Neurodevelopment and Vector-borne Diseases: Building a Research Capacity in the Tropics

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Abstract

Grenada and other Caribbean nations have experienced a rapid spread of Chikungunya (CHIKV) and it has been associated with children neurodevelopment complications.

Through a robust multi-dimensional clinical tool (Intergrowth-21st Neurodevelopmental Assessment), blood samples, team of researchers from St. George's University are analyzing the effects of CHIKV in children neurodevelopment.

So far, the results of the research's suggest the inexistence of strong association between mothers exposed to CHIKV and child neurodevelopment problems.

This study was cared out by Windref Research Institute, see picture below.

Background

Chikungunya, a mosquito-borne viral disease has been linked to neurodevelopmental problems among children such as delayed coordination and language development. Grenada and other Caribbean nations have experienced a rapid spread of CHIKV since 2013.

Aims:

1) Build capacity for arboviral and neurodevelopmental research at St. George's University in Grenada

2) Assess the burden of confounding factors to better understand the specific impact of CHIKV on neurodevelopment and inform public health priorities

3) Determine the prevalence of mother to child transmission of CHIKV in Grenadian pregnant mothers

4) Measure neurodevelopment in children at 2 years of age exposed at different trimesters in utero to CHIKV and compare with unexposed children

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Methodology

The study, which is still enrolling participants, has so far enrolled 526 mothers and 381 children born during and up to one year after the 2014 CHIKV outbreak. The study is quantitative and measures several variables:

1) A questionnaire about the home environment, relationships, food security and pregnancy outcomes;

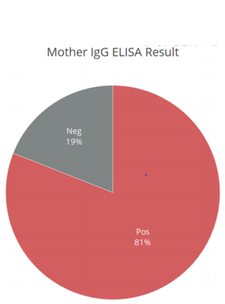
2) Multidimensional and objective assessment of early neurodevelopment in infants using a robust multi-dimensional clinical tool (Intergrowth-21st Neurodevelopmental Assessment – InterNDA); and

3) Blood samples to measure CHIKV exposure of mothers and their children by ELISA (InBios CHIKjj IgG kit). The picture below illustrates the blood sample preparation for ELISA measurement.

- CHIKV-exposed moms and infants, and time of exposure during pregnancy were used to divide groups for comparison (exposed – IgG positive and nonexposed IgG negative).

Results

- Caribbean-based research assistants have been trained in standardized neurodevelopmental assessment using the interNDA.
- Of 526 mothers tested, 426 (81%) were IgG CHIKV positive and 100 (19%) tested negative. Among 381 children tested, 16 tested positive and 365 negative (Figure 1a). The infection rates for those exposed in utero compared to not were 4.4% and 3.9% respectively (Figure 1b).
- Infected mothers had lower education compared to non-infected but were otherwise not significantly different from each other on average (Figure 2).



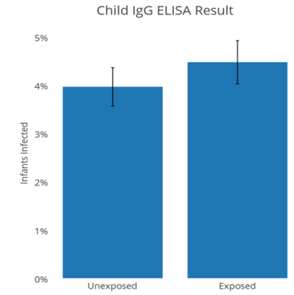


Figure 1 a and b: Mother Anti CHIKV IgG Result and child IgG Result by in utero exposure

Factor	Level	Negative	Positive	p
n		100	426	
Race (%)				0.717
	African Descent	85 (89.5)	354 (85.9)	
	Indian descent	3 (3.2)	19 (4.6)	
	Other	7 (7.4)	36 (8.7)	
	Refused/don't know	0 (0.0)	3 (0.7)	
Mother age (years) (mean (sd))		30.17 (5.99)	30.14 (6.01)	0.965
Mother's education (%)				0.02
	Primary School	13 (13.7)	51 (12.4)	
	Secondary School	45 (47.4)	234 (56.8)	
	Bachelor's degree	6 (6.3)	40 (9.7)	
	Graduate or Professional degree	8 (8.4)	9 (2.2)	
	Other	23 (24.2)	75 (18.2)	
	Refused/Don't know	0 (0.0)	3 (0.7)	
Mother is married, common-law, or lives with a partner? (%)				0.247
	No	36 (37.9)	193 (46.8)	
	Yes	59 (62.1)	218 (52.9)	
	Refused/Don't know	0 (0.0)	1 (0.2)	
Monthly income (%)				0.066
	Under $1000 EC	13 (13.7)	85 (20.6)	
	$1,001-2,000 EC	22 (23.2)	74 (18.0)	
	$2,001-3000 EC	13 (13.7)	78 (18.9)	
	Over $3000 EC	23 (24.2)	60 (14.6)	
	Refused/Don't know	24 (25.3)	115 (27.9)	
History of Hypertension (%)		8 (8.0)	44 (10.3)	0.606
History of Diabetes Mellitus (%)		4 (4.0)	10 (2.3)	0.563
Alcohol during pregnancy		10 (10.5)	27 (6.5)	0.25
Smoking during pregnancy				0.312
	No	95 (100.0)	406 (97.6)	
	Yes	0 (0.0)	6 (1.4)	
	Refused/Don't know	0 (0.0)	4 (1.0)	

Figure 2: Demographic characteristics of mothers: IgG Positive versus Negative

- The preliminary analysis of the InterNDA data revealed that children exposed to CHIKV in utero may have lower mean cognitive scores compared to unexposed children (4.1 vs 3.82, p = 0.08) (Figure 4).
- Children exposed to CHIKV versus not were similar in height, weight, age, and gender (Figure 5).

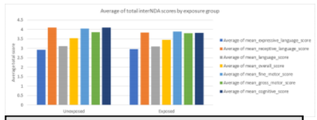


Figure 4: Average interNDA scores unex-

	NOT EXPOSED	EXPOSED TO CHIKV
N	170	179
CHILD HEIGHT (CM) (MEDIAN [IQR])	87.05 [85.11, 89.68]	87.60[85.00, 89.95]
CHILD WEIGHT (KG) (MEDIAN [IQR])	12.10 [11.20, 13.30]	12.40 [11.40, 13.57]
CHILDS AGE (MONTHS) (MEDIAN [IQR])	25.00 [24.00, 25.00]	25.00 [24.00, 25.00]
FEMALE (%)	67 (43.8)	85 (50.3)

Figure 5: Child characteristics exposed versus not

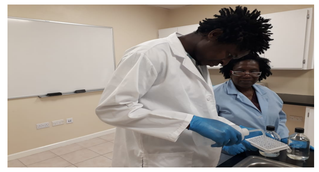
Conclusions

This study is still enrolling after the expected enrollment period in attempts to reach the targeted 1000 mother-child pairs.

So far there is no final conclusion about the association between mother's exposure to CHIKV and abnormal neurodevelopment of infant. Preliminary results suggest that there is no strong association between mothers expose to CHIKV and child neurodevelopment. However, the mean cognitive scores may be lower in those exposed at different trimesters in utero to CHIKV compared with unexposed children.

Limitations: Several factors have limited enrollment, such as the timing of testing for the infants turning 24 months and the likelihood of parent bringing their infants for assessment (i.e., summer break/Carnival season, rainy season) and inability to contact the mothers due to outdated phone numbers/contact information. However, we are continuing to reach out to nurses at the health clinics, where the mothers attend follow-up appointments with their infants to try and obtain updated contact information and locate them for involvement in the study.

Next steps: The next analysis will be to assess the burden of confounding factors to better understand the specific impact of CHIKV on neurodevelopment to inform public health priorities.



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