Original Research Article


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Study design: AJRM, Data collection: LIZ, ER, IAES, Data analysis: AJRM, LIZ, ER, IAS, Writing: All authors. All authors contributed to and approved of the final version submitted.

Competing interests: None of the authors has any conflict of interest to declare.

Words Count:


References: 56.

Tables: 2.

Supplemental Tables: 1.

Figures: 6.
Abstract

Background: After serious epidemics of chikungunya (CHIKV) and Zika (ZIKV) in the Americas, dengue (DENV) have reemerged in most countries. We analyzed the incidence, incidence rates, and evolution of DENV cases in Honduras from 2015-2018 and the ongoing 2019 epidemic.

Methods: Using epidemiological weeks (EW) surveillance data on the DENV in Honduras, we estimated incidence rates (cases/100,000 population), and developed maps at national, departmental, and municipal levels.

Results: From 1 January 2016 to 21 July 2019, a total of 109,557 cases of DENV were reported, 28,603 in 2019, for an incidence rate of 312.32 cases/100,000 pop this year; 0.13% laboratory-confirmed. The highest peak was reached on the EW 28°, 2019 (5,299 cases; 57.89 cases/100,000 pop). The department with the highest number of cases and incidence rate was Cortes (8,404 cases, 479.68 cases/100,000 pop in 2019).

Discussion: The pattern and evolution of DENV epidemic in 2019 in Honduras has been similar to that which occurred for in 2015. As previously reported, this epidemic involved the north and central areas of the country predominantly, reaching municipality incidences there >1,000 cases/100,000 pop (1%). Studies using geographical information systems linked with clinical disease characteristics are necessary to attain accurate epidemiological data for public health systems. Such information is also useful for assessment of risk for travelers who visit specific areas in a destination country.

Keywords
Dengue virus (DENV); geographical information systems (GIS); public health; travelers; arboviruses; infectious diseases epidemiology.
Introduction

Latin America and the Caribbean have been the epicenter of emerging epidemics of arboviral diseases since December 2013 [1]. Among the most important of them, chikungunya (CHIKV) [2] and Zika (ZIKV) [3] viruses infections are ranked first. Together with dengue (DENV), these arboviral diseases have affected millions during the last five years, especially those in the most tropical areas near to the Equator, as is the case of countries in the north of South America and Central America [4]. Probably due to high attack rates during such epidemics, primarily due to ZIKV as a flavivirus, DENV rates, but also of CHIKV and ZIKV, felt significantly during years 2015 to 2017. In late 2018, this arboviral disease began to increase in most countries, reaching epidemics again in most countries in 2019.

In 2017, there were 580,640 cases of dengue in the region (254,453 in Brazil, 89,893 in Mexico and 76,093 in Peru), with 561,356 in 2018 (265,934 from Brazil, 78,621 Mexico and 44,825 Colombia) [5, 6]. Such declines in dengue have been discussed by experts, indicating that multifactorial events may have accounted for this situation, including elements of immunity, increased vector control, and even vector and viruses changes or adaptations [6, 7].

Among the affected countries, Honduras is currently facing an epidemic (2019), reaching highest values at some epidemiological indicators, such as the number and proportion of severe form cases, as well the case fatality rate [6]. Honduras have prone conditions, such as climate [8, 9], international travel, foreign trade [10, 11], geographical susceptibility, that would be associated with the outbreak [12-16].
As reported before, in general, there are not many studies about arboviral diseases in Honduras [17-21], some explicitly exploring the potential impacts of climate change and variability on DENV, as well as the analysis of the 2015 DENV epidemics [9, 12].

Previous assessments for DENV and CHIKV in Honduras performed by our group demonstrated the importance of *A. aegypti* populations for informing public health decisions and travel advice [12]. This has also been shown in other Latin American countries [12, 14, 15, 22-24]. In addition to *A. aegypti*, the presence of *A. albopictus* was confirmed in the Mountain Park Juana Lainez at Tegucigalpa in 2013 [4, 25].

