# **Accepted Manuscript**

Mirroring the Zika epidemics in Cuba: The view from a European imported diseases clinic

A. Almuedo-Riera, N. Rodriguez-Valero, D. Camprubí, I. Losada Galván, C. Zamora-Martinez, J. Pousibet-Puerto, C. Subirà, M.J. Martinez, M.J. Pinazo, J. Muñoz

PII: \$1477-8939(19)30098-5

DOI: https://doi.org/10.1016/j.tmaid.2019.06.001

Reference: TMAID 1430

To appear in: Travel Medicine and Infectious Disease

Received Date: 11 April 2019
Revised Date: 20 May 2019
Accepted Date: 11 June 2019

Please cite this article as: Almuedo-Riera A, Rodriguez-Valero N, Camprubí D, Losada Galván I, Zamora-Martinez C, Pousibet-Puerto J, Subirà C, Martinez MJ, Pinazo MJ, Muñoz J, Mirroring the Zika epidemics in Cuba: The view from a European imported diseases clinic, *Travel Medicine and Infectious Disease* (2019), doi: https://doi.org/10.1016/j.tmaid.2019.06.001.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

**Title:** Mirroring the zika epidemics in Cuba: the view from a European imported diseases clinic

**Authors:** Almuedo-Riera, A.<sup>a,e</sup>, Rodriguez-Valero N<sup>a</sup>, , Camprubí, D.<sup>a</sup>, Losada Galván, I.<sup>a</sup>, Zamora-Martinez C.<sup>b</sup>, Pousibet-Puerto J.<sup>c</sup>, , Subirà, C.<sup>a</sup>, Martinez MJ.<sup>d,a</sup>, Pinazo MJ.<sup>a</sup>, Muñoz J.<sup>a</sup>

ISGlobal, Hospital Clínic - Universitat de Barcelona, Barcelona, Spain.

## Affiliations:

- a) ISGlobal, Hospital Clínic Universitat de Barcelona, Barcelona, Spain.
- b) Department of Internal Medicine, Hospital Clinic, Barcelona, Spain.
- c) Tropical Medicine Unit, H. De Poniente, El Ejido (Almeria, Spain).
- d) Department of Microbiology, Hospital Clinic, Barcelona, Spain.
- e) Department of Internal Medicine, Hospital General de Granollers, Granollers, Barcelona, Spain.

All authors participated in the study design. Almuedo-Riera, A. and Muñoz J. were the PIs of the study

Conceptualization: Almuedo-Riera, A.; Rodriguez-Valero N; Muñoz J.

Methodology: Almuedo-Riera, A.; Rodriguez-Valero N.

Investigation and Resources: Almuedo-Riera, A.; Rodriguez-Valero N; Camprubí, D.; Losada Galván, I. Zamora-Martinez C.; Pousibet-Puerto J.; Martinez MJ.; Pinazo MJ.; Muñoz J.

Data Curation: Almuedo-Riera, A.; Rodriguez-Valero N; Camprubí, D.; Losada Galván, I.; Zamora-Martinez C.; Pousibet-Puerto J.; Pinazo MJ.; Muñoz J.

Project Administration: Almuedo-Riera, A.;

Supervision, Formal Analysis: Almuedo-Riera, A.; Rodriguez-Valero N.

Writing - Original Draft: Almuedo-Riera, A., Muñoz J. Writing

Review & Editing: all the authors

Corresponding author: Alex Almuedo-Riera

Corresponding author email: almuedo@clinic.cat

Present address: ISGlobal, Hospital Clínic - Universitat de Barcelona, C/Rosselló

132 2º2ª, 08036, Barcelona (Spain)

Reserved space. Do not place any text in this section. Include the mandatory author checklist or your manuscript will be returned.

# Manuscript:

**Title:** Mirroring the Zika epidemics in Cuba: the view from a European imported diseases clinic.

**Authors:** Almuedo-Riera, A., Rodriguez-Valero N, Camprubí, D., Losada Galván, I., Zamora-Martinez C., Pousibet-Puerto J, Subirà, C., Martinez MJ., Pinazo MJ., Muñoz J.

**Keywords:** Zika virus, arboviruses, travel, Cuba.

#### Text:

Dear Editor, the changing epidemiology of Zika virus infection has been described before (1) and in this letter we would like to show how the local epidemiology of Zika in Cuba is reflected in imported cases in returning travellers to Barcelona.

The spread of the 2015 Zika epidemic was mostly reported in South America and the Caribbean. While increasing numbers of cases raised in South-America, Cuba was still free of cases (2). On 2nd March 2016 the first imported case from Cuba (Artemisa province ) was reported. The first autochthonous case was reported on 16th March 2016 in La Habana. Onwards, cases were reported in Camagüey, Cienfuegos, Guantánamo, Havana and Santiago. During 2017 transmission has been reported in municipalities of Arroyo Naranjo and Regla in the province of Havana (3).

