Neurodevelopmental Screening Tests Outcomes of Children in Wisconsin With a Prenatal History of Travel to Zika Virus-Endemic Regions During 2015-2018: A Retrospective Case-Control Study

Sabrina A. Kabakov, OTD;* Rachel V. Spanton*; Elaina Razo; Erik Sanson; Christelle Cayton; Emmy Wanjiku; Jens Eickhoff, PhD; Karla K. Ausderau, OTR, PhD; Emma L. Mohr, MD, PhD

ABSTRACT

Background: Children with prenatal Zika virus exposure are at an increased risk of developing neurodevelopmental deficits in early childhood. Travel to Zika virus-endemic regions during pregnancy elevates the risk of offspring developing complications. This study examined developmental outcomes of children from Wisconsin with maternal or partner travel history to Zika virus-endemic regions during pregnancy compared to gestation and age-matched controls.

Methods: A retrospective chart review compared outcomes of cases (n = 181) with prenatal travel history to Zika virus-endemic regions to gestational and birth date-matched controls (n = 172) up to 7 years old. We reported Zika virus testing and travel, birth outcomes, standardized developmental screening tests, and specialist referral rates.

Results: There were no differences in referral rates and standardized developmental screening test outcomes, but cases tended to have more referrals for early intervention compared to the controls ($P = 0.059$). One Zika virus-positive case was identified with complications surrounding birth, and 2.2% of children had documentation in their health records noting potential Zika virus exposure. Regardless of groups, limited referrals were made at 9 (0%), 18 (60%), and 24 (40%) months based on Ages and Stages Questionnaire-version 3 (ASQ-3) recommendations.

Conclusions: This study found similar developmental screening outcomes and referral rates between groups. Longitudinal care of children whose mothers traveled to Zika virus-endemic regions could be improved with better documentation of prenatal Zika virus exposure in the child's medical record, use of standardized developmental screening tools at every recommended well-child visit, and referral when developmental screening test scores are low.

• • •

Author Affiliations: Department of Pediatrics, University of Wisconsin (UW) School of Medicine and Public Health (SMPH), Madison, Wisconsin (Kabakov, Spanton, Razo, Sanson, Cayton, Wanjiku, Mohr); Department of Kinesiology, Occupational Therapy Program, UW–Madison, Madison, Wisconsin (Kabakov, Ausderau); Department of Biostatistics and Medical Informatics, UW SMPH, Madison, Wisconsin (Eickhoff); Waisman Center, UW–Madison, Madison, Wisconsin (Ausderau); Department of Medical Microbiology and Immunology, UW SMPH, Madison, Wisconsin (Mohr). **Denotes co-first authors.*

Corresponding Author: Emma Mohr, 600 Highland Ave, Madison WI 53792, phone 608.265.5107, email emohr2@wisc.edu, ORCID ID 0000-0003-0742-305X

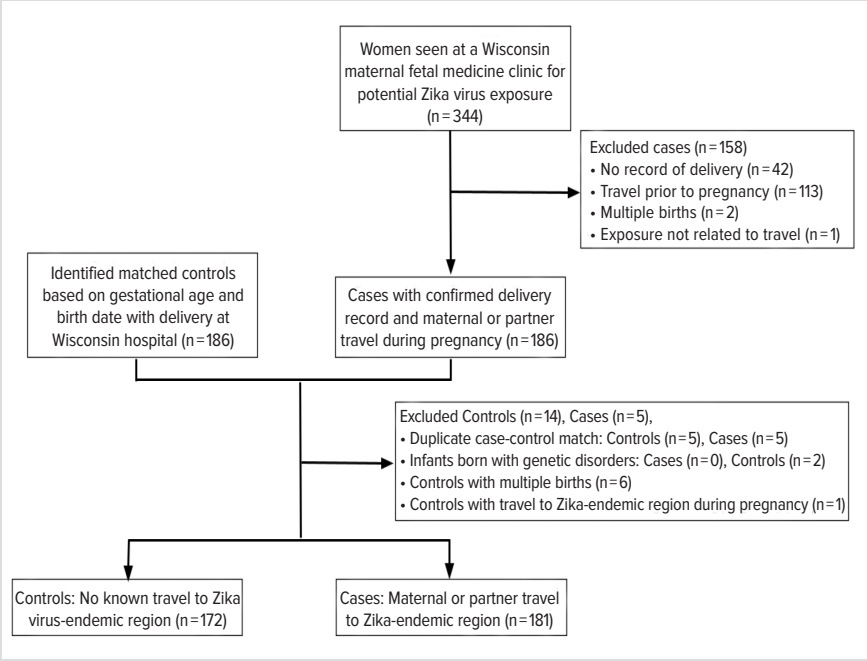
BACKGROUND

Zika virus was declared a public health emergency in 2016 when prenatal Zika virus exposure was linked to congenital defects in newborns, including microcephaly and visual and hearing deficits.[1,2] Approximately 5% of children with laboratory-confirmed Zika virus exposure in the United States are born with congenital defects.[3] An additional 30% of children who are born without congenital deficits manifest neurodevelopmental deficits in early childhood, with language development being the most affected.[4] As cohorts of children with Zika virus exposure during the 2015-2018 epidemic are now entering school age, recent research has identified neurodevelopmental deficits in preschool age.[5,6] Additional research is necessary to define how potential prenatal Zika virus exposure affects developmental outcomes in childhood, especially in pregnancies where exposure to mosquitoes occurred but no testing for Zika virus was performed.

