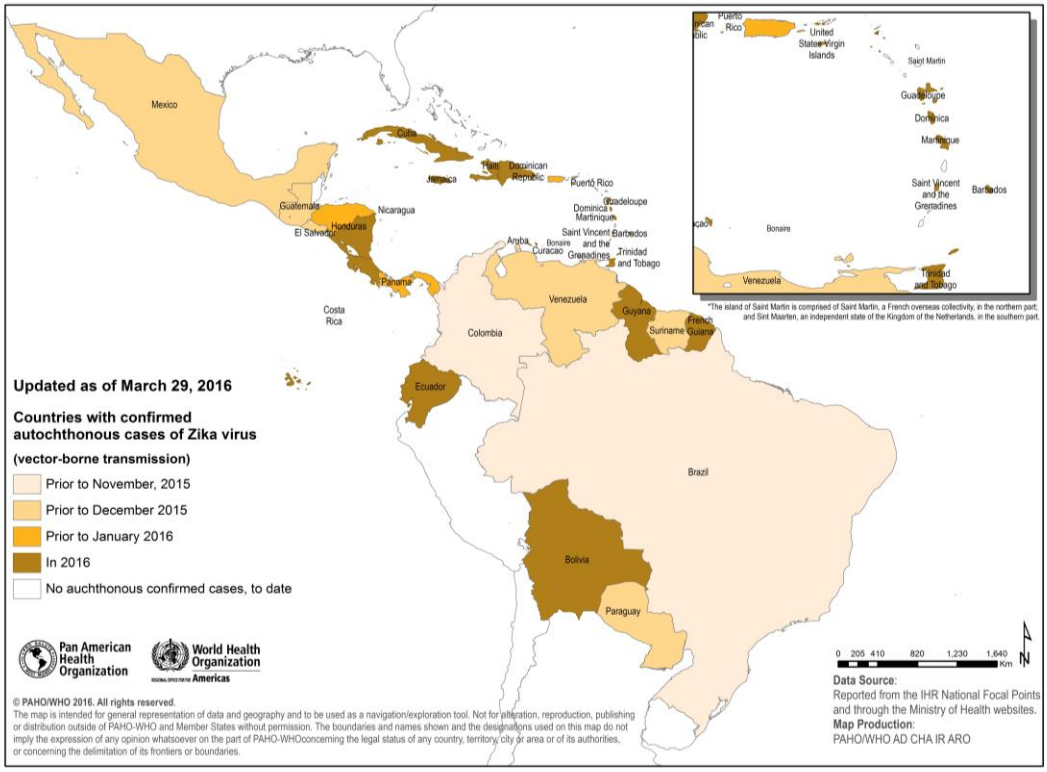
Zika - Epidemiological Update

31 March 2016

Zika virus – Incidence and trends

Since the detection of Zika virus in Brazil in 2015 to date, 33 countries and territories have confirmed autochthonous vector-borne transmission of Zika virus in the Region of the Americas (**Figure 1**). No new countries or territories have confirmed vector-borne transmission in the preceding two weeks.

Figure 1. Countries and territories in the Americas with confirmed autochthonous (vector-borne) Zika virus cases, 2015-2016 (as of 29 March 2016)



Sexual transmission of Zika virus

The most prominent mode of transmission of Zika virus is vector-borne. However, during this epidemic, surveillance system in countries without autochthonous circulation of Zika virus or presence of the vector mosquito detected cases of Zika virus via sexual transmission. For all eight cases described below, transmission occurred in partners who had sexual contact with men who

had history of travel to countries reporting Zika virus circulation, and all of them presented Zika virus symptoms shortly before or at the time of sexual contact.

In the Region of the Americas, cases of sexual transmission of Zika virus were reported in Argentina, Chile, and the United States of America.

Argentina

On 29 February, Argentina reported the first case of possible sexual transmission in a woman from Cordoba who had not traveled outside of the country, and reported sexual contact with a partner who traveled to Colombia. The partner had presented Zika virus symptoms and infection was laboratory confirmed by MAC-ELISA. To date, there is no confirmed autochthonous vector-borne transmission of Zika virus in Argentina.

