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Original Research Article

Spatial Distribution of Zika in Honduras during 2016-2017 using Geographic Information Systems (GIS) – Implications in Public Health and Travel Medicine◊

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Abstract

Background: Zika virus (ZIKV) infection has significantly affected Latin America in 2015-2017. Most studies have been reported from Brazil and Colombia, and only a few from Central America. For these reasons we analyzed the incidence, incidence rates and evolution of cases in Honduras from 2016-2017.

Methods: Using epidemiological weeks (EW) surveillance data on the ZIKV epidemics 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 31 December 2017, a total of 32,607 cases of ZIKV were reported (98.5% in 2016 for an incidence rate of 36.85 cases/100,000 pop; 1% confirmed by RT-PCR). The highest peak was reached on the EW 6°, 2016 (2,559 cases; 29.34 cases/100,000 pop). The department with the highest number of cases and incidence rate was Cortés (13,128 cases, 791.08 cases/100,000 pop in 2016).

Discussion: The pattern and evolution of ZIKV infection in Honduras has been similar to that which occurred for chikungunya in 2015. As previously reported, infection with chikungunya involved predominantly the central and capital area of the country, reaching incidences there >750 cases/100,000 pop. 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

Zika virus (ZIKV); geographical information systems (GIS); public health; travelers; arboviruses; infectious diseases epidemiology; Honduras.

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Introduction

During the past several years, a significant number of tropical and subtropical geographic areas have been threatened by an unprecedented occurrence of emerging arboviral outbreaks [1]. Factors such as climate change [2, 3], international travel, foreign trade [4, 5], geographical susceptibility, and other factors are associated with these outbreaks [6-10]. In December 2013, chikungunya virus (CHIKV) arrived in the Americas [11], and this was followed shortly by Zika virus (ZIKV) in 2013-2015 [12]. These viruses spread within a population that had already experienced previous endemo-epidemic seasons of urban dengue virus (DENV) and sylvatic yellow fever virus (YFV) [2, 4, 5, 13, 14].

According to the Pan-American Health Organization (PAHO) [15], in Central America 71,316 cases of ZIKV were reported between 2015-2017 (11% confirmed by RT-PCR), with >45% of them occurring within Honduras (Figure 1), making it the country with the highest number of cases in the region. In general, there are not many other studies about ZIKV in Honduras [16-20]. Previous publications worth mentioning are a multi-country surveillance from 1 April 2015 to 31 March 2016 of ZIKV-associated Guillain-Barre Syndrome (GBS) [21] and case reports about neurological complications of ZIKV such as sensory polyneuropathy [22]. Other publications have highlighted Honduras as a potential point source of ZIKV cases to other countries given the attraction of tourist destinations such as Roatán and the Bay Islands [17-19].

ZIKV was first detected in Honduras in late December 2015 [23, 24]. After that, mandatory reporting surveillance of ZIKV cases was established in the country, and the World Federation of Neurology (WFN) established a Zika Working Group to help understand the ZIKV epidemic [25]. Coinciding with the beginning of the epidemics in the country (Figure 1), the World Health Organization (WHO) declared a Public Health Emergency of International Concern (PHEIC) in

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February 2016. As of this time, ZIKV has spread to more than 148 countries around the world, mostly in Latin America, and its complications have challenged the existing response capacities of local health systems [5, 7, 16, 26].

The ZIKV epidemics in countries such as Brazil and Colombia stimulated multiple studies, including entomological assessments since the control of the *Aedes aegypti* mosquito is critical to curb the spread of the virus [18, 24, 26, 27]. 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 [6]. This has also been shown in other Latin American countries [6, 8, 9, 13, 28, 29]. In addition to *A. aegypti*, the presence of *A. albopictus* was confirmed in the Mountain Park Juana Lainez at Tegucigalpa in 2013 [30].

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. PAHO currently streamlines reports from ministries of health and reports weekly confirmed and suspected cases of ZIKV by country [26, 29, 31-35]. These reports provide up-to-date data about the epidemiology of ZIKV in affected global regions [6], 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 [31, 33, 36, 37].

Understanding the impact of arboviruses, especially ZIKV, in terms of clinical complications, disability and costs to health systems requires a greater 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 arboviruses [10, 13].

