

## **Dengue, Zika Fever and Chikungunya: Biological Aspects and Situation in South America between 2015 and 2020**

**Dengue, Zika Fever e Chikungunya: Aspectos Biológicos e Situação na América do Sul entre 2015 e 2020**

**Dengue, Fiebre Zika y Chikungunya: Aspectos Biológicos y Situación en América del Sur entre 2015 y 2020**

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### **Abstract**

Arbovirose are diseases caused by arthropod-borne viruses and affect the region of the Americas, including the South American continent, where provoke impact on the economy and public health. Among the more than 500 viruses registered in the International Catalog of Arbovirus, those that cause dengue, zika fever and chikungunya stand out. Thus, this article comprises a descriptive study based on secondary data where we compare biological and diagnostic aspects these diseases, as well as assessing its presence, between 2015 and 2020, in the countries that integrate the su-american continental portion. Despite the considerable progress made in recent years to better understand the molecular aspects of etiologic agents and clinical conditions, the scenario is complex and the three arboviruses caused outbreaks in South America, in the period described, even in different proportions, with dengue remaining the most common arbovirus infection, whose the incidence rates fluctuate each analyzed year. The fight against arboviruses must be permanent and requires well-founded intersectoral policies and individual responsibility. Government interventions need to tighten up to implement measures to combat, and health and education systems could align more effectively for a stronger work to raise the awareness that is triggered from basic education students, helping in the continued education of the population in favor of a more oriented and prudent society. It is also necessary to reflect on the effectiveness of information systems to decrease the problem of underreporting that prevents showing the real scenario of these diseases.

**Keywords:** Arboviruses; Underreporting; Epidemiology.

### **Resumo**

Arboviroses são doenças causadas por vírus transmitidos por artrópodes e afetam as Américas, incluindo a América do Sul, onde provocam impactos na economia e na saúde pública. Entre os mais de 500 vírus registrados no Catálogo Internacional de Arbovírus, destacam-se os que causam dengue, febre zika e chikungunya. Assim, este artigo compreende um estudo descritivo baseado em dados secundários, onde são comparados aspectos biológicos e diagnósticos em relação a essas três enfermidades, bem como avaliamos sua presença, entre 2015 e 2020, nos países que integram a porção continental sul-americana. Apesar do considerável progresso feito nos últimos anos para melhor compreender os aspectos moleculares dos agentes etiológicos e das condições clínicas, o cenário é complexo e os três arbovírus causaram surtos na América do Sul, no período descrito, em proporções diferentes, e a dengue a mais comum, cujas taxas de incidência variam a cada ano analisado. O combate aos arbovírus deve ser permanente e requer políticas intersetoriais bem fundamentadas e responsabilidade individual. As intervenções governamentais precisam estreitar-se para implementar medidas de combate, e os sistemas de saúde e educação poderiam se alinhar de forma mais eficaz a fim de um trabalho mais forte de sensibilização que seja desencadeado desde os alunos da educação básica, auxiliando na educação continuada da população a favor da uma sociedade mais orientada e

prudente. Também é necessário refletir sobre a eficácia dos sistemas de informações a fim de minimizar o problema da subnotificação, que impede de mostrar o real cenário dessas doenças.

**Palavras-chave:** Arbovírus; Subnotificação; Epidemiologia.

### Resumen

Los arbovirus son virus transmitidos por artrópodos pertenecientes a diferentes familias taxonómicas y afectan a las Américas, incluso América del Sur, donde impactan la economía y la salud pública. Entre los más de 500 virus registrados en el Catálogo Internacional de Arbovirus, están los causantes de dengue, fiebre del zika y chikungunya. Así, este artículo comprende un estudio descriptivo a través de datos secundarios, donde son comparados aspectos biológicos y diagnósticos en relación al estas tres enfermedades, así como evaluamos su presencia, entre 2015 y 2020, en los países que componen el continente sudamericano. A pesar del considerable progreso logrado en los últimos años para comprender mejor los aspectos moleculares de los agentes etiológicos de estas enfermedades y las condiciones clínicas, el escenario es complejo y los tres arbovirus continúan causaron brotes en América del Sur, en el período descrito, en diferentes proporciones, siendo el dengue la más común, cuyas tasas de incidencia varían con cada año analizado. La lucha contra los arbovirus debe ser permanente y requiere políticas intersectoriales bien fundamentadas y responsabilidad individual. Las intervenciones gubernamentales deben ser más estrictas para implementar contramedidas, y los sistemas de salud y educación podrían alinearse de manera más efectiva para construir un trabajo de conciencia más sólido que sea impulsado por los estudiantes de primaria, ayudando a la población educativa a favor de una sociedad más orientada y prudente. También es necesario reflexionar sobre los sistemas de información para minimizar el subregistro, que impide mostrar el escenario real de estas enfermedades.

**Palabras clave:** Arbovirus; Infraregistro; Epidemiología.

## 1. Introduction

Arbovirosis are diseases caused by arthropod-borne viruses (arboviruses) belonging to different taxonomic families (Donalasio, et al., 2017) and of global distribution, being present in almost all continents, although the greatest frequency is in tropics region. Such diseases persist in nature and have complex life cycles involving vertebrate hosts, that include birds, rodents, primates, bats, reptiles; and haematophagous vectors as ticks, mites, black flies, horseflies and, especially, mosquitoes (Weaver, et al., 2018).