Cuba has 11.230.142 inhabitants distributed in 15 provinces and 168 municipalities. The urbanization is up to 77% of the country. Based on WHO Zika virus classification, Cuba is categorized as Category 1 considered a region with new

Reserved space. Do not place any text in this section. Include the mandatory author checklist or your manuscript will be returned.

introduction or re-introduction with ongoing transmission. Cumulative cases extracted from reports of PAHO/WHO with data of 4 January 2018 show that Cuba had 187 confirmed cases being 58 imported cases with an incidence rate of 1.64 ((autochthonous suspected + autochthonous confirmed) / 100,000 population). At the 35th epidemiological week of 2017, no suspected nor confirmed disease from pregnant women were reported to PAHO/WHO. Neither were cases of Guillain-Barré syndrome or other neurologic syndromes, congenital syndrome or deaths associated with Zika infection informed (3).

Despite these global reports, a recent characterization of Zika outbreak in Cienfuegos was presented in the "Convención Internacional de Salud" in April 2018 in Havana, Cuba. During the outbreak, 614 cases were reported at week 28 of 2017 focused in the residential urban zone of the municipality. There was a correlation of these cases with the elevated infestation of *Aedes aegypti* in the area. A total of 115 cases affected pregnant woman being 39.1% symptomatic infections and 60.9% diagnosed by urine PCR, performed due to epidemiological vigilance. The clinical spectrum described in Cienfuegos is similar to other outbreaks, being cutaneous rash the main symptom present in 93.4% of the patients. Arthralgia and fever as following major symptoms were present in 48.5% and 38.1% respectively(4).

A prospective cohort study to monitor imported arboviral diseases was started in our Hospital from January 2016 to September 2018. During the study period, patients with suspected arboviral disease were identified and recruited in the outpatient clinic and emergency room of the Hospital. Serology and PCR for dengue, chikungunya and Zika virus was conducted for diagnosis. A total of 42 cases were diagnosed with Zika

Reserved space. Do not place any text in this section. Include the mandatory author checklist or your manuscript will be returned.

infection following the WHO definition. 6 patients had a positive PCR only in urine, 3 only in serum, and in 17 cases the test was positive in both samples, urine and serum. The remaining cases had a positive IgM for ZIKV, with simultaneous negative serology for DENV and CHIKV. These cases were defined as possible cases. For Zika virus real time RT-PCR for ZIKV (RealStar® Zika Virus RT-PCR kit, Altona Diagnostics), IgM and IgG antibodies against ZIKV (Euroimmun, Germany) were performed. Median age of patients was 35 years (ranging from 21 to 62) and 64% of them were women. The aim of the trip was tourism in 22 cases (52,4%), visiting friends and relatives in 13 (31%), cooperation in 4 (9,5%) and business travellers 3 (7,1%). Median duration of the trip was 18 days (range 6-181 days). There were two asymptomatic cases. From all these cases 29 (69%) did not seek pretravel advice.

Figure 1 shows the country of probable acquisition of Zika cases by year. While during the period from February 2016 to November 2016 we observed a variety of countries in South and Central America where Zika was acquired during 2017 in 2018 all Zika infections diagnosed in our clinic were in returning patients coming from Cuba. This might reflect a possible Zika outbreak or enduring transmission in Cuba despite the decline of reported imported cases of Zika in Europe.

During the last year, the incidence of Zika virus has declined in Latin America and the Caribbean. The projections of disappearance of Zika Virus predicts a low level of transmission in a context of high levels of immunized population in affected communities (5), although there are limited seroprevalence studies available to understand this fact. Some authors have expressed the possibility of new local and

Reserved space. Do not place any text in this section. Include the mandatory author checklist or your manuscript will be returned.

limited widespread of Zika infection in cities where contagion was not present during the first epidemic wave.

According to the first declared case in the island, Cuba was one of the last Zika free countries in the region during the spread of the epidemic. This could explain a lack of herd immunity in the population and the possibility of being one of the last places where transmission is ongoing or where the risk of little outbreaks is still present.

Cases diagnosed from August 2017 onwards highlight the importance of awareness in suspicion of Zika infections in travellers returning from Cuba.

Reports of emerging infectious diseases such as Zika virus from European and other non-endemic areas are valuable for the identification of potential risks due to hidden epidemics, also increasing awareness among physicians attending returning travellers from specific destinations. Furthermore, since Europe has been a feasible scenario for outbreaks of arboviral diseases due the possible transmission by *Aedes albopictus*, precise evaluation of risks prompt timely epidemiological surveillance and control to decrease the possibility of introduction of these diseases in areas where the vector is present. Recently, six autochthonous dengue cases of a family were confirmed in South Spain where *Aedes Albopictus* seems to be able to have activity during winter (6).

