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Review

Knowledge of a re-emerging arboviruses: Chikungunya, Strategies for control, Esmeraldas, Ecuador

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Chikungunya Fever is a disease caused by infection with Chikungunya (CHIKV) virus, alphavirus belonging to the Togaviridae family transmitted by the bite of female mosquitoes *Aedes aegypti* and *Aedes albopictus*. Due to the widespread distribution of *Ae. aegypti* and *Ae. albopictus* is not demonstrated that the presence in the country is susceptible to invasion and spread of the virus. PAHO / WHO reports that the epidemiological week 26, 2014 (updated June 27, 2014), the backlog of cases from 2013 to 2014, reported in countries or territories with indigenous transmission of CHIKV in the Americas, is 259,723 suspected cases and 4,721 confirmed cases, for an incidence rate of 296.6 cases per 100,000 population. The impact of this infection on public health by the tendency of Ecuador and its geographical distribution is unknown, however it is estimated that due to the wide spread of the vectors involved in the region, major epidemics could occur as it happened in other parts of the world where the disease has been introduced into virgin populations. Ecuador does not escape to this reality. Close surveillance, strengthening the diagnostic capacity, entomological strategies involving permanent and sustained action to prevent and control disease community participation is required.

Keywords: virus-vector-surveillance-epidemiologic-entomologic surveillance- participation

INTRODUCTION

The Chikungunya fever is a viral disease transmitted to humans by mosquitoes. It was first described during an outbreak in southern Tanzania in 1952. It is an RNA virus of the genre Alphavirus, family Togaviridae. The name

derives from the word "Chikungunya" in Makonde, ethnic group living in southeast Tanzania and northern Mozambique. Roughly means "that which bends down" in reference to the stooped appearance of patients because of joint pain (Jupp et al., 1988).

The Chikungunya virus is characterized by the sudden appear of high fever and myalgia, joint pain, accompanied by muscle aches, headache, nausea, fatigue and rash accompanied resistant to common

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allergy itching. There is no vaccine against this viral disease, it is not fatal but can affect the immune system or cause bleeding culminating in the death of the patient. Therefore, the only recommended medications are those intended to relieve pain and fever. Importantly, most people recover, but in some cases joint pain may last for months or even years.

The virus is transmitted to humans through the bite of *Aedes aegypti* and *Aedes albopictus* mosquitoes. Mosquitoes become infected when they feed on a person already infected with the virus. Infected mosquitoes can transmit the virus to others through bites. Both mosquitoes behave as transmitters of dengue virus (CDC, 2014).

In December 2013, the Pan American Health Organization, warned countries in the region of the Americas of a native transmission in Saint Martin, a situation that increased the risk of transmission in the Caribbean (Public Health Ministry of Dominican Republic, 2014). WHO recently stated that the Chikungunya epidemic is "serious" in the Americas and estimate that about 350,000 cases (OPS, 2011) are already registered.

The virus has also been introduced in Central American countries such as El Salvador and South American countries like Brazil, Paraguay, Venezuela and more recently in Colombia. Due to the alert that exists in other countries by the Chikungunya virus, the Ministry of Health, through a Press Release indicates that so far Ecuador only has registered one case of Chikungunya fever (MSP Ecuador, 2014).

The register of a case involves the need to strengthen the surveillance system and clinical expertise, to address virus introduction and management of cases that are filed, because the country has the socio-environmental and epidemiological conditions for the disease development (climate, vector, weak health control on immigration borders).

Moreover, there is the presence of the vector *Ae. aegypti* who behaves as a common vector for Chikungunya and Dengue virus. In this regard, this year (until Epidemiological week No. 42) has caused 14,314 cases of dengue: without warning signs 12,832, with warning signs 1423 and 59 severe cases, which compared to the previous year (2013) reported to the same Epidemiological week (N° 42) 10,152 cases; 9,235 no warning signs, warning signs 862 and 58 cases of severe dengue (MSPE, 2014).

Due to this situation and considering the efforts of local health teams with less community participation, arises the need to publish this information to alert the community, leaders, universities and decision-makers in relation to policies that should be implemented after the introduction of the virus in Ecuador, and the role of sectorial integration in the application of appropriate strategic actions of epidemiological and entomological surveillance of this disease.

