

The Impact of Non-Detectable Zika Infection

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Introduction

While it has been several years since the emergence of the Zika virus epidemic, the infection continues to be a threat to the development of children identified as infected or exposed. Due to the neurotropic nature of Zika virus, the mystery of how the virus manifests itself in the developing child is still largely unknown. Because of this, pediatric health professionals must remain vigilant when assessing language, motor and cognitive domains in this population of patients. These professionals must also ensure to include both age and developmentally appropriate measures in their management to identify interventions promoting neurodevelopment. Although microcephalic children have been associated with having developmental delays, the neurodevelopment of non-microcephalic Zika-exposed children should not be assumed. In this prospective case review, language development for both exposed and infected children were significantly delayed for their age. The objective of this study is to provide clinicians an update on neurodevelopmental delays observed in Zika-infected and Zika-exposed children. Through review of the current literature and clinical observations, findings related to the auditory and neurodevelopment of Zika-infected and Zika-exposed patients identify a need for continued long-term monitoring of developmental milestones in children who are exposed or infected.

Domains of Development as Observed

Motor: In clinic, some patients with Zika virus exposure appeared clumsy and unstable when standing stationary and mobile. We have observed a 36-month-old male (patient C) with extremely poor muscle tone which impacted his ability to walk confining him his stroller. Two 22-month-old twins were just beginning to walk.

Language: When compared to typically-developing toddlers, significant expressive language delays have been observed in our patient population. By 15 to 18 months, a typically-developing toddler should have a rapidly increasing vocabulary. At our clinic, we have observed patients of older ages to be significantly delayed. During our hearing evaluations, minimal expressive language was used by the patients. Receptively, these patients appeared to be developmentally on-track. Patient D has been receiving speech therapy for swallowing difficulties present since birth.

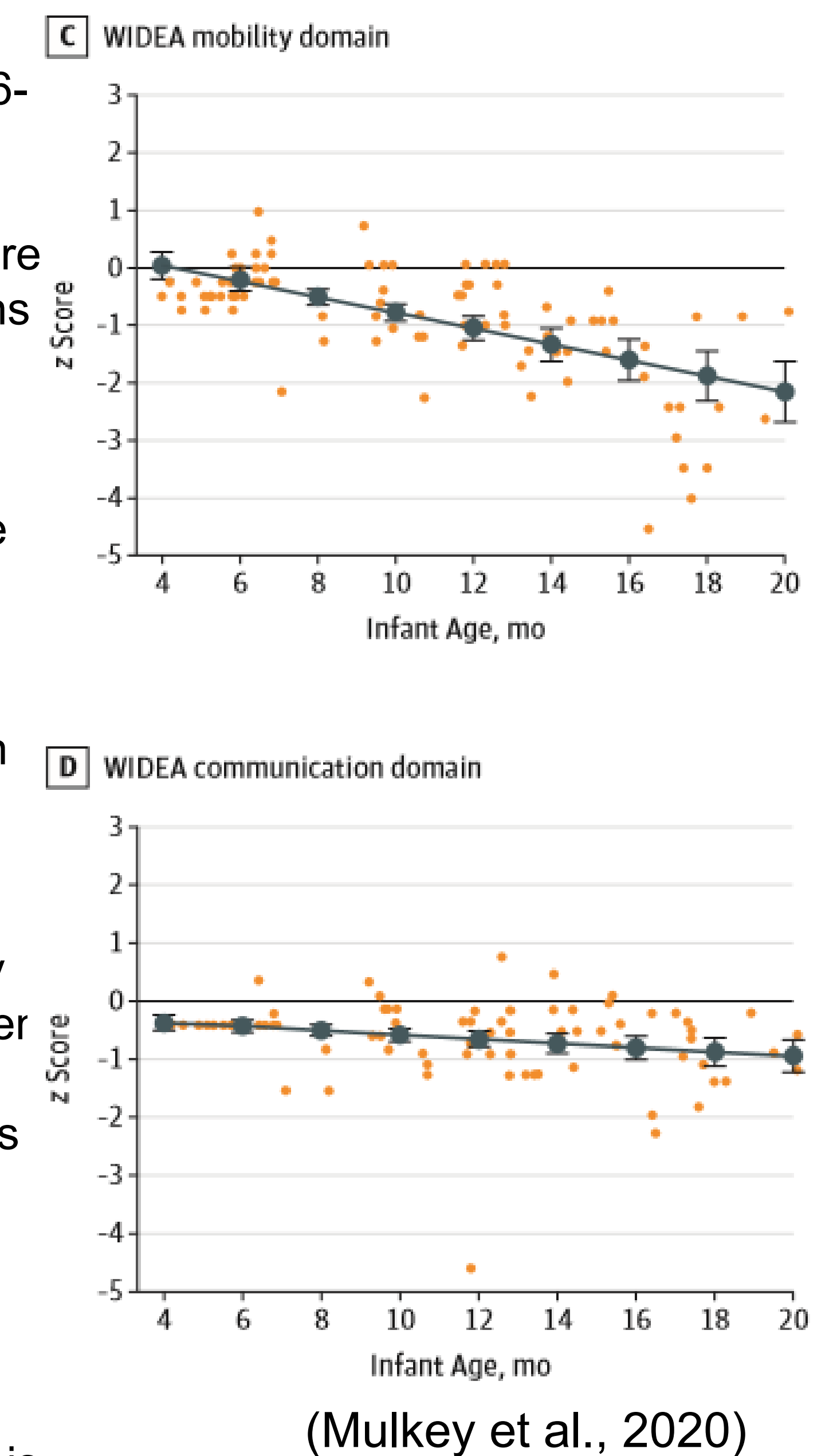
Hearing: The Zika virus is known to attack progenitor cells, which are primed for development from about 6 weeks gestation to 1 year after birth. After the first 12 months of life, late-onset hearing loss due to Zika virus exposure has not been observed. At the Mailman Center, our patients have been observed to have normal hearing sensitivity that is adequate for speech and language development needs.

