HHS Public Access

Author manuscript

Birth Defects Res. Author manuscript; available in PMC 2021 August 03.

Published in final edited form as:

Birth Defects Res. 2019 August 01; 111(13): 938–940. doi:10.1002/bdr2.1546.

Updated baseline prevalence of birth defects potentially related to Zika virus infection

Samantha M. Olson[1,2], **Augustina Delaney**[1,3], **Abbey M. Jones**[1,3], **Christopher P. Carr**[1,4], **Rebecca F. Liberman**[5], **Nina E. Forestieri**[6], **Van T. Tong**[1], **Suzanne M. Gilboa**[1], **Margaret A. Honein**[1], **Cynthia A. Moore**[1], **Janet D. Cragan**[1]

[1]National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, Georgia

[2]G[2] S Corporation, San Antonio, Texas

[3]Eagle Medical Services, San Antonio, Texas

[4]Oak Ridge Institute for Science and Education, Oak Ridge, Tennessee

[5]Massachusetts Department of Public Health, Center for Birth Defects Research and Prevention, Boston, Massachusetts

[6]North Carolina Department of Health and Human Services, Birth Defects Monitoring Program, Raleigh, North Carolina

Dear Editor,

Zika virus (ZIKV) was first recognized as a human teratogen in 2016 (Rasmussen, Jamieson, Honein, & Petersen, 2016). During the ZIKV outbreak in the Americas, we launched rapid surveillance of pregnancies with laboratory evidence of ZIKV infection and targeted surveillance of birth defects. Because little was known about the birth defects associated with congenital ZIKV infection, a broad case definition was used for surveillance of birth defects potentially related to ZIKV based on early reports of congenital ZIKV infection in the literature and expert opinion. The initial case definition included microcephaly and/or brain abnormalities, neural tube defects (NTDs) and other early brain malformations (e.g., holoprosencephaly), eye abnormalities, and consequences of central nervous system (CNS) dysfunction such as arthrogryposis and hearing loss (Honein et al., 2017). The baseline prevalence of these defects in the United States prior to the ZIKV outbreak was estimated as 2.86 per 1,000 live births (95% CI: 2.65–3.07) using data from statewide birth defects surveillance programs in Massachusetts and North Carolina in 2013 and from three counties in metropolitan Atlanta, Georgia, during 2013–2014 (Cragan et al., 2017).

Correspondence Samantha M. Olson, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA. ylz8@cdc.gov.

DISCLAIMER

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

For newly identified teratogens, case definitions often evolve over time. Based on new data, we now propose changes to the current case definition involving NTDs and other early brain malformations and consequences of CNS dysfunction. Accumulating evidence from surveillance of infants and fetuses born to mothers with laboratory evidence of ZIKV infection suggests that NTDs and other early brain malformations are not associated with ZIKV infection during pregnancy. For example, the prevalence of NTDs did not increase significantly during the ZIKV outbreak compared to before the outbreak (Delaney et al., 2018; Hurtado-Villa et al., 2017). In addition, in infants born to mothers with laboratory evidence of ZIKV infection during pregnancy, arthrogryposis was only noted in infants with structural brain abnormalities when imaging was available. This abnormality is therefore more appropriately classified with other neurodevelopmental sequelae, such as seizures and developmental delay. Moreover, many birth defects surveillance programs do not ascertain hearing loss not associated with an ear malformation making under-ascertainment likely. For these reasons, we have updated the baseline estimates of birth defects potentially related to congenital ZIKV infection prior to the outbreak to include only microcephaly and/or brain abnormalities and eye abnormalities.

Cases included in the original baseline prevalence estimates of birth defects potentially related to congenital ZIKV infection were re-reviewed and categorized by expert clinicians to remove those with NTDs and other early brain malformations or CNS dysfunction with no other qualifying defects. Methods for calculating prevalence estimates have been previously reported (Cragan et al., 2017). The report on the follow-up of infants at least one-year-old with laboratory evidence of possible ZIKV infection during pregnancy in the U.S. territories and freely associated states followed this updated case definition with microcephaly, brain abnormalities, and eye abnormalities classified as Zika-associated birth defects, and other specific outcomes (hearing abnormalities, congenital contractures, seizures, body tone abnormalities, movement abnormalities, swallowing abnormalities, possible developmental delay, possible visual impairment, and postnatal onset microcephaly) classified as neurodevelopmental abnormalities potentially linked to Zika (Rice et al., 2018).

From the original baseline population in 2013–2014, 747 infants/fetuses met the initial broad surveillance case definition; 229 with NTDs or other early brain malformations and 45 with CNS dysfunction have been excluded. The revised baseline prevalence of 1.81 infants/fetuses per 1,000 live births (95% CI: 1.65–1.98) comprised 473 infants/fetuses with microcephaly and/or brain abnormalities or with eye abnormalities (Table 1). In comparison, among infants at least 1 year of age in the U.S. territories and freely associated states born to mothers with laboratory evidence of ZIKV infection during pregnancy, an estimated 6% (or 60 infants per 1,000 live births) had a Zika-associated brain or eye defect (Rice et al., 2018). This suggests over a 30-fold increase in Zika-associated brain or eye defects compared to our updated baseline prevalence estimate prior to the ZIKV outbreak. Prospective surveillance systems continue to follow-up live born infants born to mothers with laboratory evidence of ZIKV infection to enable the evaluation of neurodevelopmental abnormalities.