Most developmental research on Zika virus has focused on cohorts in countries with high prevalence and incidence of Zika virus or on congenital defects. Zika virus has multiple modes of transmission, including (1) transmission from mosquito to human, (2) sexual transmission, and (3) vertical transmission from mother to child.[7] The Centers for Disease Control and Prevention (CDC) recommends caution when traveling to areas with reported Zika virus infections (both past and current), which are countries where there is a high prevalence of *Aedes aegypti* mosquitos.[8] Travel to a Zika virus-endemic area(s) during pregnancy increases the risk of congenital defects or late-onset

neurodevelopmental deficits compared to pregnancies with no travel history to endemic regions.[9,10] Zika virus infection is often asymptomatic, even during pregnancy, suggesting that pregnant persons who travel to endemic regions may have no knowledge of a Zika virus infection. Fetuses remain at risk for developing deficits independent of the presence of acute Zika virus infection symptoms.[3] Current CDC testing guidelines recommend testing only for symptomatic pregnant women after travel to a country with a past or current Zika virus outbreak.[11] Asymptomatic pregnant women do not meet the testing criteria despite their fetuses remaining at risk for deficits. Defining the incidence of neurodevelopmental deficits in this unique group of children is important for developing travel and testing recommendations during pregnancy and specifying which children should receive early intervention.

Figure 1. Exclusion and Inclusion Criteria



This study aimed to investigate the developmental screening outcomes of children with a prenatal travel history to Zika virus-endemic regions during the height of the Zika virus epidemic in 2015-2018, within a Wisconsin hospital health care system. This study utilized electronic health records (EHR) to define maternal Zika virus information, developmental screening outcomes, and specialist referrals.

METHODS

A retrospective chart review was conducted to determine how travel exposure to a Zika virus-endemic region(s) during pregnancy affected developmental screening outcomes. Maternal records were obtained from women seen at a Wisconsin maternal-fetal medicine clinic to evaluate for Zika virus from January 1, 2015, through December 31, 2018. Cases were defined as children with prenatal maternal or partner travel history to a Zika virus-endemic region during 2015-2018, based on the CDC classification.[8] Cases were removed from the study based on the following exclusion criteria: (1) no record of delivery in the same Wisconsin health system, (2) travel history prior to pregnancy, (3) multiple births, and (4) potential Zika virus exposure unrelated to travel (Figure 1). We identified matched-control offspring based on gestational age (+/- 1 week) and birth date (+/- 1 birth month) using PeriData.Net, a comprehensive birth registry that provides birth-level data (Ancilla Partners, Inc, Milwaukee, Wisconsin). After matching, cases and controls were excluded based on the following criteria: (1) duplicate assignments in the case/control group, (2) children with diagnosed genetic disorders, (3) controls with multiple births, (4) controls with maternal or partner travel history to a Zika virus-endemic region. After all exclusion criteria were considered (Figure 1), 181 cases and 172 controls were available for study. This chart review was approved by the UnityPoint Health Meriter Institutional Review Board (#2019-024). Data from children's EHRs were extracted from birth until 7 years of age or April 1, 2023.

The EHR provided demographic and socioeconomic information, Zika virus testing, travel history, and birth and developmental outcomes. Paper records from the maternal-fetal medicine clinic provided supplemental travel information, including travel continent, potential paternal travel, any acute Zika virus symptoms, estimated trimester of exposure, and confirmed test results. The University of Wisconsin-Madison Clinical and Health Informatics Institute was used to identify maternal demographic information, type of delivery, and birth measurements. ZIP codes were obtained from the maternal EHR in January 2024 (due to the absence of maternal ZIP codes in the delivery records). The distribution of health services across urban and rural areas is known to affect health outcomes.[12] To account for the impact of socioeconomic status on developmental outcomes, maternal ZIP codes were assigned a rural or urban status using the Health Innovation Program's Zip Code Toolkit.[13]

Multiple variables were obtained to compare birth and developmental outcomes between groups. These included delivery type, sex, gestational age at birth, Apgar scores, birth measurements, documentation of potential Zika virus exposure, specialist referrals, and developmental screeners including the Ages and Stages Questionnaire-version 3[14] (ASQ-3) and Modified

