Timing of cCMV Diagnosis:
Retrospective Study in Washington State

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October 10, 2023

Congenital Cytomegalovirus Public Health and Policy Conference

Salt Lake City, Utah

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Speaker Disclosure

Mallory R. Baker, AuD

I have no actual or potential conflict of interest in relation to this program/presentation.

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Learning Objectives

- Understand the current methods of identification of congenital CMV within Washington State

- Examine the timing of diagnosis of infants in relation to presenting symptoms and outcome

- Identify the need for a proactive CMV screening in newborns

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Introduction

- Washington State does not have a cCMV screening mandate
- In 2008, Seattle Children's Hospital Otolaryngology and Audiology clinics started testing the dried blood spot (DBS) as part of a sensorineural hearing loss etiology work up
- Subsequently, clinical experience revealed missed diagnoses of cCMV
- Late diagnosis of cCMV led to missed opportunities for treatment, early intervention, and monitoring

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Goals of Project

- To investigate the timing and pathway for diagnosis for infants with cCMV in relation to presenting symptoms and outcome

- To understand reasons for late diagnosis and gaps in the current process

- Use this information to inform advocacy within the state and education for providers

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Methods

- Retrospective review of SCH patients
  - Birth date of 2004 or later
  - Seen at SCH between 2009-2021 with a diagnosis of cCMV
- Initially identified using ICD codes for both congenital CMV and general CMV
  - Records reviewed to confirm cCMV
- Medical record review included:
  - Clinical notes, lab results, imaging, and audiology data
- Age at first CMV testing = Date the first CMV test was sent

Definitions

- cCMV
  - Positive urine culture or PCR or blood PCR within 21 days of life
  - Positive CMV PCR from a neonatal dried blood spot sample
- Symptomatic at birth
  - Small for gestational age (<10%)
  - Microcephaly (<3%)
  - Abnormal physical exam (generalize petechiae, HSM, jaundice)
  - Abnormal labs (plts <100k, ALT/AST > 2.5 ULN, conjugated bili >1 mg/dl
- Progressive sensorineural hearing loss (SNHL)
  - ≥ 20 dBHL decrease in PTA in at least one ear between evaluations
  - Passed NBHS with SNHL documented at subsequent audiologic evaluations
- Early vs Late Diagnosis
  - Early = cCMV diagnosed within 21 days of life
  - Late = cCMV diagnosed after 21 days of life

Patient Characteristics

	Total Cohort	Early Diagnosis Group (≤ 21 days)	Late Diagnosis Group (> 21 days)
N	112	60	52
Gender			
Male	54 (48%)	30 (50%)	24 (46%)
Female	58 (52%)	30 (50%)	27 (52%)
Race/ethnicity			
Black	8 (7%)	3 (5%)	5 (10%)
White	79 (71%)	46 (77%)	33 (62%)
Asian/AIAN/NHPI	13 (12%)	5 (8%)	8 (16%)
Hispanic	18 (16%)	6 (10%)	12 (21%)
Not stated	14 (13%)	7 (12%)	7 (13%)

Patient Characteristics

	Total Cohort	Early Diagnosis Group (≤ 21 days)	Late Diagnosis Group (>21 days)
N	112	60	52
Symptomatic at birth	62 (55.9%)	44 (73.3%)	18 (34.6%)
Asymptomatic at birth	44 (39.3%)	16 (14.3%)	28 (53.8%)*
Premature (<37 weeks)#	24 (21.4%)	20 (33.3%)	4 (7.7%)
Passed NBHS	37 (33%)	22 (36.7%)	15 (28.8%)
Referred NBHS	71 (63.4%)	38 (63.3%)	33 (63.5%)
No NBHS or Unknown	4 (3.5%)	0	4 (7.7%)

Median Age at cCMV Diagnosis (range)	**0.5 months (0-101.4 months)**	**0 months (0-0.7 months)**	**11.85 months (1-101.4 months)**

**6 with unknown symptomatology at birth* *# p <0.001*

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Patient Characteristics

Head imaging results

	Total Cohort	Early Diagnosis Group (≤ 21 days)	Late Diagnosis Group (> 21 days)
Cranial ultrasound			
Number with test done	62	49	11
% abnormal	58%	59%	64%
MRI			
Number with test done	69	39	30
% abnormal	87%	82%	93%
No imaging done	17	2	15