Our analysis provides an updated baseline prevalence estimate of birth defects potentially related to ZIKV infection during pregnancy based on knowledge accumulated since the beginning of the ZIKV outbreak in the Americas. Programs monitoring ZIKV infections in

mothers and infants can use the updated baseline prevalence estimate to better understand the impact of ZIKV in their own populations.

ACKNOWLEDGMENTS

The authors thank Dana Meaney-Delman, MD, Centers for Disease Control and Prevention; the Metropolitan Atlanta Congenital Defects Program, Centers for Disease Control and Prevention; the Center for Birth Defects Research and Prevention, Massachusetts Department of Public Health; and the Birth Defects Monitoring Program, North Carolina Department of Health and Human Services.

REFERENCES

Cragan JD, Mai CT, Petersen EE, Liberman RF, Forestieri NE, Stevens AC, … Honein MA (2017). Baseline prevalence of birth defects associated with congenital Zika virus infection—Massachusetts, North Carolina, and Atlanta, Georgia, 2013–2014. MMWR Morbidity and Mortality Weekly Report, 66, 219–222. 10.15585/mmwr.mm6608a4 [PubMed: 28253231]

Delaney A, Mai C, Smoots A, Cragan J, Ellington S, Langlois P, … Honein MA (2018). Population-based surveillance of birth defects potentially related to Zika virus infection—15 states and U.S. territories, 2016. MMWR Morbidity and Mortality Weekly Report, 67, 91–96. 10.15585/mmwr.mm6703a2 [PubMed: 29370151]

Honein MA, Dawson AL, Petersen EE, Jones AM, Lee EH, Yazdy MM, … Jamieson DJ (2017). Birth defects among fetuses and infants of US women with evidence of possible Zika virus infection during pregnancy. The Journal of the American Medical Association, 317, 59–68. 10.1001/jama.2016.19006 [PubMed: 27960197]

Hurtado-Villa P, Puerto AK, Victoria S, Gracia G, Guasmayán L, Arce P, … Zarante I. (2017). Raised frequency of microcephaly related to Zika virus infection in two birth defect surveillance systems in Bogotá and Cali, Colombia. The Pediatric Infectious Disease Journal, 36(10), 1017–1019. 10.1097/INF.0000000000001670 [PubMed: 28914749]

Rasmussen SA, Jamieson DJ, Honein MA, & Petersen LR (2016). Zika virus and birth defects—Reviewing the evidence for causality. The New England Journal of Medicine, 374, 1981–1987. 10.1056/NEJMsr1604338 [PubMed: 27074377]

Rice ME, Galang RR, Roth NM, Ellington SR, Moore CA, Valencia-Prado M, … Honein MA (2018). Vital Signs: Zika-associated birth defects and neurodevelopmental abnormalities possibly associated with congenital Zika virus infection: U.S. territories and freely associated states, 2018. MMWR Morbidity and Mortality Weekly Report, 67(31), 858–867. 10.15585/mmwr.mm6731e1 [PubMed: 30091967]

TABLE 1

Baseline prevalence of microcephaly and/or brain abnormalities and eye abnormalities[a] potentially related to Zika virus infection, by selected characteristics—Massachusetts, North Carolina, and Atlanta, Georgia, 2013–2014[b]

Characteristic	Microcephaly and/or brain abnormalities (%)	Eye abnormalities without brain abnormalities (%)	Total cases (%)
No. of infants or fetuses	392	81	473
Infants/fetuses with defects per 1,000 live births (95% CI)	1.50 (1.35–1.65)	0.31 (0.25–0.38)	1.81 (1.65–1.98)
Pregnancy outcome			
Live birth	349 (89)	81 (100)	430 (91)
Pregnancy loss[c]	43 (11)	0	43 (9)
Gestational age at delivery (weeks)			
<32	68 (17)	6 (7)	74 (16)
32–36	80 (20)	18 (22)	98 (21)
37–41	243 (62)	56 (69)	299 (63)
≥42	1 (<1)	1 (1)	2 (<1)
Maternal age at delivery (years)			
<25	127 (32)	15 (18)	142 (30)
25–34	178 (45)	42 (52)	220 (47)
≥35	87 (22)	24 (30)	111 (23)
Earliest age birth defect was noted[d]			
Prenatally	116 (55)	4 (7)	120 (45)
≤28 days of delivery	58 (27)	29 (54)	87 (33)
29 days to <3 months	13 (6)	10 (18)	23 (9)
3 months to <6 months	10 (5)	3 (6)	13 (5)
≥6 months	15 (7)	8 (15)	23 (9)

[a] Case reports were aggregated into two mutually exclusive defect categories: (a) microcephaly (defined as a clinical diagnosis of microcephaly and head circumference at delivery <3rd percentile for sex and gestational age) and/or brain abnormalities, and (b) eye abnormalities without mention of a brain abnormality.

[b] Data from Massachusetts (2013), North Carolina (2013), and three counties in metropolitan Atlanta, Georgia (2013–2014). Total live birth population for the three areas = 261,629.

[c] Includes stillbirths ≥20 weeks gestation, elective terminations after prenatal diagnosis of a malformation at any gestational age and, in Massachusetts, spontaneous pregnancy losses at <20 weeks and <350 g.

[d] The earliest age when a qualifying defect was first noted in the medical record. Data were only available for 266 cases from Massachusetts and metropolitan Atlanta, Georgia.