LB-5106

Assessment of persistent arthralgia associated with the chikungunya virus outbreak on the U.S. Virgin Islands

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Background

Chikungunya virus (CHIKV), an emerging alphavirus transmitted by the *Aedes aegypti* and *Aedes albopictus* mosquitoes, was newly introduced into the Americas in December of 2013. As of May 2015, almost 1.5 million suspected or confirmed cases had been reported in 45 different countries in the Caribbean, Central, South, and North America.

Acute symptoms of CHIKV infection include fever and polyarthralgia. These symptoms often resolve within 7-10 days, but 5-60% of cases in previous outbreaks have reported persistent arthralgia for months following initial infection.

To better define the long-term impact of CHIKV during the 2014-2015 outbreak on the U.S. Virgin Islands, clinical and functional outcomes were evaluated at 6 months after the onset of reported CHIKV illness.

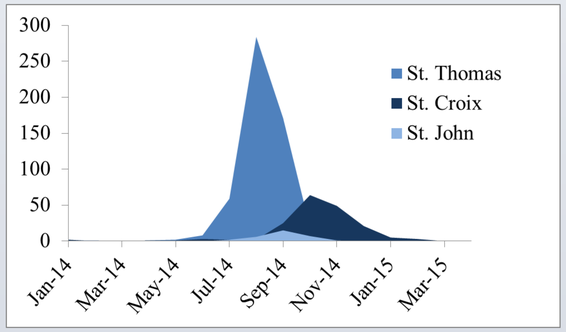

Figure A. Epidemic curve of reported laboratory-positive CHIKV cases by month of illness onset on the USVI

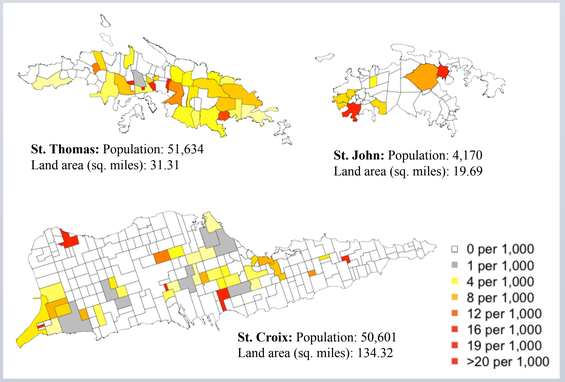

Figure B. Incidence of reported laboratory-positive CHIKV cases per 1,000 by estate (subdivision of the county-level islands) from January 2014 – March 2015.

Methodology

The outcomes of confirmed CHIKV cases were compared to healthy non-cases.

Confirmed cases were defined as a case of reported CHIKV disease, from a resident of the U.S. Virgin Islands (USVI), with an acute CHIKV infection diagnosed by:
1) Positive RT-PCR for CHIKV RNA or
2) CHIKV IgM ELISA assay with positive virus-specific neutralizing antibodies

Verbal consent was obtained from all cases prior to administering a questionnaire with information regarding acute illness, residual joint symptoms, and lost work or hampered activity due to infection.

A healthy non-case was defined as a consenting USVI resident who responded "no" to experiencing sudden onset of fever and joint pain, between June 2014 and June 2015, and was attending a healthcare facility in USVI during the last week of June 2015.

Using Poisson regression with robust standard errors, crude and adjusted prevalence ratios were calculated to estimate the association between CHIKV and persistent arthralgia

Results

	Cases (95% CI)	Non-cases (95% CI)	P-value for difference in proportions
Sample Size	151	179	-
Gender (Female)	64.2%	65.0%	-
Median age in years (range)	48.9 (1-95)	34.3 (1-78)	-
Self-reported arthralgia during day of interview	**33.1% (25.6-40.6%)**	**10.0% (5.6-14.4%)**	**<0.001**
Self-reported arthralgia within the past 30 days	**51.0% (43.0-59.0%)**	**17.9% (12.3-23.5%)**	**<0.001**
History of arthritis among individuals reporting arthralgia	28.6% (18.5-38.7%)	65.3% (48.8-81.8%)	<0.001
Difficulty walking	27.8% (20.7-34.9%)	12.9% (7.9-17.8%)	<0.001
Difficulty climbing a flight of stairs	31.8% (24.4-39.2%)	12.9% (7.9-17.8%)	<0.001