Chile

On 26 March, the Chile Ministry of Health informed that the Catholic University of Chile laboratory confirmed the first case of sexual transmission of Zika virus in continental Chile, where the vector has not been detected and autochthonous vector-borne transmission of Zika virus has not been reported. The male partner who was symptomatic at the time of unprotected sexual course, is believed to have been infected with Zika virus while traveling in Haiti shortly before the symptoms onset. See full report.

United States

Between February and March of 2016 in the United States, a total of 6 cases of Zika virus via sexual transmission have been laboratory confirmed. In all cases where type of sexual contact was documented, the contact included unprotected intercourse and occurred when the male partner was symptomatic or shortly after symptoms resolved. See full report. The median age of the patients was 22.5 years, ranging from 19 to 55 years. In three cases for which further information is available, transmission occurred in women who had contact with male partners who presented Zika virus symptoms after travel to areas with Zika transmission. The partners subsequently developed Zika virus symptoms 10 -14 days after the initial sexual contact. See full report.

Detection of Zika virus in semen

There have been at least three documented cases of Zika virus isolated from semen samples taken at least two weeks after onset of illness, when Zika virus was not detected in blood by RT-PCR. In one case, serum, urine, and semen samples were taken from a 68-year-old man who presented Zika virus symptoms after travel to the Cook Islands. See full report. At 27 days and 62 days after onset of febrile illness, only semen was positive for Zika virus by real-time RT-PCR. Serial semen specimens were not collected for these cases, and the duration of persistence of infectious Zika virus in semen remains unknown. See full report.

Zika virus infection in pregnant women

Reported cases of Zika virus infection have been reported in pregnant women in 18 countries and territories of the Americas: Barbados, Brazil, Bolivia, Colombia, Costa Rica, the Dominican Republic, Ecuador, El Salvador, French Guiana, Guadeloupe, Guatemala, Martinique, Mexico,

Nicaragua, Panama, Paraguay, Puerto Rico, and Saint Martin. Details on surveillance of pregnant women in Colombia, Honduras, and Puerto Rico are highlighted below.

In **Colombia**, a total of 10,812 pregnant women have been identified with suspected or confirmed Zika virus infection since the beginning of the outbreak up to epidemiological week (EW) 11 of 2016. Of these, 997 pregnant women have been laboratory confirmed with Zika virus, and the remaining 9,815 had presented symptoms of Zika virus without laboratory confirmation.

In **Honduras**, 68 pregnant women have been detected with Zika virus, of which 41 women presented Zika virus symptoms during the first and second trimester of pregnancy.

In **Puerto Rico**, 40 pregnant women have been laboratory confirmed with Zika virus infection. There were 27 pregnant women who presented symptoms of Zika virus, and 13 pregnant women who were asymptomatic.

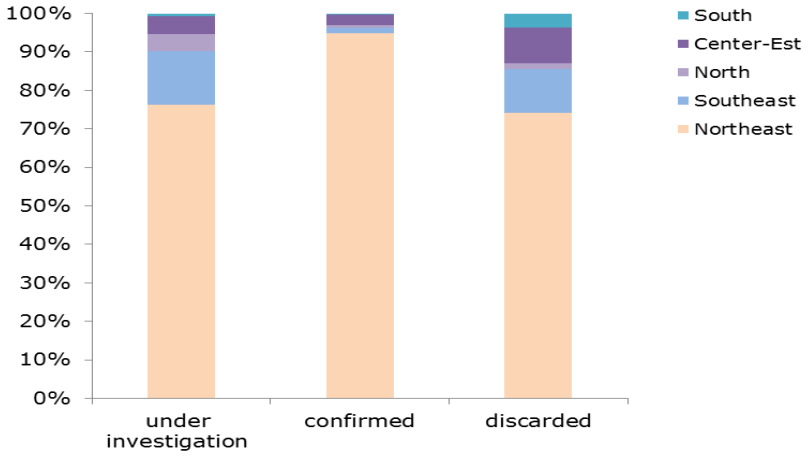
Reported increase of congenital microcephaly and other central nervous system disorders