Checklist for Autism in Toddlers-Revised[15] (MCHAT-R). The ASQ-3 is a screening tool to measure developmental milestone attainment, and MCHAT-R is a screening tool for identifying the risk of autism spectrum disorder. ASQ-3 outcomes were documented at 9, 18, and 24 months across 5 areas of development (communication, fine motor, gross motor, personal social, and problem-solving). They were interpreted as on schedule (within 1 SD), monitor (between 1 and 2 SD), or further assessment needed (>2 SD) per ASQ-3 guidelines. The MCHAT-R was documented at 2 time points (16-21 months and 22-30 months of age), with total scores categorized as no further action (0-2 score), additional screening needed (3-7 score), or refer to specialists (8-20 score).

We evaluated referrals to multiple pediatric subspecialties, therapies, and early intervention (Wisconsin Birth to 3 Program[16]) because diagnoses related to developmental deficits or complications from congenital Zika virus infection may be evaluated by all of these specialties. Referrals to dentists, dermatologists, rheumatologists, and allergists were excluded as these specialties were not determined to help evaluate or manage developmental outcomes. Specialists also were excluded if the frequency was reported less than 5 times across both cases and controls. Search terms to identify the frequency of specialists were "consult" or "referral" in the chart. Before calculating the referral rate, charts with EHR visits documented after birth hospitalization were included, indicating they were still engaged in the health care system.

Study data were collected and managed using Research Electronic Data Capture (REDCap) tools hosted by the UW-Madison School of Medicine and Public Health.[17,18] All data were verified for accuracy by the co-first authors. Statistical analyses were conducted using SAS software, version 9.4 (SAS Institute; Cary, North Carolina). Demographic characteristics were compared between cases and controls using chi-square analysis for categorical characteristics or the nonparametric Wilcoxon rank sum test for characteristics measured on a quantitative scale. Referral rates by specialists were compared between cases and controls using a chi-square or Fisher exact test. Analogously, the MCHAT-R and ASQ-3 categories were compared using a chi-square test or Fisher exact test for each area of development and time point. All reported P values are 2-sided, and $P < 0.05$ was used to define statistical significance.

RESULTS

We investigated both maternal and partner travel (due to sexual transmission of Zika virus) because paper records did not explicitly outline who traveled. Solely partner travel was indicated in 11 paper charts (6.07%). Partner travel was included in the country of travel but was excluded from the travel duration and trimester of travel (Table 1). Most prenatal Zika virus-endemic travel history occurred within North America followed by South America, with specific countries outlined in Supplemental Table 1. The mean maternal travel duration was 39.5 days (median = 8 days), which was skewed since 13.5% of maternal travel had periods of ≥ 30 days. The majority of reported travel was during the first trimester (81.8%), followed by the second (27.1%) and third trimesters (9.4%); 11.6% reported travel occurred across multiple trimesters. Records did not include activities during travel, so it is unclear what mosquito exposures were encountered. In total, 56.4% of maternal cases received Zika virus testing. Just over half of the pregnant women had Zika virus IgM testing, and fewer were tested by polymerase chain reaction (PCR) or plaque reduction neutralization test (PRNT). Only 10.5% of maternal cases reported symptoms consistent with acute Zika virus infection, including rash, acute conjunctivitis, headache, arthralgia, myalgia, and fever. Of the symptomatic maternal cases, 63.2% received testing. One maternal case had a positive Zika virus result, and the infant born had multiple comorbidities at birth (including imperforate anus, congenital rectovaginal fistula, and caudal regression syndrome); however, no infant medical records after birth were available.

Comparison of the maternal cases and matched controls demonstrates similarity in variables, such as maternal age and rural/urban location (Table 1). More cases than controls had an ethnicity or race defined as "Other" ($P = 0.002$) or reported "Hispanic or Latino" ($P = 0.001$) in the maternal health record. Immediate delivery and birth outcomes, including delivery type, infant sex, gestational age, Apgar scores, and measurements, did not differ between cases and controls. Only 4 of the 181 child cases had potential Zika virus exposure included in their problem list.