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Reason for CMV testing

	Total Cohort	Early Diagnosis Group (≤ 21 days)	Late Diagnosis Group (> 21 days)
N	112	60	52
Symptoms at birth	23 (21%)	23 (38%)	0
SGA	14 (13%)	14 (23%)	0
Failed NBHS	6 (5%)	5 (8%)	1 (2%)
Mother diagnosed during pregnancy	16 (14%)	15 (25%)	1 (2%)
Abnormal prenatal ultrasound	19 (17%)	18 (30%)	1 (2%)
SNHL diagnosed beyond a month of life	37 (33%)	NA	37 (71%)
Other	19 (17%)	6 (10%)	13 (25%)
Reason not stated	1 (1%)	1 (1.7)	0

Department Initiating Testing

	Total Cohort	Early Diagnosis Group (≤ 21 days)	Late Diagnosis Group (> 21 days)
Birth hospital	47 (42%)	46 (77%)	1 (0.2%)
NICU	7 (6%)	6 (10%)	1 (0.2%)
OTO/Audiology	35 (31%)	0	35 (67%)
Primary Care Provider	5 (4.5%)	3 (5%)	2 (0.4%)
Neurology	6 (5%)	1 (0.2%)	5 (10%)
Genetics	7 (6%)	0	7 (13.5%)
Other	5 (4.5%)	3 (5%)	2 (0.4%)

Late Diagnosis group:

Reason for testing and age at diagnosis

Reason for testing	n	Median Age at Diagnosis* (range)
Total	52	11.85 (1.0- 101.4)
Referred NBHS	1	1.7
Abnormal prenatal ultrasound	1	1.1
SNHL diagnosed beyond a month of life	37	15.5(1-91)
Other	3	2.3 (1.2-3.4)
Developmental delay ± abnormal imaging	10	17.4 (5.9 -101.4)

*months

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Late Diagnosis Group:

Audiology Outcomes

	n	Median Age at Diagnosis (range)
No Documented SNHL	5 (9.6%)	22.6 months (1.2-53.2)
SNHL in one or both ears	46 (88.5%)	9.4 months (1-91)
Unilateral SNHL	21 (45.7%)	13.7 months (1-91)
Bilateral SNHL	25 (54.3%)	7.7 months (1.1-78)
Progressive SNHL	29 (63.0%)	25.4 months (1-91)
Passed NBHS, then developed SNHL	14 (30.4%)	50.9 months (1.1-85.2)
Unknown Hearing	1 (2.2%)	101.4 months

Median age at first audiologic evaluation = 28.4 months

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Late Diagnosis Group:

Developmental Outcomes

	Total Cohort	Early Diagnosis Group	Late Diagnosis Group
N	112	60	52
Age appropriate	34	18 (30%)	16 (31%)
Mild delay	22	9 (15%)	13 (25%)
Mod/severe delay	32	16 (27%)	16 (31%)
Unknown	24	17 (28%)	7 (13%)

Age at longest follow-up – *median 79 months (range 8-201)*

Late Diagnosis Group:

Missed Antiviral Opportunities

- 12/52 (23%) would have qualified for valganciclovir treatment based on severity of symptoms at birth and/or abnormal MRIs*
- 36/52 (69%) would have qualified for valganciclovir if isolated SNHL was considered a reason for treatment as per some guidelines#

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* AAP 2021 Red Book

Luck S et al, JPIDS 2017;36:1205-13

Applying Different Screening Strategies

Universal screening

- 52 **additional** infants would have been identified at birth
  - 46% of total group (52/112)

Screening based on referred NBHS

- 33 **additional** infants would have been identified at birth
  - 29.5% of the total cohort (33/112)
  - 63% of the late diagnosis group (33/52)

Expanded screening *(Suarez et al, 2023)*

- 99/108* (91.7%) of the total cohort would have been identified at birth
- 42/48* (87.5%) of the late diagnosis group would have been identified at birth

**4 infants without enough data to assess*

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Conclusion

- Without a systematic screening process in place, almost half of the infants eventually diagnosed with cCMV were missed at birth
- Many **symptomatic at birth** infants are not appropriately identified through the clinician-led screening model
- Many **asymptomatic at birth** infants have hearing and CNS abnormalities related to cCMV

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Conclusion

- Delayed cCMV diagnosis results in delays for audiology and developmental intervention
- Delayed diagnosis also misses the window of opportunity for antiviral treatment
- ***Any*** formal screening protocol (universal, hearing targeted, or expanded targeted) would result in earlier diagnosis for the majority of infants

