

Clinical Findings and Neurodevelopmental Outcomes in Jamaican Children with suspected Congenital Zika Syndrome

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Introduction

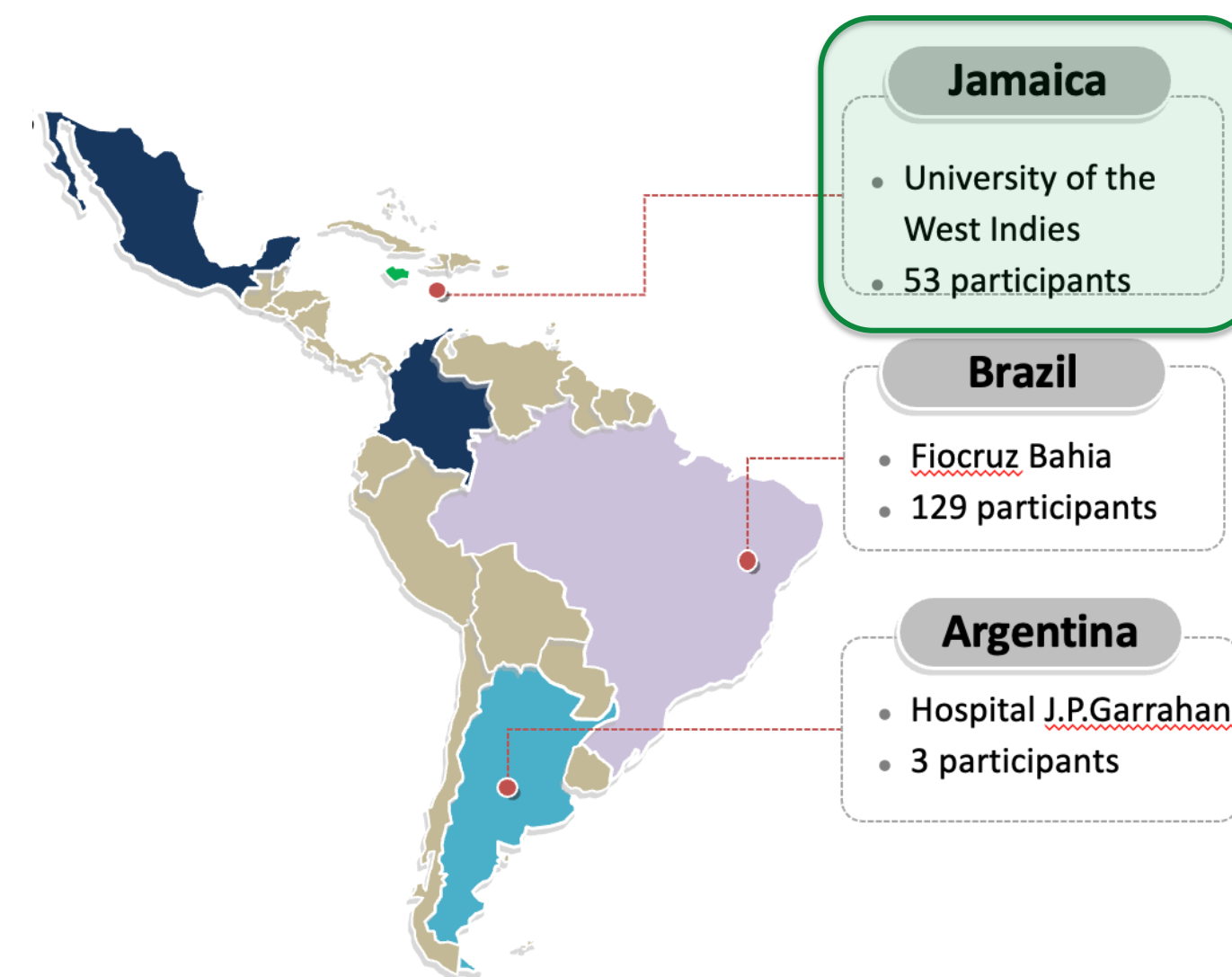
- The first recorded outbreak of Zika virus (ZIKV) infection was in 2007. A large epidemic began in Brazil in 2015 and Jamaica recorded its first case in January 2016.
- Vertical transmission with ZIKV has been associated with congenital Zika syndrome (CZS). Features include severe microcephaly, craniofacial disproportion, eye abnormalities, severe arthrogryposis, intrauterine growth retardation and sensorineural hearing loss.
- In 2016, after noting the increased numbers of newborns with microcephaly in the ZIKV-affected areas of Brazil and in French Polynesia, the World Health Organization declared a “public health emergency of international concern”.
- By late 2016, cases of newborns with microcephaly and arthrogryposis were being recognized in Jamaican hospitals.
- In June 2016, the European Commission funded the “ZIKAction” consortium, to perform collaborative population-based research to better characterize the epidemic in Latin America, Caribbean, Europe and other sites.
- As part of a multi-center registry, this study aimed to characterize the clinical, radiological, neurodevelopmental and laboratory features of children antenatally exposed to ZIKV and/or presenting with suspected CZS in Jamaica.

