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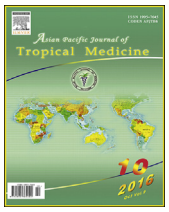

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Zika virus is arriving at the American continent

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Dear editor,

Zika virus (ZIKV) is the last arbovirosis to arrive to the American continent, following dengue virus (DENV) in 1990, West Nile virus (WNV) in 1999 and chikungunya (CHIK) at 2013. At this time, it represents a pandemic at this continent [1].

It was first isolated from a rhesus monkey at the Zika forest near Kampala, Uganda in 1947 and from mosquito *Aedes africanus* in 1948 [2]. It is a member of Flaviviridae family, along with yellow fever virus (YFV), DENV, WNV and Japanese encephalitis virus [1,3]. The first reports of human infection were in Uganda and Tanzania, in 1952 [4]. Since then, ZIKV has spread from Africa to Southeast Asia and Pacific Islands [1,4,5]. The first epidemic started in 2007 at Yap Islands, Micronesia, which was also the first detection of ZIKV outside of Africa and Asia, with an estimate of 73% population infected and 49 confirmed cases [6]. The second and largest epidemic was at French Polynesia, reaching 28 000 medical attentions which represented about 11% of population [7] and almost 70% in some islands [8]. Hence it spreads through the Pacific, where it is still actually circulating in New Caledonia, Cook Islands, Vanatu, Solomon Islands, Fiji and Easter Island [7]. It is believed that the last one make the epidemiological entrance of the virus to the Americas, on May 2015 in Brazil [8,9].

Today ZIKV has autochthonous transmission in 33 countries and regions of the American continent [10], where the main vector is *Aedes aegypti* (*A. aegypti*), also carrier of DENV, YFV and CHIK. In 1947 *A. aegypti* was eradicated from 18 countries through efforts of Pan-American Health Organization (PHO) and the use of organophosphate DDT. However, DDT use was left in the 1960s and the mosquito returned, so it is present now [11]. There are reports of six countries (Argentina, Chile, France, Italy, New Zealand and United States) without the presence of the vector and local acquisition of the disease, probably by sexual intercourse [10].

In Peru, *A. aegypti* reemerged in 1984 at Loreto and spread to San Martin region and country's central rainforest zone. Towards 2000 the vector was detected in Lima region, at five districts (La Victoria, El Agustino, Rimac, San Juan de Lurigancho, Cercado de Lima) and later on it spread to other 29 districts. By 2011, the mosquito presence involved 269 districts and 18 regions of Peruvian territory, where about a third of the total population lived [12]. Five haplotypes of *A. aegypti* have been found, which indicates that genetic variability is not only because of its active migration but also because of the passive migration by human activities [13,14]. Also, *A. aegypti* has expanded its habitat due to climate change and El Niño phenomenon, both of which increase temperature and humidity [15].

ZIKV incubation period is estimated between three and seven days (range 3–14) after host infection [16]. Course tends to be mild, last days or weeks and it is suspected that individuals acquire immunity after first episode because reinfection has not been reported yet [17,18]. Clinical symptoms, present in 20% of cases, consist in onset of fever and pruriginous maculopapular rash, arthralgia and/or non-purulent conjunctivitis. Common manifestations are nonspecific including fever, malaise, headache and joint pain associated to rash [17–19]. There are neither reports of hemorrhagic complications, nor synergy or increased severity when there is coinfection with DENV or CHIK [20,21].

Infection is associated with neurological complications, being the main and most alarming Guillain–Barré syndrome (GBS). French Polynesia epidemic showed an increase of GBS cases, which was lately associated in a case–control study of 42

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patients [22]. Thirteen countries and territories reported raising incidence of GBS while ZIKV was circulating [10]. Also, in Brazil, within the 2014–2015 period, the incidence of microcephaly in newborns increased 20 times [1], reporting initially 141 suspected cases in Pernambuco, followed by other northeastern states (Paramaiba, Rio Grande do Norte), alongside spontaneous abortions and miscarriages [23]. First months of pregnancy of the newborns match the highest incidence periods of ZIKV at northeastern Brazil and there was not family history of either genetic diseases or positive tests for other infections [24].

Causal association was carried out by Instituto Evadro Chagas through isolation of ZIKV from brain tissue and detection of virus in cerebrospinal fluid (CSF) and, brain tissue and fragments of viscera (heart, lungs, liver, spleen, kidney) of a newborn that died shortly after birth [23,24]. In addition, ZIKV IgM was found in CSF of 12 newborns with microcephaly and negative to TORCH test (*Toxoplasma gondii*, other agents, rubella, cytomegalovirus and herpes simplex virus types 1 and 2), DENV and CHIK [24]. Two cases reported ZIKV in amniotic fluid and microcephaly by ultrasound [25]. Centre for Disease Control and Prevention (CDC) confirmed the presence of virus in cerebral tissue and placenta using polymerase chain reaction (PCR) and immunohistochemistry methods [26]. Besides neurological damage, there is evidence of ocular compromise as macular atrophy, and both macular and perimacular injuries with optical nerve atrophy [24]. Brazil has reported 739 microcephaly cases and other fetal malformations until 21st November, 2015 [9].

One of the major difficulties is the lack of commercial serological and molecular diagnostic tests. Those now available are limited to reference laboratories and cannot fulfill public health demand. It is necessary to develop fast tests (immunochromatography), and serologic (ELISA IgM, IgG) and molecular methods for early diagnosis of ZIKV infection, according to circumstances of involved countries, most of which are low or middle income countries [1,24]. Use of the diagnosis tests should be prioritized for susceptible population as pregnant women and individuals with chronic or autoimmune diseases [24]. On the other hand, these tests will contribute to a better case manage, preventing and treating the complications according etiology [1].

ZIKV is not well known comparing to other virus. However, due to its neurotropism it causes microcephaly and is associated with GBS. Presence of *A. aegypti* in many regions of Peru makes it easier to spread and could be present in population, not being detected well timed because there is a lack of diagnosis methods. It is important to take appropriate control measures and lower case numbers for the control of mosquito. A quick, effective and combined response is needed by the World Health Organization (WHO) Member States through financial aid and assistance. Also, a vaccine for this virus should be developed to prevent not only the infection but also its main complications.

Conflict of interest statement

We declare that we have no conflict of interest.

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