Developmental screening test results were evaluated to define whether prenatal travel history increases the likelihood of poor performance on standardized screening tests. Results from the MCHAT-R were reported in 45.3% to 56.4% of cases and 41.3% to 41.9% of controls across all timepoints (Supplemental Table 2). At the 16- to 21-month timepoint, more cases (11%) scored in the "additional screening needed" category compared to controls (0%, $P = 0.0038$) (Supplementary Table 4). However, at 22 to 30 months administration, there were no significant differences between the MCHAT-R assessment results for cases and controls (Figure 2). Overall, the majority of children scored in the "no further action" category in both groups and time points. The ASQ-3 was reported in 34.8% to 39.8% of cases and 35.4% to 39.5% controls (Supplemental Table 2) across all timepoints. There were limited significant differences between the cases and controls in ASQ-3 scores across 9, 18, and 24 months (Figure 2, Supplemental Table 3). The only significant ASQ-3 difference was in the 18-month problem-solving domain, with more cases (6.3%) performing in the monitor zone compared to the controls (0%, $P = 0.045$). Overall, the ASQ-3 (24 months) and MCHAT-R (22-30 months) at the latest timepoint revealed that the majority of children, regardless of prenatal travel history, perform within the expected range (Figure 2).

Table. Maternal and Infant Demographic and Exposure Information

	Controls (n = 172)	Cases (n = 181)	*P* value
Travel and Exposure Information			
Travel continent,[a] n (%)			
North America	–	152 (84.0)	–
South America	–	20 (11.0)	–
Europe	–	0 (0)	–
Africa	–	4 (2.2)	–
Asia	–	11 (6.1)	–
Oceania	–	2 (1.1)	–
Travel durations,[b] no. days			
Mean (SD)	–	39.5 (145.6)	–
Median	–	8	–
Trimester with travel history recorded,[c] no. days			
1st trimester	–	139 (81.8)	–
2nd trimester	–	46 (27.1)	–
3rd trimester	–	16 (9.4)	–
Maternal Zika symptoms, n (%)			
Any reported symptom(s)[d]	–	19 (10.5)	–
Rash	–	3 (1.7)	–
Acute conjunctivitis	–	2 (1.1)	–
Headache	–	6 (3.3)	–
Arthralgia	–	7 (3.9)	–
Myalgia	–	9 (5.0)	–
Fever	–	7 (3.9)	–
Zika virus testing performed[e]/symptomatic mothers	–	12/19 (63.2)	–
Tests performed, n (%)			
Zika virus testing performed[e]		102 (56.4)	
IgM	–	99 (54.7)	–
PCR	–	29 (16)	–
PRNT	–	1 (0.6)	–
Maternal Zika symptomatic, n (%)			
Unknown	–	5 (2.8)	–
Zika positive test, n	–	1[f]	–

	Controls (n = 172)	Cases (n = 181)	*P* value
Maternal Demographics			
Maternal race and ethnicity, n (%)			
White	120 (69.8)	125 (69.1)	0.972
Black (African American)	12 (7.0)	7 (3.9)	0.290
Asian	21 (12.2)	12 (6.6)	0.106
Other	13 (7.6)	35 (19.3)	0.002
Hispanic or Latino	14 (8.1)	44 (24.3)	< 0.001
Unknown or not reported	5 (3.0)	1 (0.6)	0.113
Maternal age at birth, mean (SD)			
Years	30.7 (5.0)	31.6 (5.7)	0.175
Maternal socioeconomic status, n (%)			
Rural	32 (19.3)	30 (16.9)	0.559
Urban	134 (80.7)	148 (83.1)	
Birth Outcomes			
Delivery type, n (%)			
Vaginal	131 (76.2)	128 (70.7)	0.247
Cesarean birth	41 (23.8)	53 (29.3)	
Infant sex, n (%)			
Male	84 (48.8)	87 (48.1)	0.561
Female	88 (51.2)	94 (51.9)	
Gestational age at birth, mean (SD)			
Weeks	39.16 (8.2)	39.24 (10.6)	0.175
Apgar scores, mean (SD)			
1-minute	8.2 (1.3)	8.0 (1.7)	0.643
5-minute	8.8 (0.6)	8.7 (1.1)	0.232
Birth measurements, mean (SD)			
Head circumference (cm)	34.6 (4.7)	34.2 (2.0)	0.643
Length (cm)	50.8 (3.5)	51.3 (2.6)	0.250
Weight (kg)	3.4 (0.5)	3.4 (0.5)	0.310
Infant Record Information			
Problem list includes prenatal history of potential Zika virus exposure, n (%)			
"Zika virus exposure" or "potential Zika" virus exposure"	–	4 (2.5)	–

Abbreviations: IgM, immunoglobulin M; PCR, polymerase chain reaction; PRNT, plaque reduction neutralization tests.

[a]Some women disclosed travel to multiple countries, so the sum of all women at each travel location does not equal the sample size. Partner travel was included in the travel destination. We were unable to differentiate travel from immigration status using medical records.

[b]Travel duration includes time in the country by maternal travel dates. Unable to capture travel duration for 26 records and charts solely with partner travel were additionally excluded from the calculation. The final sample size was 143.

[c]Some women reported travel across multiple trimesters, so the sum of all women with travel does not equal the sample size. Charts solely with partner travel were excluded from the calculation (n = 170).

[d]Number of women with 1 or more symptoms consistent with acute Zika virus infection.

