born to mothers age 20-24 (Table 2). Infants born to white mothers accounted for the majority (63.6%) compared to black mothers (32.7%, Table 2). Nearly half the infants (45.4%) were born preterm (less than 37 weeks; Table 2).

Table 2: Confirmed Cases Reported to the MBDR by Maternal Demographic Characteristics: cCMV Case Review, 2004-2011

Demographic Variable	Number	Percent
Maternal Age		
<20	13	23.6
20-24	14	25.5
25-29	10	18.2
30-34	12	21.8
35+	6	10.9
Maternal Race		
Whites	35	63.6
Blacks	18	32.7
Other[1]	*	*
Gestational Age		
<37 weeks	25	45.4
37+ weeks	30	55.5

[1]Encompasses women who do not define themselves as black or white and includes Native American, Asian/Pacific Islander, Chinese, Japanese, and Filipino.

*Data omitted when fewer than 6 infants were confirmed with a diagnosis of cCMV.

Delivery Type and Case Status for Reviewed Cases

A statistically significant relationship between delivery type and case status was observed (p-value <.0001). Infants born by vaginal delivery (4.1%) were less likely to have a negative status than infants born through C-section (8.6%; Table 3).

Table 3: Delivery Type and Case Status for all Reviewed Cases: cCMV Case Review, 2004-2011

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 (0.0%)	35 (100%)
Unknown	8 (53.3%)	1 (1.0%)	6 (40.0%)	15 (100%)
Total	85	6	8	99

Physical, Clinical and Laboratory Presentation

Over two-thirds of the infants (70.5%) presented with hematologic symptoms, including petechiae or purpura, hemolytic anemia, a direct bilirubin of less than 3 mb/dl, a platelet count of less than 75,000/mm, elevated alanine aminotransferase levels, and jaundice at birth (Table 4). Approximately half the infants (53.4%) had neurologic deficits, including intracranial calcifications, microcephaly, seizures, neurologic abnormality, and chorioretinitis with nearly a fifth (19.3%) having hearing impairment (Table 4). About 20% of the infants had hepatosplenomegaly and about 13% had pneumonia (Table 4). Results also revealed that about 14% of the infants had individual cases of other congenital complications, including, but not limited to, hemangioma of skin and subcutaneous tissue, benign neoplasm of spinal meninges, and retrolental fibroplasia (Table 4). More detailed information about how these infants presented clinically can be found in Table 4 below.

Table 4: Clinical Presentation of Confirmed Cases: cCMV Case Review, 2004-2011

Clinical Presentation	Number	Percent
Hematologic Symptoms[1]	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
Hepatosplenomegaly[3]	17	19.3
- Hepatomegaly	19	21.6
- Splenomegaly	18	20.5
Pneumonia	10	13.0
Other congenital complications	12	13.6

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

[2]Functional abnormality of a body area due to a decrease in the function of the brain, spinal cord, muscles, or nerves.

[3]Encompasses infants that have both hepatomegaly and splenomegaly.

Public Health Implications and Future Directions

∗Congenital CMV has serious consequences for those affected, including lasting disabilities or even death.

∗Pregnant women may lower their risk of exposure and the risk of fetal CMV infection by hand washing.

∗Public health programs can promote knowledge and awareness to lower the occurrence of cCMV. For example, The Michigan Early Hearing Detection and Intervention Program developed a strategic plan to address CMV (See page 4).

Following trends, promoting prevention and linking families to resources

For more information please contact:
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Call Toll Free: 1-866-852-1247
E-mail: BDRFollowup@michigan.gov
Website: www.michigan.gov/birthdefectsinfo