Human being is an accidental host for most arboviruses due to your presence in forest area, with the exception of the virus that causes dengue, which uses him as the primary host to maintain cycles in urban and peri-urban areas. Other elements as climate and habitats that allow viruses to adjust to new reservoirs and vector species, also determine and influence the biological cycle of arboviruses (Figueiredo, 2019), in addition to demographic factors, strengthened by the expansion of global transportation systems (Gould, et al., 2017). In the Americas, changes in the anthropogenic sphere and mutations allow arboviruses to have the potential to emerge or re-emerge (Ganjian, et al., 2020).

Arbovirosis share many characteristics, making them difficult to distinguish from each other. Among the more than 500 viruses registered in the International Catalog of Arbovirus (CDC, 2021), those that cause dengue, chikungunya and zika fever stand out. South American continent has been scenery of these arboviruses, and they promote impacts on the economy and public health of affected countries. Thus, understanding the nature of these diseases and their transmission, additionally to epidemiological situation in territories, is important to help in the development of resource management strategies to combat them, which needs prioritizing in continuing education and in accurate future research in the field.

In this context, the present article comprises a descriptive study about dengue, zika fever and chikungunya, based on secondary data, where we compare biological and diagnostic aspects in relation these diseases, as well as assessing its presence, between 2015 and 2020, in the countries that comprise the South American continental portion.

## 2. Methodology

The present work is an integrative review, according to concept established by Botelho et al. (2011) about, built through scientific production concerning dengue, zika fever and chikungunya and its epidemiological situation between 2015 and 2020 in the countries that make up South America. The search for publications on general aspects related to their biology,

diagnosis and peculiarities of each nation of the South American regarding to diseases was carried out in the databases Medical Literature Analysis and Retrieval System Online (MEDLINE), ScienceDirect, Scopus, Scientific Electronic Library Online (SciELO), Latindex and Latin American and Caribbean Literature in Health Sciences (LILACS), using the terms: arbovirus; epidemiology; diagnosis; South America; notification; arboviruses; dengue, chikungunya; zika fever; vaccination, in consonance with the Health Sciences Descriptors (DeCS), and their correspondents in Portuguese and Spanish languages. Epidemiological informations were obtained through the Health Information Platform for the Americas (PLISA) from Pan American Health Organization / World Health Organization (PAHO / WHO).

To refinement of the material, the publications were included in the form of scientific articles, research or revision, or book chapters, according to the criteria: (i) the molecular structure and pathogenesis of viruses that cause dengue, zika fever and chikungunya; (ii) the diagnostic methods used for each of them; (iii) the forms of transmission; (iv) factors that favor the emergence and reemergence of diseases; (v) approach to arbovirus control in the corresponding South American countries. Concerning to epidemiology, we considered data related to (i) total cases; (ii) confirmed cases and (iii) incidence rate of dengue, zika fever and chikungunya between 2015 and 2020, of the last epidemiological week available for each country that make up South America continental portion, including the territory of French Guiana, although belongs to French government. The results include a description of molecular, taxonomic, transmissibility and diagnosis aspects of dengue, zika fever and chikungunya, as well as a discussion on the panorama of the three diseases in South American territory during the mentioned period.

### 3. Results and Discussion

#### 3.1 General aspects of dengue, zika fever and chikungunya

Dengue has as etiologic agent Dengue virus (DENV), belonging to the genus *Flavivirus*, Flaviviridae family. Its genome consists of a single-stranded RNA chain, approximately 10.8 kb in length and open reading frame (ORF) that encodes a single polyprotein which is cleaved into the structural proteins: capsid (C), membrane (M) and envelope (E); and eight nonstructural proteins (NS): NS1, NS2A, NS2B, NS3, NS4A, NS2K, NS4B and NS5, responsible for assist in viral genome replication. The M protein is synthesized as a precursor protein (prM), being cleaved by cellular protease to generate mature status (Murugesan & Manoharan, 2020).

DENV is transmitted by *Aedes* mosquitoes, mainly *Aedes aegypti*, but may also be *Aedes albopictus*, and has four antigenically distinct serotypes: DENV-1, DENV-2, DENV-3 and DENV-4 (Hoyos-Lopez, 2019). The variation of them is due to differences in specific amino acids and genetic material, factors that allow differentiation in viral fitness, pathology and viremia (Niu, et al., 2020). Thus, the genetic content of the pathogen signals the host immune response and, consequently, the clinical manifestations and severity of the disease (Katzelnick, et al., 2017).

Although there is no association between distinct types of DENV and the clinical course of the disease, researchers have suggested that DENV-2 and DENV-3 cause more severe disease states more frequently than other serotypes, and that DENV-4 is responsible for a softer condition (Zanotto & Leite, 2018). DENV-2 was the most prevalent serotype in several outbreaks in the Americas, epidemiologically ranked as the most relevant worldwide due to its association with the highest numbers of intense outbreaks, followed by DENV-3, DENV-1 and DENV-4 (Fares, et al., 2015).