In the past decade, the near real-time availability of novel and disparate internet-based data sources has motivated the development of complementary methodologies to track the incidence and spread of disease. The Pan American Health Organization (PAHO) currently streamlines reports from ministries of health and reports weekly confirmed and suspected cases of arboviral diseases such as DENV, CHIK, and ZIKV by country [24, 26-31]. These reports provide up-to-date data about the epidemiology of arboviral diseases in affected global regions [12]. However, there is no detailed information about specific places, departments or municipalities, which is necessary to make more specific recommendations to travelers as well for public health prioritization and policies [4, 27, 29, 32, 33], especially during epidemics, as is the case for Honduras in 2019.

Understanding the impact of arboviruses, in terms of clinical complications, disability, and costs to health systems, require a more significant number of investigations involving multiple medical specialties, mainly in susceptible countries such as Honduras. This information is essential to develop and prepare for possible future epidemics of new emerging arboviruses [4, 16, 22].
As part of the enhanced efforts in control and risk assessment for arboviral diseases in Latin America, the Universidad Tecnológica de Pereira, the Ministry of Health of Honduras and the Universidad Nacional Autónoma de Honduras, are working together in the analysis of epidemiological information of infectious diseases in regional and national scales [12, 34], including conditions such as ZIKV, DENV and CHIKV [9, 12, 24, 27-29, 32]. In this setting, this study aimed to estimate incidence rates of DENV in 2016-2019 for Honduras and its departments and municipalities and to develop GIS-based epidemiological maps for this arboviral disease, mainly focusing in 2019 epidemic.

Methods

Honduras is a Central American country constituted by 18 departments (main administrative level) and 298 municipalities (second administrative level). The Honduran territory presents climatic, geographic, and epidemiological conditions suitable for the transmission of many vector-borne diseases [4]. *Aedes aegypti*, the primary vector of DENV, CHIKV and ZIKV, is widely distributed over all the territories [12, 35], constituting large areas where environmental factors such as temperature, humidity, precipitation, latitude, and altitude, as well as social, cultural, economic and political factors are suitable for sustained vector-transmission [4, 12].

For this observational, retrospective and cross-sectional study, the epidemiological data were collected from the national surveillance system, obtaining the number of cases for each department and each municipality of the country by the year 2016-2019 (detailed by weeks). Data and analysis of DENV for 2015 have been previously reported by our group [12]. Data were constituted from clinically confirmed cases (suspected cases by clinical criteria definition) and laboratory-confirmed by RT-PCR, which have been revised in terms of data quality. Data analyzed for this study came from 298 primary municipal notification units, collected at the 18 department
notification units, and consolidated in Tegucigalpa (Francisco Morazán department, Capital District, CD) [12]. Determination of DENV infection included syndromic and laboratory surveillance.

Using official reference population data (National Institute of Statistics, INE), estimates of the annual incidence rates for all the departments and municipalities of the country were calculated (cases/100,000 pop) to provide estimates of DENV incidence by department and municipalities [4, 12].

Besides, national GIS-based maps, by departments and municipalities with the distribution of DENV were generated. Microsoft Access® was used to design the spatial databases to import incidence rates by departments, municipalities, and disease to the GIS software. The Client GIS software Open source used was Kosmo Desktop 3.0 RC1®. The shapefiles of departments (.shp) were linked to data table database through spatial join operation, in order to produce digital maps of annual incidence rates by departments and municipalities [4, 12, 27, 30].

Results

From 1 January 2016 to 21 July 2019, a total of 109,557 cases of DENV were reported, 44,834 of them in 2016 (40.9%), then decreasing to 5,217 in 2017 (4.8%) and increasing up to 28,603 in the ongoing 2019 (26.1%), for incidence rates varying from 522.75 cases/100,000 pop in 2016, to 312.32 cases/100,000 pop till the epidemiological week (EW) 28 of 2019 (Figure 1A).

The highest peak was reached on the EW 28°, 2019 (5,299 cases; 57.89 cases/100,000 pop) (Figure 1B). The closest comparison in figures is with 2015 cases, where the highest number occurred during EW 25 with 1,789 cases (Figure 1B). Last four EW of 2019, 25 to 28, have been
higher than any previous EW since 2015 (Figure 1C), reaching rates per week above 20 cases/100,000 pop, after EW 25 of 2019 (Figure 1C). Looking at the four last EW, these comprise 55% of the cases reported in 2019 (15,725) (Figure 1B).