Congenital microcephaly in Brazil

According to the Brazil Ministry of Health, as of EW 12 of 2016, there were 6,776 suspected cases of microcephaly or other nervous system malformation among newborns reported since 22 October 2015. Of these, 2,485 cases (37%) have been investigated, revealing 944 confirmed cases of microcephaly and/or other central nervous system (CNS) malformations with evidence suggestive of congenital infection. Out of the total reported cases, 1,541 cases were discarded as being due to non-infectious causes or not fitting the case definition, and 4,291 remain under investigation.

The confirmed cases are distributed in 21 out of 27 Federal Units; the Northeast region continues to report the majority of the cases with 76% (3,276) of suspected cases and 95% (895) of confirmed cases. The Southeast region is reporting 14% (594 cases) of suspected and 2% (15 cases) of confirmed cases of microcephaly in Brazil (**Figure 2**).

Figure 2. Cases of microcephaly reported in sub-national region of Brazil by classification, EW 2 to 11 of 2016



Source: Brazil Ministry of Health

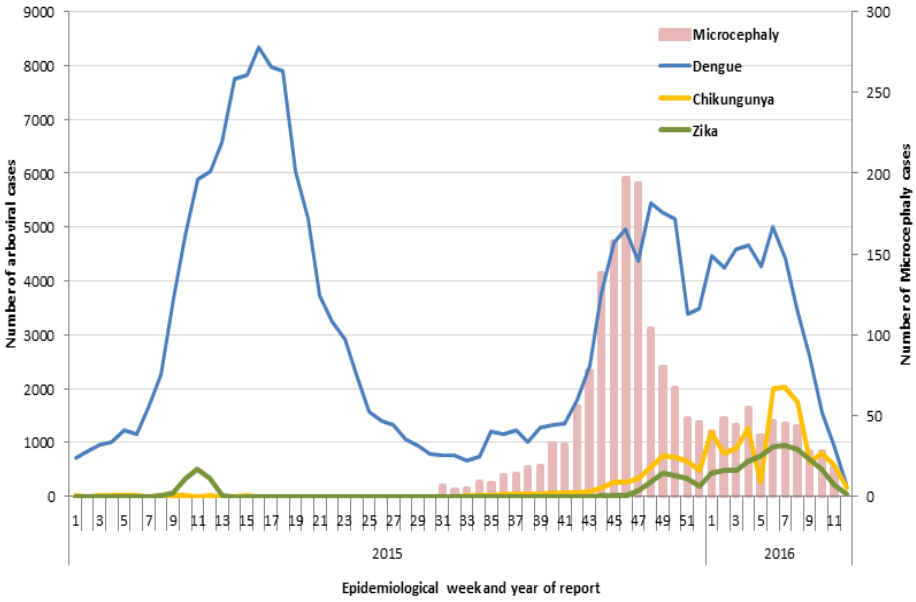
There have been 208 deaths (including miscarriages or stillbirths) reported cases of microcephaly and/or CNS malformation, of which 47 has been confirmed as suggestive of congenital infection. See full report.

In a cohort study, clinical characterizations in 104 infants born in 2015 with microcephaly in Pernambuco State, Brazil, were studied. The researchers interviewed 100 mothers, and 59 mothers retrospectively reported having rash during their pregnancy. Seventy infants were identified as having severe microcephaly, defined in the study as having head circumference <30 cm. Imaging tests performed for 58 infants showed radiologic abnormalities, including calcifications mainly in the cortical/subcortical junction (93%), evidence of malformations of cortical development including lissencephaly (69%), and ventriculomegaly (66%). Initially, testing was not available for Zika virus and TORCH agents and was only partially completed. However, the timing of microcephaly and the history of rash illness in more than 50% of the pregnant mothers suggests an outbreak of severe microcephaly consistent with congenital infections in Pernambuco that peaked in October 2015. These findings illustrate not only congenital microcephaly but other severe birth defects in newborns. See full report.