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As part of the enhanced efforts in control and risk assessment for ZIKV 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 [6, 38], including diseases such as ZIKV, DENV and CHIKV [3, 6, 29, 31-33, 36]. In this setting, this study aimed to estimate incidence rates of ZIKV in 2016-2017 for Honduras and its departments and municipalities and to develop GIS-based epidemiological maps for this arboviral disease.

Methods

Honduras is a Central American country constituted by 18 departments (main administrative level) (Figure 2) and 298 municipalities (second administrative level) (Figures 3 and 4). The Honduran territory presents climatic, geographic and epidemiological conditions suitable for transmission of many vector-borne diseases. *Aedes aegypti*, the main vector of ZIKV, is widely distributed over all the territories [6, 39], 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 [6].

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 year 2016-2017 (detailed by weeks). Data were constituted from clinically confirmed cases (suspected cases by clinical criteria definition) and 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) [6]. Determination of ZIKV infection included syndromic and/or laboratory

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surveillance (clinical definition of fever, rash, conjunctivitis and arthralgias in a place with previously ZIKV circulation; at least one case confirmed by RT-PCR). This clinical definition has been recommended by the WHO, PAHO, and the US Centers for Disease Control (CDC).

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 ZIKV incidence by department and municipalities [6].

In addition, national GIS-based maps, by departments and municipalities with the distribution of ZIKV 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 [6, 31, 34].

Results

From 1 January 2016 to 31 December 2017, a total of 32,607 cases of ZIKV were reported (1% confirmed by RT-PCR for ZIKV), 98.5% of them in 2016, for an incidence rate of 36.85 cases/100,000 pop.

The highest peak was reached on the epidemiological week (EW) 6°, 2016 (2,559 cases; 29.34 cases/100,000 pop) (Figure 1). During the first 10 EW, a total of 16,415 cases were reported (50% of the 2016-2017 period). Number of cases decreased at EW 12° to 93 cases (1.07 cases/100,000 pop). A second peak of cases occurred during EW 24° reaching 988 cases (11.33 cases/100,000 pop) (Figure 1). By EW 35° more than 95% of the cases of the period were reported.

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Of the 18 departments of Honduras, all except Gracias a Dios reported cases during the study period. Rates ranged from 0 to 791.08 cases/100,000 (Cortés, 2016), followed by Francisco Morazán (663.53 cases/100,000, 2016) and Yoro (350.93 cases/100,000, 2016), Santa Barbara (308.64 cases/100,000, 2016), and Olancho (265.65 cases/100,000, 2016) (Figure 2, Table 1). These 5 departments, which are located in the central and northwestern areas of Honduras (figure 2), reported more than 88% of the ZIKV cases of the country (Table 1).

When comparing Cortés and Francisco Morazán incidence over time, clear differences were evident. At Cortés a high number of cases was reported during the first 12 EWs of 2016 reaching up to 109.8 cases/100,000 pop (1815 cases) during that week, for a total of 11,514 cases in the three first months (35% of the cases reported in Honduras during 2016-2017) (Figure 1). In contrast, there was a low incidence in Francisco Morazán (below 20 cases/100,000 or <300 cases per week) during the same period. Thereafter, there was a low reported number of cases in Cortés (<10 cases/100,000 pop) and a significant increase in Francisco Morazán, which reached its peak during the EW 23° with 50.3 cases/100,000 (793 cases that week) for a total of 5,453 cases (17% of the cases reported in Honduras during 2016-2017) (Figure 1). Until EW 23° more than 52% of the cases of the 2016-2017 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).

From the total number of municipalities (298) of Honduras, 69.4% of them reported cases of ZIKV (Table 2). Rates ranged from 0 to 2,495.79 cases/100,000 (Ceguapa, Santa Barbara department, 2016), followed by Cane (La Paz department, 1,648.91 cases/100,000, 2016) and San Vicente Centenario (Santa Bárbara department, 1.565,18 cases/100,000, 2016) (Figure 3, Table 2).

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Tegucigalpa, at the Capital District, reported 10,386 cases in 2016 for a rate of 860,03 cases/100,000 pop. (Figure 3).