Years 2015 to 2018, showed that most cases concentrated during mid-year months (Figure 2A), a seasonality probably related to climate change and variability, as reported before by us [9]. The median number of cases per EW during 2015-2018 reached two peaks, during EW 20 (507 cases) and EW 25 (485 cases), with an interquartile range (IQR) of 197-1000 and 206-1014, respectively (Figure 2B). The current epidemic (2019), reached 2.5 times higher number of cases for the EW 25 compared to previous years (2015-2018) and 7.6 times for the EW 28 (Figure 2C).

All the 18 departments of Honduras reported cases during the study period (Table 1). In 2019, rates ranged from 7.82 cases/100,000 pop (Gracias a Dios) to 479.68 cases/100,000 pop (Cortés), followed by Yoro (357.71 cases/100,000 pop), Santa Barbara (274.00 cases/100,000 pop), and Olancho (271.53 cases/100,000 pop), till EW 26 (Table 1, Figure 3). Francisco Morazán department, where the capital city is located, have reported 1,924 cases (116.59 cases/100,000 pop) till EW 26 (Table 1, Figure 3). These five departments, which are located in the northwestern and central areas of Honduras (Figure 3), have reported more than 80.9% of the DENV cases of the country (Table 1). Cortes department is currently concentrating 44.3% of the reported cases (8,404) (Table 1) till EW 26.

When comparing Cortés and Francisco Morazán incidence over time, apparent differences were evident. At Francisco Morazán a high number of cases was reported during the first 17 EWs of 2018 reaching up to 11.4 cases/100,000 pop (186 cases) during that week, for a total of 1170 cases in the four first months (Figure 4). In contrast, there was a low incidence in Cortes during that period (below 5 cases/100,000 or <60 cases per week) during the same period. Thereafter,
there was a low reported number of cases in Francisco Morazán (<5 cases/100,000 pop) until EW 22 of 2019, and a significant increase in Cortes, which reached a higher incidence compared to Francisco Morazán, since EW 31 of 2018 (1.28 cases/100,000 pop versus 1.23) and then staying always significantly above in subsequent EW. The higher rates ratio from that EW and beyond, begun to increase from 1.04 times higher (EW 31 of 2018) reaching its maximum difference at EW 4 of 2019 (9.67 times higher) and EW 13 of 2019 (9.24 times higher), and after that staying above 2.3 times higher (Figure 4).

The peak during the EW 23° with 50.3 cases/100,000 (793 cases that week) reached 5,453 cases that week (for a total of 17% of the cases reported in Honduras during 2016-2017) (Figure 1). Until EW 26° more than 54% of the cases of the 2019 epidemic were reported from these two departments, documenting a concentrated occurrence in the most populated departments containing the capital (Tegucigalpa, Francisco Morazán) and second-largest city of the country (San Pedro Sula, Cortés) (Table 1, Figures 3 and 4).

From the total number of municipalities (298) of Honduras, 59.7% of them reported cases of DENV in 2019 (Table 2, Supplemental Table 1). From those municipalities that have no reported DENV in 2019 (120), there are 18 (15%) that reported cases in 2018, but also 34 (28.3%) that reported cases in 2017, and 58 (48.3%) that reported cases in 2016 (Table 2, Supplemental Table 1).

Rates ranged from 0 to 1,468.26 cases/100,000 pop (Choloma, Cortes department), followed by Santa Barbara (Santa Barbara department, 1,255.04 cases/100,000 pop) and Santa Lucia (Intibucá department, 1,155.54 cases/100,000 pop.) (Table 2, Figure 5). Tegucigalpa, at the Capital District, reported 1,813 cases till EW 26 of 2019 for a rate of 43.93 cases/100,000 pop. (Figure 5).
From the total number of cases till EW 28, 26.89% of them (7,691) were classified as severe dengue (Figure 6), which is a proportion higher than previous years (201-2018) (Figure 6). From the severe dengue cases, 92% (7,054) occurred in Cortés (3,666), San Pedro Sula (2,690), Santa Bárbara (508) and Yoro (190) (Figure 5). Till EW 28, 97 suspected deaths have been reported, with 52 laboratory-confirmed, for a case fatality rate (CFR%) of 0.128% (1.82 deaths/1,000 cases). Of these confirmed deaths, 39 (75%) corresponded to patients <15 y-old (21 [54%] between 5 and nine y-old). From the laboratory investigation, DENV-1 and DENV-2 serotypes have been identified, with a predominance of DENV-2.

