Arboviruses in Latin America and The Caribbean: A Workshop Report of the 9th INTERNATIONAL CONFERENCE ON GLOBAL HEALTH, Miami, May 7th – 9th, 2019

Abstract

The Global Health Consortium of the Robert Stempel College of Public Health and Social Work, Florida International University (GHC@FIU) conducted a workshop on "Arboviruses in Latin America and the Caribbean". The workshop was held in Miami on May 7th, 2019, within the scope of the 9th Global Health Conference organized by GHC@FIU and co-sponsored by PAHO/WHO.

This a report on the workshop, where staff from PAHO/WHO country offices in the region, representatives of scientific and academic institutions, civil society organizations, public agencies, and experts chosen for their active participation and knowledge in the field were brought together to discuss the state of the art, processes and experiences applied to the control, treatment and prevention of arboviral diseases.

Dengue: Current Epidemiological Situation and Innovation in Reporting Systems: Health Information Platform for the Americas (PLISA)

Approximately 500 million people in the Americas are today at risk of dengue. After the noticeable reduction in reported dengue incidence cases within the Americas in 2017, probably attributable to crossed immunity between Dengue and Zika, scientists envisioned three potential scenarios for the following years, said Dr. Gamaliel Gutiérrez from PAHO/WHO Regional Program for Arboviral Diseases. An explosive re-emergence is expected for 2019. The four dengue serotypes (DENV-1, DENV-2, DENV-3 and DENV-4) circulate throughout the Americas, and in some countries simultaneously.

In response to the dengue situation in the Americas, the PAHO/WHO Regional Dengue Program, along with the countries in the Americas, implemented the Integrated Management Strategy for dengue prevention and control in the Americas known as IMS-Dengue. This strategy integrates six components; patient care, social communication, environment, integrated vector management, laboratory and epidemiology. The epidemiological surveillance is part of this last component and represents one of the main challenges at Regional level, however, significant achievements are being made in terms of standardization of indicators, which will allow for timely interventions.

PLISA is the Health Information Platform for the Americas where WHO/PAHO collect and process the epidemiologic data published by the countries in their national reports.

Currently, 46 countries systematically report each week the number of cases, incidence, severe cases, number of deaths and dengue mortality and the circulating serotypes.

Sentinel Surveillance and Geo-Health Approaches

Dr. Jairo A. Méndez-Rico, Regional Advisor of Viral Diseases at PAHO Health Emergencies, shared his perspective on the challenges for laboratory surveillance or emerging and endemic arboviruses.

International Health Regulations (IHR) recommend countries to maintain active surveillance of diseases and public health events and urges to strengthen and respond quickly to events of international dispersion, and contain any threat to public health, both pathogens under elimination or control (small-pox, poliovirus, etc.) and emerging or re-emerging pathogens (Zika, Yellow Fever, SARS, MERS, Influenza).

Core capacity # 8 of the IHR (2005) obligates WHO Member States to establish mechanisms to provide reliable and timely identification and characterization of infectious agents and other hazards that may cause public health emergencies of national and international interest, including sending specimens to the appropriate laboratories if necessary.

Building the so called "IHR Laboratory core capacity" should not consist in a new vertical program but rather be an opportunity for better coordinating the existing laboratory programs and networks. A thorough examination of these networks permits the synthesis of common laboratory elements that serve as a basis for identifying the laboratory core capacity for IHR.

Four elements are particularly important to comply with IHR requirements: laboratory capacity for the priority diseases/events, specimen collection and transport, biosafety, and laboratory based surveillance.

The laboratory algorithms are NOT static and should be adjusted depending on the needs, epidemiological profile, and to respond to emergencies, taking into account new findings, biological evidence and performance of new assays

For early detection of emerging agents the negative samples are as important as the positive ones. In case of emergencies due to natural disasters, the differential diagnosis must be considered with other types of agents. Efficient mechanisms are required to identify new events, new agents (viruses), or new variants with pandemic potential.

The laboratory is critical to confirm (or rule out) new agents: Zika, Mayaro, Oropouche, EEV, West Nile Virus. Laboratory surveillance programs must be prepared to detect and report new agents in a timely manner (mandatory notification within 24 hours). However, the detection capacity does not refer only to the installed capacity; it implies networking: the possibility of having access to a laboratory that has the capacity.