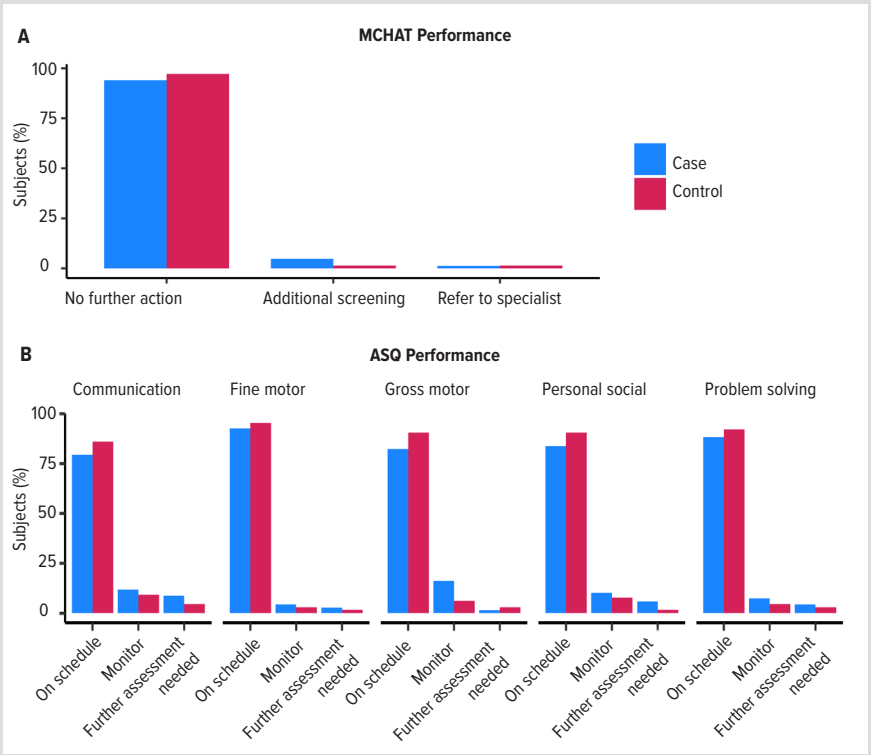
[e]The number of women with any Zika virus test (IgM, PCR, PRNT, and/or unknown) performed.

[f]Zika positive case (n = 1) by IgM enzyme-linked immunoassay and PRNT.

Rates of referrals to specialists were evaluated as a proxy marker of clinician or parental concern for additional specialized evaluation. The number of children included in this "specialist referral rate" evaluation is smaller because fewer children in both groups had medical visits documented after the birth hospitalization (Figure 3A). Overall, 48.1% of cases and 49.0% of controls were referred to at least 1 specialist. There were no significant differences between cases and controls in the referral rate to multiple specialists (Figure 3). However, there was a trend for more cases (20%) than controls (12%) having referrals to the Wisconsin Birth to 3 Program ($P = 0.058$). We also evaluated whether children were referred appropriately after receiving scoring in the "further assessment needed" category on the ASQ-3. There were similar referral rates for both the cases and controls. Combining cases and controls, zero referrals were made at 9 months and only 40% to 60% of children received a referral at 18 months ($P < 0.001$) or 24 months ($P = 0.003$) when a referral was recommended by ASQ-3 screening (Supplemental

Table 5). In summary, there were no differences in referrals to pediatric subspecialties and therapies, but many children were not referred appropriately to specialists after receiving a score indicating further assessment needed on the ASQ-3 developmental screening test.

Figure 2. Standardized Developmental Screening Tests



A) Modified Checklist in Toddlers-Revised (MCHAT-R) at 22–30 months (sample size: 71 controls, 84 cases).
B) Ages and Stages Questionnaire-version 3 (ASQ-3) at 24 months (sample size: 64 controls, 68 cases).

DISCUSSION

This retrospective case-control study identified children in Wisconsin who had maternal or partner travel during pregnancy to Zika virus-endemic areas during 2015-2018. This study found that 56.4% of maternal cases received Zika virus testing during pregnancy, and only 1 pregnant woman tested positive. We found similar developmental screening and referral outcomes between the travel-exposed cases and matched controls.

We found no differences in developmental screening outcomes between the cases and controls up to 30 months of age. However, our evaluation of developmental screening tests is limited because there are no standardized developmental screening tests for school-age children during their well-child visits.[19] Current American Academy of Pediatrics (AAP) guidelines recommend screening at 9, 18, and 24 or 30 months during well-child visits.[20,21] Because new deficits emerge–specifically in executive function and emotional regulation–in school-age children with prenatal Zika virus exposure,[5,6] our finding that developmental screening results were similar between cases and controls only applies to up to 30 months of age. Families and clinicians should obtain specific developmental evaluations if there are concerns during the preschool and elementary school years.

