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Risk of *Aedes Aegypti* as Biological Vector Transmissibility between Dengue Virus and Heartworm: Impact on the Pathogenesis of Zoonotic Diseases in Rural and Urban Environments

Nicoly Guimaraes Amaral Cabral [1], Giovanna dos Reis Brasiliense Cavalcante [1], Alexia Costa Leite [1], Guilherme Britto [1] and Rachel Siqueira de Queiroz Simões [2, 3, *]

[1] *Veterinary Medicine Undergraduate Student, Department of Health and Agriculture Sciences, Santa Úrsula University, Fernando Ferrari, 75 – Botafogo Campus, Rio de Janeiro, Brazil.*
[2] *Coordinator of Veterinary Medicine and Professor of Zoonoses & One health, Department of Health and Agriculture Sciences, Santa Úrsula University, Fernando Ferrari, 75 – Botafogo Campus, Rio de Janeiro, Brazil. Correspondence: rachel.simoes@usu.edu.br and coordenacao.medicinaveterinaria@usu.edu.br*
[3] *Tropical Medicine, Vector Medical Malacology lato sensu postgraduate, Oswaldo Cruz Institute, Oswaldo Cruz Foundation, Avenida Brazil 4.365 – Manguinhos, Rio de Janeiro, Brazil.*

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Abstract

Dengue is a vector-borne viral disease caused by the *flavivirus* dengue virus (DENV) that continue to circulate worldwide. A positive-stranded enveloped RNA virus (DENV) is principally transmitted by *Aedes* mosquitoes. It has four antigenically distinct serotypes, DENV-1 to DENV-4. This review highlights pathophysiology and clinical signs of Dengue Virus correlated with Heartworm Disease by *Aedes aegypti* mosquitoes, which transmit Dengue, Zika, Chikungunya and other arboviruses, had been modified genetically which carries a *Wolbachia pipientis* bacterium that stops the insect from transmitting viruses. There have been recent advances in the development of therapeutic drugs, and vaccines that are currently being pursued at several phases of preclinical and clinical development. The preventive measures of dengue transmission and challenging the epidemiological surveillance of the zoonotic diseases are the key role to control the spread of this vector through the improve the health promotion campaigns in water supply, personal protection, biological and mechanism vector approaches.

Keywords: *Aedes aegypti*; Dengue virus; Heartworm; Vector-borne; Zoonotic diseases

1. Introduction

The involvement of the *Aedes Aegypti* vector in the transmission of Heartworm and Dengue fever in rural and urban environments had been few associated. DENV as previously mentioned is transmitted by the infected *Aedes Aegypti* mosquito during its hematophagous feeding. This transmission cycle can happen either in the wild ecosystem, involving the transmission of the virus between primates, or in the urban environment, being maintained within the population helped by mosquitoes [1]. The combination of the disseminated vector and the susceptible human population, favorable environmental conditions for proliferation associated with infectious human influx, can lead to seasonal outbreaks that are currently disease-free. The wild cycle of dengue involves the transmission of the virus and mosquitoes prevalent from the forest to the urban transmission cycle. While the virus can spread in rural environments, it will also be maintained within the human population, helped by urban mosquitoes, such as *Aedes Aegypti* [1].

* Corresponding author: Rachel Siqueira de Queiroz Simões

2. Dengue virus (DENV)

Dengue is a disease caused by a dengue virus (DENV), which is classified as an arboviral infection with the highest prevalence and importance in the world. DENV belongs to the Flavivirus genus, transmitted mainly by mosquitoes of the *Aedes aegypti* genus [1]. The virus is transmitted by the bite of an infected mosquito, during a blood meal that exists in wild and urban ecosystems [2]. The DENV genome represents a positive-sense single-stranded RNA that encodes three structural proteins (capsid, prM/M and E) and seven non-structural proteins that are translated at the time of viral replication. [3].