At Francisco Morazán department, areas closer to Tegucigalpa presented high incidence numbers. For instance, Santa Lucia reported 193.13 cases/100,000pop and San Buenaventura reported 101.25 cases/100,000pop (Figure 4). Similarly, at Cortés department, municipalities such as Villanueva, Choloma, Puerto Cortes, San Manuel, which surround the department capital of San Pedro Sula, demonstrated incidence rates >100 cases/100,000 pop (Figure 4) (Table 2) (Supplemental Table 1 shows all the municipalities of Honduras by incidence rates).

Discussion

As expected, after the arrival of ZIKV to Brazil and other countries in Latin America [12, 31], Honduras was significantly affected by ZIKV cases. As occurred with DENV and CHIKV in 2015 [6], Francisco Morazán and Cortés, the most populated departments, were the most affected. ZIKV has followed the path of dengue and chikungunya in Honduras. Those areas with high incidence rates of these infections also exhibited the highest risk for ZIKV [6]. Although more than 32,000 cases were reported in the country, only 1% of cases have been 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 and reliable serological tests. Nonetheless, we used the PAHO case definition which is based upon a clinical definition of ZIKV infection for surveillance data.

Social and eco-epidemiological conditions in Honduras make the whole country susceptible to spread of arboviral diseases such as DENV, CHIKV and ZIKV [3, 6]; therefore, analyses such as the one presented herein are relevant for understanding future emerging arboviral diseases in the

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region and the country. Other relevant viral diseases to consider include Mayaro (MAYV), Oropouche (OROV), Venezuelan Equine Encephalitis (VEEV), West Nile virus (WNV), among others [1, 13, 40, 41]. 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 ZIKV and other arboviruses into other regions and countries. Although the last case of ZIKV in Honduras was officially reported in mid-December 2017, transmission is still occurring, albeit with a lower number of incident cases (between 0 and 13 cases/week during first 38 EW of 2018). However, as seen in other countries [7, 31-34], marked variation occurred in reported incidence in areas within countries and between 2016 and 2017. This can be explained in part due to previous high attack rates and a decrease in the number of susceptible populations due to herd immunity. As has been recently hypothesized for dengue [42], but also for Zika and chikungunya, this decline is unlikely due to changes in epidemiological surveillance systems, as similar designs of surveillance systems exist across the region. However, future studies should address the effect of prior DENV infection on ZIKV incidence and severity, the epidemiological effect of prior ZIKV infection on dengue incidence and severity, immune correlates based on new-generation ELISA assays, and the impact of prior DENV/other arbovirus infection on ZIKV immune response in relation to number of infections and the duration of antibodies in relation to interval of protection [42]. Also, in 2015-2016, environmental conditions in the Americas were ripe for ZIKV transmission [43].

As mentioned previously, in Central America Honduras was the country with the highest number of ZIKV cases [15]. But, some small countries such as Belize actually had a higher incidence rate (636 cases/100,000pop), with more than 2.000 cases during 2015-2017 [44-46]. One also has to keep in mind that exact numbers of ZIKV cases are difficult to obtain from many of the other countries in Central America [47, 48]. Adding the ZIKV cases from Central America which are known to the rest of the continent, more than 800,000 cases have been reported [15].

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So far, in Honduras only 8 cases of congenital Zika syndrome (CSZ) have been reported. But, this figure may not be accurate and may be an underestimate. Further studies are necessary to determine the true frequency of ZIKV infection during pregnancy in Honduras and the association of microcephaly and other birth defects with ZIKV infection [20], as has been reported in Brazil and Colombia, among other countries in Latin America [49-52]. Abortion is currently illegal under any circumstances in Honduras.

In this setting, public health tools for detailed analyses, such as the use of GIS-epidemiological maps [6, 34, 36], are of high relevance for any affected country. In the case of Central American territories, there is a clear lack of studies developing such maps for arboviral and other infectious diseases. In Honduras, a previous assessment using GIS mapped DENV and CHIKV during 2015 found a similar spatial distribution as has been found for ZIKV in 2016. In 2016, according to the Ministry of Health of Honduras, 22,961 cases of DENV and 15,896 cases of CHIKV were reported. Combining the three arboviral diseases, almost 71,000 cases were reported. In spite of the fact that Honduras has been especially affected by DENV, CHIKV and ZIKV, there is a great lack of scientific and public health studies dealing with these arboviruses [53].