Since the last Zika Epidemiological Update, all three arboviruses circulating in Pernambuco (chikungunya, dengue, and Zika virus) and the reported cases of microcephaly are continuing a downward trend into EW 11 as indicated in **Figure 3**. Between EW 47 of 2015 and 11 of 2016, reported cases of chikungunya and Zika virus were noticeably higher compared to the same period in 2015. In addition, 40,462 cases of dengue were reported between EW 1 and EW 11 of 2016, which is almost twice the number of dengue cases reported during the same EWs of 2015.

Between EW 5 and EW 11 of 2016, a weekly average of 39 microcephaly cases were registered; this is 10 cases lower than the weekly average from the previous week.

Figure 3: Reported cases of chikungunya, dengue, Zika virus, and microcephaly in Pernambuco state, Brazil by EW, 2015 to 2016



Source: Pernambuco State Secretary of Health

Martinique

On 21 December, Martinique became the first island in the Caribbean to confirm autochthonous vector-borne transmission of Zika virus. On 24 March, the France Ministry of Health confirmed the first case of microcephaly related to Zika virus in Martinique. The diagnosis was made by ultrasound at 22 weeks of gestation. Zika virus was detected in the amniotic fluid and fetal blood by PCR. In the mother, serology in blood samples was positive for Zika virus in January and February.

Guillain-Barré syndrome (GBS) and other neurological disorders

To date, eight countries and territories in the Region (Brazil, Colombia, the Dominican Republic, El Salvador, Honduras, Martinique[1], Suriname, and Venezuela) have reported an increase in cases of Guillain-Barré syndrome (GBS) with at least one case laboratory confirmed for Zika virus. Four other countries and territories have not recorded an increase but identified Zika virus-associated cases of GBS (French Guiana, Haiti, Panama, and Puerto Rico) (**Table 1**).

Table 1. Countries and territories in the Americas with GBS in the context of Zika virus circulation (as of 30 March 2016)

Increase in GBS plus Zika virus lab confirmation in at least one case of GBS	Zika virus lab confirmation in at least one case of GBS
Brazil	French Guiana
Colombia	Haiti
Dominican Republic	Panama
El Salvador	Puerto Rico
Honduras	
Martinique[1]	
Suriname	
Venezuela	

Other neurological manifestations associated with Zika virus are being detected in the Region. Guadeloupe reported one case of myelitis with Zika virus detected in the cerebrospinal fluid (CSF), and Martinique has reported three cases of unspecified severe neurological condition among confirmed Zika virus cases.

Information on the observed increase of GBS in Colombia, the Dominican Republic, and Martinique is presented below.

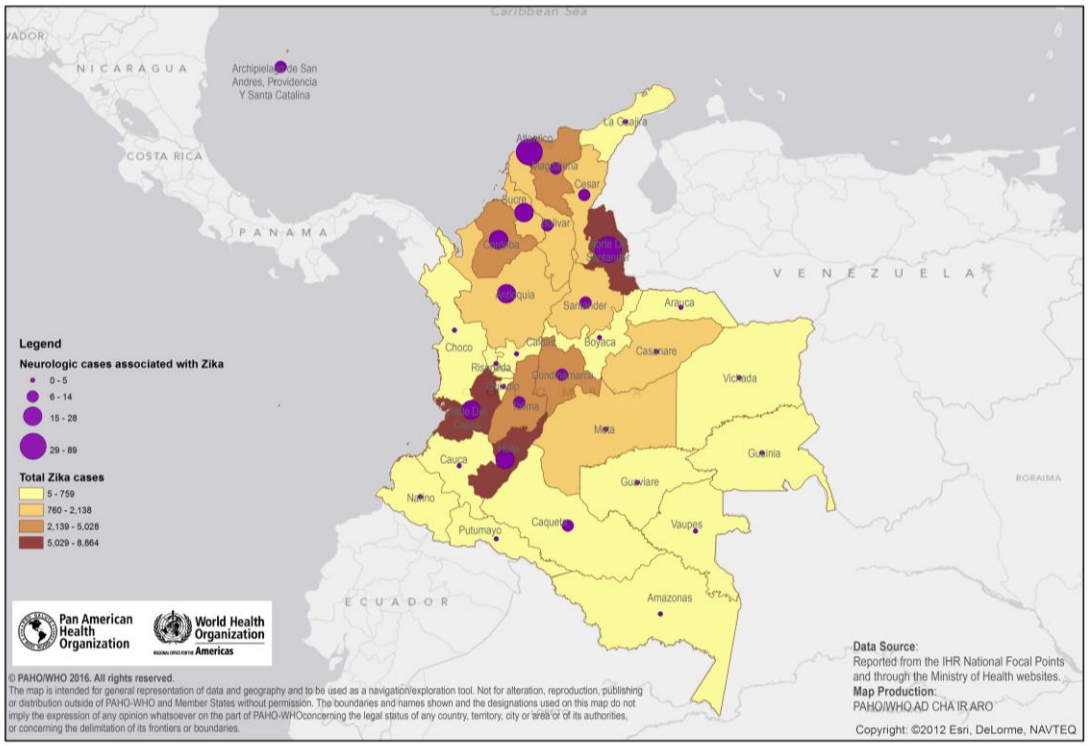
[1] Data regarding the expected baseline for the number of GBS cases for Martinique is unavailable, however, an increase in the number of GBS cases compared to the previous weeks has been observed.