2.1. History

The origin of dengue dates to 1823, when slaves from West Africa introduced the terms “dinga” and “dyenga” to the Americas, terms used to name an epidemic of the disease in their homeland [4, 5]. This term was later reformulated into Spanish, originating the word “dengue”, also ensuring the Swahili origin “Ki-denga-pepo” (sudden attack like a spasm or tremor caused by an evil spirit), with antecedents in epidemics that occurred in Jakarta in 1779 and the "break-bone fever" of Philadelphia in 1790 [5, 6].

This historical fact shows that the dengue virus dates back several centuries, but it was only in 1953, in Manila, Philippines that a new form of the disease was recognized, affecting mainly children, being characterized by hemorrhagic manifestations, shock and high mortality, being called from "Philippine Hemorrhagic Fever". This new form served to differentiate it from other hemorrhagic diseases that occurred in Korea and from previous records of hemorrhagic manifestations and shock in dengue patients in Taiwan. [5,7]. After the 1954 Philippine epidemic, new cases occurred in Thailand (1958) and Singapore (1960) [5,8]. In 1958 at Bangkok, cases with the symptoms of dengue hemorrhagic fever appeared, resulting in the explosion of an epidemic. The King of Thailand asked for help, mentioning the possibility of an outbreak like the one that occurred in the Philippines. The dengue virus was isolated and confirmed the suspicion [5,7].

In 2003, around 483 thousand cases of dengue were reported in the Americas, of which approximately ten thousand were hemorrhagic dengue fever. More than 250 thousand cases come from the South American, where, although the Andean Region reports several around 50 thousand cases, 80% of cases of hemorrhagic dengue fever are concentrated there. In Brazil, dengue fever has a seasonal pattern, with a higher incidence of cases in a hotter and more humid period, typical of tropical climates. In 1986, dengue acquired epidemiological importance when the epidemic arrived in Rio de Janeiro State and the circulation of serotype 1, which soon reached the Northeast Region. Thus, dengue fever became endemic in Brazil, interspersing epidemics, generally associated with the introduction of new serotypes, in previously free areas. In the period between 1986 and 1990, dengue epidemics were restricted to some states in the Southeast (Rio de Janeiro, São Paulo and Minas Gerais) and Northeast (Pernambuco, Alagoas, Ceará and Bahia) regions. In 1990, the introduction of a new serotype – DEN-2 –, also in Rio de Janeiro, worsened the disease situation [9].

In 2001, the DEN-3 serotype was introduced in Rio de Janeiro, where it was also detected in Roraima Sate, probably due to the intense movement of people on the border between Brazil and Venezuela. In 2002, around 800 thousand cases of dengue were registered in Brazil, which corresponds to 80% of the cases in all of America in the same year, with 150 deaths. At the time, this absolute number of deaths exceeded, for the first time, the number of deaths from malaria. In the same year, dengue transmission was recorded in all states, except for Santa Catarina and Rio Grande do Sul, where the detected cases were imported [9].

2.2. Pathophysiology and Clinical Signs of Dengue

Dengue is an arbovirus caused by the dengue virus (DENV), belonging to the *Flavivirus* genus, transmitted mainly by the *Aedes aegypti* mosquito [1]. After the bite of an infected mosquito, the virus enters the bloodstream and replicates it into mononuclear blood cells, such as macrophages and dendritic cells. This replication triggers a complex immune response, with the release of pro-inflammatory cytokines, notably interleukin-6 (IL-6). The activation of CD4+ T lymphocytes and Natural Killer (NK) cells occurs in sequence, leading to the involvement of CD8+ T lymphocytes and the production of immunoglobulins M (IgM) by B lymphocytes [10].

2.3. Incubation Period and Clinical Manifestations

After an incubation period ranging from 4 to 10 days, symptoms begin to manifest. Dengue can be classified into two forms: non-severe dengue and severe dengue, according to the clinical signs presented and the presence of alarm signs [1].

2.3.1. Non-Serious Dengue

Mild cases of dengue are characterized by sudden high fever, severe headache, retro-orbital pain, myalgia, arthralgia, nausea, vomiting and rash. In general, these symptoms are self-limiting and resolved with symptomatic treatment and adequate hydration [11].