In this study, we estimated the incidence rates of ZIKV, and generated epidemiological maps in two geographical levels (departments and municipalities). ZIKV appears to followed the patterns of other arboviral diseases in the country [6]. Further studies are clearly essential to understand the epidemiological and medical characteristics of this and other arboviruses in Honduras. Although this may not provide all the answers, such information is particularly useful for public health evidenced-based decisions [54]. Developed maps would provide baseline epidemiological information for assessment of the differentiated risk related to acquiring such diseases in certain

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areas (departments and municipalities) of Honduras. Similar recommendations have previously been made for DENV and CHIKV [3, 6].

Use of GIS-based epidemiological maps are very useful to develop preventative/control strategies and public health policies for joint control of these vector-borne diseases in Honduras [6, 31-33, 36, 37], as well as other countries in Central 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.

These maps can also provide relevant information concerning the risk to individuals traveling to specific regions of the world [6, 31-33, 36, 37, 55]. A correlated and very important 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*), just 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 Zika-endemic areas).

In the case of ZIKV, previous studies at the department of Islas de la Bahía (Bay Islands), which include Roatan, indicate that this is a highly visited tourist destination during all seasons. This area has a considerable occurrence of DENV and CHIKV [6], 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 [18].

Roatan is constantly receiving international cruise ships, with the consequent epidemiological implications, as described [6]. Now, in the department of Colon (with 47.39 cases/100,000 pop

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of ZIKV in 2016), which includes Trujillo (3.14 cases/100,000 pop of ZIKV in 2016) with its port Puerto Castilla, there is large 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 ZIKV and other arboviral diseases in Honduras. Such tourist destinations are epidemiologically suitable for acquisition of ZIKV by international travelers in Honduras. In fact, such acquisition of infection with both ZIKV and CHIKV has been reported in a young woman who returned to Madrid, Spain after visiting Tegucigalpa and Chouteca [19].

In the near future, other eco-epidemiological assessments should be performed in Honduras for these arboviral diseases. With warm temperatures during the whole year, susceptible individuals, and high density of mosquito vectors, many municipalities have become endemic regions for ZIKV in addition to CHIKV and DENV [6].

Limitations

Only 1% of cases of ZIKV infection were laboratory confirmed. We used the PAHO case definition in surveillance to be as accurate as possible in obtaining the epidemiological data [37]. This situation is similar to other countries and published reports about GIS-mapping of Zika and other arboviral diseases in the Americas [31-34, 36]. But certainly, in Honduras, as in other areas of the tropical Americas, DENV and CHIKV also circulate with ZIKV, and there is overlap in their clinical features. All three viruses have similar clinical presentations, and coinfections may be more common than previously known [4, 5, 40, 56-59]. In addition, there is probably under-reporting of cases in certain areas as compared with more accurate reporting in certain municipalities.

Conclusions

GIS-based maps provide relevant information to assess the risk to individuals travelling to specific destinations in endemo-epidemic areas allowing detailed prevention advice [37]. Such maps allow

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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 [60]. Simultaneous or sequential arboviral infections occur and should be assessed and mapped as a subject of surveillance [57-59]. Preparedness in this setting should also consider the potential arrival of Mayaro [13, 41], Oropouche and yellow fever viruses in *Aedes* infested areas [61].

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Data availability

Raw data for is available and will be provided on request.

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Table 1. ZIKV incidence rates (cases/100,000pop) by departments, Honduras, 2016-2017.

	Cases		Population		Rates*	
Department	2016	2017	2016	2017	2016	2017
Cortés	13,082	90	1,653,699	1,686,094	791.08	5.34
Francisco Morazán	10,465	189	1,577,178	1,601,291	663.53	11.80
Yoro	2,092	58	596,138	604,844	350.93	9.59
Santa Bárbara	1,364	13	441,939	448,942	308.64	2.90
Olancho	1,450	12	545,835	554,282	265.65	2.16
Choluteca	1,037	3	453,360	458,871	228.74	0.65
El Paraíso	905	13	465,864	473,277	194.26	2.75
Copán	361	6	388,810	394,890	92.85	1.52
La Paz	181	3	209,783	213,499	86.28	1.41
Atlántida	373	19	457,031	464,288	81.61	4.09
Islas de la Bahía	51	0	67,704	69,493	75.33	0.00
Comayagua	392	22	521,748	531,676	75.13	4.14
Valle	101	1	180,772	182,996	55.87	0.55
Colón	154	19	324,950	330,105	47.39	5.76
Ocotepeque	58	25	154,251	157,018	37.60	15.92
Intibucá	45	1	246,258	250,959	18.27	0.40
Lempira	21	1	339,310	345,489	6.19	0.29
Gracias a Dios	0	0	96,384	98,337	0.00	0.00
Total	32,132	475	8,721,014	8,866,351	368.44	0.54

*Cases per 100,000 pop.