The symptomatology promoted results in an unapparent condition or spectrum of clinical diseases ranging from self-limiting dengue fever to its severe form, a potentially lethal haemorrhagic and capillary leak syndrome, formerly dengue haemorrhagic fever and dengue shock syndrome (Bajwa, et al., 2017). Primary infection with a DENV confers long-term immunity only to this serotype, but not to the other three (Tang, et al., 2020). However, when resorted to by a heterologous subtype, the clinical picture worsens circumstantially (Castillo, et al., 2014), with a possibility that such severe clinical signs

are related to the rapid expulsion of the virus from the organism (Whitehorn & Simmons, 2011). Thus, the course of the infection does not correlate with the high viral load. In contrast, primary infections in infants born to dengue immune mothers develop severe symptoms such as hemorrhage (Ranjit, et al., 2018).

Zika virus (ZIKV) also is transmitted by *Flavivirus*, belonging to the family Flaviviridae. Contamination in humans occurs through the bite of *Aedes* mosquitoes (Sharma, et al., 2020), especially *A. aegypti*, *A. albopictus* and *Aedes africanus* (Faria et al., 2018), but can be transmitted in other ways as maternal-fetal, during the pregnancy, and sexual. ZIKV can infiltrates in breast milk, urine, tears and saliva (Romero, et al., 2019), however, scientific evidences about contamination through direct contact with these fluids do not exist until then.

The virus genome ZIKV is formed by 11 kb long single-stranded RNA, which encodes a polyprotein that yields three structural: C, prM and E; and nonstructural proteins: NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5. (Lowe, et al., 2018) e Asian/American, with the subtypes Pacific, American and Southeast Asia and, with differences between the amino acids in prM, NS3 e NS5 proteins (Kawai, et al., 2019).

When transmission occurs through the mosquito bite, it inoculates ZIKV into human skin by feeding on blood, and the target cells of the viral infection are likely to localize to the epidermis and dermis, which also constitute the body's first line of defense against invasion. Human primary dermal fibroblasts, epidermal keratinocytes and immature dendritic cells have been shown to be permissive to ZIKV infection and replication, as well as immune system cells (Zhang, et al., 2019). The virus also replicates and produces infectious particles in the mesenchymal stem cells of the prostate stroma, in the sertoli cells (Clinton, et al., 2020), in maternal decidua and placenta monocytes (Parker, et al., 2020).

Chikungunya, which in the makonde language means *the illness of the bended walker* (Mehdi, et al., 2019), is an arbovirus caused by the Chikungunya virus (CHIKV), belonging to the genus *Alphavirus*, family Togaviridae, and as dengue and zika fever, is transmitted to humans through the bite of mosquitoes belonging to genus *Aedes*, especially *A. aegypti* and *A. albopictus* (Cardoso, et al., 2019).

This CHIKV has only one serotype and as genetic material, a  $\pm$  11.8 kb single-stranded RNA with two ORFs for structural proteins: of capsid and of envelope (E3, E2, 6K / TF and E1); and the nonstructural proteins: NSP1, NSP2, NSP3 and NSP4. All are translated as cis- and trans- cleavage polyproteins to form mature viral proteins (Taylor, et al., 2017). Its genome evolved into four linhagens, with distinct genotypes, according to the E1 gene sequence: West African (WA), East Central South African (ECSA), Asian and Indian Ocean Lineage (IOL), these two identified in America (Stelitano, et al., 2019).

Several cell types have been shown to be permissive to CHIKV infection: fibroblasts, satellite cells, myofibers, osteoblasts, and connective and muscle tissue macrophages (Young, et al., 2019). The virus also replicates in lymphoid organs either before (axillary lymph nodes) and/or after the passage in the blood stream (lymph nodes and spleen) (Matusali, et al., 2019). CHIKV infection and replication result in the local production of inflammatory mediators that recruit and activate such defense cells. Those infiltrators activate additional immune cells, such as natural killer (NK) cells, which contribute to tissue damage (Maucourant, et al., 2019).

A comparative summary of the three diseases about taxonomy, molecular characteristics, cell specificity and forms of transmission of their etiological agents is shown in table 1.

**Table 1:** Comparison between dengue, zika fever and chikungunya concerning to taxonomy, molecular characteristics, cell specificity and forms of transmission of their etiological agents.