2.3.2. Severe Dengue and Warning Signs

Progression to severe forms of dengue involves manifestations such as plasma extravasation, significant bleeding and organ failure. Alarm signs include severe and continuous abdominal pain, persistent vomiting, mucous bleeding, increased hematocrit accompanied by a rapid drop in platelets, and lethargy or irritability [1].

2.4. Pathophysiology of Severe Dengue

In severe cases, the virus directly affects endothelial cells, increasing vascular permeability. This process leads to fluid leakage into surrounding tissues, resulting in hypovolemia and shock, known as Dengue Shock Syndrome (DSS). Multiple organ failure can occur in cases that are not adequately treated [2,12].

2.5. Clinical Dengue Management

Dengue treatment mainly consists of controlling symptoms and preventing complications. Management involves continuous monitoring of the patient's vital signs and hydration status. In severe cases, administration of intravenous fluid therapy is essential to restore intravascular volume and avoid shock. In critical situations, it may be necessary to perform blood transfusions to correct bleeding [1].

2.6. Importance of Early Dengue Diagnosis

Early diagnosis is essential to prevent progression to serious forms of disease. Rapidly identifying warning signs and immediately seeking medical attention can significantly reduce the morbidity and mortality associated with dengue fever [13]. So, to make a positive diagnosis of DHF/SSD, clinical and laboratory criteria are required, as established by the WHO expert group and used in various epidemics.

2.6.1. Clinical criteria

High fever, continuous and sudden onset, lasting 2 to 7 days; hemorrhagic manifestations, including a positive loop test, followed or not by petechiae, ecchymosis, epistaxis, hematuria, melena and other bleeding; hepatomegaly and shock are the most evident and characteristic clinical signs of the viral disease.

2.6.2. Laboratory criteria

Thrombocytopenia with platelet count less than 100,000/mm^3 and hemoconcentration with hematocrit elevated by 20% or more above the normal value (above 45%, with great therapeutic and prognostic value) are the most evident laboratory values of this viral disease. For a positive diagnosis of DHF, the first two clinical criteria and the two laboratory criteria are required as mandatory signs. An early diagnosis is essential to prevent serious complications and death [5].

The diagnosis of dengue is crucial for adequate patient management and the implementation of epidemiological control measures. Laboratory methods play a fundamental role in this process, including the detection of viral antigens, serological tests and molecular biology techniques for identification of viral RNA genome [14, 15]. Viral antigen detection tests, the most used being the NS1 test, could identify the presence of the dengue virus in the early stages of the disease. Serological tests, such as IgG and IgM, are very useful for confirming infection and differentiating primary and secondary cases of the disease, contributing to a better therapeutic approach. [14, 15].

2.7. Dengue treatment

The WHO (World Health Organization) published a document with guidelines for the treatment of dengue. These guidelines will be carried out in hospitals until the patient is admitted to the Intensive Care Unit. The procedures to be followed vary according to the health status of each patient, including:

2.7.1. Management of the febrile phase

It is recommended to rest, take oral fluids, and to reduce fever, apply a warm sponge after using paracetamol, with a dosage of 10-15 mg/kg/day for high fever above 39°C, repeating the medicine every 4 to 6 hours. Paracetamol produces

antipyresis, acting centrally on the hypothalamic temperature-regulating center, producing peripheral vasodilation that results in an increase in blood flow to the skin, consequently leading to sweating and heat loss. Then, nutritional support is provided, being nutritious and balanced, with the addition of juices and electrolytes. Avoid foods that are black or reddish in color to avoid causing confusion in cases of bleeding. The patient must be monitored every day, observing and monitoring the history of bleeding, abdominal pain, vomiting, appetite and the amount of fluid intake. However, the physical assessment must be carried out by observing vital signs, increased liver volume and sensitivity to palpation. The platelet count should be a test that should be requested for the patient, as it evaluates the number of platelets present and changes in the clotting mechanisms [16].

