Spatial distribution of Zika virus infection in Northeastern Colombia

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SUMMARY

In this study, we investigated the weekly reported spatio-temporal distribution and topographic risk factors for Zika virus (ZIKV) infection in northeastern Colombia. Weekly reported surveillance data, including clinical, suspected and confirmed cases from the ongoing ZIKV epidemic in the *Santander* and *Norte de Santander* departments (*Santanderes*) in Colombia were used to estimate cumulative incidence rates. Spatial analysis was performed to develop hot spot maps and to identify spatial topographic risk factors for infection. From January 1, 2016 to March 19, 2016, 11,515 cases of ZIKV were reported in *Santanderes*, with cumulative rates of 316.07 cases/100,000 population for the region (representing 18.5% of the cases of the country). Five municipalities (four in *Norte de Santander*) reported high incidence of ZIKV infection (>1,000 cases/100,000 pop); these municipalities are close to the border with Venezuela. Most of the cases reported occurred mainly in low altitude areas, and persistent hot spots were observed. Higher infection rates were reported in the northeastern part of the study area. Use of risk maps can help guide decisions for the prevention and control of ZIKV. Hotspots on the Colombia-Venezuela border can have implications for international spread.

Keywords: Zika, epidemiology, public health, geographical information systems, Latin America.

INTRODUCTION

Zika virus (ZIKV) infection is causing epidemics in Latin America [1]. Colombia has officially reported a total of 58,838 cases of ZIKV infection in the first 32 epidemic weeks (21 in 2015 and 11 in 2016) [2]. According to the Pan American Health Organization (PAHO) and the World Health Organization (WHO), Colombia has fewer cases than Brazil in terms of absolute number of infections (58,838 cases, 4% laboratory confirmed in Colombia compared to 72,596 cases, 0.74% laboratory confirmed in Brazil) [3,4]. However, Colombia has a higher per capita incidence rate (IR) than Brazil due to its smaller population size (209,157,170 pop, IR = 34.71 cases/100,000 population in Brazil; 48,747,632 population, IR=120.70 cases/100,000 population in Colombia) [4]. The ZIKV incidence rate is 3.5 times higher in Colombia than in Brazil. Thus, Colombia currently faces the greatest burden of disease for ZIKV, worldwide.

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Up-to-date surveillance data are crucial to better understand ZIKV epidemiology, including the distribution of disease burden across landscapes and time. Spatial epidemiological analysis can produce risk maps that can be used to describe communities at higher risk for infection to prioritize interventions and to advise travel policies for visitors.

Previous studies have reported on the burden of ZIKV infection in Colombia and used geographical information systems (GIS) to produce maps for La Guajira (northern Colombia) and for Tolima (central Colombia) [5,6]. No GIS-based epidemiological maps of ZIKV have been developed for *Santander* and *Norte de Santander* (together, *Santanderes*), two departments in northeastern Colombia with the highest incidence rates [7]. Because this region shares a border with Venezuela, a country where ZIKV incidence is expected to be high but is not well-characterized, the observed incidence rates in *Santanderes* could have implications for the international spread of the disease [7].

Information about the spatio-temporal distribution and risk factors for ZIKV is limited in Colombia, particularly in northeastern part of the country [5,6]. This region has been significantly affected by the current outbreak as evidenced by *Norte de Santander* having the highest number of reported cases in 2016 (8,484 as of March 19, 2016) [2]. Here, we estimated the cumulative incidence rate of ZIKV infection and created risk maps for *Santander* and *Norte de Santander* regions.

PATIENTS AND METHODS

Surveillance data on weekly reported ZIKV cases, including both laboratory confirmed and clinically suspected cases, for 2016 were reported by the National Institute of Health, Colombia and were used to estimate cumulated incidence rates. Population data for 2016 from the 2005 National Colombian Census with population annual projections (www.dane.gov.co) was used as denominator to estimate per capita ZIKV infections (cases/100,000 population) in each *Santander* and *Norte de Santander*, and together for the *Santanderes* [7].

Diagnosis

Diagnosis of ZIKV infection included laboratory and/or syndromic surveillance (clinical definition of fever, rash, conjunctivitis and arthralgias in a municipality with previously ZIKV circulation, at least one case confirmed by real time-polymerase chain reaction (RT-PCR) [7]. Until April 15, 2016, there were no serological tests available for diagnosis of ZIKV infection in Colombia, only RT-PCR is available.

Those fitting the clinical definition but who were diagnosed in a municipality without laboratory-confirmed cases, were considered "suspected" (Figure 1).