Discussion

After CHIKV and ZIKV epidemics in Brazil and other countries in Latin America [3, 27], dengue is reemerging in multiple countries, such as Brazil, Colombia, Bolivia, Nicaragua, and Honduras, among other [6]. As showed herein, Honduras is being hit by a significant DENV epidemic in most of its territory. As occurred with DENV, CHIKV, and ZIKV in previous years [4, 12], Francisco Morazán and Cortés, the most populated departments, were the most affected. DENV has followed the path of areas in Honduras previously affected by CHIKV, ZIKV, and DENV in the past. Those areas with high incidence rates of these infections also exhibited the highest risk for DENV reemergence [4, 12]. Although more than 28,000 cases were reported in the country, only 0.13% of cases (those that died) have been laboratory-confirmed by RT-PCR. This is directly related to the financial limitations that preclude assessment of all patients by laboratory confirmation and to a lack of readily available. Nevertheless, the current epidemics, is becoming the worst in 50 years in Honduras, with 26 out of 32 public hospitals that are near to collapse as a result.
Social and eco-epidemiological conditions in Honduras make the whole country susceptible to spread of arboviral diseases such as DENV, CHIKV, and ZIKV [9, 12]; therefore, analyses such as the one presented herein are relevant for understanding future emerging arboviral diseases in the region and the country, but have been expectable also based in previous analyses for DENV, CHIKV, and ZIKV in Honduras [4, 12]. Other relevant viral diseases to consider in the immediate future should include Mayaro (MAYV) [36], Oropouche (OROV), Venezuelan Equine Encephalitis (VEEV), West Nile virus (WNV), among others [1, 22, 37, 38]. In the case of MAYV, some authors have recently suggested that the exported cases observed in European and North American countries where the competent mosquito vectors exist indicate a global risk in addition to the regional implications [36]. With the rapid increasing trends of globalization, a high potential for this arbovirus emerging in urban centers in the tropics that are infested with competent mosquito vectors is a threat that should be considered. Recent social and political movements such as migration of large numbers of people from Central America through Mexico toward the United States of America present the potential for spread of DENV cases related to this epidemic in Honduras, as well as also other arboviruses, into other regions and countries.

During the 2019 DENV epidemic in Honduras, one prominent aspect is the high proportion of severe DENV forms, more than a quarter of them, which is 20-times higher than in any other country in the Americas, making currently Honduras the territory with the highest proportion, but also number of severe DENV cases, even above Brazil [6]. Till EW26, Honduras reported over 6,000 severe DENV cases, and Brazil only 710 (out of 1,127,244 cases till EW 23, 0.06%) [6]. Then, is reasonable, given the limitations of more data, to consider if this is related or not to an effect of prior ZIKV infection on DENV incidence and severity. The epidemiological effect of prior ZIKV infection on dengue incidence and severity, as well as immune, correlates based on new-generation ELISA assays, should be considered. The impact of prior ZIKV/other arbovirus infection on DENV immune response concerning different infections and the duration of
antibodies concerning the interval between, for possible protection, is a matter of discussion [39].

In expectation to the high proportion of severe cases, the proportion of deaths or the CFR% is also higher than in any other country in the Americas (0.128%), including Brazil (0.032%) [6]. Also, in 2018 and especially in 2019, environmental conditions, including global warming, in the Americas, as well as in other regions of the world, were ripe for DENV transmission [8, 9, 40-43]. The World Health Organization (WHO) have identified Ten Threats to Global Health in 2019, including air pollution and climate change; noncommunicable diseases; global influenza pandemic; fragile and vulnerable settings; antimicrobial resistance; Ebola and other high-threat pathogens; weak primary health care; vaccine hesitancy, dengue and HIV [44].

In this setting, public health tools for detailed analyses, such as the use of GIS-epidemiological maps [12, 30, 32], are of high relevance for any affected country [4]. In the case of Central American territories, there is an evident lack of studies developing such maps for arboviral and other infectious diseases. In Honduras, previous assessments using GIS mapped DENV and CHIKV during 2015 and ZIKV in 2016, found a similar spatial distribution as has been found for DENV in 2019. In 2019, according to the Ministry of Health of Honduras, 129 cases of CHIKV and 117 cases of ZIKV have been reported. Although Honduras has been especially affected by DENV, CHIKV, and ZIKV, there is a significant lack of scientific and public health studies dealing with these arboviruses [4, 6, 45], that can lead to acute and chronic complications, even fatal outcomes [46, 47].