Geographical Distribution

The Chikungunya virus is native to sub-Saharan Africa where it is kept in a sylvatic cycle between mosquitoes and nonhuman primates. The virus causes sporadic outbreaks of disease in humans. There are references of this disease in Africa since the eighteenth century. Apart from Africa, it has been detected sporadically in parts of Asia (including Sri Lanka), probably introduced from Africa (Lumsden, 1955). During the years 2005-2006 the virus caused major epidemics in some islands in the Indian Ocean, particularly in the islands of Reunion, Comoros, Mayotte, Madagascar, Mauritius, Seychelles and Maldives (Konstantin *et al.*, 2011). Apparently this epidemic wave began in 2004 in coastal areas of Kenya (Mombasa) from where it spread to the affected islands in subsequent years. In turn, between 2006 and 2008 were major epidemics of Chikungunya in India, with hundreds of thousands of reported cases (Yergolkar *et al.*, 2006). International travel has facilitated the introduction of the virus in endemic areas, documented cases in France, Italy, Australia and the USA (Lanciotti *et al.*, 2007; Pistone *et al.*, 2009).

The agent

Chikungunya virus (CHIKV) belongs to the genus Alphavirus, family Togaviridae. Corresponds to antigenic Semliki Forest virus complex that also contains the Mayaro, O'Nyong-Nyong and Ross River virus. The virus emerged from a sylvatic cycle in Africa, resulting in three genotypes: Asian, West African and East / Central / South African, known by the acronym ECSA (RENAVE, 2013).

Through the years the virus has spread in the world and has undergone several genetic mutations that have allowed it to adapt to new epidemiological conditions. During the 2005 outbreak in Reunion Island it acquired a mutation called A226V in the envelope protein E of CHKV of the ECSA genotype and it was associated with increased replication capacity of the virus in *Ae. albopictus* (Vazeille *et al.*, 2007).

Mutated virus has spread from the Indian Ocean to East Africa and Asia, as well as the transmission in Italy. However, phylogenetic analysis showed that the CHKV with the ECSA genotype infected native cases of Reunion island had no mutation in the A226V (Vazeille *et al.*, 2007) position. Likewise, phylogenetic analysis of the complete nucleotide sequence of the virus detected in the first cases of San Martín, showed that belongs to the Asian genotype (Leparc –Goffart *et al.*, 2014). Since then, virus carrying this mutation (not known whether if acquired once or several independent mutation events converged) have spread rapidly and efficiently by all those Indian regions where *Ae. albopictus* predominates

(Jiménez –Clavero, 2013). In this regard, studies show that populations of *Ae. albopictus* in the Americas are capable of transmitting New Caledonia strain (NC / 2011-568) belonging to the Asian genotype (Edward et al., 2007). However, the first two cases in the Americas native belong to the ECSA strain, but not the mutation at position 226 (Yergolkar et al., 2006).

Having a high mutation rate of the virus increases the chance of replication in different hosts (Weaver, 2006). In this regard, the alphaviruses are specific to the vectors employed. This specificity is because a long evolutionary process and adaptation of the virus to efficient vectors (Forshey et al., 2010; Weaver, 2006) which may be located in the receptors in the midgut of bloodsucking mosquitoes, which allows them to pass through different barriers within vector and go to their circulatory system (Pascoa et al., 2002).

Transmission

After the bite of a mosquito infected with CHIKV, most individuals showed symptoms after an incubation period of three to seven days (range: 1-12 days), with possibilities of asymptomatic cases in patients with antibodies to CHIKV and according to serological studies range from 3-28%, who also contribute to the spread of the disease in the presence of the vector (OPS, 2011). The natural cycle of Chikungunya is human-mosquito-human; *Ae. aegypti* and *Ae. albopictus* are the vectors responsible for transmission. These species bite during the day with peak activity in the early morning and late evening. Both are outside of homes, although *Ae. aegypti* also shows activity in the interiors. In studies of blood feeding activity of *Ae. aegypti* conducted in Uganda in East Africa, activity at dusk (one or two hours before sunset) was found; smaller peak, two or three hours after sunrise (Mc. Clelland, 1959) was also observed. Similarly, in Bangkok Thailand, a first peak of blood feeding activity was observed after 08:00 hours of the morning (Yasuno and, Tonn, 1970). As for the pattern of feeding activity of *Ae. albopictus*, a study carried out in parks and green areas in the city of Caracas, Venezuela, located between 3,000 and 5,000 feet showed two peaks of activity, the first at 07:30 - 9:30 and the second 14:30 - 17:30 (Zorilla et al., 2011).