Table 1. Demographics and prevalence of self-reported arthralgia 6 months post acute CHIKV infection among cases and non-cases

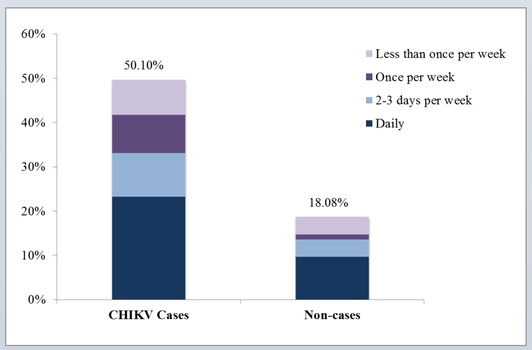

Figure C. Frequency of self-reported arthralgia 6 months post-acute CHIKV infection among cases and non-cases

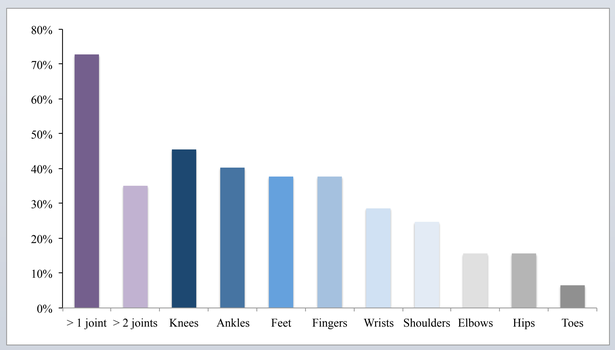

Figure D. Affected joints among laboratory-positive CHIKV cases

	No history of arthritis (95% CI)	History of arthritis (95% CI)
Crude prevalence ratio	3.16 (2.38 – 4.18)	1.91 (0.86 - 4.21)
Age-adjusted prevalence ratio	3.02 (2.19 – 4.15)	1.62 (0.83 – 3.15)
Overall prevalence ratio of persistent arthralgia (adjusted for age and history of arthritis):		
2.53 (1.87 - 3.41)		

Table 2. Prevalence ratios of persistent arthralgia, defined as joint pain at least once per week, in CHIKV cases compared to non-cases 6 months post-acute infection before and after adjustment for age and stratified by history of arthritis

Impact of persistent arthralgia on absenteeism

- 42.3% of all CHIKV cases reported being employed 6 months post-acute infection
  - 78.8% of those individuals reported missing work due to CHIKV-related illness
  - On average, CHIKV cases reported missing 8.5 days of work (range: 2 – 60 days)
- 48.1% of CHIKV cases who reported arthralgia 6 months post-acute infection, reported being employed
  - 86.5% of those individuals reported missing work due to CHIKV-related illness
  - On average, those individuals reported missing 10.9 days of work (range: 2 – 60 days)

Impact of persistent arthralgia on daily life

- 84.6% of CHIKV cases reported missing their daily activities and household chores due to CHIKV-related illness within 6 months of infection.
  - On average, all CHIKV cases reported missing 30.2 days of their daily activities or household chores
  - On average, CHIKV cases who reported arthralgia 6 months post-acute infection, reported missing 41.5 days of their daily activities or household chores

Conclusions

Based on our findings, the estimated prevalence of persistent daily arthralgia among CHIKV cases in the USVI is more than twice that of healthy non-cases. After adjustment for age and history of arthritis, CHIKV cases are estimated to be 153% (95% CI: 87 - 241%) more likely to have persistent arthralgia compared to non-cases, 6 months post-acute infection.

73% of CHIKV cases who reported persistent arthralgia, reported pain in more than one joint and 35% reported pain in 2 or more joints.

CHIKV cases, regardless of presence of persistent arthralgia missed a substantial number of days of work and of daily activities due to infection.

CHIKV cases will be interviewed at 12 months after acute infection to determine whether the prevalence of persistent arthralgia remains.

Acknowledgements

Thank you to Dr. Erin Staples and Dr. Morgan Hennessey of the Centers for Disease Control and Prevention for their support on this project and to Christina Sancken, Zachary Heth and Elyse Phillips, masters students from the Rollins School of Public Health, for their assistance in data collection.

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Funding provided by NIH\NIAID R37 AI032042 and by the USVI Department of Health