	Dengue	Zika Fever	Chikungunya
<b>Etiological agent</b>	DENV	ZIKV	CHIKV
<b>Family of etiologic agent</b>	Flaviviridae	Flaviviridae	Togaviridae
<b>Genus of the etiologic agent</b>	<i>Flavivirus</i>	<i>Flavivirus</i>	<i>Alphavirus</i>
<b>Nature of viral genetic material</b>	RNA	RNA	RNA
<b>Viral genome size</b>	10.8 kb	11 kb	11.8 kb
<b>Viral strains</b>	DENV-1, DENV-2, DENV-3, DENV-4	African (subtypes Eastern and African) and Asian/American (Pacific, American and Southeast Asia subtypes)	WA, ECSA, Asian and IOL
<b>Viral Vectors</b>	<i>A. aegypti</i> ; <i>A. albopictus</i>	<i>A. aegypti</i> ; <i>A. albopictus</i> ; <i>Aedes africanus</i>	<i>A. aegypti</i> ; <i>A. albopictus</i>
<b>Other forms of transmission</b>	–	Materno-fetal; Sexual	–
<b>Target cells</b>	Dendritic cells, monocytes; macrophages.	Human primary dermal fibroblasts; epidermal keratinocytes; immature dendritic; prostate and ertoli cells	Fibroblasts, satellite cells, myofibers, osteoblasts, connective and muscle tissue macrophages

Source: Authors (Adapted).

### 3.2 Diagnosis

The differential diagnosis of these three arbovirosis is made by laboratory tests. Detection of viral genetic material is the technique of choice, and the reverse transcription polymerase chain reaction (RT-PCR) has high specificity and sensitivity for the analysis of its RNA (Zhou, et al., 2019). Generally, the most used material in diagnostic tests is serum, however, samples of plasma, blood and tissues (liver, spleen, lymph nodes and lung) are effective in the analyzes (Hunsperger, et al., 2016). Similarity of symptoms represents an impasse today in arbovirosis diagnosis.

Classical dengue is an acute condition, usually asymptomatic; however, 20% of infections are symptomatic, beginning with the feverish phase (40 °C), which lasts from 2 to 7 days (WHO, 2019). Bleeding is observed in the progression of the disease, a condition that helps in the positivity of the tourniquet test (Sangkaew, et al., 2021). The Tourniquet test or Rumpel-Leede test is characterized as a marker of capillary fragility (Grande, et al., 2016). The blood pressure cuff used marks an intermediate point between the individual's systolic and diastolic pressure, a procedure that occurs for about 5 min (Feder, et al., 2016). Patients with hemorrhagic dengue fever present, after the test, petechiae in the antecubital fossa region (Raafat, et al., 2019).

The symptoms of chikungunya are similar to those of dengue, typically in both of cases can notice pyrexia, myalgia, headache, and in some cases rash (Vega, et al., 2019). It mainly affects the peripheral joints, including wrists, knees, ankles, and additional symptoms of the disease include arthritis, tenosynovitis, rash and myalgia, especially in the lower back and leg muscles (Chen, et al., 2016). The elderly and pediatric populations are the most sensitive to the severe condition of the disease and the symptoms persist for long periods (Paixão, et al., 2018). However, unlike dengue, most cases are symptomatic, preceded by a silent incubation interval of the virus that lasts 4 to 7 days (Fagour, et al., 2015). In contrast, the clinic of Zika is not specific and may be confused with the symptoms of dengue and chikungunya and has a high association with microcephaly and other brain disorders, such as Guillain-Barré syndrome (Mayer, et al., 2017).



ZIKV infection is usually asymptomatic, but can cause dengue-like symptoms. Severe complications include neurological disorders such as Guillain-Barre syndrome and fetal microcephaly (Wang, et al., 2017). Evidence of the association between this virus and microcephaly was cited by the US Center for Disease Control and Prevention (CDC) in 2016 (CDC, 2021).

The pathogen can cross placental and blood-brain barriers, causing disruptions in brain development, thus impairing the growth of neural progenitor cells (De Oliveira, et al., 2019). This is followed by virus infections in the first trimester of pregnancy (Prata-Barbosa, et al., 2019). Moreover microcephaly, exposure to ZIKV during pregnancy can result in visual and hearing impairment in the newborn (Peloggia, et al., 2018). The clinical and laboratory characteristics of dengue, chikungunya and zika are represented in Table 2.

**Table 2:** Comparison of dengue, zika fever and chikungunya regarding to clinical and laboratory diagnosis.

Disease	Clinical diagnosis	Laboratory diagnosis
<b>Classic dengue</b>	Fever, severe headache, myalgia, rash, nausea, vomit, muscle and joint pain	Viral isolation; Detection of viral RNA - RT - PCR; NS1 antigen capture;
<b>Dengue hemorrhagic</b>	Photophobia, rubeoliform rash	Anti-IgM and Anti-IgG Antibodies -ELISA Assay
<b>Shock Syndrome (Dengue)</b>	Bleeding in nose and in the gastrointestinal tract, gums, hematuria, petechiae; Plasma leakage	Blood count: Hemoconcentration, Thrombocytopenia
<b>Chikungunya</b>	Pyrexia, myalgia, headache, rash; Intense arthralgia in locomotor limbs (mainly in the knees, ankles, phalanx and wrist); Mild arthralgia in children; Children under 1 year of age have severe fever, seizures, peripheral cyanosis and bullous skin lesions Chronic complications – persistent joint pain, stiff joints	Viral isolation; Viral RNA detection Antibodies, Anti-IgM and Anti-IgG; Viral Antigen Detection - Nonstructural protein 1 (NSP1), NSP2, NSP3 and NSP4 - Viral envelope glycoprotein E1
<b>Zika</b>	Fever, headache, retro-orbital pain, non-purulent conjunctivitis, rash, myalgia and arthralgia; Edema, vomiting; Neurological complications; Association with Guillain-Barré syndrome Meningoencephalitis; Acute myelitis; Fetal Microcephaly	Usually, normal blood count Leukopenia, thrombocytopenia; Viral isolation; Viral RNA Detection IgM antibody detection by IgM capture enzyme-linked immunosorbent assay; Viral protein ns1

Sources: Brasil (2016); OPAS, (2017) (Adapted).