According to National Statistical and Information Office of Cuba (ONEI), a total of 1383939 European travellers visited Cuba in 2016, with an increasing trend over the last years. Targeted travel risk assessment become essential for monitoring the risk of travellers and the introduction of diseases in Europe. Data obtained from imported diseases clinics in non-endemic areas are essential to achieve these objectives.

Reserved space. Do not place any text in this section. Include the mandatory author checklist or your manuscript will be returned.

## **Acknowledgments -**

#### **Disclaimers** -

#### References

- Rodriguez-Morales AJ, Ruiz P, Tabares J, Ossa CA, Yepes-Echeverry MC,
   Ramirez-Jaramillo V, et al. Mapping the ecoepidemiology of Zika virus infection in urban and rural areas of Pereira, Risaralda, Colombia, 2015–2016: Implications for public health and travel medicine. Travel Med Infect Dis. 2017 Jul 1;18:57–66.
- Guzman MG, Barrington C, Castro M, Pérez D. Why Did Zika Not Explode in Cuba? The Role of Active Community Participation to Sustain Control of Vector-Borne Diseases. Am J Trop Med Hyg [Internet]. 2017 Aug 2 [cited 2018 Nov 7];97(2):311–2. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28722613
- Pan American Health Organization / World Health Organization. Zika Epidemiological Report. United States of America. September 2017. Washington,
   D.C.: PAHO/WHO; 2017 Pan. 2017 [cited 2018 Nov 8]; Available from:
   https://www.paho.org/hq/dmdocuments/2017/2017-phe-zika-situation-report-cub.pdf
- Acosta D, María H, Díaz M. Caracterización de la enfermedad por virus zika.
   Cienfuegos 2016-2017 [Internet]. [cited 2018 Nov 8]. Available from: http://www.convencionsalud2018.sld.cu/index.php/connvencionsalud/2018/paper/viewFile/228/426
- O'Reilly KM, Lowe R, Edmunds WJ, Mayaud P, Kucharski A, Eggo RM, et al.
   Projecting the end of the Zika virus epidemic in Latin America: a modelling

Reserved space. Do not place any text in this section. Include the mandatory author checklist or your manuscript will be returned.

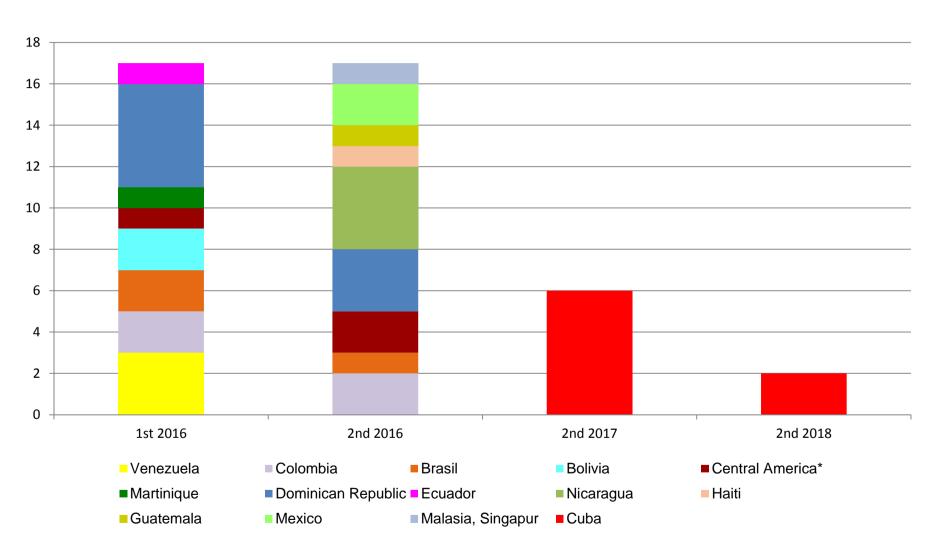
- analysis. BMC Med [Internet]. 2018 Oct 3 [cited 2018 Nov 8];16(1):180. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30285863
- Executive summary NEWS World malaria report 2018 [Internet]. [cited 2019 May
   Available from:

https://ecdc.europa.eu/sites/portal/files/documents/CDTR\_week47-2018.pdf

Address for correspondence: Alejandro Almuedo-Riera, ISGlobal, Hospital Clínic - Universitat de Barcelona. C/ Roselló 132 4th floor, 08036, Barcelona, Spain. Email: almuedo@clinic.cat

Figure 1 Trends of country of acquisition of Zika infection by semester

Figure 1 Trends of country of acquisition of Zika infection by semester



<sup>\*</sup>Central America: in 3 travellers was impossible to determine the origin of infection (1 case travelled to El Salvador-México during the 1st semester of 2016, 1 case to Panamá-Costa Rica during the 2nd semester of 2016 and 1 case to Nicaragua-Guatemala-Costa Rica during the 2 semester of 2016.