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Table 2. Top ten risky municipalities by ZIKV incidence rates (cases/100,000pop), Honduras, 2016-2017.

		Cases		Population		Rates*	
Departments	**Municipalities**	**2016**	**2017**	**2016**	**2017**	**2016**	**2017**
Santa Bárbara	Ceguapa	131	5	5,249	5,353	**2,495.79**	93.41
La Paz	Cáne	66	1	4,003	4,150	**1,648.91**	24.10
Santa Bárbara	San Vicente Centenario	58	0	3,706	3,736	**1,565.18**	0.00
Cortés	Villanueva	1,765	14	161,609	165,602	**1,092.14**	8.45
Copán	San Pedro Sula	**8,022**	29	754,061	765,999	**1,063.84**	3.79
Santa Bárbara	Quimistan	474	0	52,884	54,638	896.30	0.00
El Paraíso	Jacaleapa	36	1	4,126	4,186	872.55	23.89
Yoro	El Progreso	1,678	52	193,567	195,247	866.88	26.63
Francisco Morazán	Tegucigalpa M.D.C.	**10,386**	189	1,207,635	1,225,043	860.03	15.43
Cortés	Choloma	2,100	14	249,217	255,625	842.64	5.48
Olancho	Silca	65	0	8,087	8,135	803.73	0.00
Santa Bárbara	La Arada	79	1	10,220	10,433	773.00	9.58
Olancho	Juticalpa	821	9	132,484	135,076	619.70	6.66
Santa Bárbara	Nuevo Celilac	49	0	8,166	8,185	600.04	0.00
Islas de la Bahía	Utila	24	0	4,277	4,400	561.08	0.00
Copán	Santa Rosa	354	6	65,233	66,629	542.67	9.01
Santa Bárbara	San José de Colinas	104	2	19,266	19,407	539.82	10.31
Santa Bárbara	Trinidad	101	0	20,325	20,563	496.93	0.00
Choluteca	San Antonio de Flores	27	1	5,463	5,470	494.25	18.28
Olancho	Guayape	60	0	13,027	13,152	460.60	0.00

*Cases per 100,000 pop.

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Figure 1. Temporal distribution by epidemiological weeks of number of cases of Zika in Honduras, 2015-2016 (A), and the comparison between the evolution during 2016 at Cortés and Francisco Morazán departments (B).