There is no direct transmission from person to person (MSSSI, España, 23). Theoretically, the virus can be transmitted by transfusion, transplantation of tissues, organs and cells (CDC, 2011; Couderc, 2012). Although until now has not been reported secondary to transfusion case, infection was reported from exposure to blood (health workers). Vertical transmission has been documented in pregnant women affected by the Chikungunya fever with a vertical transmission rate close to 50% in viremic patients (Robillard et al., 2006).

Reservoir

The reservoirs are humans during epidemic periods. In inter-epidemic periods, nonhuman primates and some other wild animals such as bats, rodents, birds or other vertebrates act as a reservoir (OMS, 2014 27). However, this situation has not been proven in the Americas.

Natural history of the disease

It refers to the proper way to evolve that each disease has when it leaves its own course without any other intervention (Padrón- Malpica, 2013 28). The onset of the disease process involves the main vectors for CHIKV: *Ae. aegypti* and *Ae. albopictus* and reservoirs. Humans are the main reservoir of the virus during epidemic periods. Presymptomatic phase is the incubation period in which the mosquitoes acquire the virus from a viremic host, after an average incubation extrinsic period of 10 days (IPK, 2014; MS SSI, Span, 2014 29 30). After that, the mosquito is capable of transmitting the virus to a susceptible host. During the symptomatic or clinical phase, CHIKV can cause acute (OMS/OPS, 2014 31), subacute and chronic disease.

Acute disease is usually characterized by sudden onset of high fever and severe joint pain. The acute phase lasts between 3 and 10 days (Renault et al., 2007 32). The most common symptom is persistent inflammatory arthralgia in the same joints that were affected during the acute stage. During the acute phase of this disease, virus produces high-titer viremia. Later in the subacute phase rheumatic symptoms reappear as distal polyarthritis, exacerbation of pain in previously injured joints and bones and subacute hypertrophic tenosynovitis in wrists and ankles two or three months after the onset of the disease (Fourie and Morrison 1979 33). Finally, the chronic symptoms phase remain for more than four months (Alladi et al., 2010 34).

The CHIKV fever may not have the characteristic manifestations or may coexist with other infectious diseases. In this sense, the differential diagnosis should include other diseases such as dengue, leptospirosis, malaria, meningitis, post - infectious arthritis and other viruses such as rubella, measles, parvovirus and enterovirus (Jiménez- Corona, 2014 35).

Epidemiological Surveillance

Currently, native transmission exist in 45 countries or territories in the Americas, seven of them are for the continental massif (USA, Mexico, El Salvador, Costa Rica, Venezuela, Guyana, Suriname and French Guyana) (Jiménez- Corona, 2014 35). In Chikungunya fever attack rate of virgin populations may be up to 50%

(OPS/OMS, 2013 36). In localities affected by the recent epidemic ranges from 38 - 63%, according to WHO (OPS, 2011 4). Letality rate is 0.45% and the incidence rate is 76.3 per 100,000 inhabitants (33).

In this regard, the incidence rate of dengue in Ecuador for 2012 is situated at 122.26 cases per 100,000 inhabitants and by 2013 was 86.00 per 100,000 inhabitants, being more prevalent in the provinces of the coast and eastern region (Guayas, Manabi, Los Rios, El Oro, Esmeraldas, Santa Elena, Sucumbios, Napo, Orellana, Santo Domingo de los Tsáchilas, Morona Santiago, Pichincha, Bolívar, and Canar), which is associated with a high rate of infestation of the vector *Ae. aegypti*, and hence a high potential for viral transmission Chikungunya and Dengue (MSP Ecuador, 2014 5).

The epidemiological monitoring of virus must include strengthening the surveillance of dengue, taking the differential diagnosis and should be aimed at: (i) detect the introduction of Chikungunya virus in one area, (ii) to track the disease once introduced or (iii) monitoring of the disease when it is established. It is recommended for those countries without indigenous cases of Chikungunya: testing for stopping the virus in a percentage of patients with fever and joint pain, or fever and arthritis of unknown etiology such as in cases with negative tests for malaria and dengue (OPS/OMS, 2013).