Materials and Methods

Retrospective study of infants and children potentially exposed to ZIKV antenatally and who were outpatients and/or inpatients in any one of four public hospitals in the Greater Kingston Metropolitan Region of Jamaica between June 1, 2016, and October 31, 2019, who were identified by review of admission logbooks and out-patient clinic records.

- Inclusion criteria - ≥ 1 of:
 - Exposed to ZIKV in utero (i.e., a mother with laboratory confirmation of ZIKV infection during pregnancy)
 - Have laboratory-confirmed congenital ZIKV infection
 - Meet the Registry definition of suspected CZS: microcephaly (head circumference (HC) greater than two standard deviations (SD) below the mean for age and sex) and/or fetal brain disruption sequence and/or arthrogryposis or joint contractures
- Exclusion criteria: Neonates with lab-confirmed congenital infection other than ZIKV e.g., TORCHS or with genetic or other confirmed cause of microcephaly or congenital anomaly
- Pseudoanonymised data were entered into a REDCap (Research Electronic Data Capture) database. Descriptive analyses were performed. All significance tests were conducted at the 0.05 level. SPSS v26 (IBM Corp., Armonk, NY, USA).
- Ethical approval was obtained.

Results



Key Results

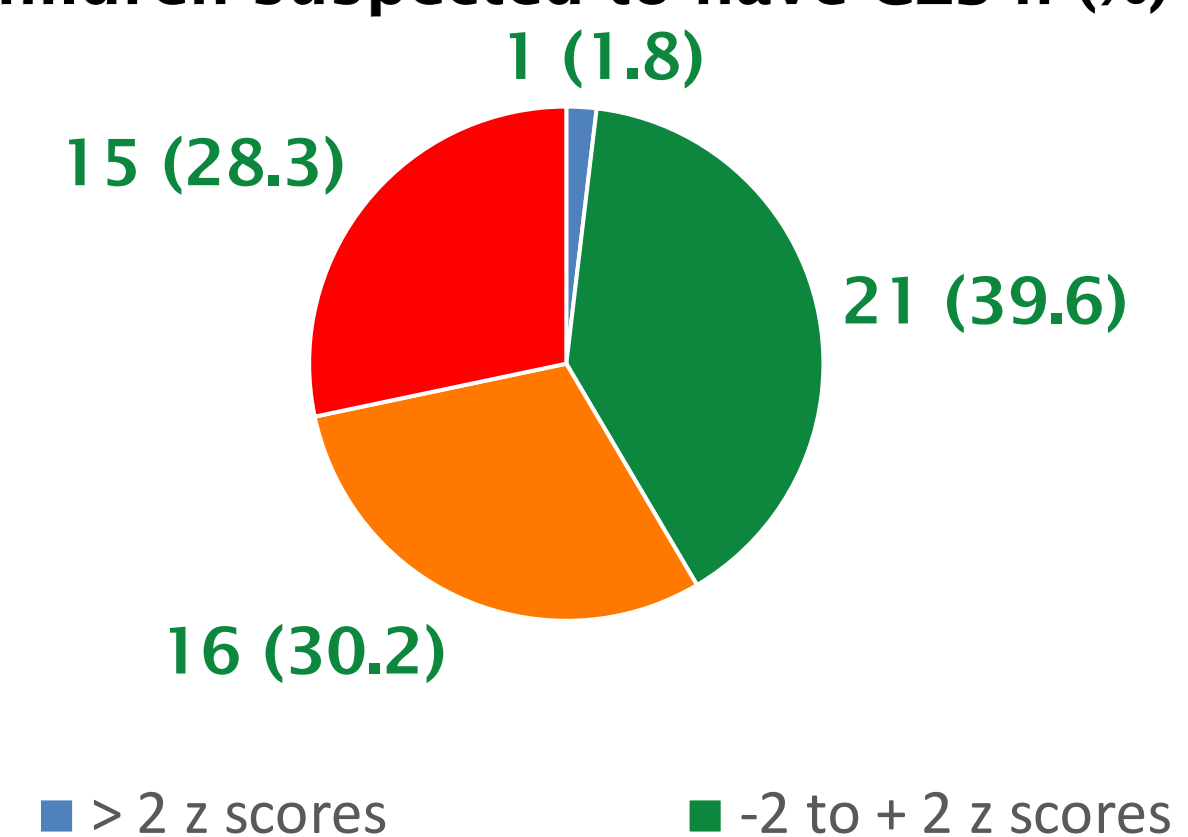
- 6 (11.3%) mothers - lab confirmed ZIKV
- 1 (1.9%) infants had ZIKV results available
- 31 (58.5%) participants were microcephalic
- 24/27 (88.9%) infants had abnormal neuroimaging
- 19/34 (55.8%) infants had developmental delay
- Developmental delay was associated with abnormal neuroimaging and clinical neurologic findings.