2.7.2. Critical phase management

At this stage, platelet blood transfusion is indicated, using fresh whole blood or packed red blood cells. The dose to be used will vary according to the type of blood that will be performed, with fresh whole blood at 10 ml/kg/dose or with red blood cell concentrate at 5ml/kg/dose. The indication for platelet transfusion is based on a parameter when there is significant hemorrhage with the presence of thrombocytopenia or if the platelet count is less than 10,000/mm3 (10-20 mL/kg of platelets). Some criteria are established for the patient to be released, namely: absence of fever without the use of antipyretic medications, performing a platelet count with a result of above 100,000/mm3, adequate diuresis and stable hematocrit, absence of signs of external bleeding or internal [16].

2.8. Dengue prevention

Dengue prophylaxis is carried out mainly through control of the mosquito vector, Aedes aegypti, preventing its reproduction and dissemination into the environment. Therefore, restrictive measures must be taken to eradicate it:

- **Improvement in water supply**: Implementation of measures to improve water supply, including protection against mosquitoes in water tanks, cisterns and underground reservoirs.
- **Personal protection**: Use of appropriate clothing to protect against insect bites, application of insecticides in tablets and spirals (pyrethrum), use of repellents with DEET and fabrics impregnated with permethrin, in addition to the installation of mosquito nets and curtains treated with insecticides.
- B**iological control:** Use of biological methods to control larvae, with the use of larvophagous fish, such as *Gambusia affinis* and *Poecilia reticulata*, as well as the application of bacteria, such as the strains of *Bacillus thuringiensis* H-14 and *Bacillus sphaericus*, in polluted waters.
- **Mechanical control**: Involves the elimination or appropriate destination of breeding sites sucheliminating and recyclable materials, under the supervision of Agents to Combat Endemic Diseases or Community Health Agents, with the collaboration of residents with the main objective eliminate or prevent the accumulation of standing water [16].

3. Heartworm disease

Heartworm disease is a parasitic disease transmitted by *Culicidae* that primarily affects the cardiovascular system of dogs, which are common in tropical and coastal areas. The etiological agent *Dirofilaria immitis*, as it is seen in pulmonary arteries, causes the development of hypertension and pulmonary thromboembolism. In more advanced stages, vena cava syndrome and/or right congestive heart failure may occur [17]. Adult worms cause successive trauma to the wall of pulmonary vessels, triggering the release of inflammatory mediators and causing hypertrophy of the endothelium with the formation of villi (proliferative pulmonary endarteritis) [18].

3.1. History

The first reference to canine heartworm disease dates to around 400 years ago, in 1626, by Birago, with observations in hunting dogs in northern Italy. However, it was only in 1856 that this parasite was described at a morphological level, being named by Leidy as “immitis”. Heartworms are nematodes belonging to the *Filarioidea* superfamily, *Onchocercidae* family, *Dirofilaria* genus, divided into two subgenera *Dirofilaria* (D. immitis) and *Nochtiella* (*D. repens, D. tenuis* and *D. ursi*) [19].

In 1911, Railliet and Henry, two French parasitologists described the *Dirofilaria* genus and, thus, the current taxonomic classification, *D. immitis* (Leidy, 1856). In 1979, due to the importance of this parasitosis, not just the damage which it causes to infected animals, but also to the human population, and due to the intimate relationship between domestic animals and humans, the disease spread to be considered a zoonosis by the World Health Organization. In Brazil, its introduction is probably associated with the importation of infected domestic dogs, showing high adaptability to the climate and the presence of vectors [20].