A good laboratory diagnosis depends on a good sample and a well-recognized case. Surveillance results should not be used or expected to make medical decisions, the clinical diagnosis should be prioritized. Articulation of the laboratory with the epidemiology and clinical components is essential to ensure an appropriate response to the IHR

Dr. Rebecca Christofferson, Assistant Professor of Pathobiological Sciences with the Vector-borne Disease Laboratories at the Louisiana State University School of Veterinary Medicine, investigates arboviruses and much of her research focuses on uncovering the patterns that dictate why and when humans get sick. She described the Targeted Proactive Arthropod Surveillance (TaPAS) model which is aimed at the early detection of vectors for local, national, regional and international awareness and protection. The most important factors for success are the identification of the geographical areas most at risk for introduction and/or emergence, and the characterization of local and international arboviral threats: vector interactions, environmental constraints, potential reservoirs, and potential expanded ecologies in disparate geographical areas.

One of the research areas of Dr. Andria E. Rusk, from Duke University, is geospatial analysis. Dr. Rusk pointed out that WHO is calling for geospatial analysis techniques to be used for vector born disease (VBD) control and eradication. Geographical Information Systems should greatly assist targeting of interventions at the focal and household levels, leading to improved effectiveness and cost effectiveness of control.

Human behavior and environmental factors are key to understand VBD and have been found to be statistically significant. One of the way to consider these factors is through the use of mapping: geospatial methods are helpful in discovering if geographic location plays a role in the relationship between determinants and outcomes. Where things are occurring has relevance to what is actually causing our behavior and outcome.

Interventions are often not as effective as they could be. Improvements are frequently inconsistent across study sites, showing better results in one area and not in other areas. Geo-Health Framework applications can help monitor and evaluate control efforts, analyse determinants and systems, assess risks, and to monitor interventions.

Delmelle, Hagenlocher, et al. in their study of a spatial model of socioeconomic and environmental determinants of dengue fever in Cali, confirmed the role of environmental factors, as well as population density and socioeconomic status in the spread of Dengue disease. They also showed the usefulness of spatial regression in predicting Dengue fever rates with limited data availability and provided the foundation for sub-neighborhood level research investigating specific risk areas

WHO has promulgated leveraging geospatial analysis techniques for arboviral diseases control and eradication and called to use these techniques to support targeted interventions, to lead to increases in cost and intervention effectiveness.

Country experiences

Livia Vinhal Frutuoso, on behalf of the Ministry of Health Brazil, shared data on the vector control strategies and results in the country.

In 2017 more than 86% of the Brazilian municipalities were infested with *Aedes aegypti*. Their integrated vector management approach includes disseminating larvicide pyriproxyfen traps to evaluate the efficacy of the larvicide in reducing the vector population. The Wolbachia method is also applied, looking to reduce the mosquito's transmission capacity.

Among several challenges, Brazil needs to establish surveillance and integrated clinical management of arboviruses to provide a timely response, support for diagnosis, and to reduce incidence and deaths.

Ecuador is working with PAHO/WHO in the IMS for dengue prevention and control in the Americas. Dr. Aída Mercedes Soto Bravo, from the PAHO/WHO office at Ecuador, commented on the four pillars of the strategy: advocacy, developing, evaluating and communicating robust strategic information, funding, and capacity building.

Thanks to this cooperation, all areas benefited from IMS: epidemiological surveillance, laboratory capacity and networking, patient care, and the environment.

The country still faces several challenges, primarily financing and governance.

Congenital Zika virus highly impacted Brazil since the emergence of the virus. Dr. Giovanny V A França, from the Brazilian Ministry of Health, commented on the impact of these outbreaks and the integrated health and social management of congenital Zika population being developed in the country.

Over 2,000 coordination and control rooms throughout the country monitor the actions to combat *A. aegypti*. In the current epidemiological situation 11 states concentrate 85% of the 3,364 confirmed cases of congenital Zika Virus syndrome (CZS) and TORCH (93% newborn/infants; 3% fetus/miscarriage/stillborn). The national network of experts on Zika and related diseases promote joint data discussion and analysis of cohort studies on CZS in Brazil to speed up the production of more robust evidence on selected research questions.

The country's challenges are centered in promoting actions aimed at sexual and reproductive health for women and men in all life cycles, tracking children's growth and development, expanding psychosocial care, strengthening primary health care, expanding access to diagnosis, treatment and rehabilitation of children, and prioritizing the strategies to qualify surveillance and health care for congenital anomalies.

Modeling and Disease Surveillance

Modeling interventions for dengue control are a tool to support decision making. Diana Patricia Rojas, from the Department of Biostatistics at FIU, discussed the current challenges on arbovirus modeling, which range from the incidence of asymptomatic infections, overlapping symptoms, epidemiological surveillance, and vector geo-spatial localization.