Increase of GBS and other neurological disorders in Colombia

During the period of enhanced surveillance for neurological syndrome from December 2015 up to EW 11 of 2016, Colombia detected 381 cases of neurological syndrome with history of Zika virus symptoms including 258 cases of GBS and other similar neurological conditions such as ascending polyneuropathy. Laboratory testing for Zika virus was conducted with 7% (18 cases) of GBS cases and 6% (24 cases) of the total neurological syndrome cases were confirmed by PCR.

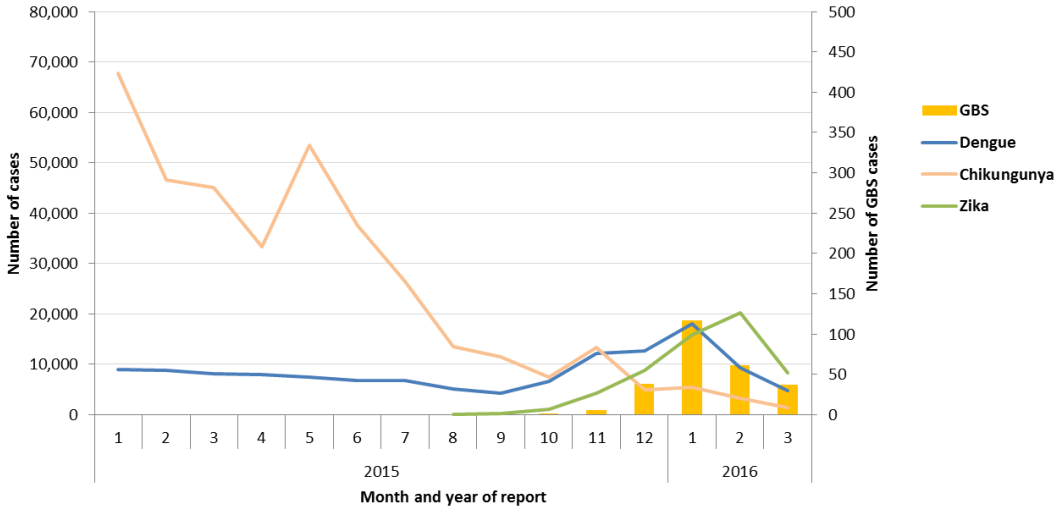
A large number of cases of neurological syndrome is reported from states in the Caribbean region of Colombia (Antioquia, Atlantico, Barranquilla, Cordoba, and Sucre), where the first Zika virus outbreaks were detected in the country (**Figure 4**). Norte Santander is reporting the highest number of GBS cases (77 cases), and the highest number of Zika virus cases in the country. Valle and Huila are reporting the second and third highest number of Zika virus cases respectively, where there is also high numbers of GBS cases reported. The geographic distribution of cases of neurological syndrome by Departments indicates that there is a spatial association with states also reporting high number of Zika virus cases.