3.2. Diagnosis

3.2.1. Laboratory diagnosis

One of the most used diagnostic methods is the test for antigen research in adult females of *D. immitis*, which is a quick, easy and sensitive method. In dogs, antigens can increase between 5 and 6.5 months after infection, but false negatives can occur due to infections caused by: immature forms, only males or a low parasite load (common in felines), for these reasons, This test resulting in negative is not enough to exclude the suspicion of *D. immitis* infection in felines, and it is necessary to complement it with anti-*D. immitis* antibody research kits. In dogs, this test is not used due to its low specificity due to cross-reactions with intestinal parasites. Techniques can be applied to visualize microfilariae, such as fresh drops, blood smears and concentration techniques to differentiate microfilariae, such as the modified Knott technique and the acid phosphatase technique. The differentiation of microfilariae is very important, as the species present different degrees of pathogenicity [21, 22].

3.2.2. Clinical diagnosis

During the physical examination, some signs can be seen that lead to suspicion of heartworm disease, namely cardio-respiratory signs for *D. immitis* and cutaneous signs for *D. repens*. For confirmed diagnosis, chest x-ray and echocardiogram are useful techniques used. The radiographic changes seen are branches of the pulmonary arteries with an enlarged, tortuous and incomplete shape. Changes in the lung parenchyma, initially in the diaphragmatic lung lobes, in more severe cases, right dilation of the heart is shown [21, 22].

Echocardiography is effective in visualizing massive infections, in evaluating the functional and anatomical impact of the disease at the cardiac level and in confirming the diagnosis of visualization of worms in the tricuspid valve. However, it is important to be careful when using echocardiography to diagnose fast infections, where, in these cases, the worms will be in the peripheral branches of the pulmonary arteries, remaining out of the view of the echocardiograph [21, 22].

3.3. Pathophysiology and Clinical Signs of Heartworm Disease

Heartworm disease is a zoonosis caused by the nematode *Dirofilaria immitis*, transmitted by hematophagous mosquitoes, such as Aedes, Culex and Anopheles. It mainly affects the cardiovascular system of dogs and, in rare cases, can affect cats and humans [17, 23, 24].

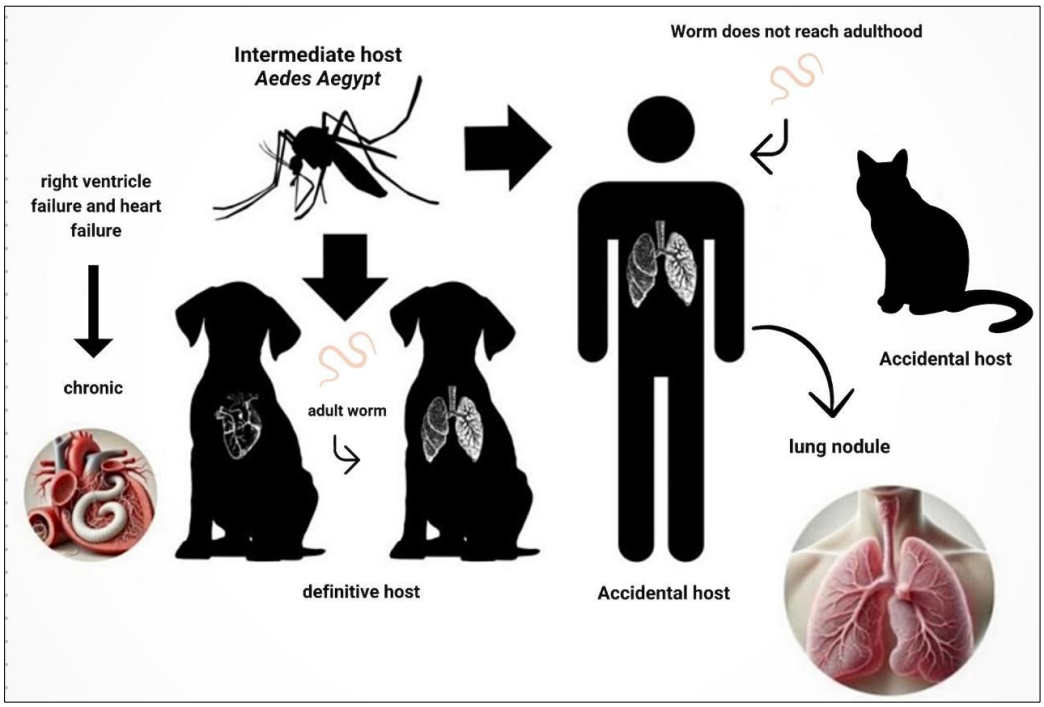

Figure 1 Pathophysiology and clinical signs of Dengue virus associated Heartworm Disease by *Aedes aegypti* mosquitoes and challenging the epidemiological surveillance of the zoonotic diseases (design by the authors)

