

Possible Zika Virus Infection Among Pregnant Women — United States and Territories, May 2016

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Zika virus is a cause of microcephaly and brain abnormalities (1), and it is the first known mosquito-borne infection to cause congenital anomalies in humans. The establishment of a comprehensive surveillance system to monitor pregnant women with Zika virus infection will provide data to further elucidate the full range of potential outcomes for fetuses and infants of mothers with asymptomatic and symptomatic Zika virus infection during pregnancy. In February 2016, Zika virus disease and congenital Zika virus infections became nationally notifiable conditions in the United States (2). Cases in pregnant women with laboratory evidence of Zika virus infection who have either 1) symptomatic infection or 2) asymptomatic infection with diagnosed complications of pregnancy can be reported as cases of Zika virus disease to ArboNET* (2), CDC's national arboviral diseases surveillance system. Under existing interim guidelines from the Council for State and Territorial Epidemiologists (CSTE), asymptomatic Zika virus infections in pregnant women who do not have known pregnancy complications are not reportable. ArboNET does not currently include pregnancy surveillance information (e.g., gestational age or pregnancy exposures) or pregnancy outcomes. To understand the full impact of infection on the fetus and neonate, other systems are needed for reporting and active monitoring of pregnant women with laboratory evidence of possible Zika virus infection during pregnancy. Thus, in collaboration with state, local, tribal, and territorial health departments, CDC established two surveillance systems to monitor pregnancies and congenital outcomes among

women with laboratory evidence of Zika virus infection[†] in the United States and territories: 1) the U.S. Zika Pregnancy Registry (USZPR),[§] which monitors pregnant women residing in U.S. states and all U.S. territories except Puerto Rico, and 2) the Zika Active Pregnancy Surveillance System (ZAPSS), which monitors pregnant women residing in Puerto Rico. As of May 12, 2016, the surveillance systems were monitoring 157 and 122 pregnant women with laboratory evidence of possible Zika virus infection from participating U.S. states and territories, respectively. Tracking and monitoring clinical presentation of Zika virus infection, all prenatal testing, and adverse consequences of Zika virus infection during pregnancy are critical to better characterize the risk for congenital infection, the performance of prenatal diagnostic testing, and the spectrum of adverse congenital outcomes. These data will improve clinical guidance, inform counseling messages for pregnant women, and facilitate planning for clinical and public health services for affected families.

Zika virus disease and congenital Zika virus infection are defined by the interim CSTE case definition and include confirmed and probable cases with laboratory evidence of infection (2). The clinical criteria for Zika virus disease include the presence of one of four symptoms (fever, rash, arthralgia, and conjunctivitis), or Guillain-Barré syndrome, or an adverse pregnancy outcome (fetal loss, or in utero findings of

* <http://www.cdc.gov/westnile/resourcepages/survsources.html>.

[†] In the surveillance systems, laboratory evidence of Zika virus infection is defined as a positive Zika virus real-time reverse transcription–polymerase chain reaction test or a positive Zika virus immunoglobulin M (IgM) antibody test using the CDC IgM antibody capture enzyme-linked immunosorbent assay (ELISA). Plaque reduction neutralization testing (PRNT) performed in conjunction with the IgM ELISA must have Zika PRNT titers ≥ 10 .

[§] <http://www.cdc.gov/zika/hc-providers/registry.html>.



microcephaly or intracranial calcifications) in a symptomatic or asymptomatic mother with compatible illness or epidemiologic risk factors for Zika virus infection. Clinical criteria for Zika virus congenital infection in infants include microcephaly, intracranial calcifications, or other central nervous system abnormalities (2). Jurisdictions report cases meeting these criteria to ArboNET. Although jurisdictions can report asymptomatic infection in pregnant women without pregnancy complications to ArboNET, this reporting is at the discretion of the local jurisdiction and is not universal. Current ArboNET reporting includes cases of Zika virus disease that meet the interim CSTE case definition.

For the purposes of the USZPR and ZAPSS, laboratory evidence of possible Zika virus infection is defined as a positive Zika virus real-time reverse transcription–polymerase chain reaction (rRT-PCR) test result (i.e., a confirmed case of Zika virus infection) or an equivocal or presumptive positive Zika virus immunoglobulin M (IgM) antibody capture enzyme-linked immunosorbent assay (ELISA) test result (3–5).[¶] Plaque reduction neutralization testing (PRNT) performed in conjunction with the IgM ELISA must have Zika PRNT titers ≥ 10 for inclusion. Pregnant women who meet laboratory criteria are included in the surveillance systems whether they report symptoms or not. Women are included retrospectively if laboratory evidence of congenital Zika virus infection is identified in fetal tissues, the placenta, or the infant.