Case Review

Patient Identification	Age/Sex	Diagnosis	Clinical Observations
Patient A (Twin "A")	22 months/ female	Zika virus exposure (first trimester); expressive speech delay; significant motor delay; born @ 35 weeks gestation	Less than 6 words ("mama & papa") as reported by mother
Patient B (Twin "B")	22 months/ female	Zika virus exposure (first trimester); expressive speech delay; significant motor delay; born @ 35 weeks gestation	Less than 6 words ("mama & papa") as reported by mother
Patient C	36 months/ male	Zika virus exposure; microcephaly; anomalous optic nerve; abnormal muscle tone, gait, and motor coordination	Less than 50 words as reported by mother
Patient D	22 months/ female	Zika virus exposure (second trimester); expressive speech delay; developmental delay	Receiving speech therapy as reported by mother
Patient E	18 months/ female	Zika virus exposure; reported normal gross motor, fine motor and speech/language development	Growing vocabulary as reported by mother

Literature Review

In the present clinical findings at the Mailman Center, we have observed 10% of our pediatric cohort, ages 18-months-old to 36-months-old, to have significant language and motor delays. Similar to our findings, Gordon-Lipkin & colleagues (2019) reported that 19 infants aged 19 to 24 months with Zika exposure were nonverbal and scored below an age equivalent of 6 months in the Ages and Stages Questionnaire, Third Edition (ASQ-3). Similarly, when using the Bayley Scales of Infant Toddler Development-Third Edition (BSID-III; cognitive, language, and motor domains), Faical & colleagues (2019) observed language delays in 31% of infants and motor delays in 3% of infants exposed in-utero to Zika virus. Nielsen-Saines & colleagues (2019) reported 12% of their Zika-exposed cohort aged 7 to 32 months scored below two standard deviations on the BSID-III in at least one domain. Of the 146 children in the cohort, 35% scored below average in the language domain. The objective measures reported in the literature support the clinical findings that we have recently been observing in this population. Mulkey & colleagues (2020) identified that as Zika virus exposed children develop, they typically score within one standard deviation in mobility, communication, self-care, and social cognition domains as measured by the Warner Initial Developmental Evaluation of Adaptive Functional Skills (WIDEA). As depicted by the graphs, this trajectory appears to continue until the child is around 18 months of age. At this age, similar to our clinical findings, children appeared to subtly regress and score outside two standard deviations in mobility and communication domains. This prompts a primary concern and challenge to clinicians, why are these children not being found earlier.



Conclusion

Early detection and identification of developmental delays in any domain is essential for early intervention services. A thorough case history, including potential maternal Zika virus exposure and developmental milestones, can ensure early detection and appropriate referral. Because multiple domains of development are affected by Zika virus exposure, an interdisciplinary approach should be considered when managing this population. Infants with Zika virus exposure should be presumptively eligible for IDEA Part C due to the developmental trajectory measured and observed by clinicians. Pediatricians and clinicians should regularly monitor this population as the manifestations of the Zika virus continue to be discovered.

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