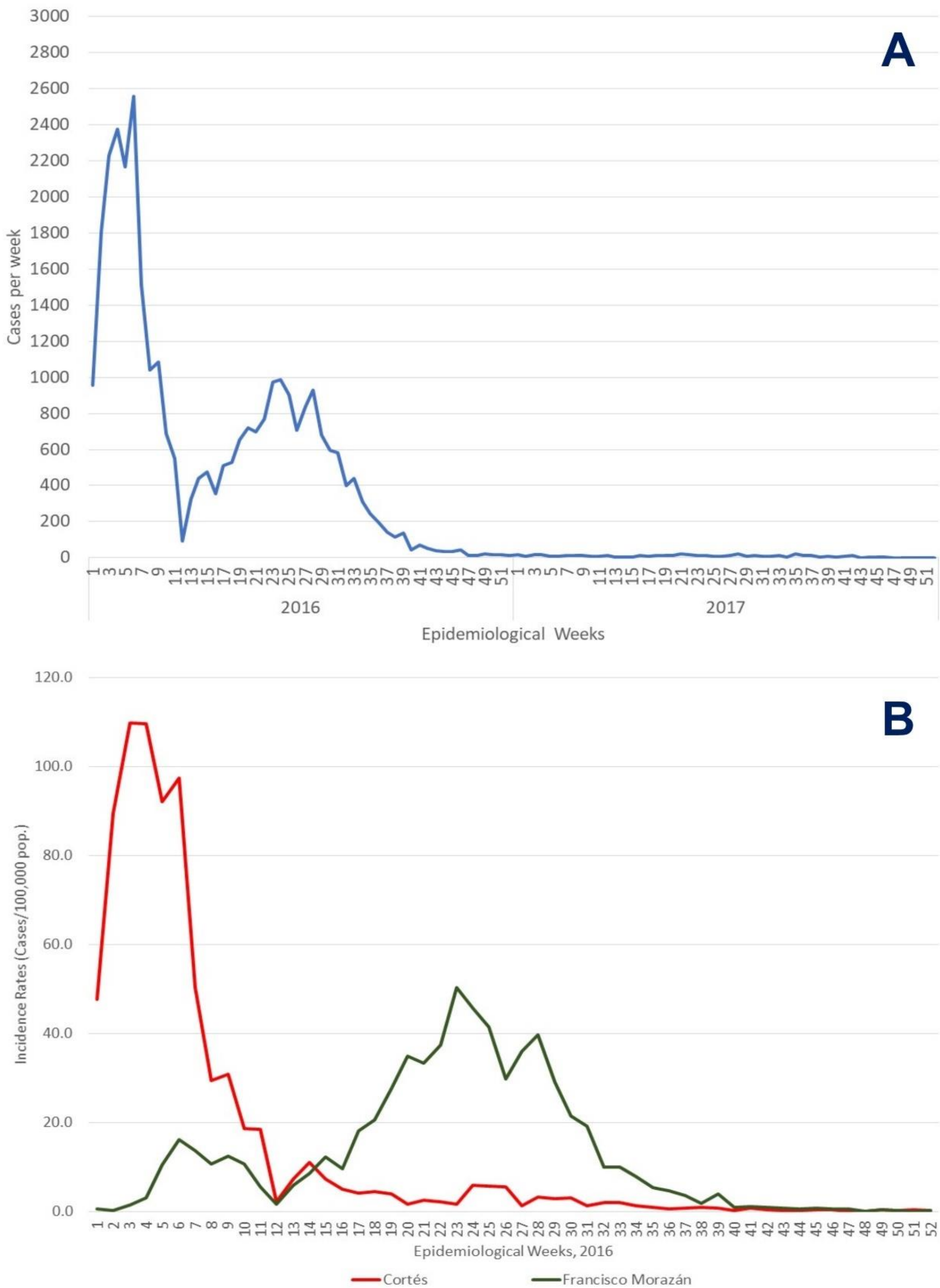

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Figure 2. Geographic distribution by GIS-based map of the calculated incidence rates for Zika in Honduras, 2016-2017 by departments.