The USZPR was initiated primarily to monitor outcomes in pregnant women returning from travel to areas with local Zika virus transmission (6). To date the majority of cases in pregnant women reported to USZPR are associated with travel, but it also includes cases of sexual transmission (7) and local transmission from the U.S. territories. ZAPSS was developed separately for Puerto Rico to conduct enhanced surveillance in pregnant women at risk for Zika virus infection as a result of ongoing local Zika virus transmission. Using USZPR and ZAPSS, CDC will report the number of pregnant women with laboratory evidence of possible Zika virus infection weekly on its website. Data reported by noon Eastern Standard Time each Thursday (for this report, May 12, 2016) will be verified and reported in aggregate the following Thursday. Reporting is subject to a lag of 1 week to verify data from each participating jurisdiction. Reports from Arizona and Idaho have not yet been verified and are excluded from the current report.

As of May 12, 2016, combined data from USZPR and ZAPSS include 279 reports of pregnant women with laboratory evidence of possible Zika virus infection, including 157 pregnant women residing in U.S. states and the District

of Columbia (Figure 1) and 122 residing in U.S. territories (Figure 2). As of May 11, 2016, 113 pregnant women meeting clinical criteria for Zika virus disease were reported to CDC through ArboNET, 48 in U.S. states, and 65 in U.S. territories.

Among the 157 pregnant women from U.S. states and the District of Columbia monitored through USZPR, 73 (49%)^{**} reported clinical symptoms consistent with Zika virus disease. Among these symptomatic pregnant women, 64 (88%) reported rash, 36 (49%) arthralgia, 37 (51%) fever, and 17 (23%) conjunctivitis. Among all pregnancies included from U.S. states, Zika virus nucleic acid detection by rRT-PCR was reported in 39 (25%).

Among 122 pregnant residents of the U.S. territories^{††} being monitored in USZPR or ZAPSS, 80 (66%)^{§§} reported clinical symptoms consistent with Zika virus disease. Among these symptomatic women, 60 (75%) reported rash, 29 (36%) arthralgia, 27 (34%) fever, and 15 (19%) conjunctivitis. Among all women included from U.S. territories, Zika virus nucleic acid detection by rRT-PCR in serum was identified in 67 (55%).

Discussion

Through the establishment of these pregnancy surveillance systems, CDC, in collaboration with state, local, tribal, and territorial partners, is reporting and actively monitoring pregnant women with laboratory evidence of possible Zika virus infection. These surveillance systems monitor pregnant women at risk for adverse congenital outcomes attributable to possible Zika virus infection. Including pregnant women with laboratory evidence of possible Zika virus infection but without a reported history of symptoms more than doubles the number of pregnancies being monitored, compared with pregnancies meeting the interim CSTE case definition and reported by ArboNET.

Limiting surveillance to symptomatic women with confirmed or probable Zika virus disease or to women already affected by an adverse pregnancy outcome excludes a substantial proportion of women with asymptomatic and possible Zika virus infection during pregnancy. In contrast, the broader case definition used for the USZPR and ZAPSS surveillance systems might overestimate Zika virus infection among women screened for infection because of crossreactivity with dengue and other flaviviruses, particularly among residents of U.S. territories and travelers with a history of prior flavivirus infection or flavivirus vaccination (8), or nonspecific reactivity.