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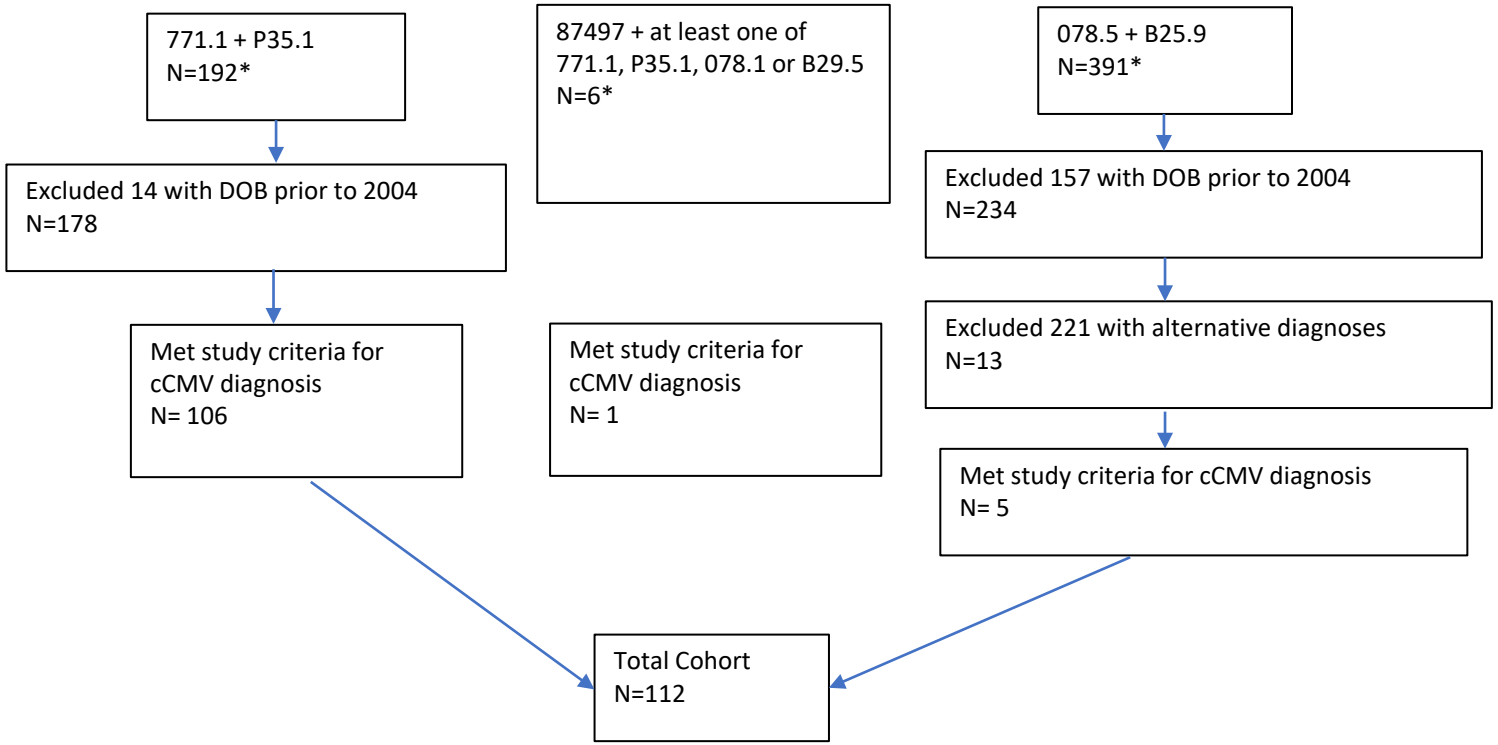

* Excluding duplicates

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OTO/Audiology clinic process

- 2008-2015
  - Infants and children > 21 days of age with a documented SNHL without clear alternative etiology
    - Request neonatal DBS sample from the state- assay for CMV DNA PCR
- 2019 – present
  - Infants and children > 21 days - ≤6 months of age with a documented SNHL without clear alternative etiology
    - Send saliva swab for CMV PCR
    - If positive - request neonatal DBS sample from the state- assay for CMV DNA PCR
  - Infants and children > 6 months of age with a documented SNHL without clear alternative etiology
    - Request neonatal DBS sample from the state- assay for CMV DNA PCR