### 3.3 Epidemiology in South America

We obtained informations about total cases, confirmed cases and incidence rate of dengue, zika fever and chikungunya in South American countries between 2015 and 2020, until the last epidemiological week notified for each country in PLISA. The values related to the cases of dengue, zika fever and chikungunya are exposed (tables 3 – 5).

**Table 3.** Number of total and confirmed cumulative cases, and incidence rate of dengue for each country in South American countries, 2015 – 2020. TC: Total Cases; CC: Confirmed Cases; IR: Incidence Rate per 100,000 inhabitants; (–): Data not available.

		2015	2016	2017	2018	2019	2020
<b>Argentina</b>	<b>TC</b>	4,774	79,455	557	1,829	3,130	61,553
	<b>CC</b>	1,208	41,211	254	1,175	1,703	60,666
	<b>IR</b>	11.32	181.21	1.26	4.09	7	137.74
<b>Bolivia</b>	<b>TC</b>	27,099	32,386	9,923	7,597	16,193	83,552
	<b>CC</b>	2,432	4,413	917	1,348	7,240	14,743
	<b>IR</b>	245.8	297.45	89.78	67.73	144.97	744.94
<b>Brazil</b>	<b>TC</b>	1,649,008	1,500,535	252,054	265,934	2,248,570	1,378,592
	<b>CC</b>	500,972	31,6687	42,101	174,724	1,290,861	735,596
	<b>IR</b>	809.7	716.01	120.43	126.11	1,078.48	661.21
<b>Colombia</b>	<b>TC</b>	96,444	101,016	25,284	44,825	127,553	74,043
	<b>CC</b>	39,475	45,809	6,784	4,063	38,016	17,401
	<b>IR</b>	194.72	207.62	53.56	90.62	257.87	149.69
<b>Chile</b>	<b>TC</b>	40	33	10	18	29	9
	<b>CC</b>	7	0	10	18	28	9
	<b>IR</b>	0.22	0.18	0.06	0.1	0.16	0.05
<b>Ecuador</b>	<b>TC</b>	42,499	13,612	11,387	3,099	8,416	14,800
	<b>CC</b>	1,475	13,612	11,387	131	821	–
	<b>IR</b>	261.92	83.08	68.49	18.38	49.91	87.77
<b>Guyana</b>	<b>TC</b>	388	303	4	286	230	403
	<b>CC</b>	388	303	0	286	230	403
	<b>IR</b>	48.02	39.3	0.51	36.57	29.41	51.53
<b>French Guyana</b>	<b>TC</b>	2,603	522	625	240	250	8,244
	<b>CC</b>	357	9	0	0	250	4,807
	<b>IR</b>	993.51	189.13	220.85	82.76	86.21	2,842.76
<b>Paraguay</b>	<b>TC</b>	68,652	70,215	1,832	32,359	11,811	22,1085
	<b>CC</b>	5,258	2,556	616	3,414	1,161	61,249
	<b>IR</b>	976.14	1,004.09	26.9	469.18	171.25	3,205.52
<b>Peru</b>	<b>TC</b>	35,837	31,868	76,093	6,930	17,143	42202
	<b>CC</b>	32,511	17,055	27,241	–	–	23,473
	<b>IR</b>	115.01	100.3	236.57	21.29	52.66	129.64
<b>Suriname</b>	<b>TC</b>	15	6	1	123	86	519
	<b>CC</b>	6	1	0	1	42	277
	<b>IR</b>	2.74	1.09	0.18	21.65	15.14	91.37
<b>Uruguay</b>	<b>TC</b>	13	1,337	0	0	0	2
	<b>CC</b>	0	60	0	0	0	2
	<b>IR</b>	0.38	38.82	0	0	0	0.06
<b>Venezuela</b>	<b>TC</b>	54,152	29,268	8,615	19,118	16,015	5,8583
	<b>CC</b>	13,837	5,833	1,588	2,440	880	238
	<b>IR</b>	173.05	92.86	26.94	59.04	49.46	18.08

Source: PLISA (2021).

**Table 4.** Number of total and confirmed cumulative cases, and incidence rate of zika fever for each country in South American countries, 2015 – 2020. TC: Total Cases; CC: Confirmed Cases; IR: Incidence Rate per 100,000 inhabitants; (-): Data not available.