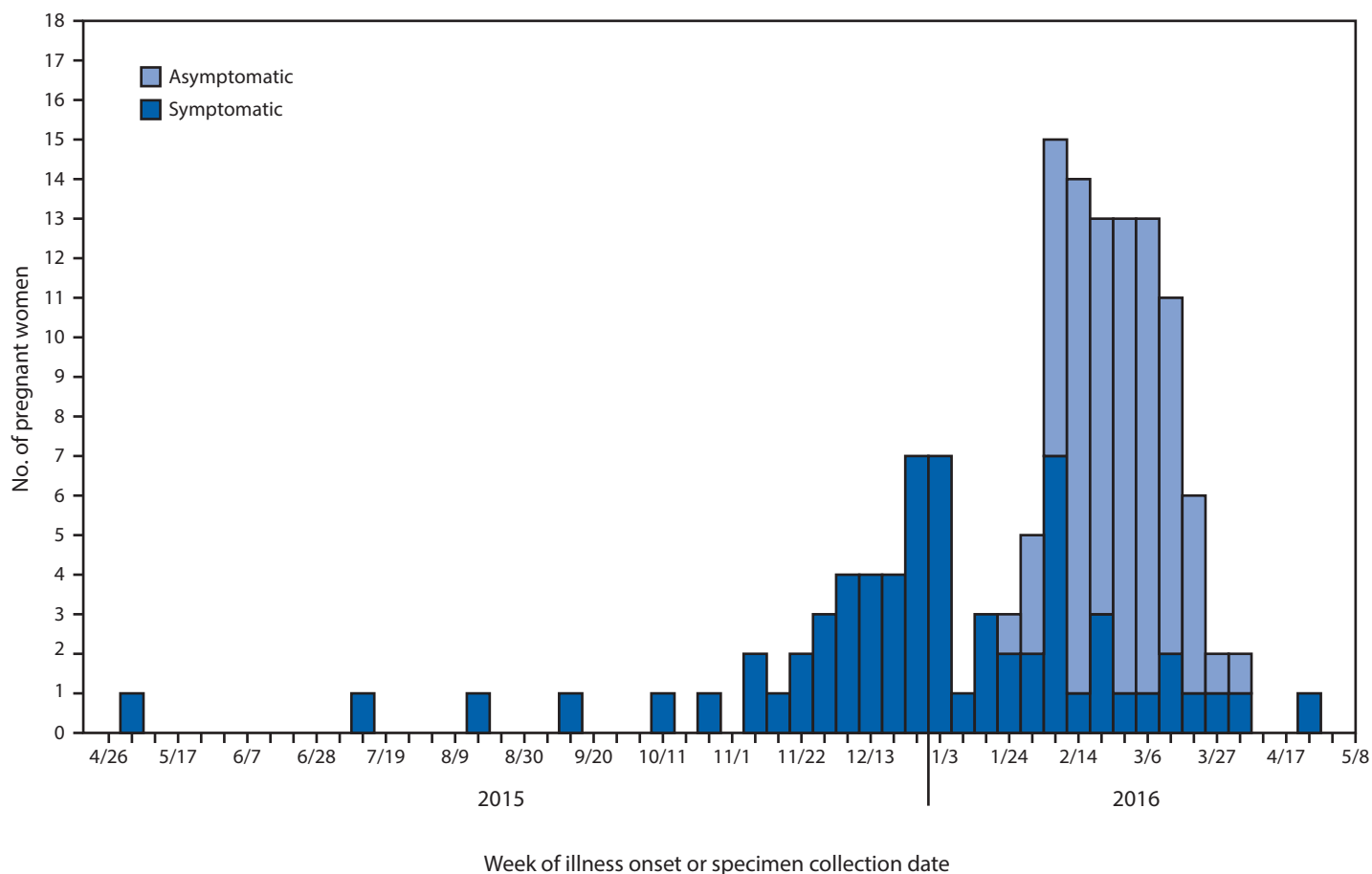
^{**} Eight missing information on symptom status.

^{††} All U.S. territories are participating.

^{§§} One missing information on symptom status.

[¶] <http://www.cdc.gov/zika/hc-providers/diagnostic.html>; <http://www.cdc.gov/zika/hc-providers/qa-pregnant-women.html>.

FIGURE 1. Week of illness onset for symptomatic pregnant women or specimen collection date* for asymptomatic pregnant women^{†,§} with laboratory evidence[¶] of possible Zika virus infection, by symptom status (N = 142)** — 48 states^{††} and the District of Columbia, April 26, 2015–May 12, 2016



Abbreviations: ELISA = enzyme-linked immunosorbent assay; IgM = immunoglobulin M; PRNT = plaque reduction neutralization test.

* Date of onset of symptoms or testing.

[†] Specimen collection dates for asymptomatic pregnant women might not coincide with the period of exposure or infection with Zika virus.

[§] CDC issued updated interim guidelines on February 5, 2016, to include recommending serologic testing of asymptomatic pregnant women 2–12 weeks after travel to an affected area.