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Table 1 Characteristics of children suspected to have CZS – ZIKAction Jamaica Registry

Birth weight (BW) (kg), mean (SD)	2.7 (0.4)
Crown heel length (CHL) (cm), mean (SD)	47.4 (2.7)
Occipitofrontal circumference (cm), mean (SD)	30.9 (2.3)
Gestational age (weeks), mean (SD)	38.4 (1.5)
Apgar score (5 min), mean (SD)	8.7 (1.1)
Neonatal High Dependency Unit admission**, n (%)	34 (66.7)
ZIKV (RNA PCR & IgM) n (%)	1 (1.9)
Neuroimaging abnormality (N=27)	24 (88.9%)
Developmental delay (N=34)	19 (55.8%)
Abnormal ophthalmology examination (N=32)	8 (25.0%)
Abnormal hearing evaluation (N=9)	5 (55.5%)
Seizures (N=36)	6 (16.7%)
Weakness (N=36)	9 (25.0%)
Hypotonia (N=34)	10 (29.4%)
Spasticity (N=35)	19 (54.2%)
Death	1 (1.8%)

Head Circumference Categories in Jamaican children suspected to have CZS n (%)



Head circumference categories of participants, year of birth, Jamaican children suspected to have CZS

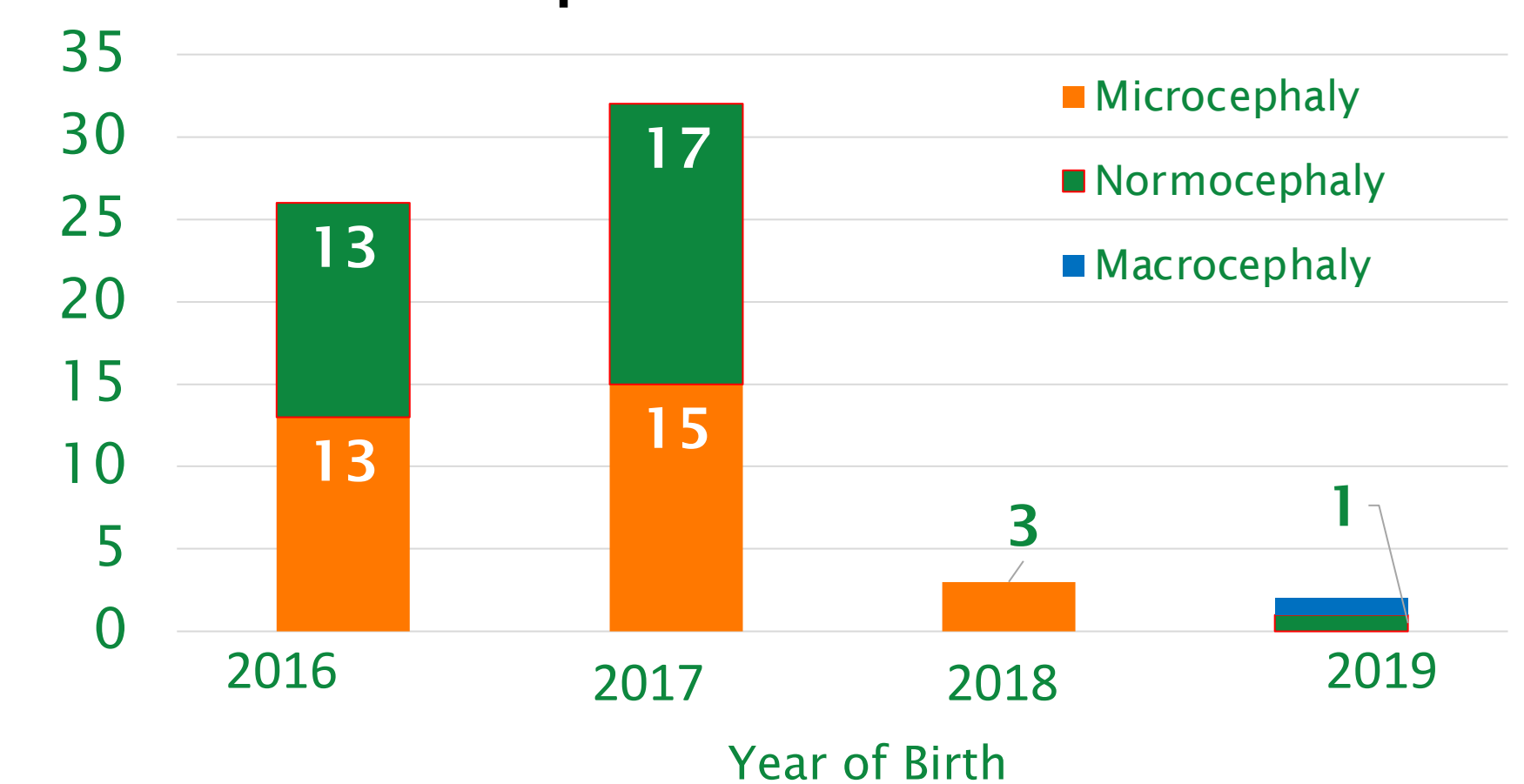
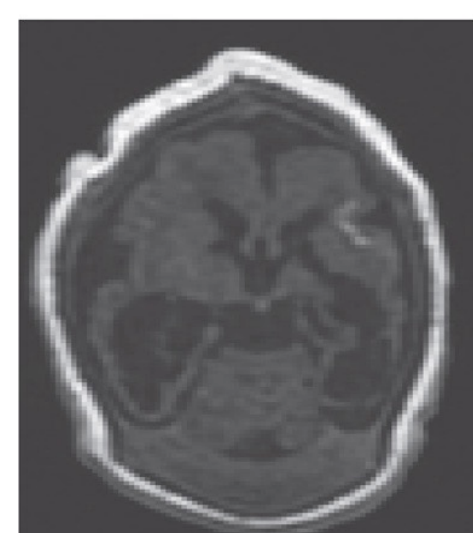
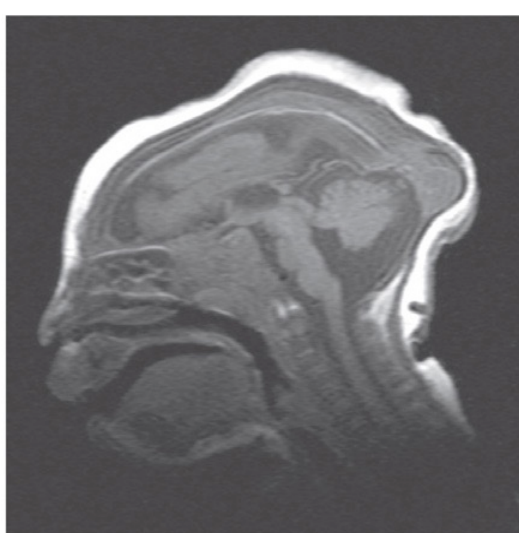


Table 2 Variables associated with developmental delay in study participants- ZIKAction Jamaica Registry

	Developmental Delay		P value
	Yes	No	
Weakness, n			
Yes	8	0	0.005*
No	10	13	
Hypotonia, n			
Yes	8	1	0.020*
No	9	12	
Spasticity, n			
Yes	13	3	0.011*
No	5	9	
Pathologic reflexes, n			
Yes	10	1	0.002*
No	4	10	
Neuroimaging results, n			
Normal	0	4	0.003*
Abnormal	14	4	

Conclusions

- This registry identified a subset of children born during and immediately after the ZIKV epidemic in Jamaica with physical features of CZS, adverse neurodevelopmental outcomes and with increased needs for health resources and social support.
- Adverse neurodevelopmental outcomes were associated with abnormal neuroimaging and clinical neurologic abnormalities.
- Few infants had ZIKV and TORCH results available highlighting the gaps which existed in the diagnostic capabilities for these infectious diseases during the period of the registry.
- These data will facilitate planning for diagnostic, rehabilitative and support services should there be another ZIKV or similar epidemic in Jamaica with the potential for teratogenicity and adverse neurodevelopmental outcomes.



6-week-old Jamaican infant with typical clinical and radiological features of CZS
From: James-Powell T, Brown Y, Christie CD, Melbourne-Chambers R, Moore JT, Morgan O, et al. Trends of microcephaly and severe arthrogryposis in three urban hospitals following the Zika, Chikungunya and Dengue fever epidemics of 2016 in Jamaica. *West Indian Med J* 2017 Jul 14;66:10-19.



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