Data for this study were gathered from 127 primary notification units, one per municipality, and later consolidated at the department's level for *Santander* and *Norte de Santander*.

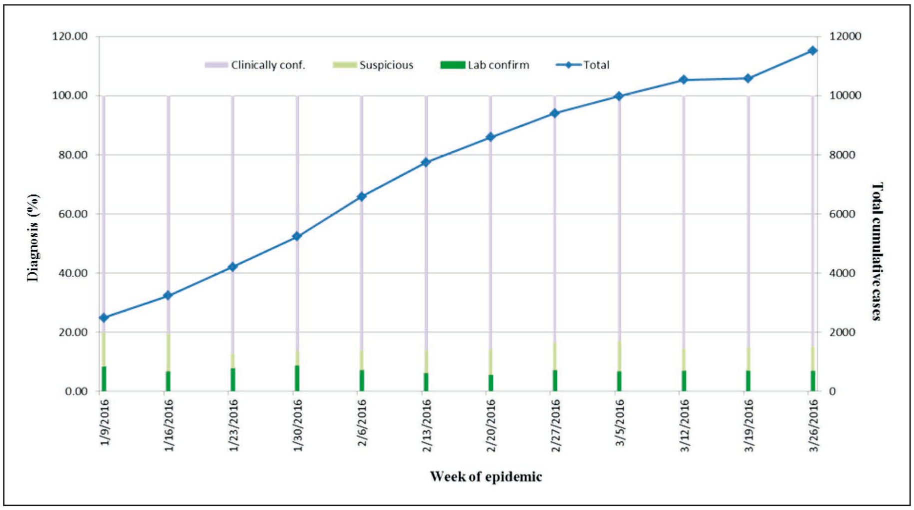

Figure 1 - Weekly reported Zika virus infection in Northeastern Colombia.

Spatial analysis

Microsoft Access (version 365)® was used to design the spatial database, and to import incidence rates for municipalities to the GIS software Kosmo Desktop, which was used to develop the maps (Figure 2). Geographic data (municipalities and department polygons) required for the department were provided by the Regional Information System of the Coffee-Triangle region (http://www.sirideec.org.co/). The 90-meter resolution Shuttle Radar Topographic Mission Digital Elevation Model was downloaded from NASA's website. Road and rail ways and water bodies were downloaded from DIVA-GIS [8]. The shape files (based on official cartography) of municipalities and communes were linked to the database. We developed risk maps in the municipalities of both *Santander* and *Norte de Santander*. ArcGIS 10.2 and Kosmo® 3.1 were used to generate the risk maps. Space-time pattern mining tools in ArcGIS Pro 1.1 were used for hot spots analysis. All municipalities within *Santanderes* over the 12 weeks were imported into this tool and analyzed for spatial correlations across space and time to identify clusters of ZIKV infection over space and time. Each centroid location in the department was assigned 10,000 meter × 10,000 meter spanning area.

RESULTS

Through March 19, 2016, *Santanderes* have reported 11,515 cases (6.8% were confirmed by RT-PCR and 84% were suspected cases); 22% of these cases came from *Santander* and 77% from *Norte de Santander* (Figure 1). The cumulative incidence rate of ZIKV across all 127 municipalities within the two departments for all reported cases (both confirmed and suspected) was 316 cases/100,000 populations (Figure 1). The cumulative incidence rate for laboratory-confirmed cases was 21 cases/100,000 population (Figures 1 and 2). In *Norte de Santander*, cumulative incidence rates ranged from 0 to 4,535 cases/100,000 population in each municipality; *Santiago* municipality had the highest cumulative incidence rate (4,535 cases/100,000 population), followed by *Durania* (1,686 cases/100,000 population), *Bochalema* (1,182 cases/100,000 population) and *Los Patios* (1,046 cases/100,000 population) (Figure 2). *Cucuta*, the capital of *Norte de Santander*, shares a border with