		2015	2016	2017	2018	2019	2020
<b>Argentina</b>	TC	0	128	684	57	2	–
	CC	0	26	250	37	0	–
	IR	0	0.29	1.55	0.13	0	–
<b>Bolivia</b>	TC	2	1,294	1,736	1,736	290	567
	CC	2	186	628	486	47	11
	IR	0.02	11.88	15.71	15.48	2.59	5.06
<b>Brazil</b>	TC	56,159	273,904	31,754	19,020	30,500	18,941
	CC	17,825	128,793	9,202	1,379	4,257	2,66
	IR	27.58	130.7	15.17	9.02	14.63	9.08
<b>Colombia</b>	TC	16,763	91,711	1,498	857	429	165
	CC	1,697	8,017	3	607	12	1
	IR	33.84	188.5	3.05	1.73	0.87	0.33
<b>Chile</b>	TC	–	0	–	0	0	0
	CC	–	0	–	0	0	0
	IR	–	0	–	0	0	0
<b>Ecuador</b>	TC	3	3,547	3,183	4	0	0
	CC	3	874	2,134	4	0	0
	IR	0.02	21.65	19.15	0.02	0	0
<b>Guyana</b>	TC	1	33	–	–	–	–
	CC	1	33	–	–	–	–
	IR	0.12	4.28	–	–	–	–
<b>French Guyana</b>	TC	0	10,790	–	50	–	–
	CC	0	48	–	–	–	–
	IR	0	39.0942	–	17.24	–	–
<b>Paraguay</b>	TC	6	30	84	145	2	593
	CC	6	6	2	4	0	0
	IR	0.09	0.45	1.23	2.1	0.03	8.60
<b>Peru</b>	TC	0	1,669	5,361	984	2,500	119
	CC	0	778	513	–	2,292	14
	IR	0	5.25	16.67	3.02	7.23	0.37
<b>Suriname</b>	TC	509	3,031	9	3	1	1
	CC	110	622	1	–	1	0
	IR	92.88	553.1	1.6	0.53	0.18	0.18
<b>Uruguay</b>	TC	–	–	0	0	0	0
	CC	–	–	0	0	0	0
	IR	–	–	0	0	0	0
<b>Venezuela</b>	TC	17	6,1691	684	209	76	34
	CC	0	0	250	–	0	0
	IR	0.05	195.73	1.55	0.65	0.6	0.10

Source: PLISA (2021).



**Table 5.** Number of total and confirmed cumulative cases, and incidence rate of chikungunya for each country in South American countries, 2015 – 2020. TC: Total Cases; CC: Confirmed cases; IR: Incidence Rate per 100,000 inhabitants; (-): Data not available.

		2015	2016	2017	2018	2019	2020
<b>Argentina</b>	TC	–	3,394	0	0	0	0
	CC	–	322	0	0	0	0
	IR	–	8.47	0	0	0	0
<b>Bolivia</b>	TC	143	19,614	3,345	97	806	1,517
	CC	916	1,190	22	91	97	54
	IR	9.6	191.07	30.47	0.86	7.19	13,91
<b>Brazil</b>	TC	15,276	263,598	185,737	87,687	178,147	98,177
	CC	374	145,059	151,966	68,962	100,963	39,461
	IR	7.7	195	90.1	41.58	85.963	47.09
<b>Colombia</b>	TC	354,228	19,357	1,052	663	535	160
	CC	3,189	203	28	157	48	5
	IR	721.6	40.07	2,2	1.34	1.08	0.32
<b>Chile</b>	TC	0	0	–	0	0	0
	CC	0	0	–	0	0	0
	IR	0	0	0	0	0	0
<b>Ecuador</b>	TC	29,354	280	–	8	2	1
	CC	4,157	1,745	196	8	–	0
	IR	206.5	12.36	1.18	0.05	0.01	0.01
<b>Guyana</b>	TC	5,310	149	–	–	–	–
	CC	29	0	–	–	–	–
	IR	661.6	19.33	–	–	–	–
<b>French Guyana</b>	TC	6,960	805	215	140	–	–
	CC	1,759	18	46	–	–	–
	IR	3,340.6	298.19	92.55	48.28	–	–
<b>Paraguay</b>	TC	3,418	880	739	1,237	52	316
	CC	873	38	8	67	0	0
	IR	61	13.65	10.97	17.94	0.75	4.58
<b>Peru</b>	TC	85	133	1,733	341	136	138
	CC	100	124	717	–	–	80
	IR	0.6	0.82	7.62	1.05	0.42	0.42
<b>Suriname</b>	TC	–	3	–	9	2	0
	CC	–	0	–	–	1	0
	IR	–	0	–	1.58	0.35	0
<b>Uruguay</b>	TC	–	–	0	0	0	0
	CC	–	–	0	0	0	0
	IR	–	–	0	0	0	0
<b>Venezuela</b>	TC	15,492	3,107	302	295	180	67
	CC	347	68	39	11	9	2
	IR	50.6	10.07	1.07	0.91	0.56	0.21

Source: PLISA (2021).

Until 2020, the three arboviruses continued to cause outbreaks in South America, even in different proportions, according to disponible data. The incidence rates for each arbovirus fluctuate each year, with an increase and decrease in

values for some countries. In agreement with informations, dengue is the disease that has the largest number of cases, leading the records and occurring in all countries.

