

Cytomegalovirus (CMV) Infection in the First Year of Life in a Cohort of Infants in Rural Guatemala

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Background

- Little is known about the epidemiology of CMV infection in low resource countries.
- No data exists regarding congenital or post-natal CMV infection in rural Guatemala.

Objectives

- We evaluated the frequency and effects of post-natal CMV infection in infants from a prospective cohort study designed to assess the effects of post-natal Zika on neurodevelopment (ND) in rural Guatemala (DMID 16-0057).

Methods

- Infants (0-3 months old) were enrolled from June 2017 to July 2018 into this longitudinal observational study
- Infants were evaluated for CMV infection by PCR testing of urine samples collected at 0-3 months of age.
- At 0, 3, 6, and 12 months after enrollment, infants were assessed by study physicians and neurodevelopmental psychologists for the following outcomes:
 - * Weight, Height-Z score
 - * Head circumference (HC)
 - * Neurological examination
 - * Hearing and vision behavioral screening
 - * Ophthalmologic examination
 - * Hearing screening by otoacoustic emissions
 - * Mullen Score of Early Learning (MSEL), Early Learning Composite (ECL) Score
- We explored associations between CMV infection and microcephaly, neurological, visual and hearing deficits, malnutrition, and ND outcomes at 1 year of age (Chi square or Fisher's exact).

Results

- The infant cohort (N = 469) had a mean age at enrollment of 1.5 (SD 0.75) months; 47% were female and 71% were breastfeeding at 1 year. Gender was not correlated with CMV positivity.
- A total of 103 (22%) were CMV positive** and the majority of these (97%) were ≥ 4 weeks of age at testing.
- Infants ≥ 4 weeks of age were more likely to be CMV positive (P < 0.0001) (Figure 1).**
- Among children with HC measurements, microcephaly (HC ≤ 2 SD) was present in 9/87 (10.3%) CMV positive and 35/338 (10.4%) CMV negative infants at 0-3 months of age (p = 0.99). **(Table 1)**
- Malnutrition at 0-3 months (RR: 1.53, 95% CI 0.89-2.66, p = 0.13) and 1 year (RR: 1.10, 95% CI 0.77-1.58, p = 0.59) was not associated with CMV infection at 0-3 months. **(Table 2)**
- Abnormal neurological exams in the first year of life occurred in 50/100 (50%) CMV positive and 166/365 (45.5%) CMV negative infants (p = 0.56).
- Among 438 infants who underwent screening for hearing deficits and a complete ophthalmologic evaluation, none of the CMV positive children had abnormal vision or hearing.
- There was no association between CMV infection at 0-3 months and ND MSEL overall or subdomain scores at 1 year (overall Relative risk (RR) 1.02, 95% CI 0.99-1.05, p = 0.16). **(Table 3)**

Table 1 and 2: Association between CMV infection and Microcephaly or Malnutrition at First (0-3 months of age) and Last study visit (12-15 months of age) in infants, stratified by age at first CMV positivity \leq or $>$ 4 weeks of age.

TABLE 1 - MICROCEPHALY	Rel. Risk	95% CI	p-value
Microcephaly at FIRST visit:			
Overall	1.0	0.50 – 2.00	0.99
CMV at ≤ 4 weeks of age	n/c	n/c	0.99
CMV at > 4 weeks of age	0.93	0.46 – 1.91	0.85
Microcephaly at LAST visit:			
Overall	1.15	0.67 – 1.96	0.61
CMV at ≤ 4 weeks of age	n/c	n/c	0.99
CMV at > 4 weeks of age	1.21	0.69 – 2.13	0.50