We also found that more cases than controls tended to receive referrals for early intervention services (Birth to 3 Program). While not statistically significant, the trend is meaningful because it suggests that early intervention services may be needed more commonly by children with potential prenatal Zika virus exposure. We also found that many children are still not referred when developmental concerns are identified.[22] None of the infants in either group were appropriately referred to specialists at 9 months of age when they received a low developmental screening score, and only half were appropriately referred at a later age. For successful intervention, it is crucial that children are referred for specialty care after scoring low on screening tests. This may reflect the physicians and caregivers opting to use a "wait and see" approach, disregarding AAP recommendations that all children be referred after a low score.[20]

Accurately diagnosing maternal Zika virus infection is challenging, and better diagnostics need to be developed. Only 1 pregnant woman had a positive Zika virus test in our chart review. This may reflect the true maternal infection rate or could reflect the inaccuracy of tests done outside of the targeted test range.[11,23] Developing better tests to diagnose maternal Zika virus infection is critical as children remain at equal risk for developmental deficits whether maternal cases are symptomatic or asymptomatic.[3]

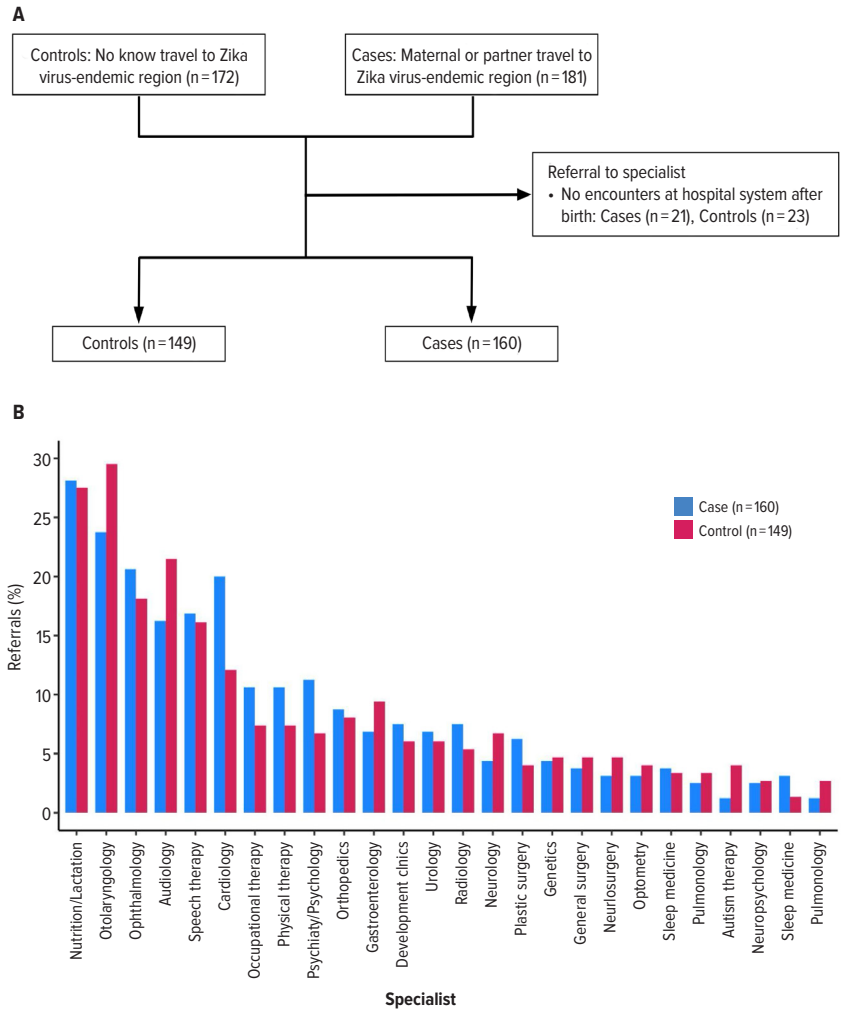
There was inadequate documentation in the EHR stating that a child was exposed to Zika virus. Our study identified only 4 children's charts with "potential Zika virus exposure" listed. This may be the result of the lack of an appropriate ICD-10 (*International Classification of Diseases, 10th Edition*) code at this date.[24] Improving documentation within the EHR is one approach to alert all future medical providers that a child is at risk for developmental deficits. Creating better documentation of prenatal travel history in the child's EHR can support the identification of children who could benefit from appropriate referrals so that early referral rather than a "wait and see" approach is used.