In 2020, Brazil, Colombia, Chile, Paraguay and Venezuela had a lower dengue incidence rate when compared to 2019. For Zika, Bolivia and Paraguay had a higher rate compared to the antecedent year. Chile and Uruguay had an incidence rate of zero for zika fever and chinkungunya. Argentina and Suriname had an incidence rate equal to zero for chinkungunya, and the rest had not increased in any country so far. Zika fever and chinkungunya, as reported available data, they do not appear in all countries and at lower incidence rates when compared to dengue.

Differences also be verified between values of total and confirmed cases after laboratory diagnosis. Some countries in periods such as: Peru (2018 and 2019), French Guiana (2017 and 2018) and Ecuador (2020), for dengue; Venezuela (2015, 2016, 2018, 2019 and 2020) for Zika; and Suriname (2018), Guyana (2017) and French Guiana (2018) for chinkungunya, have no laboratory confirmed cases or information contained in the epidemiological bulletins issued by their health authorities, certainly having rate obtained from clinical cases.

About to countries with zero cases, it is not clear whether there was in fact a decline or the data available in PLISA correspond to a reduction in notifications in a timely manner, which is particularly noticeable in 2020 in agreement with the collected. The data from Argentina regarding chinkungunya had zero values, however, the report refers only to the epidemiological week 33, while other, for epidemiological week 53, the corresponding to the number of epidemiological weeks in 2020. For dengue, data on the epidemiological week were no longer available for 2020 or previous years.

The informations reflect a complex scenario liable to some interpretations that converge to underreporting. In the first, data is usually assembled only during outbreaks and the patients are examined when looking for a local health unit. Yet, according to Franco, et al. (2019), dengue, for example, as it is considered a benign virus by the population, it does not always impose the search for medical attention. This can also occur for zika and chinkungunya, which makes it possible that not all cases are investigated to be notified, perhaps not indicating the real situation, and it can be one of explanations for the image presented here.

In second, the co-circulation of these arboviruses is a challenging public health problem in terms of clinical spectrum, (Estofolete, et al., 2019). Some patients may have a series of signs and symptoms that together will be sufficient to reach a clinical diagnosis, however in others these manifestations can be limited, making the diagnosis more difficult, requiring laboratory tests. The lack of these to differentiate viruses is one of the challenges, where clinical management remains the basis for the control of these arboviruses (Espinal, et al., 2019). When the patient seeks health care, only experienced and well-trained doctors can correctly diagnose a patient, but mistakes still occur without specific tests. The Brazilian public sector, for example, serves more than 70% of the population, but only a small part of the reported cases is confirmed by specific tests in public reference laboratories, influencing official government notifications due to the inaccuracy of clinical diagnoses and serological cross reaction results (Magalhães, et al., 2020).

Another element that may be associated to falling in the number of notifications in 2020 and 2021 is the population fear of seeking their respective health services by virtue of COVID-19 pandemic, which is still ongoing. As well, it is possible that the community has also shown preoccupied of receiving health professionals by the SARS-COV-2 contamination risks, and these due to exposure to entering the home to investigate breeding sites and guide the community (Andrade, et al., 2020), which can weaken patrolling, and strengthens underreporting. Another notable aspect is that it is possible that suspected dengue cases are camouflaged with the clinical similarity of COVID-19 (Mascarenhas, et al., 2020), and as a consequence, they are not being reported in the information systems, besides the potential exhaustion of surveillance systems to investigate and to notify cases of arboviruses in a timely manner with the confrontation of COVID-19.

For Zika fever, notifications in pregnant women are also important and need to be considered to recognize the disease in advance, establish adequate monitoring and awaken individual awareness to the importance of combating, besides another forms of transmission cannot be disregarded either. In view of the importance of notification as an instrument to understand reality, periodic assessment of the system to identify its weaknesses is important.

Climatic factors are already well defined as contributors in the transmission of arboviral diseases. Part of South America is located in the tropical zone, with higher temperatures and wetter periods, which as the transmitting mosquito takes advantage of standing water to lay its eggs, and by temperature, which influences hatching of its larvae (Winokur, et al., 2020), furthermore the diverse mast fauna which providing various types of reservoirs for arboviruses (Marcondes, et al., 2017).

The human movement assists in the reintroduction of viruses to trigger disease transmission. In Córdoba, Argentina, for example, imported cases have been reported from endemic dengue regions, including Brazil, Bolivia, Venezuela, Colombia, Mexico and Costa Rica (Robert, et al., 2019). Human activity also generates artificial sites of vector oviposition, aided by uncontrolled urbanization resulting from the demographic increase, and the region of the Americas is characterized by a high degree of urbanization. South America itself is home to four megacities: São Paulo and Rio de Janeiro in Brazil; Buenos Aires in Argentina; and Lima in Peru (Masciadri, et al., 2019). Uncontrolled urbanization, added to other elements of a socioeconomic nature such as basic sanitation and poor health system infrastructure, and inefficient garbage collection, as well as individual indifference, allows the transmission of these arboviruses to be maintained (Da Silva, et al., 2019).