[¶] Laboratory evidence of possible Zika virus infection is defined as a positive Zika virus real-time reverse transcription–polymerase chain reaction test or a positive Zika virus IgM ELISA test; if PRNT is performed in conjunction with the IgM ELISA, Zika PRNT titers must be ≥ 10 for inclusion.

** Excludes 15 women with missing symptom status or missing date of symptom onset.

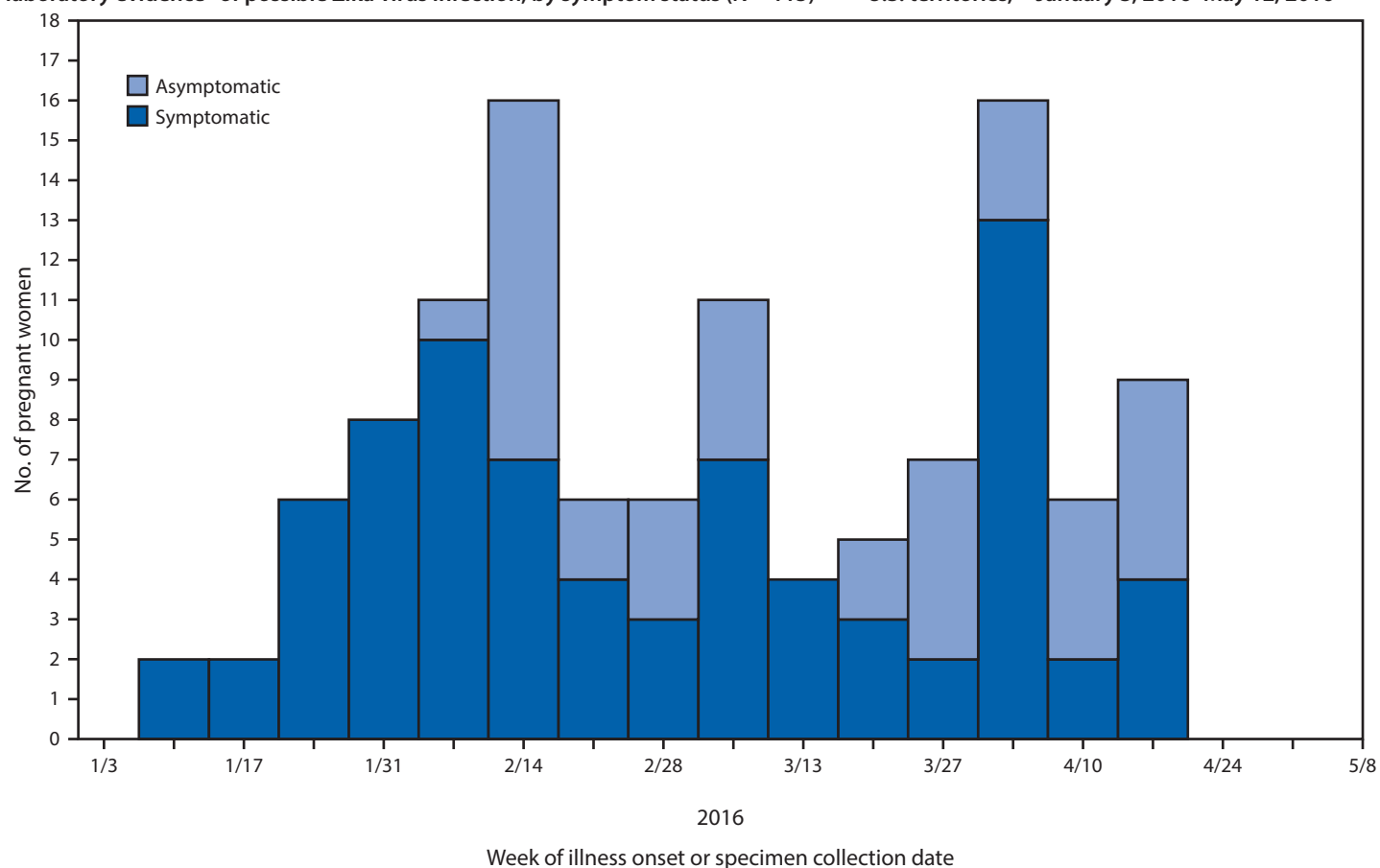
^{††} Figure includes data for U.S. states from the U.S. Zika Pregnancy Registry, excluding Arizona and Idaho.