In this study, we estimated the incidence rates of DENV and generated epidemiological maps in two geographical levels (departments and municipalities), not only for the current year of epidemic 2019 but also for previous years 2016-2018. DENV appears to follow the patterns of the previous spatial distribution of arboviral diseases in the country [4, 12]. At departments level, the major shift was observed from the spatial distribution on the capital and south area in 2016 to low
incidence rates in all the departments along the years 2017 and 2018, with the epidemic focused mainly in the north area of the country in 2019 (Figures 3 and 4). At municipalities level (Figure 5), multiple areas in 2016 presented high incidence rates in north, central, and east regions, falling significantly for 2017 and 2018, and reaching high incidence rates again in 2019 at many north municipalities, particularly those most populated such as Choloma, Santa Barbara, El Progreso, Yoro, and San Pedro Sula, among others. This spatial distribution is similar to the epidemics of ZIKV and DENV in 2016 (Figure 5) [4].

Further studies are essential to understand the epidemiological and medical characteristics of this and other emerging and reemerging arboviruses in Honduras. Although this may not provide all the answers, such information is particularly useful for public health evidenced-based decisions [4, 48]. Developed maps would provide baseline epidemiological information for the assessment of the differentiated risk related to acquiring such diseases in certain areas (departments and municipalities) of Honduras. Similar recommendations have previously been made for DENV, CHIKV, and ZIKV in previous epidemics [4, 9, 12].

Use of GIS-based epidemiological maps is beneficial to develop preventative/control strategies and public health policies for joint control of these vector-borne diseases in Honduras [12, 27-29, 32, 33], as well as other countries in Central and South America. These tools, such as GIS-based maps can also be developed and used for making public health decisions about other emerging diseases in Honduras [4, 6].

These maps can also provide relevant information concerning the risk to individuals traveling to specific regions of the world [12, 27-29, 32, 33, 49]. A correlated and crucial role is using the data to help prevent further spread of viruses such as DENV, CHIKV, and ZIKV from other countries (imported cases) to Honduras and other countries in Latin America. According to the Secretary of
Tourism of Honduras (Instituto Hondureño de Turismo), in 2014, the country received 1.133 million international tourists (51.3% from Europe and 23.2% from Asia-Pacific region); 107,710 visited the archaeological site of Copán, and 20,118 the fortress of Santa Barbara, both located in arboviral endemic areas) [4]. According to the World Tourism Organization (https://data.worldbank.org/indicator/ST.INT.ARVL), the number of international arrivals to Honduras in 2017 was 851,000 [6].

Touristic areas, such as Roatan in the department of Islas de la Bahía (Bay Islands), are highly visited destination during all seasons. This area has a considerable occurrence of DENV (24.62 cases/100,000, and previously of CHIKV and ZIKV [4, 12], highlighting the need for increased measures to prevent arbovirus infection in these areas. A recent study specifically at Roatán found by molecular diagnosis the co-circulation of ZIKV, DENV, and CHIKV [19].

Roatan is constantly receiving international cruise ships, with the consequent epidemiological implications, as described [4, 12]. Now, in the department of Colon (with 202.16 cases/100,000 pop of DENV in 2019), which includes Trujillo (152.65 cases/100,000 pop of DENV in 2019) with its port Puerto Castilla, there is sizeable industrial development and an international hub for cruise ships. This area should also be a focus of concern for travel medicine and public health for DENV, ZIKV, and other arboviral diseases in Honduras [4]. Such tourist destinations are epidemiologically suitable for the acquisition of arboviral diseases, including DENV, by international travelers in Honduras [4]. Acquisition of ZIKV and CHIKV has been reported in a young woman who returned to Madrid, Spain, after visiting Tegucigalpa and Choluteca [20].

Shortly, other eco-epidemiological assessments should be performed in Honduras for these arboviral diseases. With warm temperatures during the whole year, but especially in the middle
of it, susceptible individuals, and high density of mosquito vectors, many municipalities are suitable for transmission of DENV as well as for other arboviruses [4, 12].

