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Zika virus-induced neurological critical illness in Latin America: Severe Guillain-Barre Syndrome and encephalitis

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ABSTRACT

Zika virus (ZIKAV) is classically described as causing minor symptoms in adult patients, however neurologic complications have been recognized. The recent outbreak in Central and South America has resulted in serious illness in some adult patients. We report adult patients in Latin America diagnosed with ZIKAV infection admitted to Intensive Care Units (ICUs).

Methods: Multicenter, prospective case series of adult patients with laboratory diagnosis of ZIKAV in 16 ICUs in 8 countries.

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Results: Between December 1st 2015 and April 2nd 2016, 16 ICUs in 8 countries enrolled 49 critically ill patients with diagnosis of ZIKAV infection. We included 10 critically ill patients with ZIKAV infection, as diagnosed with RT-PCR, admitted to the ICU. Neurologic manifestations concordant with Guillain-Barre Syndrome (GBS) were present in all patients, although 2 evolved into an encephalitis-like picture. 2 cases died, one due to encephalitis, the other septic shock.

Conclusions: Differing from what was usually reported, ZIKAV infection can result in life-threatening neurologic illness in adults, including GBS and encephalitis. Collaborative reporting to identify severe illness from an emerging pathogen can provide valuable insights into disease epidemiology and clinical presentation, and inform public health authorities about acute care priorities.

1. Introduction

In March 2015, the first autochthonous transmission of Zika virus (ZIKAV) was described in continental South America [1,2]. This flavivirus likely originated in Uganda, and is presumed to have migrated eastward [3,4]. As of March 28, 33 countries in the region of the Americas have since reported confirmed cases of transmission [5].

Epidemics provide a crucial and time-sensitive opportunity to understand the epidemiology of a new or emerging infectious threat. Using prior experience with severe H1N1 influenza and Dengue outbreaks [6,7], we organized a network of 24 sentinel Intensive Care Units (ICUs) in 8 Latin American countries to detect critically ill patients with diagnosis of ZIKAV requiring admission to ICU.

Laboratory confirmation of the cases during an epidemic outbreak can be difficult, particularly in middle- or low-income countries. According to Pan-American Health Organization (PAHO), the majority of cases of ZIKAV are suspected cases (65,524 in the countries that report to our database) with only a minority having laboratory confirmation (1647) [8].

The best test to confirm infection is the Reverse Transcription Polymerase Chain Reaction (RT-PCR) in serum or cerebrospinal fluid, but it is not without disadvantages. Although first reports limited the usefulness of analyzing serum to 5–7 days after infection [9,10], recent data challenges this assertion and sets the median and 95th percentile for time until loss of positivity at 14 days (95% CI, 11 to 17) and 54 days (95th CI, 43 to 64) respectively. (Paz-Bailey G, Rosemberg ES, Doyle K et al. Persistence of Zika virus in body fluids — preliminary report. N Engl J Med. February 2017). Most cases are diagnosed on a clinical and epidemiological basis, using protocols and case definitions established in each country according to WHO definitions [11-15].

Clinical ZIKAV infection typically has a milder presentation when compared to other *Aedes*-related viral infections. However, it has been increasingly recognized to cause serious illness, particularly with cases identified during this epidemic. Evidence supporting the relationship between the ZIKAV infection and fetal microcephaly, Guillain-Barre Syndrome (GBS) and myelitis is increasing [16-19].

While microcephaly in the children of infected mothers has been the most dramatic manifestation of this neurotropic virus, various neurological disorders have been increasingly recognized in affected hosts [20,21]. In French Polynesia, a total of 42 cases of GBS were recorded during the ZIKAV outbreak (2013–14), an estimated risk of 0.24 cases per 1000 ZIKAV infections [22]. Cases of myelitis have been described during the acute phase of the infection, while GBS is more commonly a post-infectious complication [23].

The description of the clinical features of new emergent diseases is a challenge that might require gathering data concurrently with the epidemic outbreak. The present study had its focus on detecting and describing severe medical complications caused by ZIKAV infection in adults in a short period of incidence, through a multicenter, prospective and observational study of admitted patients in participating hospitals and intensive care units (ICUs) with diagnosis of ZIKAV.

1.1. Objectives

Describe the clinical presentation, demographic features, and evolution of critical ill adult patients admitted to ICUs with recent diagnosis of ZIKAV infection, through a surveillance network in 8 countries of Latin America.

2. Materials and methods

We developed a network of 24 sentinel ICUs in 8 participating Latin American countries to detect critically ill patients with diagnosis of ZIKAV between December 2015 and April 2016.

2.1. Eligibility criteria

We recruited all critically ill adult patients admitted to participant ICUs with recent diagnosis of ZIKAV infection. We established a confirmed diagnosis when the patient tested positive by RT-PCR against ZIKAV [24].

2.2. Exclusion criteria

We excluded patients without laboratory confirmation or with a plausible alternative diagnosis.

2.3. Data recollection

Clinical and demographic data were collected using an online case report form modified from the International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) [22], with modifications relevant to critically ill patients, diagnosis and treatment of neurological complications. This case report form was made available to all 24 participating ICUs through Google Forms and data pooled in Google Drive.

2.4. Statistical analysis

Data were recorded in Excel and analyzed using Stata 11 v (College Station, Texas, USA). Quantitative variables are presented with measures of central tendency and dispersion, as appropriate for the data distribution. Categorical variables are presented as counts.

2.5. Ethical statement

International ethics guidelines for biomedical research on human beings were followed (WHO, CIOMS). As no intervention or purposeful modification of biological, physiological, psychological or social variables was intended, it is considered an exempt risk research and no informed consent was required. Data were obtained anonymously, assigning different codes for hospital records and never posing a risk to professional confidentiality agreement. The research occurred in the context of a ZIKAV outbreak. Protocol was defined and one Case Report Form (CRF) was the only information-gathering instrument.