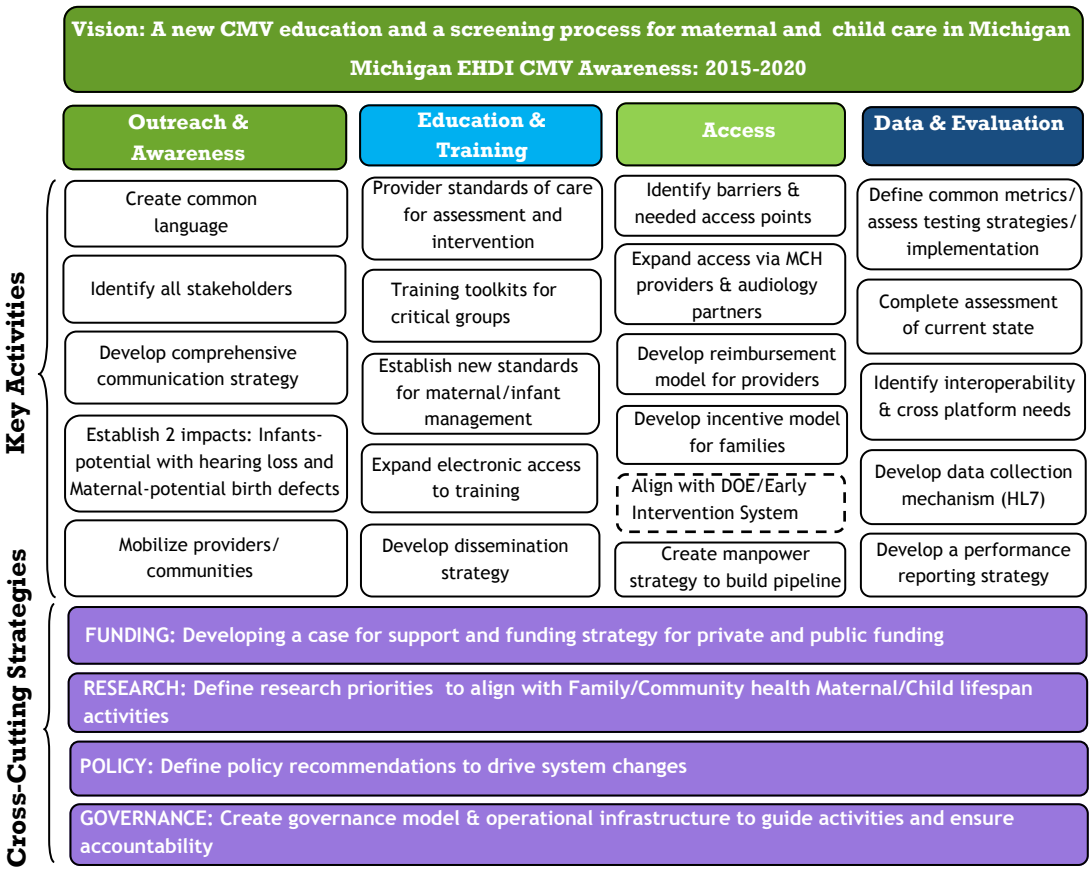
The *Michigan Monitor* is online at
www.michigan.gov/mchepi

Find information about MBDR reporting at:
http://www.michigan.gov/mbdr

Program Updates

ICD-10-CM is almost here! The Birth Defects Registry has been busy preparing for the change to ICD-10-CM Diagnosis and Procedure codes. Many of our reporting partners have sent us test data, and we will be ready to accept data with the new codes by October 1st. We are looking forward to a more detailed and descriptive code set that ICD-10-CM has to offer.

Early Hearing Detection and Intervention (EHDI) Program: Strategic Plan to Address CMV in Michigan



Helpful websites for health professionals and families

Michigan Early Hearing Detection and Intervention (EHDI) Program: **www.michigan.gov/ehdi**
National EHDI: **www.cdc.gov/ncbddd/hearingloss/ehdi-programs.html**
Children's Special Health Care Services (CSHCS) Program: **www.michigan.gov/cshcs**
Early On®, Michigan's early intervention system: **www.1800earlyon.org**
CDC CMV and Congenital CMV Infection: **www.cdc.gov/cmv/index.html**
Teratology Primer—2nd Edition: **www.teratology.org/primer.asp**
Stop CMV Action Network: **www.stopcmv.org**

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