Frequent Cytomegalovirus Shedding in Breastmilk in Healthy Women Persists Up to 17 Weeks Postpartum

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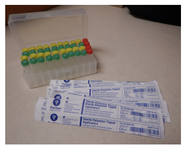
Introduction

- Cytomegalovirus (CMV) can cause severe disease in premature or very low birth weight infants.
- Postnatal mother to child transmission of CMV is rare and occurs mainly via breastmilk.
- CMV seroprevalence in reproductive-age women is 45-100%.[1]
- Of CMV-seropositive women, 40-96% shed CMV DNA in their breastmilk.[2]

Research Aim: To characterize CMV viral shedding at multiple anatomical sites in CMV-seropositive healthy postpartum women.

Methods

Population: CMV-seropositive healthy women < 4 months postpartum were enrolled at the University of Washington in 2014-2015.



Samples: Breastmilk, oral and vaginal swabs, and urine were self-collected daily every other week for 8 weeks. Samples were assayed for CMV DNA using polymerase chain reaction (PCR).

Outcomes

- Proportion of days with CMV detected from each site on a per-person and population basis.
- Associations between CMV quantity and shedding frequency at different sites using Poisson regression.

Results

- 9 participants a median of 7 weeks postpartum (range 5-15 weeks) self-collected samples for a median of 28 days (range 26-31 days).
- Samples include 253 breastmilk, 258 oral and vaginal swab, 257 urine, and 81 plasma samples.

Figure 1. Proportion of Women with CMV Detection by Site

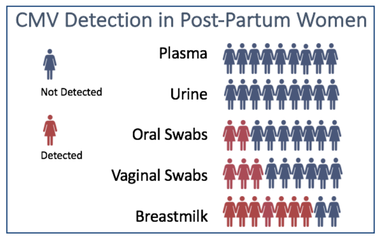
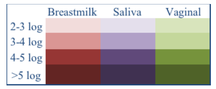


Table 1. Frequency and Quantity of CMV Shedding by Site (N=9)

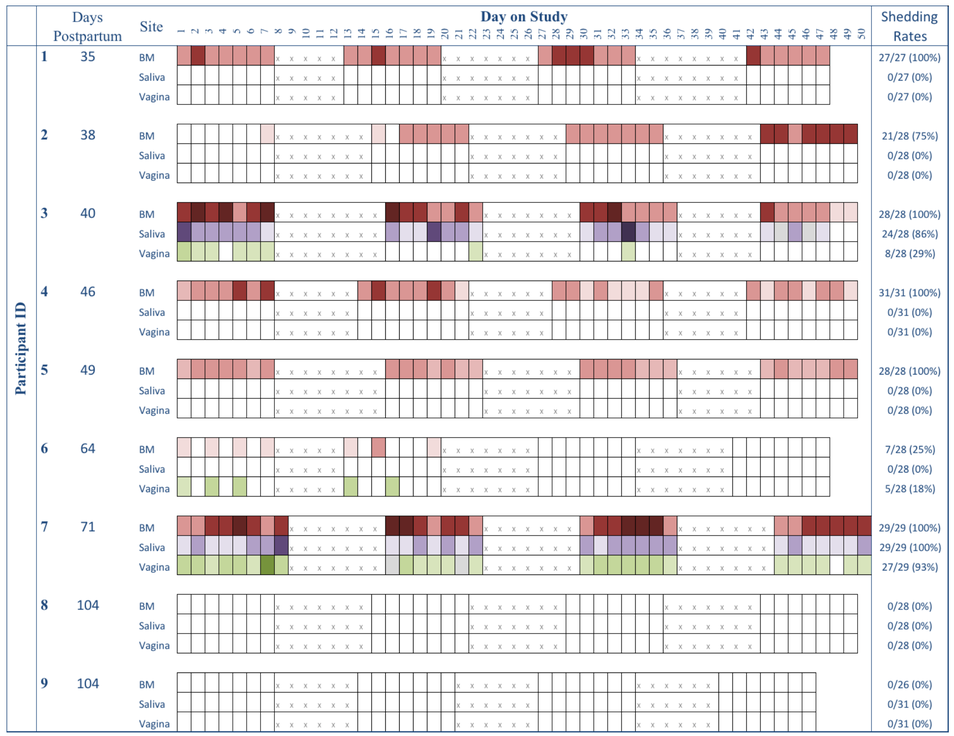
	Breastmilk	Vaginal	Oral	Urine
Days sampled per person, median (IQR)	28 (28-28)	28 (28-29)	28 (28-29)	28 (28-29)
Persons with any CMV detection, No. (%)	7 (77.8)	3 (33.3)	2 (22.2)	0 (0)
PCR-positive days/total PCR swabs, No. (%)	171/253 (67.6)	39/258 (15.1)	53/258 (20.5)	
log_{10} CMV viral copies per ml, median (IQR)[a]	3.6 (3.1-4.1)	2.8 (2.5-3.3)	3.2 (2.8-3.7)	
Per person CMV shedding rate, median (range)[b]	100 (0-100)	0 (0-90)	0 (0-100)	

Abbreviations: IQR, interquartile range; PCR, polymerase chain reaction. [a] Among positive samples.
[b] Shedding rate is defined as percent days positive for CMV DNA by RT-PCR with a detection threshold of > 150 copies /ml.

Figure 2. CMV Presence and Quantity in Self-Collected Breastmilk Samples, Oral Swabs, and Vaginal Swabs per Participant



CMV PCR results from each woman are shown in order of days postpartum at study initiation. Sample sites are shown in the following order for each participant: breastmilk (BM), saliva, vagina. Swabs with CMV detected are indicated by color with viral quantity indicated by the heatmap. The number of swabs with CMV detected/ number of swabs collected and proportion of swabs with CMV detected by site for each participant is indicated under the header "Shedding Rate."



Associations

- Vaginal CMV detection was significantly more likely to occur on days with oral CMV detection.
  - **RR = 26.1**, 95% CI 3.9 to 176.0, p = 0.0008
- Oral CMV detection was **not** significantly more likely to occur on days with vaginal CMV detection.
  - RR = 1.1, 95% CI 1.0 to 1.1
- Breastmilk CMV quantities greater than 3.6 log_{10} copies/mL was significantly associated with simultaneous oral CMV detection.
  - **RR = 4.1,** 95% CI 1.9 to 8.8, p = 0.0002
- Breastmilk CMV quantities greater than 3.6 log_{10} copies/mL were **not** significantly associated with simultaneous vaginal CMV detection.
  - RR = 1.8, 95% CI 0.9 to 3.7, p = 0.11

Conclusions

- We detected CMV in breastmilk of women up to 17 weeks postpartum.
- We found that on days when oral shedding was present, vaginal detection was much more likely and that high breastmilk quantities were associated with oral shedding.
- This suggests simultaneous CMV reactivation in several anatomical sites in healthy women, as shown in HIV+ women.[3]

Future Directions

- Less frequent sampling of larger numbers of women may provide better estimates of shedding postpartum.
- Future studies may correlate these data with mother-to-child CMV transmission via breastmilk.

Our findings are relevant to the increasing practice of raw breastmilk sharing, particularly for pre-term infants.

References

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Image: www.pinterest.com/dinnae/breastfeeding-milk-sharing/

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