Limitations

Less than 1% of cases of DENV infection were laboratory confirmed. However, considered the PAHO case definition in surveillance to be as accurate as possible in obtaining the epidemiological data [33]. This situation is similar to other countries and published reports about GIS-mapping of DENV and other arboviral diseases in the Americas [27-30, 32]. However, indeed, in Honduras, as in other areas of the tropical Americas, ZIKV and CHIKV also circulate with DENV, and there is overlap in their clinical features, maybe also with other arboviruses not yet detected, such as MAYV [37]. All three viruses have similar clinical presentations, and coinfections may be more common than previously known [10, 11, 37, 50-53], even with other endemic pathogens such as Leptospira [54]. Also, there is probably under-reporting of cases in certain areas as compared with more accurate reporting in individual municipalities.

Conclusions

GIS-based maps provide relevant information to assess the risk to individuals traveling to specific destinations in endemic-epidemic areas allowing detailed prevention advice [4, 6, 33]. Such maps allow integration of prevention and control strategies, as well as public health policies, for joint control of this vector-borne disease in this and other countries of the region [55]. Simultaneous or sequential arboviral infections occur and should be assessed and mapped as a subject of surveillance [51-53]. Preparedness in this setting should also consider the potential arrival of MAYV [22, 38], Oropouche, and yellow fever viruses in Aedes infested areas [56]. Finally, considering the reemergence of DENV in other countries, these assessments would be useful in other territories with ongoing epidemics.
Acknowledgments

This study was partially presented as a conference at the I Regional Symposium of Tropical Diseases of the Coffee-Triangle Region of Colombia, Manizales, Caldas, Colombia, July 13, 2019. The Faculty for Health Sciences of the Universidad de Caldas, Manizales, Caldas, Colombia, supported A. J. Rodriguez-Morales, for his participation at the meeting. Authors thanks the Unit of Health Surveillance (Unidad de Vigilancia en Salud, UVS), of the Secretary of Health (Secretaria de Salud, SESAL), Honduras, for providing the data.

**Funding:** Universidad Tecnologica de Pereira, Pereira, Risaralda, Colombia. This study is part of the project “Desarrollo de Mapas Epidemiológicos a través de Sistemas de Información Geográfica para la Caracterización Geográfica de Enfermedades Infecciosas y Tropicales en el Eje Cafetero de Colombia” (Code 5-15-5 [2015-2017]), Universidad Tecnológica de Pereira, Pereira, Risaralda, Colombia. Training on GIS for A. J. Rodriguez-Morales was funded by Universidad Tecnológica de Pereira, Pereira, Risaralda, Colombia.

**Ethical Approval:** Not required.

**Conflicts of Interest:** The authors have no conflict of interest to disclose.

**Data availability**

Raw data is available and will be provided on request.

**References**


Table 1. DENV incidence rates (cases/100,000pop) by departments, Honduras, 2016-2019.*

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* Till EW26-2019. **Cases per 100,000 pop.
Table 2. DENV incidence rates (cases/100,000 pop.) in the top 20 municipalities, including additionally San Pedro Sula and Tegucigalpa, Honduras, 2016-2019.*

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*TB EW/2-2019. **Cases per 100,000 pop.
Figure 1. Dengue in Honduras, 2015-2019*. Number of cases and incidence rates (cases/100,000 pop.) (A), temporal distribution of case number by epidemiological weeks (EW) (B), and the comparison of EW of incidence rates (cases/100,000 pop) per years (C). *Till EW28.
Figure 2. Seasonality of Dengue in Honduras, 2015-2019*. Percentage distribution of cases (%) per weeks (A), projection of median, quartile 1 and 3 of cases during 2015-2018, per week (B), and comparison with 2019 weekly cases. *Till EW28.
Figure 4. Temporal distribution of the calculated incidence rates per week for Dengue in Cortés and Francisco Morazán departments, Honduras, 2018-2019. *Till EW26.
**Figure 5.** Geographic distribution by GIS-based map of the calculated incidence rates for Dengue in Honduras, 2016-2019 by municipalities. *Till EW26.
Figure 6. Number and proportion of severe dengue, Honduras, 2016-2019*. *Till EW28.