n/c = not calculable

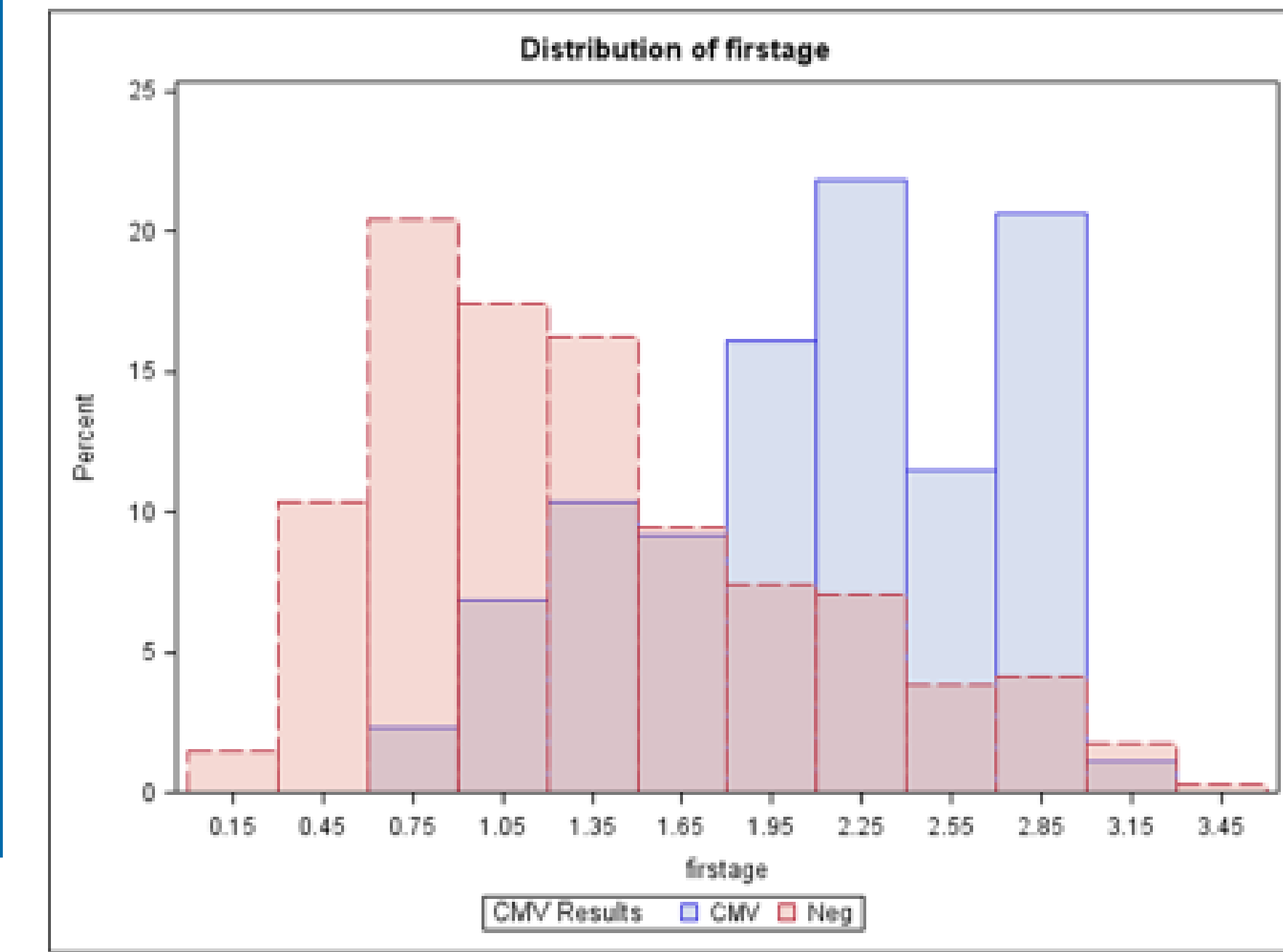
TABLE 2 - MALNUTRITION	Rel. Risk	95% CI	p-value
Chronic malnutrition at FIRST visit:			
Overall	1.53	0.89-2.66	0.13
CMV at ≤ 4 weeks of age	n/c	n/c	0.99
CMV at > 4 weeks of age	1.55	0.87-2.79	0.14
Chronic malnutrition at LAST visit:			
Overall	1.10	0.77 – 1.58	0.59
CMV at ≤ 4 weeks of age	n/c	n/c	0.99
CMV at > 4 weeks of age	1.12	0.77 – 1.63	0.56

Table 3: Association* between CMV positivity at 0-3 months and MSEL ECL Score at 12-15 months of age

Mullens score	Relative Risk	95% Confidence Interval	p-value
ECL	1.02	0.99 – 1.05	0.16
Gross motor	1.02	0.97 – 1.06	0.42
Fine motor	1.02	0.99 – 1.05	0.27
Visual receptive	1.02	0.99 – 1.06	0.24
Expressive language	1.03	0.97 – 1.10	0.36
Receptive language	1.01	0.98 – 1.04	0.41

* Adjusted for age at Mullens testing

Figure 1. CMV positive PCR distribution by age



Conclusions

- In a cohort of Guatemalan infants, postnatal CMV infection was common (22%) and more likely to occur after the neonatal period.
- There was no correlation between CMV infection and microcephaly at 0-3 months or at 1 year of age, nor with abnormal nutritional, neurologic, ophthalmologic, hearing or neurodevelopmental deficits at 1 year of age.
- This is the first epidemiologic report on CMV infection in early life in rural Guatemala.

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