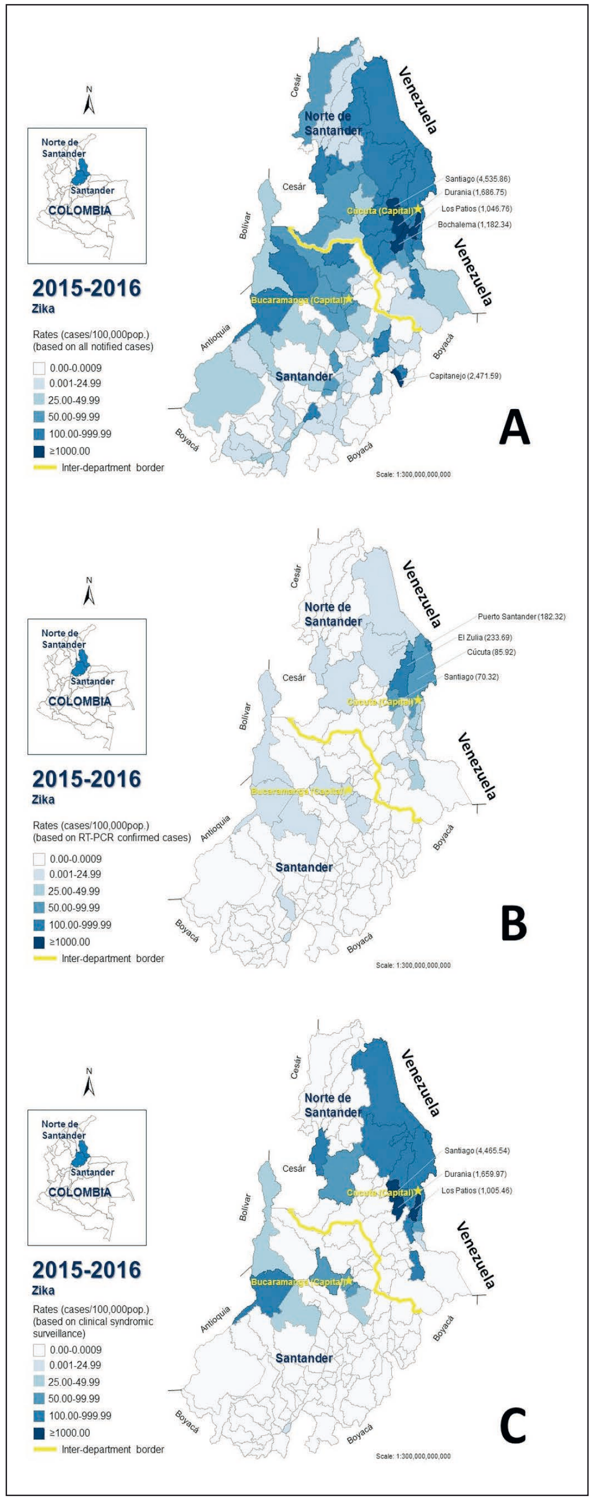

Figure 2 - Spatial distribution of Zika infection in Northeastern Colombia.

Venezuela and contributed 64% of total cases in the department and 54% in the *Santanderes* (Figure 1) with a cumulative incidence rate of 904 cases/100,000 population. Out of the 40 municipalities in *Norte de Santander*, only three did not report any suspected or confirmed ZIKV cases.

Capitanejo is the municipality in *Santander* with the highest cumulative incidence rate, 2,471 cases/100,000 population (Figure 2). *Bucaramanga*, the capital of *Santander*, contributed 30% of all cases in the department (Figure 2) and 4.5% of cases in the entire *Santanderes* region. Out of the 87 municipalities in this department, 41 have not reported any ZIKV cases (Figure 3A).

Persistent hot spots, defined as points where at least 90% of the time step intervals are hot, with no trend up or down, were reported in the northern and southern parts of the study area and in altitudes around 2000 to 2800 meter (Figure 3B). Municipalities in higher altitudes (>2800 meter) did not report any ZIKV cases. Presence of bodies of water, railways and road networks were not statistically significantly associated with the spread of ZIKV in *Santanderes* and *Norte de Santander*.

DISCUSSION

In northeastern region of *Santanderes*, the burden of ZIKV infection has been concentrated in the eastern area, with *Cucuta*, a municipality close to the border with Venezuela, presenting more than half of all cases in the two departments. Municipalities such as *Cucuta*, that share common border with Venezuela, tend to have high levels of cross-border movement, which can pose a significant risk for the international spread of ZIKV (Figure 2) [7]. Although Zika arrived in Colombia at the end 2015, regions outside the Caribbean coast, such as *Santanderes*, have largely been affected during 2016.

These results suggest that the *Santanderes* region is a high-risk area for ZIKV infection; it is already endemic of Dengue and CHIKV, which share the same mosquito vector [9,10]. Among cases in *Santanderes*, 2,475 (22%) were in pregnant women (393 confirmed by RT-PCR for ZIKV) [2]. Detailed maps for ZIKV in pregnant women would be useful for describing the epidemiology of ZIKV-associated outcomes, such as microcephaly, other birth defects and Guillain-Barré syndrome [11].