Operational Definitions

Health teams should meet the guidelines established for the management of cases (OPS/OMS, 2011 25). However, today each country has adopted the guidelines in response to the prevention and / or characterization of cases (MSPPS de Colombia, 2014; MSP Ecuador, 2014; MSP Rep. Dominicana, 2014; RENVE, 2013 3 5, 12, 37). In this regard, it must be considered any person with fever and arthritis acute onset or severe arthralgia, resident or visiting areas with transmission of CHIKV during the two weeks preceding the onset of symptoms, with contact to a confirmed case and find some epidemiological link transmission areas. In addition, all suspected cases with positive result by any of the following specific laboratory tests: detection of viral RNA by RT-PCR in serum samples taken in the first five days of onset of fever, serum IgM from 6m, 5^{to} day ° to the onset of fever, detection of IgG antibodies in paired samples, with difference of at least one week in making and increased at least four times the antibody titer for CHIKV (Ministerio de Salud y Protección Social Colombia; RENAVE, 2013 4,37).

Diagnosis Methods

To establish the diagnosis several methods can be used. Serological tests such as enzyme-linked immunosorbent assay (ELISA), may confirm the presence of IgM and IgG antibodies against Chikungunya virus. The highest concentrations of IgM are recorded between 03 and 05 weeks after the onset of disease and persist about 02 months (Alladi et al., 2014 34).

The virus can be isolated in the blood in the first days of the infection. There are several methods of Reaction in the Polymerase Chain, but its sensitivity is variable. The PCR-TR is currently the most sensitive method to detect and quantify viral mRNA VCHIK (CDC.OPS/OMS, 2014; Jiménez-Corona, 2014; Saxena et al., 2008 35, 38). The RT-PCR products from clinical samples can also be used in the genotyping of the virus, allowing the virus to compare samples of different geographical origins (OPS-OMS, 2013 36).

However, for immunological identification the cross-reactivity should be considered with other members of serogroup mainly to the O'nyong nyong virus (ONNV) which also produces a similar clinical picture and it shares the geographical distribution in Africa and the vector transmission (OPS, 2011 4).

Entomological Surveillance

Before the presence of CHIKV entomological surveillance system must constantly maintain fixed monitoring stations, adequate coverage, weekly data collection and systematic reporting. Entomological surveillance must be recognized using ovitraps. This strategy will identify the presence, distribution and density of vectors (González-Roldán, 2014 39).

Also in those countries with the availability of a Level III Biosafety laboratory, entomo-virological surveillance identifies the presence of virus (Mazzali de Ilja, 2004 40). Short-term supervised and monitored entomological surveillance must be undertaken for the elimination of breeding (containers guasarapos) and vector control strategies. Where possible introduce or retain sentinel unit if exists for temporal space → risk analysis in localities that have shown the historical high rates of transmission by the vector for dengue.

When addressing this aspect is important to consider the entomological community epidemiological surveillance, as it will allow the participation of the community and indicate which shall be started and concentrate specific actions to combat the vector.

Community active search for Chikungunya is called for tracking of intentional cases that may be happening and have not consulted a lending institution for health services, through epidemiological structured interview (MSPS Colombia, 2014 37) crawl. This monitoring is performed by the presentation of a suspect or confirmed imported case who entered the country in the acute phase and has been in dengue endemic areas, before detection of the case. Therefore, it is important the knowledge of the community about the disease. When communities are oriented they will inform appropriate levels or will start searching the geographical perimeter around the place where they reside or stay and will investigate all the places visited during the transmission period which are also considered at risk. Thus, community participation rests with different social actors: neighbors, community leaders, neighborhood associations, among others and socialized disclosure of information in schools: schools, colleges, educational institutes and universities constitutes the fundamental support to reduce outbreaks of vector.

Measures and Management of CHIKV fever cases

There is no specific antiviral drug treatment for CHIKV. It is recommended symptomatic treatment after excluding more serious diseases such as malaria, dengue and bacterial infections (OPS, 2011 4).

Acute cases

Symptomatic treatment includes support rest and the use of acetaminophen for relieving fever, and ibuprofen, naproxen or other nonsteroidal anti-inflammatory agent (NSAID) to alleviate arthritic disease component. It is not advisable to use aspirin because of the risk of bleeding. In patients with severe joint pain corticosteroid use short-term approach is to make a risk-benefit assessment. It should be advised patients to consume large amounts of fluids to replace lost fluid by sweating, and other insensitive (Sissoko et al., 2009 41).

Cases of Subacute and Chronic Disease

The period of convalescence may be prolonged (sometimes up to a year or more) and persistent joint pain may require analgesic treatment, including prolonged anti-inflammatory therapy (OPS, 2011 4). Disabling peripheral arthritis tends to persist for months, if refractory to other agents may occasionally respond to short-term corticosteroid. Ortiz, 2013 42).