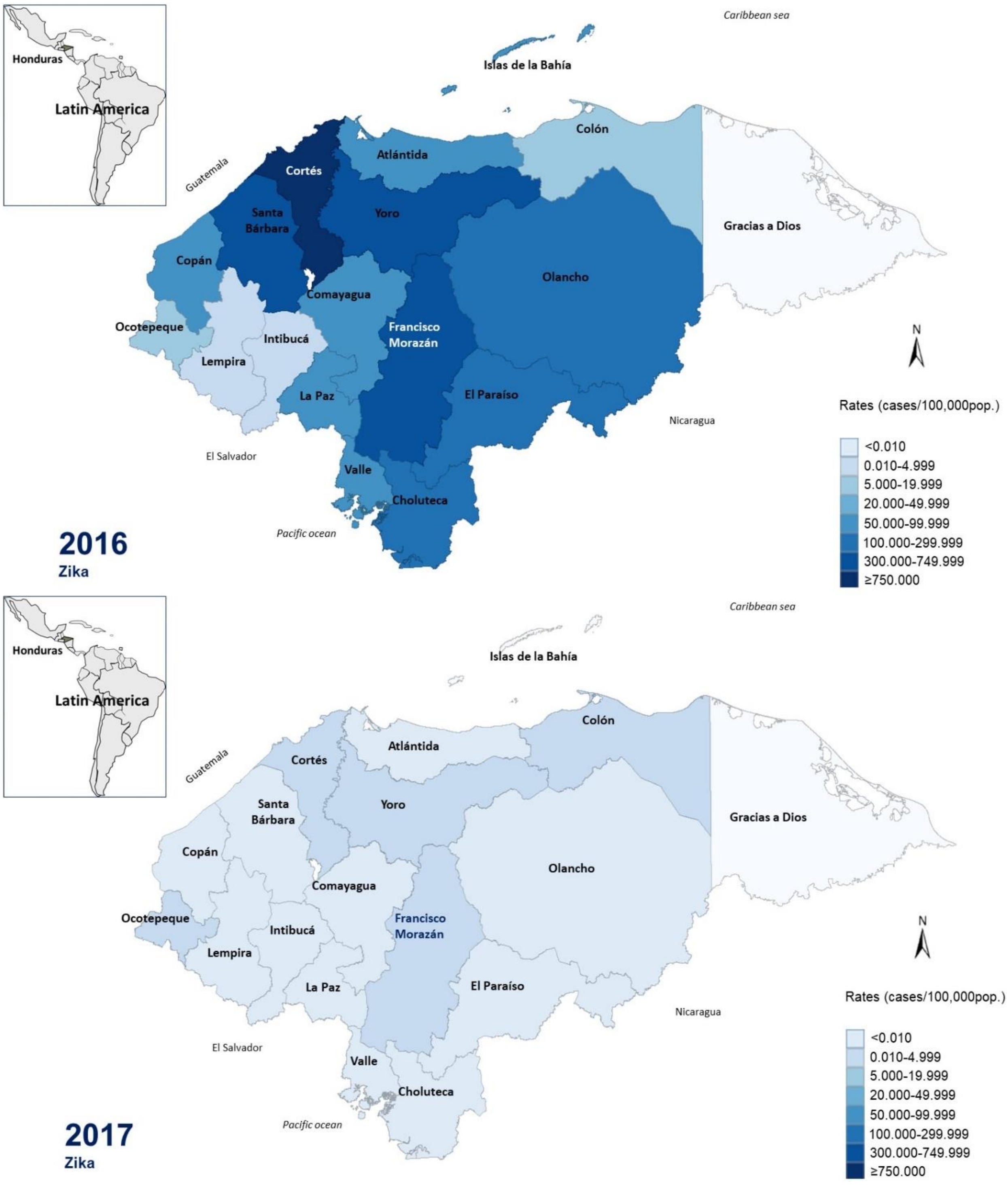

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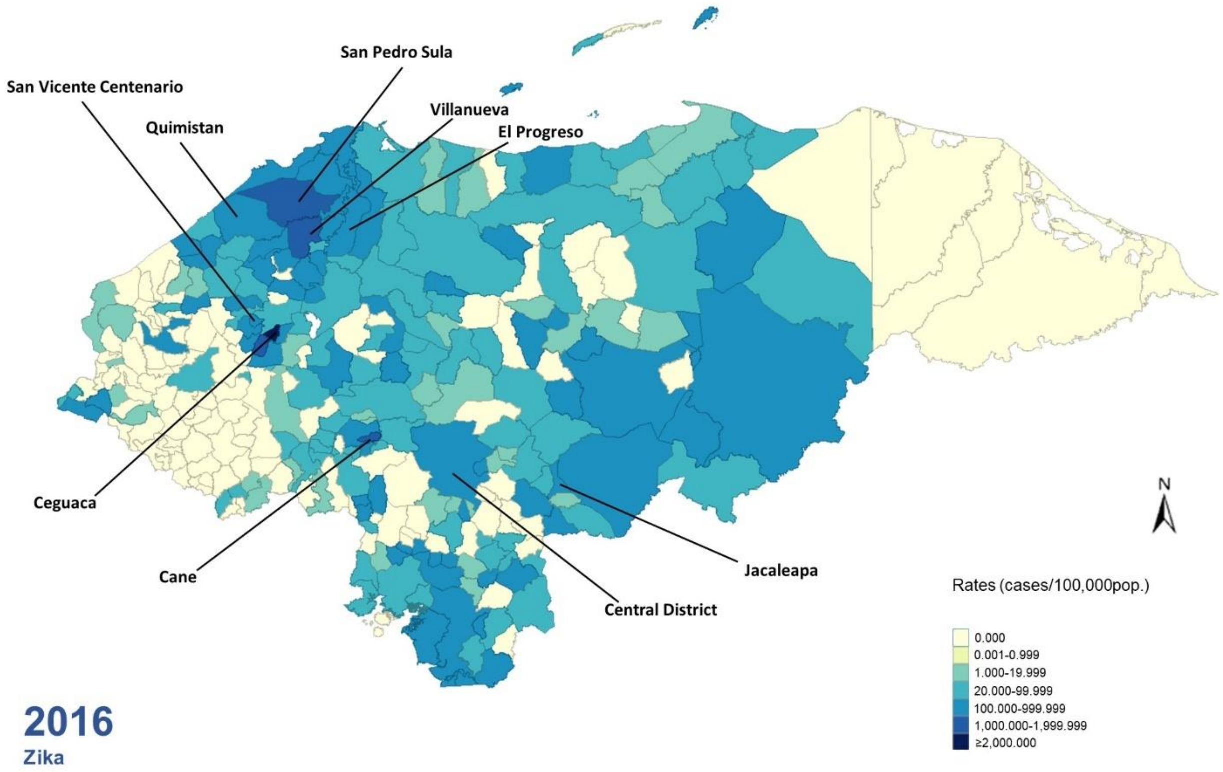
Figure 3. Geographic distribution by GIS-based map of the calculated incidence rates for Zika in Honduras, 2016-2017 by municipalities.