Limitations

Even though there were limited differences, there are multiple limitations that may have prevented early identification of children with developmental deficits in this chart review. The main limitation is that we could not determine whether any of these

infants were exposed to Zika virus prenatally because (1) travel does not inherently equate to Zika virus exposure, (2) different travel activities may have different risk (eg, cruises and high altitudes), and (3) there are lower rates of Zika virus transmission by sexual contact compared to mosquito exposure. Additionally, we could not determine whether the testing was performed within the targeted test range (within 3 weeks of exposure for the Zika virus PCR and 3 months of exposure for Zika virus IgM) given the lack of specific dates available in this chart review. If done within the targeted time period, serology testing has a sensitivity of approximately 75% to 90% depending on the test provided, with PRNT being the most sensitive and IgM being the least sensitive.[25] Another limitation of our developmental screening test evaluation is that results were not available for many children at later time points, perhaps because screening tests were delayed or canceled during the COVID pandemic As a result, children with possible prenatal exposure may still be at a high risk of developmental deficits and there is a need for better referrals and documentation in health record systems.

Figure 3. Referral Rate by Specialist



A) Final sample of children that had medical visits after the birth hospitalization and were included in the count for specialist referrals.

B) Percent referrals were calculated using the total number of referrals per group divided by the denominator for cases (n = 160) and for controls (n = 149), ordered from the most common to least common.

CONCLUSIONS

Zika virus is likely to reemerge and cause future epidemics.[26] Although we found no screening test differences between the children born to mothers with and without a travel history, there is a need to continue to monitor children born after prenatal Zika virus exposure. Monitoring children can be achieved with better documentation of prenatal Zika virus exposure in the child's medical record, use of standardized developmental screening tools at every recommended well-child visit, and referral when developmental screening test scores are low rather than waiting to see if the problem improves. The increased rate of referrals to the Wisconsin Birth to 3 Program seen in the children with prenatal travel history is interesting and warrants further evaluation to see the program was more heavily utilized following the Zika virus pandemic.

Acknowledgments: The authors wish to thank Donovin Widmann, a medical student who supported the data acquisition of this chart review; the members of Dr Mohr and Dr Ausderau's lab for supporting this work; Dr. Kathleen Antony, a maternal-fetal medicine specialist, who provided them with the paper records; and Ancilla Partners, Inc for its comprehensive birth registry data of PeriData.net.

Funding/Support: This work was supported by departmental funding to Dr Mohr, National Institutes of Health (NIH) funding (K08AI139341) to Dr Mohr, and the UW School of Medicine and Public Health Shapiro Summer Research Program. The UW–Madison Clinical and Health Informatics Institute was supported by the Clinical and Translational Science Award (CTSA) program, through the NIH National Center for Advancing Translational Sciences (NCATS) grant UL1TR002373.

Financial Disclosures: None declared.

REFERENCES

1. de Araújo TVB, Ximenes RA de A, Miranda-Filho D de B, et al. Association between microcephaly, Zika virus infection, and other risk factors in Brazil: final report of a case-

control study. *Lancet Infect Dis.* 2018;18(3):328-336. doi:10.1016/S1473-3099(17)30727-2

2. Krow-Lucal ER, de Andrade MR, Cananéa JNA, et al. Association and birth prevalence of microcephaly attributable to Zika virus infection among infants in Paraíba, Brazil, in 2015–16: a case-control study. *Lancet Child Adolesc Health.* 2018;2(3):205-213. doi:10.1016/S2352-4642(18)30020-8

3. Roth NM, Reynolds MR, Lewis EL, et al. Zika-associated birth defects reported in pregnancies with laboratory evidence of confirmed or possible Zika virus infection — U.S. Zika Pregnancy and Infant Registry, December 1, 2015–March 31, 2018. *MMWR Morb Mortal Wkly Rep*. 2022;71(3):73-79. doi:10.15585/mmwr.mm7103a1

4. Marbán-Castro E, Vazquez Guillamet LJ, Pantoja PE, et al. Neurodevelopment in normocephalic children exposed to zika virus in utero with no observable defects at birth: a systematic review with meta-analysis. *Int J Environ Res Public Health.* 2022;19(12):7319. doi:10.3390/ijerph19127319

5. Mulkey SB, Peyton C, Ansusinha E, et al. Preschool neurodevelopment in Zika virus-exposed children without congenital Zika syndrome. *Pediatr Res.* 2023;94(1):178-184. doi:10.1038/s41390-022-02373-5

6. Mulkey SB, Corn E, Williams ME, et al. Neurodevelopmental outcomes of normocephalic Colombian children with antenatal Zika virus exposure at school entry. *Pathogens*. 2024;13(2):170. doi:10.3390/pathogens13020170

7. Holtzman M, Golden WC, Sheffield JS. Zika virus infection in the pregnant woman. *Clin Obstet Gynecol*. 2018;61(1):177-185. doi:10.1097/GRF.0000000000000343