Patients with refractory joint symptoms can evaluate alternative therapies such as methotrexate (Sissoko et al., 2009 41). In addition to pharmacotherapy, cases with prolonged joint pain and stiffness can find benefits from a progressive physical therapy program. The movement and moderate exercise tend to improve morning stiffness and pain, but intense exercise can exacerbate symptoms.

Recommendations for patient isolation

To avoid infecting other people at home, communities or hospitals, patients with acute CHIKV should be avoided getting bitten by mosquitoes *Ae. aegypti* and *Ae. albopictus* during the viremic phase, which generally coincides with the first week of illness. As these mosquitoes bite during the day, from dawn to dusk and after dark if artificial light is high it is recommended them to be protected with insecticide-treated nets (TI) or stay in a place protected with mesh (CDC,2014; MSP Rep. Dominicana 2014 2,3). In addition, physicians or health workers who visit CHIKV-infected patients should avoid mosquito bites by using insect repellent and wearing long sleeves and pants.

Preventive Measures

The main epidemiological key strategy on the issue to avoid circulation and disease progression in a region is to detect "native cases", this means that the infected mosquito is already transmitting the virus to people from one place with no registered cases.

Monitoring in airports, seaports and informal border crossings should be kept active, due to the possibility of introducing the virus in the country. In this sense, the action is to check and control of people arriving to the region and especially, those whose area of origin is highly transmissible as Colombia, Venezuela, Dominican Republic and other Caribbean islands.

In parallel, SNEM teams in different cantons catalogued as risky for dengue transmission, where the incidence curve translates to an epidemic situation until Epidemiological week N° 28, with frankly downward trend until Epidemiological week N° 31, with its lowest level and maintained until week 41, reaching at a success area in the endemic channel of the Province of Esmeraldas, compared to the same period in 2013; unlike the national curve that translates an alert situation at week 28, decreasing slightly until week 30, a safety zone on the incidence of the previous year to EW 41 where it remains in the same area (6); in this regard epidemiological surveillance with emphasis on permanent entomological studies and sustained ethology of *Ae. Aegypti* must be

