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Commentary

Trends of the microcephaly and Zika virus outbreak in Brazil, January–July 2016

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Summary In the last two months, there have been indications that the Zika virus epidemic is on the decline in Brazil. We reviewed the surveillance data published by the Brazilian Ministry of Health to assess trends of microcephaly and neurological abnormalities suggestive of congenital infection, as well as Zika virus disease in Brazil as a whole and its various regions. From November 2015 to July 2016, 8301 cases of microcephaly were reported in Brazil, mainly in the Northeast region. The number of newly reported cases is declining throughout the country, except in the Southeast region. The numbers of cases that remain under investigation still represent 37.7% of all reported cases in early July. Meanwhile, from January to June, 2016, 165,241 cases of Zika virus disease were reported in Brazil. The state of Rio de Janeiro (Southeast) experienced the third highest incidence, lagging behind only the states of Bahia (Northeast) and Mato Grosso (Midwest). In early June, the number of new Zika virus cases showed a marked decline in all of the regions, except the North. Although the Zika epidemic seems to be diminishing, continued monitoring and surveillance of reported microcephaly and neurological abnormality cases is essential, and investigation efforts need to be vastly improved, as some states still reported high incidences of Zika disease in the first half of 2016.

Abbreviations: MoH, Ministry of Health; RT-PCR, reverse transcriptase protein chain reaction; WHO, World Health Organization.

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In November 2015, the Brazilian Ministry of Health (MoH) implemented a monitoring and surveillance system for microcephaly when increased numbers of cases began to be reported following an outbreak of Zika virus disease in Northeastern Brazil [1]. Since then, weekly bulletins have been published that include the most recent information about reported cases of microcephaly and neurological abnormalities in the country and in its various regions [2]. Available evidence supports a causal relationship between Zika virus infection in pregnancy and microcephaly in newborns [3]. Recently, the risk of Zika virus transmission during the Olympics has been the subject of much debate and speculation in the press. The aim of the present study was to analyze publicly available data to promote an evidence-based discussion about the trends in cases of microcephaly and Zika virus disease throughout Brazil as well as specific regions within the country.

Data extracted from the epidemiological reports from the Secretary of Health Surveillance of the Brazilian MoH to monitor cases of microcephaly and neurological abnormalities associated with congenital infections from November 08, 2015 to July 2, 2016 [1,2] were analyzed. Reported cases of Zika virus disease in Brazil from January 3, 2015 to June 11, 2016 were also analyzed to look for any parallels between the disease and microcephaly cases. Beginning in January 2016, the total cumulative number of reported microcephaly cases were classified as being 1) under investigation, 2) confirmed (by neuroimaging and/or laboratory testing), or 3) excluded; and among confirmed cases, whether or not they were associated with Zika virus infection during pregnancy. It should be noted that the MoH microcephaly case definition changed over the study period, resulting in changes in the reported number of cases of microcephaly at different times [4,5]. For the present analysis, investigated cases were defined as those for which neuroimaging or laboratory testing was completed (i.e., confirmed and excluded cases). Newly reported cases *per* week (Zika virus disease) or *per* two-week periods (microcephaly and neurological abnormalities suggestive of congenital infection) were examined to assess trends.

During November 2015–July 2016, 8301 cases of microcephaly and/or other neurological abnormalities were reported, including 6079 (73.2%) in the Northeastern region of Brazil, where the Zika virus disease epidemic was first recognized (Table 1). Among reported cases, investigation was complete for 5171 (62.3%) cases, of which 1656 (32.0%) were confirmed and 3515 (68.0%) were excluded. Overall, 255 (15.4%) of the 1656 confirmed cases were found to be associated with Zika virus infection by specific positive tests (reverse transcription–polymerase chain reaction [RT-PCR] and/or serology) in samples from the newborn and/or the mother.

New reported cases of microcephaly have declined since the end of February 2016 in all regions except the Southeast (chi-square test for trend; $p = 0.103$) (Table 1, Fig. 1A–F). Marked fluctuations in the number of new reported cases coincided with changes in the definition criteria for microcephaly in early December and with the Carnaval Holiday in mid-February. Aside from the Carnaval period, the number of new reported cases has been decreasing since the end of January, mainly in the Northeast. Some of this decline in mid-March occurred after the last change in the definition criteria for microcephaly (Fig. 1A). The number of newly completed investigations (confirmed + excluded cases) in every two-week period from January to July, 2016, fluctuated and ranged from 139 (June 19–July 2) to 694 (March 27–April 9) (Table 1). Meanwhile, the cumulative number of cases under investigation continued to increase until the end of March, and then began to decline afterwards, with the exception of a slight increase that occurred in the last two-week period studied. By early July, the number of cases under investigation still accounted for 37.7% of all reported cases (3130/8301) (Table 1). From January 16 to July 2, the total of new confirmed cases *per* two-week period was 1452 for the entire country, with 1206 in the Northeast and 110 in the Southeast (Table 1). The calculated incidences of new confirmed cases were 9.7/10,000 live births in Brazil, 8.1/10,000 live births in the Northeast and 0.7/10,000 live births in the Southeast.

In regard to Zika virus disease, 165,932 cases were reported in Brazil during January 3-June 11, 2016 (Table 2). The mean number of new cases *per* week indicated a declining trend in the country as a whole (β −242.42; chi-square test for trend $p < 0.001$) in all the regions except the North (β +21.52; chi-square test for trend $p < 0.001$) (Fig. 1A–F). In early May, the mean number of new cases in the country seemed to be declining, but at the end of May it increased again, and was still as high as 12,336 *per* week in the country (Fig. 1A and Table 2). Since May 28, the mean number of new cases showed a marked decline across the country, in all regions except the Northern region (Fig. 1A–F). In the Northeast, new cases began to decline in the last week of April, increased again at the end of May and declined from May 28 onward (Fig. 1B). In mid-June, the region still contributed the highest number of new cases in the country (1042 *per* week) (Table 2). The Southeast had the highest mean number of new cases in early May (6776 new cases *per* week), but showed a dramatic fall from May 28 onward (246 new cases *per* week) (Table 2). From January to June, the Southeastern state of Rio de Janeiro had the third highest incidence of Zika virus disease cases (278.1/100,000), behind only Bahia in the Northeast region (305.5/100,000) and Mato Grosso in the Midwest region (612.0/100,000) (incidence data from states not showed in tables).

Beginning in early March, the number of newly reported cases of microcephaly declined in Brazil, especially in the Northeast region where the largest number of cases is concentrated. The second highest number of cases occurred in the Southeast, followed by the Midwest, the North and the South, all of them with numbers well below the Northeast. Meanwhile, newly reported cases of Zika virus disease in Brazil were still increasing by mid-May, mainly in some states of the Northeast, Southeast and Midwest, but fell dramatically from the end of May onward, in all of the regions except the North.

Some specific events might have contributed to the decline in the new reported cases of microcephaly. In November 2015, when the increase in microcephaly was recognized to be temporally associated with the Zika virus disease outbreak, the MoH implemented an overly-sensitive