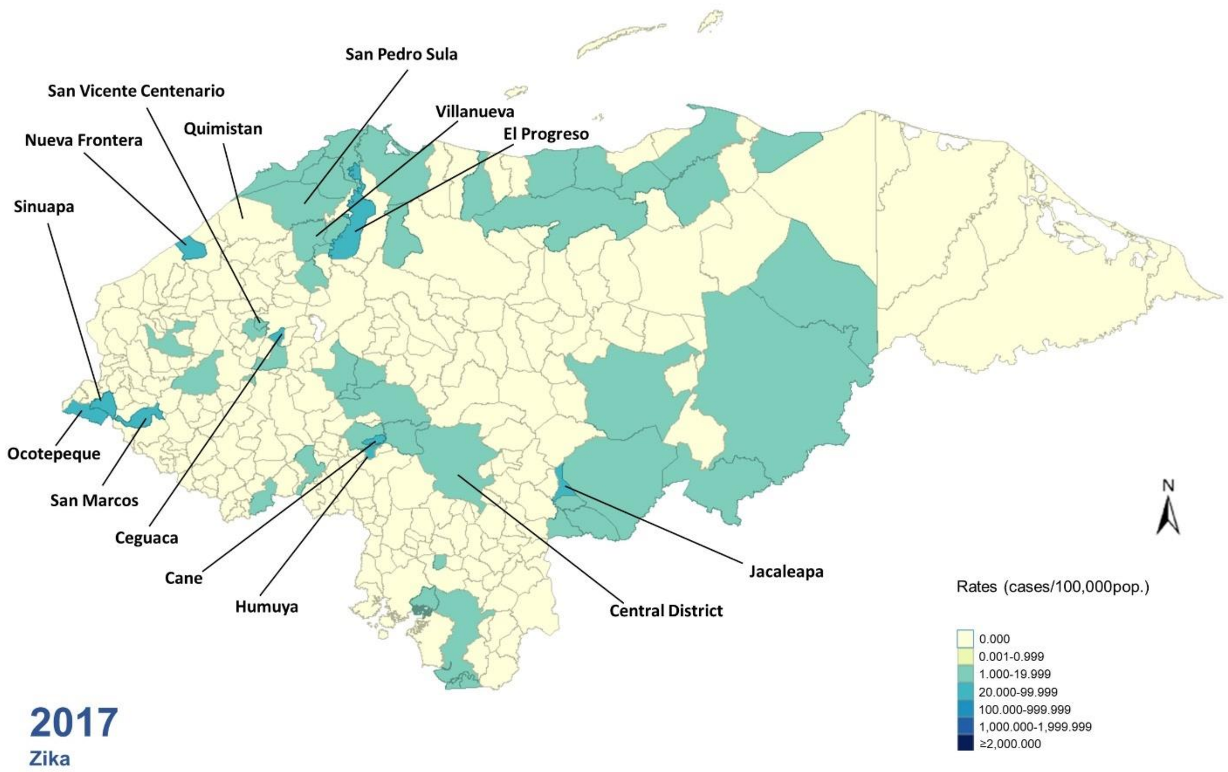


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Figure 4. Geographic distribution by GIS-based map of the calculated incidence rates for Zika in municipalities of Cortés and Francisco Morazán departments, Honduras, 2016.