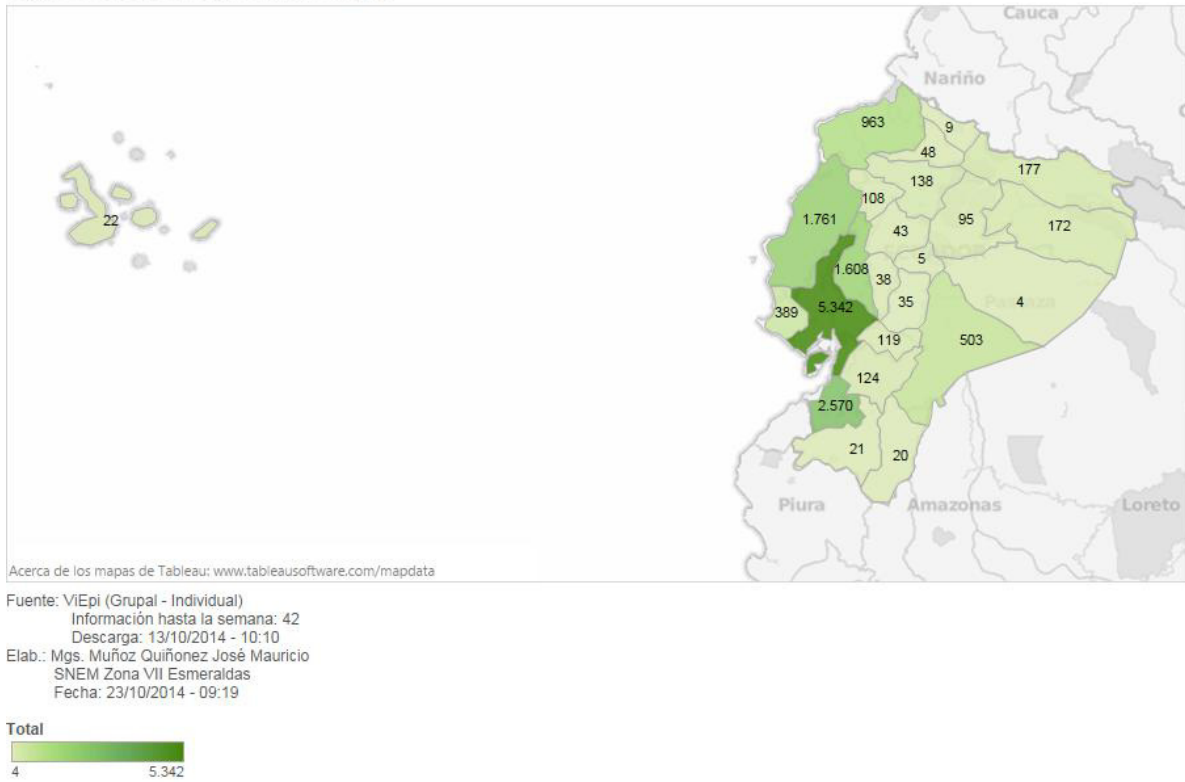


Figure 1. Number of cases of Dengue by provinces in Ecuador. Year 2014.

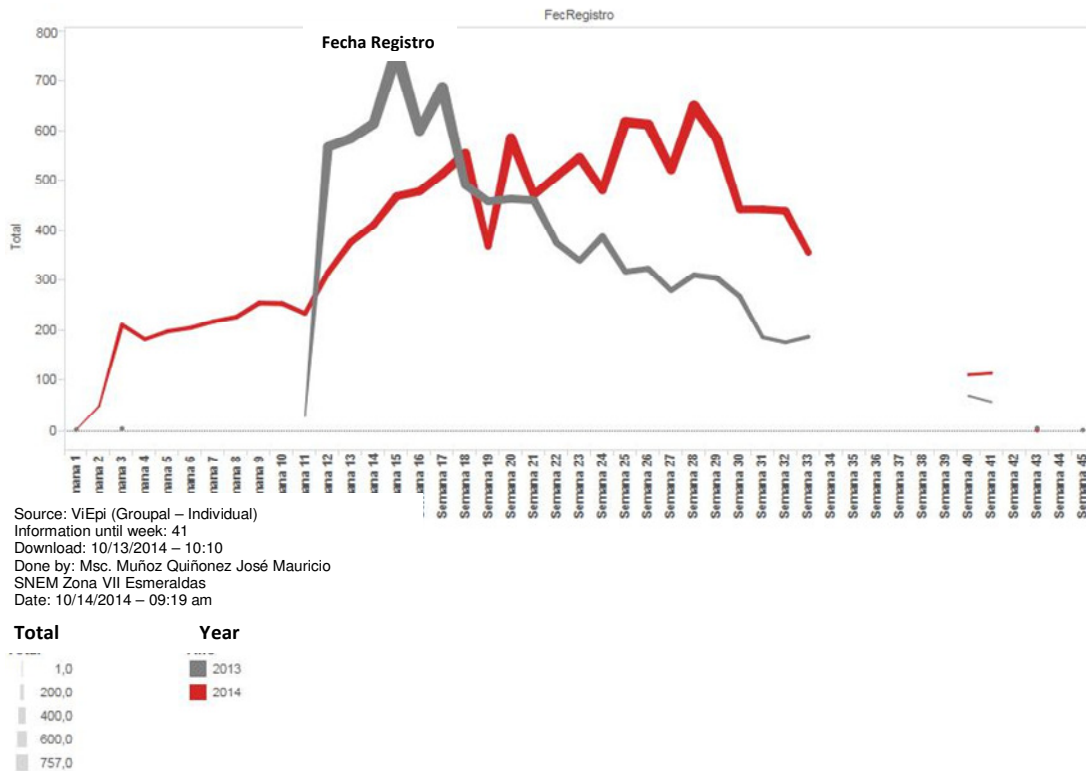


Figure 2. Behaviour of Dengue in Ecuador per epidemiological weeks. Years 2013 and 2014.