Approximately 92% of cases in this study were diagnosed based on clinical signs and symptoms, rather than laboratory testing [12-15]. This would be interpreted as one study limitation, as Chikungunya and Dengue have similar clinical and epidemiological characteristics as Zika, and all of them are infections already endemic in the area as well in the country and Latin America [16-18]. Unfortunately, locally, but also nationally, no sig-

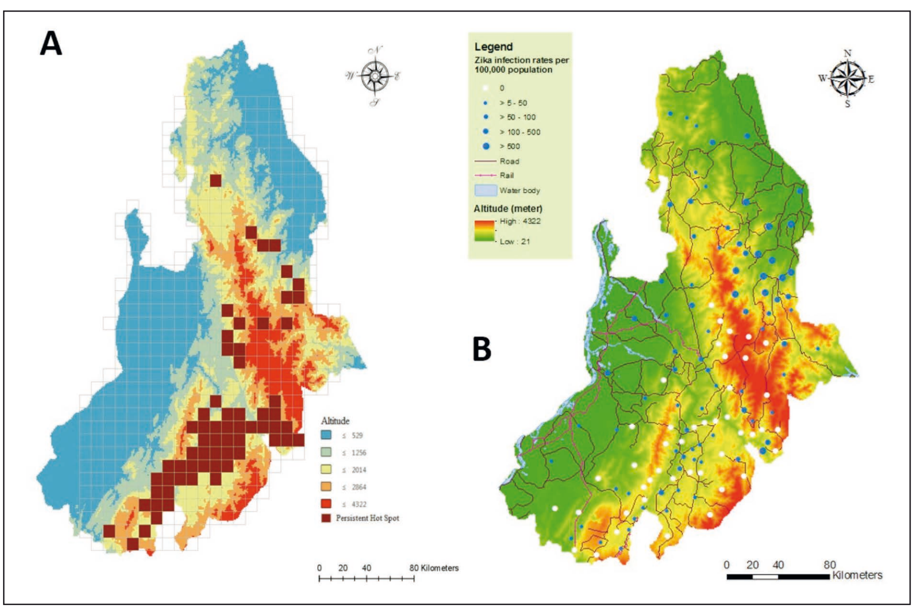

Figure 3 - Persistent Zika hot spots (A) and spatial distribution overlapped with the physiography, water body and roads of the region (B), Northeastern Colombia

nificant efforts had been made, from surveillance, to differentiate suspected ZIKV infections from Dengue and/or Chikungunya infections. Then, it should be considered in the interpretation of these results.

In this setting, even more, strengthening the surveillance system and diagnostic capacity are critical for improving the public health responses to ZIKV in high-risk zones. Colombian Ministry of Health should target ZIKV persistent hot spots and high-risk municipalities. This study also reported the presence of ZIKV in every municipality except in those higher than 2800 meters above sea level, which was expected because the vectors (mainly *Aedes aegypti* and *A. albopictus*) have difficulty surviving and reproducing in higher altitudes. Similarly, there are fewer people living in the high-altitude areas.

Further research about ZIKV transmission dynamics in Colombia, is critical for informing control efforts. As already reported, ZIKV can spread through sexual contact and blood transfusion [12, 13]. Mass awareness campaign by radio, television, mass public health alerts to people via mobile communication and newspaper advertisement may help the public understand and limit their risk behaviors associated with infection [1, 4].

We suggest employing real-time GIS-based epidemiological maps to visualize ZIKV transmission dynamics at the national, departmental and municipality levels to identify intervention priorities. Future study should focus on clinical symptoms for all PCR positive cases along with geocoded locations, travel history and socio demographic risk factors. Additionally, further work should quantify the effect that cross-border movement has on the distribution of ZIKV in Colombia and all of Latin America, to allow for the development emergency preparedness protocols in newly affected areas [5, 6, 14, 15]. Also in the future, GIS-based maps of ZIKV congenital syndrome, ZIKV-associated Guillain-Barré syndrome and even of deaths, would be useful [19, 20].

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Ethical approval

No ethical approval is needed to analyze and publish this public data. In addition, we have been granted by the Ministry of Health with access to surveillance data (SISPRO) which in addition is fully publicly available [11].

Conflicts of interest

The authors have no conflict of interest to disclose.

Author contribution

Study design: AJRM, UH, Data collection: CJGL, MLGM, JASR, SML, AFA, COLR, Data analysis: AJRM, UH, COLR, JDB, Writing: All authors. All authors read the final version submitted.

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