In addition, the threat posed by arboviruses also places where public combat campaigns are perhaps still inefficient, associated with a delicate public educational model and also with a powerless surveillance system, which makes epidemiological data unclear and which also causes underreporting. Although these elements are expressive about the permanence of the diseases, each country has its particularity regarding variations in climate, public policies to treat them and personal preventive education, which can also influence the data profile.

Brazil has the highest incidence rate of the three diseases, except in 2015 and 2016, and a geographical location in the region between 5° North and 10° South, between the Capricorn and Cancer tropics, which makes it receive a high incidence of solar radiation, while the intertropical convergence zone over the equatorial Atlantic is one of the main inducers of rain over the Amazon region (Da Silva, et al., 2019), moreover presenting socioeconomic stratification, with a Gini index of 51.3, being among the most unequal countries in the world with historically wide income and social status gaps between different occupations and sectors (Hartmann, et al., 2019).

French Guiana, a French overseas department in the Americas, has been part of France since 1946 and has a political and administrative organization similar to it (Epelboin, et al., 2018). Bordering Suriname and northern Brazil, it has 90% of its territory occupied by the Amazon Forest. With an appropriate location for the proliferation of arbovirus vectors, the country also has a constant immigration rate and, thus, a growing population. Despite ongoing efforts to regulate and remove mosquito breeding sites, the lack of infrastructure contributes to the production of urban mosquitoes (Brasil, 2019) which ends up maintaining the pattern presented according to the data presented.

In Ecuador, the Ministry of Health monitors vector control and public health services, including mosquito surveillance, indoor residual spraying, application of larvicide and ultra-low volume nebulization, including to conducting larval index surveys at home, which is among the most common indicators used by public health agencies to establish the existence of mosquitoes and quantify their abundance, constituting important considerations for understanding the potential for localized transmission and planning for reducing the source of larvae. However, despite the good cost-benefit ratio in provision of clinical services, such activities are limited by financial restrictions, requiring informed strategies to focus resources and personnel (Lippi, et al., 2019).

A study carried out in Mendellín, Colombia, researchers identified barriers that limit the coverage of thermal fogging as an action to combat the vector. One of them was the absence of residents at the time of the visitation and, when they met, they rejected it due to misinformation such as: fumigation affects health or is unnecessary when there are no mosquitoes in the house. Another problem was the substantial gap between notification of the epidemiological surveillance system and fumigation. This system should be simplified so that treatments can, ideally, kill potentially infectious mosquitoes before their extrinsic incubation period has passed (Usuga, et al., 2019).

In another study in Colombia, whose objective was to estimate the association of risk perception and experience with dengue with factors such as knowledge about the disease and its transmission, the application of practices and an attitude of will aimed at controlling this arbovirus, the authors observed that the experience with dengue cases was related to a positive attitude towards its control, showing the importance of the individual and collective context (Benítez-Díaz, et al., 2020).

Chile has managed to eradicate the transmitting mosquito; however, the reintroduction of the mosquito was reported in 2016 (Gonzalez-Pacheco, et al., 2020), but in consonance with the data presented here, it only presents confirmed cases of dengue. Some data for Guyana regarding zika and chinkungunya were not available from PAHO / WHO, and according studies (Aerts, et al., 2020), in the country there is a deficient surveillance system. Uruguay only had confirmed cases of dengue in 2016, according to PAHO data, and researchers point the notified cases are all imported from neighboring countries (Basso, et al., 2015). By the location, at the southernmost geographical limit of the distribution of the dengue vector in the South American continent, climatic conditions limit, but do not prevent, the increase of this vector during the non-winter. Thus, the population of mosquitoes decreases during the winter and increases again when temperatures rise.

#### **4. Final Considerations**

Although there is a good understanding in the literature about the determinants that favor the proliferation of these arboviruses in the urban environment, the challenge now is to identify ways to overcome the set of them to achieve effective prophylactic results. However, with the exposed panorama, based on macro-structural data, in practice seems that this intention is not being circumvented. Despite considerable progress was made in recent years to better understand the molecular aspects of the etiologic agents, the clinical conditions, and the cycle complexes of three arboviruses, they kept circulating between 2015 and 2020. The scale of these diseases in 2020 is lower than in 2019, but the reasons are uncertain with the ongoing COVID-19 pandemic, which may be hampering the operation of vector control programs.

It is necessary continue with planning, executing and monitoring public policies to combat arboviruses in parallel with activities to intercept the spread of COVID-19, because the fight against them must be permanent considering they are liable to reemergence. Perhaps government interventions need to tighten up to implement measures to combat the vector, strengthen intersectoral actions between countries. Health and education systems could be encouraged to align themselves stronger to raise students' awareness from basic education, helping to continuously train the population in favor of a more oriented and responsible society, maybe accompanied by legal mechanisms that encourage the community.

It is also recommended to reflect on the effectiveness of information systems, which should include the most powerful continuous training of all those involved in filling out notifications and in the management of health information, and people need be encouraged to look for the health service and be forwarded to the laboratory diagnosis, that is the safest in view of the clinical similarities between the three arboviruses and with other illnesses. Furthermore, it is imperative not to lose sight of the existing funding for vector control programs and vigorously motivate research targeted at vaccine development.

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