Case reports indicate that fetuses and infants of pregnant women with asymptomatic Zika virus infection might be at risk for microcephaly and other severe brain defects (9,10). Following pregnant women with laboratory evidence of possible Zika virus infection in the surveillance system, regardless of symptoms, allows better characterization of the full impact and consequences of infection to the mother and her offspring, and might allow for better stratification of risk for adverse congenital outcomes (1). An important role of the USZPR and ZAPSS surveillance systems is evaluating the range of outcomes associated with Zika virus infection during pregnancy. Pregnancy outcomes are currently being monitored and will be shared in future reports. It is critical that health care providers inform state, local, tribal, and territorial

health departments of any pregnant women with laboratory evidence of possible Zika virus infection under their care.

The findings in this report are subject to at least three limitations. First, data provided to the jurisdictions and CDC regarding symptoms and symptom onset might not be accurate or complete because of variability in recall by patients or data available to jurisdictions. Second, only pregnant women who are tested for Zika virus infection are included, thereby potentially underestimating the prevalence of infection and outcomes among all pregnant women. Finally, all states are not included in the USZPR, possibly affecting the representativeness of these data with regard to all pregnant women identified with a possible Zika virus infection.

FIGURE 2. Week of illness onset for symptomatic pregnant women or specimen collection date* for asymptomatic pregnant women^{†,§} with laboratory evidence[¶] of possible Zika virus infection, by symptom status (N = 115) — U.S. territories,^{††} January 3, 2016–May 12, 2016**



Abbreviations: ELISA = enzyme-linked immunosorbent assay; IgM = immunoglobulin M; PRNT = plaque reduction neutralization test.

* Date of onset of symptoms or testing.

[†] Specimen collection dates for asymptomatic pregnant women might not coincide with the period of exposure or infection with Zika virus.

[§] CDC issued updated interim guidelines on February 5, 2016, to include recommending serologic testing of asymptomatic pregnant living in an area with active Zika virus transmission in the first and second trimester.

[¶] Laboratory evidence of possible Zika virus infection is defined as a positive Zika virus real-time reverse transcription–polymerase chain reaction test or a positive Zika virus IgM ELISA test; if PRNT is performed in conjunction with the IgM ELISA, Zika PRNT titers must be ≥ 10 for inclusion.

** Excludes seven women with missing symptom status or missing date of symptom onset.

^{††} Figure includes data for U.S. territories from the U.S. Zika Pregnancy Registry and the Zika Active Pregnancy Surveillance System.

One challenge of this Zika virus outbreak is the lack of understanding of the magnitude of risk and spectrum of outcomes associated with Zika virus infection during pregnancy. The USZPR and ZAPSS are surveillance systems established to enumerate and describe pregnancies with Zika virus infection and risk for adverse outcomes associated with infection during pregnancy. Findings from these U.S. surveillance systems are expected to improve understanding of Zika virus infection during pregnancy, enhance risk assessment and counseling of pregnant women and families, advance clinical care, and assist states and territories to anticipate and plan needed resources and increase prevention efforts.^{¶¶}

^{¶¶} <http://www.cdc.gov/zika/pregnancy/question-answers.html>.

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Summary

What is already known about this topic?

Zika virus infection during pregnancy causes microcephaly and other serious brain abnormalities. However, the full range of outcomes of asymptomatic and symptomatic Zika virus infection during pregnancy are not yet well understood.

What is added by this report?

In February 2016, CDC, in collaboration with state, local, tribal, and territorial health departments, launched comprehensive surveillance systems to report and actively monitor pregnancies and congenital outcomes among symptomatic and asymptomatic women with laboratory evidence of possible Zika virus infection. As of May 12, 2016, there were 157 and 122 pregnant women with laboratory evidence of possible Zika virus infection residing in U.S. states and U.S. territories, respectively.

What are the implications for public health practice?

This report launches the weekly reporting of pregnant women with laboratory evidence of possible Zika virus infection in U.S. states and territories. Monitoring all pregnant women with possible Zika virus infection during pregnancy, whether asymptomatic or symptomatic, will enhance understanding of possible adverse outcomes and allow better estimates of the number of pregnancies at risk for adverse outcomes. This information will assist health care providers who counsel pregnant women and will facilitate planning services for affected families.

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