8. Zika virus: recommendations for travelers and people living abroad. Centers for Disease Control and Prevention. May 30, 2024. Accessed July 14, 2024. https://www.cdc.gov/zika/travel/index.html

9. Marbán-Castro E, Goncé A, Fumadó V, et al. Zika virus infection in pregnant travellers and impact on childhood neurodevelopment in the first two years of life: a prospective observational study. *Travel Med Infect Dis*. 2021;40:101985. doi:10.1016/j.tmaid.2021.101985

10. Vouga M, Chiu YC, Pomar L, et al. Dengue, Zika and chikungunya during pregnancy: pre- and post-travel advice and clinical management. *J Travel Med.* 2019;26(8):taz077. doi:10.1093/jtm/taz077

11. Zika virus: testing for Zika. Centers for Disease Control and Prevention. May 15, 2024. Accessed July 14, 2024. https://www.cdc.gov/zika/testing/?CDC_AAref_Val=https://www.cdc.gov/zika/symptoms/diagnosis.html

12. Blumenthal SJ, Kagen J. MSJAMA. The effects of socioeconomic status on health in rural and urban America. *JAMA*. 2002;287(1):109. doi:10.1001/jama.287.1.109-JMS0102-3-1

13. ZIP Codes by Rural and Urban Groupings Toolkit (Model 2b). University of Wisconsin-Madison Health Innovation Program; 2024. Accessed July 14, 2024. https://hipxchange.org/toolkit/ruralurbangroups/

14. Squires J, Twombly E, Bricker D, Potter L. *The ASQ-3 Users Guide*. 3rd ed. Paul H. Brookes Publishing; 2009.

15. Robins DL, Casagrande K, Barton M, Chen CM, Dumont-Mathieu T, Fein D. Validation of the modified checklist for autism in toddlers, revised with follow-up (M-CHAT-R/F). *Pediatrics*. 2014;133(1):37-45. doi:10.1542/peds.2013-1813

16. Birth to 3 Program. Wisconsin Department of Health Services. Accessed December 11, 2024. https://www.dhs.wisconsin.gov/birthto3/index.htm

17. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381. doi:10.1016/j.jbi.2008.08.010

18. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: building an international community of software platform partners. *J Biomed Inform.* 2019;95:103208. doi:10.1016/j.jbi.2019.103208

19. Lipkin PH, Macias MM; Council on Children with Disabilities, Section on Developmental and Behavioral Pediatrics. Promoting optimal development: identifying infants and young children with developmental disorders through developmental surveillance and screening. *Pediatrics*. 2020;145(1):e20193449. doi:10.1542/peds.2019-3449

20. Council on Children with Disabilities, Section on Developmental Behavioral Pediatrics, Bright Futures Steering Committee, Medical Home Initiatives for Children with Special Needs Project Advisory Committee. Identifying infants and young children with developmental disorders in the medical home: an algorithm for developmental surveillance and screening. *Pediatrics*. 2006;118(1):405-420. doi:10.1542/peds.2006-1231

21. Hyman SL, Levy SE, Myers SM, et al. Executive summary: identification, evaluation, and management of children with autism spectrum disorder. *Pediatrics*. 2020;145(1):e20193448. doi:10.1542/peds.2019-3448

22. Lipkin PH, Macias MM, Baer Chen B, et al. Trends in pediatricians' developmental screening: 2002–2016. *Pediatrics*. 2020;145(4):e20190851. doi:10.1542/peds.2019-0851

23. Jorge FA, Thomazella MV, de Castro Moreira D, Lopes LDG, Teixeira JJV, Bertolini DA. Evolutions and upcoming on Zika virus diagnosis through an outbreak: a systematic review. *Rev Med Virol.* 2020;30(3):e2105. doi:10.1002/rmv.2105

24. World Health Organization. *The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines.* World Health Organization; 1992.

25. Medialdea-Carrera R, Levy F, Castanha P, et al. A systematic evaluation of IgM and IgG antibody assay accuracy in diagnosing acute Zika virus infection in Brazil: lessons relevant to emerging infections. *J Clin Microbiol.* 2021;59(12):e0289320. doi:10.1128/JCM.02893-20

26. Van Wyk H, Eisenberg JNS, Brouwer AF. Long-term projections of the impacts of warming temperatures on Zika and dengue risk in four Brazilian cities using a temperature-dependent basic reproduction number. *PLoS Negl Trop Dis.* 2023;17(4):e0010839. doi:10.1371/journal.pntd.0010839

advancing the art & science of medicine in the midwest

WMJ

WMJ (ISSN 1098-1861) is published through a collaboration between The Medical College of Wisconsin and The University of Wisconsin School of Medicine and Public Health. The mission of *WMJ* is to provide an opportunity to publish original research, case reports, review articles, and essays about current medical and public health issues.

Visit www.wmjonline.org to learn more.