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DEVELOPING A ROBUST PUBLIC HEALTH SURVEILLANCE SYSTEM: THE KEY TO MONITORING ZIKA

[1]RUCHI PANCHOLY, MPH & AURORA SANCHEZ-ANGUIANO, MD, PHD, CPH[2]

[(1&2)]The University of South Florida, College of Public Health

INTRODUCTION

Zika virus (ZIKV) is an emerging arboviral infection, affecting over 2 million residents in 33 out of 196 (17%) countries between 2015 to 2016, and is primarily transmitted by *aedes aegypti* mosquitoes through a mosquito to human transmission cycle (World Health Organization [WHO], 2016). WHO recently declared that ZIKV is a "Public Health Emergency of International Concern" and predicted that approximately 4 million people may become infected by the end of 2016 (WHO, 2016). The geographical distribution of ZIKV is increasing due to foreign travel and climate change, and to date a total of 52 travel-associated cases were identified in the Continental United States (Centers for Disease Control & Prevention [CDC], 2016). In 2016, 50% of the reported ZIKV cases in the Continental United States were identified in Florida and Texas (N= 26) (CDC, 2016). From 2015 to 2016, 29 locally acquired ZIKV cases were identified in Puerto Rico (CDC, 2016). CDC is continuing to receive specimens for ZIKV testing and the national case count is expected to increase (CDC, 2016). The purpose of this paper is to discuss ZIKV surveillance strategies in order to monitor the ongoing spread of this epidemic which may support the rationale for the development of novel and timely interventions.

ZIKV CASE DEFINITIONS

In 2016, ZIKV become a nationally notifiable disease in the United States and the Council of State and Territorial Epidemiologists (CSTE) developed the following case definition for a suspected case: "a patient with rash or elevated body temperature (> 37.2 C) with one or more of the following symptoms (not explained by other medical conditions): arthralgia or myalgia, non-purulent conjunctivitis, headache or malaise" in someone who resides in or has visited epidemic or endemic areas within two weeks prior to the onset of symptoms (PAHO, 2016). A confirmed case of ZIKV infection is defined as: "a suspected case with a laboratory confirmed diagnosis of ZIKV through one or more tests" (PAHO, 2016). Interim case definitions developed by WHO includes the same

suspected case definition as defined by CSTE; however a probable ZIKV case is defined as a "suspected case with presence of IgM antibody against ZIKV and an epidemiological link" (WHO, 2016). According to WHO, a confirmed case is a patient. "with a laboratory confirmation of recent ZIKV infection" which includes the "presence of ZIKV RNA or antigen in serum or other samples (e.g. urine, saliva, tissues, whole blood) or IgM antibody against ZIKV and exclusion of other flaviviruses" (WHO, 2016).

MONITORING THE ONGOING SPREAD OF ZIKV

Application of CSTE and WHO case definitions involves actively monitoring for infection in travelers returning from ZIKV endemic regions and evaluating suspected cases for timing of symptom development, travel and medical history, clinical and demographic data. It is imperative that clinicians are notified regarding the case classification of ZIKV, continuously monitor for infections in suspected cases, and report cases to the local health department in order for epidemiologists to conduct timely investigations and halt locally-transmitted outbreaks from occurring. It is critical that appropriate laboratory testing is performed on suspected ZIKV cases and medical personnel should be trained on appropriate methods of specimen collection, submission, and testing procedures. Finally, the case definitions are useful for providing health departments with guidance regarding prioritization of case investigations (e.g., deciding which cases should be prioritized including: pregnant/immune compromised cases) during outbreaks.

SENSITIVITY & SPECIFICITY OF CASE DEFINITIONS

The WHO case definition can be applied to all potential ZIKV cases both internationally and in the United States. However, the CSTE and WHO case definitions do not include patients that have not travelled, but were in contact with a ZIKV fever case within the infectious period.

In addition, the definitions do not include cases' development of neurological and/or autoimmune conditions in conjunction with other ZIKV symptoms. Testing is recommended for pregnant women developing an illness with one or more symptoms mentioned in the WHO suspected case definition during or within two weeks of returning from an area with local ZIKV transmission (WHO, 2016). The WHO confirmed case definition has high specificity since it indicates that individuals must be diagnosed with ZIKV through one of several different methods including: serum, urine and/or saliva and it consists of a specific differential diagnosis for ZIKV. Since the ZIKV case definitions are considered interim and current knowledge regarding risk factors and symptoms may evolve through ongoing research, it is important for epidemiologists to remain open to the identification of novel risk factors and epidemiological links associated with the development of the virus.