Figure 4. Territorial Entities in Colombia with reported Zika virus cases and neurological syndrome, December 2015 to 19 March 2016



In addition, observed increase of GBS cases detected in the country corresponds to the epidemiological curve of suspected cases of Zika virus cases (**Figure 5**). A temporal association is observed between GBS and Zika virus cases detected in Colombia.

Figure 5. Reported cases of chikungunya, dengue, Zika virus, and GBS in **Colombia** by month, 2015 to 2016

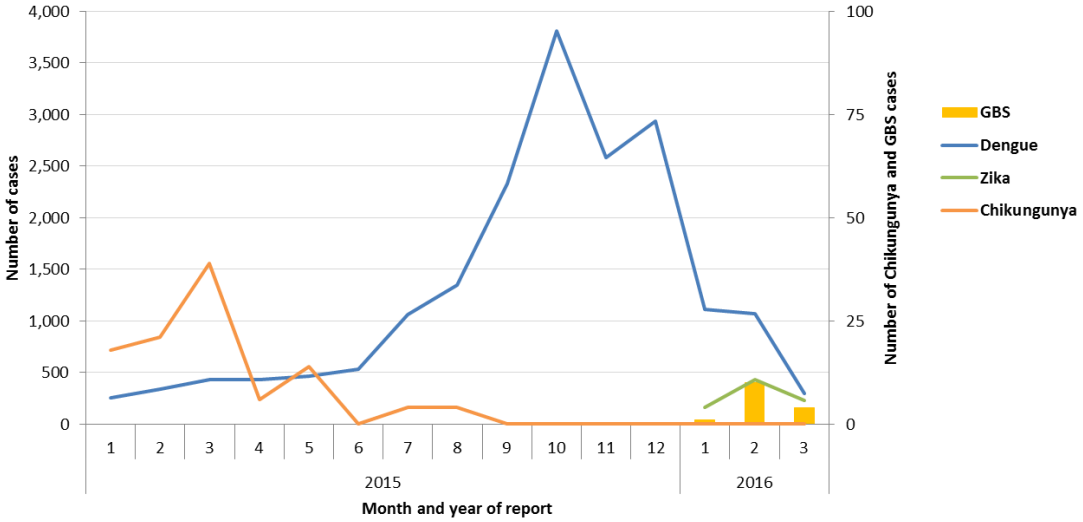


Source: Colombia Ministry of Health

Increase of GBS in the Dominican Republic

Before the introduction of Zika virus to the Region of the Americas, outbreaks of dengue and chikungunya had been registered in the **Dominican Republic**. Following a low number of dengue cases reported in there in the beginning of 2015, an increase was observed in the second semester of 2015, with a peak in October 2015. First cases of chikungunya were recorded in March 2014. When comparing the dynamics of dengue, chikungunya, and Zika virus with the incidence of GBS cases which peaked in February of 2016, a temporal correlation between GBS and Zika virus peak is observed, as seen previously in Colombia and El Salvador (See the Zika Epidemiological Update, 24 March).

Figure 6. Reported cases of chikungunya, dengue, Zika virus, and GBS in the **Dominican Republic** by month, 2015 to 2016