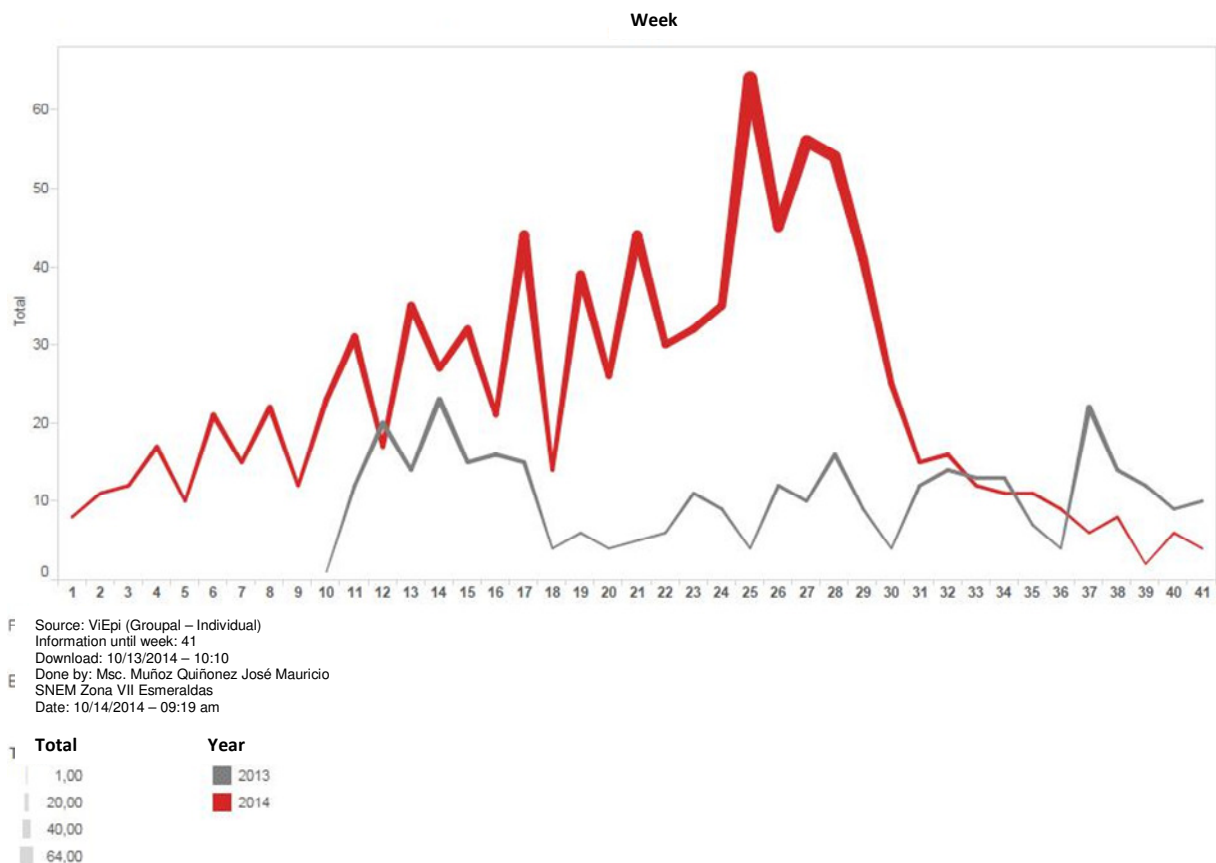


Figure 3. Comparison of Dengue cases in Ecuador per weeks and years. Years 2013 and 2014.

made, since they behave as a parallel transmitter of Dengue virus and Chikungunya virus (Figures 1, 2 and 3).

At places with busiest sites and concentration of people, strategies should involve training communities through “mingas” towards the elimination of breeding sites, cleaning and brushing casks.

Another aspect of particular importance should be initiated and strengthened by the institutions of public and private health, and local authorities who have responsibility for ensuring the health of the residents, such as MSP, IESS, gubernation, municipality, police, armed forces, parish councils and others, channeled through health institutions.

Susceptibility

All previously infected with CHIKV individuals are at risk of becoming infected and developing the disease. It is believed that once exposed to CHIKV, individuals develop lasting immunity that protects against reinfection (OMS, 2014 27).

Risk for travelers

Travellers returning from affected areas suspected of being infected with Chikungunya virus after its stay in the Caribbean, Central and South Americans countries affected, who have experienced the above symptoms until seven days after arrival, should seek immediate medical care and report on their recent trip and origin (MSSSI, España, 2014 30).

The Pan American Health Organization and World Health Organization-PAHO / WHO does not recommend any measure restricting travel to affected countries in relation to this event.

CONCLUSIONS

Due to the rapid spread of the virus, cases should be reported immediately. Added to this, prioritize the existence of public health laboratories in the country with differential diagnosis of dengue and CHKYV and increase responsiveness to detect and confirm cases. It is important to strengthen the actions of health promotion

and implement an effective communication strategy with the population in order to reduce the density of the vector.

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