ZIKV DISEASE SURVEILLANCE

As per PAHO guidelines, ZIKV surveillance should model existing surveillance systems for arboviral diseases including: dengue and chikungunya, while accounting for differences in the clinical presentation among these diseases (PAHO, 2016). A passive disease surveillance system is the most appropriate type of surveillance in tracking the ongoing spread of ZIKV at this time since it is rapid and serves as the least expensive method to monitor cases. As cases are reported by medical providers during ongoing ZIKV epidemics, a greater percentage of time and resources can be allocated to investigating individual cases. Epidemiologists from health departments can spend additional time on monitoring demographic trends in data (e.g., median age, gender distribution, and racial/ethnic breakdown of case count), major risk factors, modes of disease transmission, and timing of symptom development. Furthermore, epidemiologists should review the clinical presentation of cases, emphasize efforts on initiating novel research studies. (e.g., case-control study of infants developing microcephaly versus those that did not develop microcephaly), and developing effective control measures to halt the rapid spread of the ongoing epidemic. Syndromic surveillance via receipt of electronic lab reports in a disease surveillance system such as the Maven Outbreak Management Software is critical to identifying potential ZIKV cases (Miliard, 2016). Syndromic surveillance is critical to improving the early detection of outbreaks as cases are reported in real-time and health departments are alerted of potential ZIKV cases prior to physician reporting (Henning, 2004). However it does not replace other surveillance systems or clinician reporting of diseases (Henning, 2004).

Epidemiologists in states with higher case counts such as Florida may become engaged in active disease surveillance depending on resources available by the health department. Active surveillance may be useful in states that have high ZIKV transmission risk year round which involves the potential for *aedes* mosquitoes to replicate exponentially in subtropical climates. Active surveillance is beneficial during outbreaks as increasingly accurate case counts can inform public health decisions, policy development, and targeted interventions. In addition, a number of potentially infected cases could be missed as a result of passive surveillance and therefore conducting an aggressive campaign to determine whether existing cases remain may serve as an important factor in halting the spread of an epidemic. Finally, mosquito-based surveillance in conjunction with human surveillance is critical to monitoring the potential spread of a ZIKV outbreak, as regions with an abundance of *aedes* mosquitoes in close proximity to one or more ZIKV cases can result in local transmission. Geocoding the distribution of *aedes* mosquito pools in specific areas can assist with determining future ZIKV epidemiological patterns and predict where new cases are likely to emerge.

DISCUSSION

The actual incidence and clinical spectrum of ZIKV has not been well established. The key to monitoring ZIKV is not limited to a single surveillance system and case investigation guidelines should be developed according to the epidemiological situation in a particular region (PAHO 2016). Although interim case definitions were developed to provide global standardization and reporting of cases, surveillance efforts should be tailored according to the epidemiological spread of the disease in an area which includes tracking the spread of ZIKV into new states (PAHO, 2016). The use of the Global Public Health Intelligence Network in conjunction with an established surveillance system can enhance our ability to monitor ZIKV by providing information on potential ZIKV cases reported via the media prior to the official reporting of cases which is critical to the timely investigation of cases (Freifeld, Mandi, Reis, & Brownstein, 2008).

Long-term surveillance efforts may involve evaluating the economic impact of ZIKV on the medical infrastructure, identifying novel risk factors and circulating ZIKV lineages, and detecting epidemiological and entomological changes that may impact ZIKV transmission patterns (PAHO, 2016). Future research efforts should evaluate the incidence of maternal-fetal transmission of ZIKV by trimester, risk of developing neurological complications and adverse birth outcomes if pregnant, and investigation of possible transmission routes. Further analysis of epidemiological data is needed to understand the demographic distribution of ZIKV and risk factors associated with those developing co-infection with one or more arboviral diseases (e.g., dengue and chikungunya). Advances in our understanding of potential ZIKV transmission routes, co-infection among ZIKV and other arboviral diseases, high risk groups, and epidemiological distribution of the disease will support the rational development and application of novel interventions including: vaccines, antivirals, and integrated pest control strategies.

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