Compartmental models have been used to characterize the impacts of Zika emergence on endemic dengue transmission. Borchering et al. published the results of simulations showing that regardless of the mechanism, low periods of dengue incidence are followed by a resurgence in dengue cases. It is therefore likely that countries currently experiencing low levels of dengue incidence will experience large dengue seasons in the near future. Correlations in DENV and ZIKV reproduction number could contribute to complicating or masking an association between their case counts.

Hladish et al. used realistic simulation of dengue and plausible control programs in the state of Yucatán, Mexico to show that vaccination programs can have amplifying or interfering dynamic effects when combined with expanded vector control effort.

Other applications of modeling on the transmission dynamics of Arboviruses include randomized trials to assess new technologies for vector control such as Wolbachia, irradiated mosquitoes, dispersing stations of Pyriproxyfen, and sterile mosquitoes to reduce the density of *A. aegypti.*

Gabriela Paz-Bailey, from the Dengue Branch at the US Centers for Disease Control and Prevention talked about the Dengue epidemiology in the US and its territories, to consider where a dengue vaccine may be beneficial. Passive surveillance data from Puerto Rico for 2010-2013 shows that the highest numbers and rates were in 2010 and 2013. Since then there have been few cases reported. In the past 25 years there have been several periods of increased dengue virus transmission in the US Virgin Islands, the most recent occurred in 2012-13. The US Pacific territories and affiliated independent states include American Samoa, Guam, the Northern Mariana Islands, Palau, the Marshall Islands and the Federated States of Micronesia. Periodic dengue outbreaks have been detected among the Pacific Islands since 1958, usually with only one dengue serotype at a time. Whether continuous endemic transmission occurs in any of the islands is unclear. However, a 2010 study in American Samoa among adults found

96% percent of the sampled population had dengue IgG antibody. In 2016-2018 a large dengue outbreak occurred in American Samoa with over 1,000 cases laboratory confirmed.

The current dengue vaccine requires screening for dengue serostatus before vaccination (IgG testing). Dengvaxia (Sanofi Pasteur), has been approved for use in the United States by FDA. The indication of the vaccine includes children 9-16 years of age, who have a laboratory confirmed previous dengue infection and live in an endemic area such as the US territories of American Samoa, Guam, Puerto Rico, and the US Virgin Islands.

Models and challenges for dengue forecasting were presented by Dr. Michael A. Johansson, also from the Dengue Branch, Division of Vector-Borne Diseases at the CDC. There are several models for dengue forecasting, most of which are retrospective and vary in targets and evaluation metrics. No quantitative models are being routinely used for decision-making. Both accuracy and confidence (i.e. certainty/uncertainty) needs to be assessed. Infectious disease forecasting can improve by improving the data collected, the analytical tools, the computational power, and also by standardizing evaluation and interoperability.

The CDC epidemic prediction initiative looks to connect researchers to data and build a community among the CDC, researchers, multiple US Departments & Agencies, Councils of States and territorial epidemiologists.

Surveillance and forecasting go hand in hand, the current forecasting methods improve expert knowledge and can be helpful for situational awareness. Yet, improved analytics can improve our ability to predict and respond effectively to arboviral disease epidemics.

Dr. Haroldo Bezerra, from PAHO/ WHO, talked about the plan of action for entomology and vector control (2018 – 2023). The objective of the plan is to strengthen regional and national capacity for the prevention and control of key vectors and reduce the transmission of VBDs. The Plan of Action focuses on prevention, surveillance, and integrated vector control for arboviruses (e.g., Chikungunya, Dengue, Yellow Fever, and Zika), Malaria, and selected neglected infectious diseases (Chagas disease, leishmaniasis, lymphatic filariasis, onchocerciasis, schistosomiasis, and others) through integrated and innovative strategies, using efficacious, sustainable, low-cost, evidence-informed interventions, and best practices for vector control.

For the period 2018-2023, it is important that the countries of the Americas pledge to support this Plan of Action to reduce the burden and threat of VBD through effective, locally adapted, and sustainable vector control and best practices, including IVM. With technical support from the Pan American Sanitary Bureau, the countries will implement strategic lines of action, as appropriate to their contexts, needs, vulnerabilities, and priorities: *a)* to accelerate regional progress toward enhanced prevention and control and, in some cases, the elimination of selected VBDs; *b)* to standardize IVM, tailor it to the Region's needs, and expand it to include the use of new technologies, when feasible; *c)* to improve insecticide resistance monitoring and management; and *d)* to strengthen human resource capacity in public health entomology through more and greater opportunities for entomology education and training.