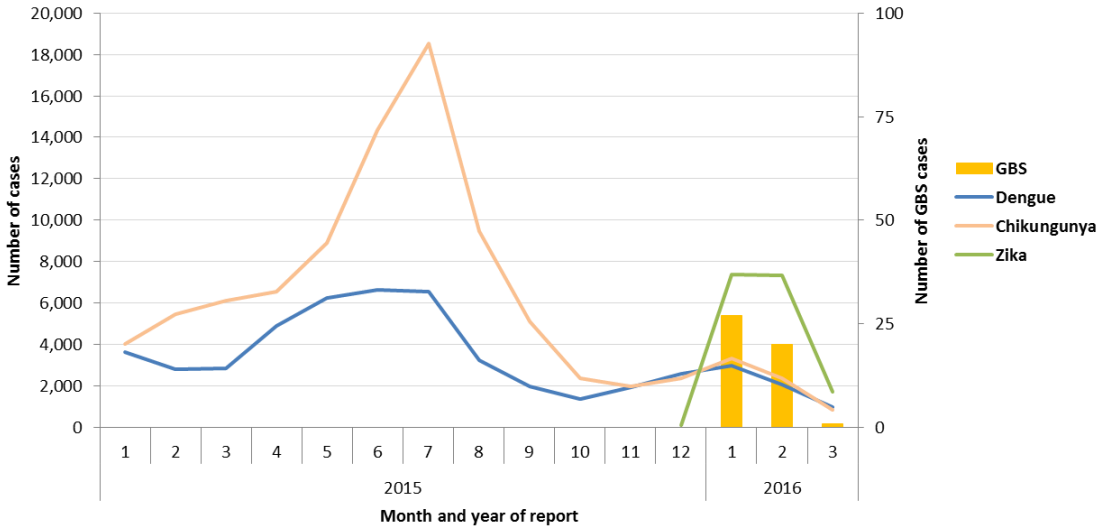


Source: The Dominican Republic Ministry of Health

Increase of GBS in Honduras

In 2015, **Honduras** experienced a dengue and chikungunya outbreak with peaks of both diseases in July of 2015. The epidemic curve for dengue and chikungunya have since shown a downward trend towards the end of 2015, when a slight increase is observed starting in December, coinciding with the detection of the first autochthonous cases of Zika virus in the country. Similar to the Dominican Republic, a temporal correlation between GBS and Zika virus is observed, with GBS cases peaking in January and February of 2016.

Figure 7. Reported cases of chikungunya, dengue, Zika virus, and GBS in **Honduras** by month, 2015 to 2016



Source: Honduras Ministry of Health

GBS and other neurological syndrome in Martinique

Among the French overseas collectivities in the Americas which include French Guiana, Guadeloupe, Martinique, Saint Barthélemy and Saint Martin, Martinique is reporting the highest number of Zika virus cases with a total of 14,320 suspected cases. When compared to other French collectivities in the Americas, Martinique is also reporting the highest number of GBS cases, including five GBS cases with confirmed Zika virus infection, and four additional GBS cases with pending laboratory results. Data regarding the expected baseline for the number of GBS cases for Martinique is unavailable, and therefore no threshold has been statistically defined. However, an increase in the number of cases compared to the previous weeks has been observed. Furthermore, three cases of unspecified severe neurological condition were identified among confirmed Zika virus cases.

Novel Findings

Zika Virus Infection with Prolonged Maternal Viremia and Fetal Brain Abnormalities

The New England Journal of Medicine published a report on a 33-year-old pregnant woman who developed Zika virus symptoms after her travels to Mexico, Guatemala and Belize in the 11th gestational week (late November 2015), and tested positive by IgG and IgM. The current recommendations for laboratory diagnosis of Zika virus indicate that Zika virus viremia lasts for less than a week after the onset of infection. However, Zika virus RNA was detected in the serum of the pregnant woman at 4 weeks and 10 weeks after the onset of Zika virus symptoms, but not after delivery. The patient elected termination of pregnancy at 21 weeks of gestation. When studying the fetal and maternal viral loads, the highest Zika virus viral loads were found in the fetal brain, with substantial viral loads in the placenta, fetal membranes, and umbilical cord as detected on quantitative RT-PCR. Lower amounts of Zika virus RNA were found in fetal muscle, liver, lung, and spleen, as well as the amniotic fluid. The researchers suspect the persistent Zika virus viremia in the mother described was a consequence of viral replication in the fetus or placenta, which had high viral loads. Other TORCH agents were not detected in the amniotic fluid. The study also conducted postmortem histopathological studies, indicating loss of intermediately differentiated postmigratory neurons through apoptotic mechanism. However, preservation of differentiated neurons in basal ganglia, limbic region, and dorsal spinal cord was observed. See full report.