After the bite of an infected mosquito, the third stage larvae (L3) are released into the host's bloodstream and, in approximately six months, develop into adult worms that lodge in the pulmonary arteries and right heart chambers. These worms cause significant damage, promoting inflammation and endothelial hypertrophy, which results in proliferative endarteritis and vessel obstruction [17. Continuous inflammation favors the development of pulmonary hypertension and thromboembolism. In advanced stages, serious complications arise, such as right congestive heart failure and vena cava syndrome, in which worms migrate to the right ventricle, blocking blood flow and causing hemolysis and disseminated intravascular coagulation [23, 24]. The infection can also cause kidney damage through the deposition of immune complexes, leading to glomerulonephritis (Figure 1) [25].

3.4. Clinical Signs

The clinical signs of heartworm disease vary depending on the parasite load and the stage of the disease. Many dogs remain asymptomatic for long periods. When symptomatic, signs include chronic non-productive cough, which worsens with exercise; fatigue and effort intolerance; presence of heart murmurs and lethargy; dyspnea and, occasionally, hemoptysis [17, 23]. In the most severe cases, cachexia, fever and anorexia appear. Vena cava syndrome is a clinical emergency that manifests as shock and pale mucous membranes, requiring immediate intervention [24, 25].

Diagnosis includes laboratory tests to detect microfilariae in the blood and imaging tests, such as radiography and echocardiogram, to evaluate heart and lung lesions. Staging is essential to guide treatment and avoid complications, such as thromboembolism, during adulticidal therapy [23, 24].

3.5. Heartworm Treatment

Patients with milder forms of the disease have a more favorable response to treatment. On the other hand, individuals with more severe manifestations of the disease have a significantly higher risk of complications and death. The presence of serious illnesses associated with severe form may, in some cases, make it impossible to carry out adequate treatment. The death of parasites, both in dogs and cats, is often related to severe parenchymal lung lesions, and limiting physical exercise is essential during the post-treatment period with adulticides. Thiacetarsamide, although effective against most male and some female parasites, demonstrates limited efficacy against immature parasites and young females.

For dogs, melarsomine dihydrochloride is the only substance approved by the United States Food and Drug Administration (FDA) and has proven to be the most effective and safe among the therapeutic options available. This drug may be indicated in cases of mild and moderate infections, at a dose of 2.5 mg/kg, administered in two doses 24 hours apart. In animals with severe disease and a high parasite load, the medicine should be administered in a single dose, with administration repeated after 30 days. Melarsomine, when administered in two intramuscular doses, 24 hours apart, is more effective, being able to inactivate more than 95% of parasites.

A safe alternative for dogs with severe disease and high antigen loads consists of administering an intramuscular dose followed by monthly boosters, in addition to two subsequent doses, administered 24 hours after the first, also 24 hours apart. Dogs undergoing this therapeutic regimen must be previously evaluated and hospitalized for administration of the drug. The pharmacodynamics of melarsomine is associated with its action as adulticide, that is, its ability to eliminate adult worms of the parasite responsible for heartworm disease. Melarsomine is an organic arsenical that exerts a mechanism of action that is not yet completely understood. It is known to cause damage to the nervous system of adult *Dirofilaria immitis* worms, resulting in their paralysis and death. It is assumed that melarsomine alters the permeability of cell membranes, which interferes with the transmission of nerve impulses and leads to paralysis of adult worms.

3.6. Heartworm Prevention

On the current market, there are several options for preventing infection in dogs, including tablets and gums based on the oxime milbemycin and ivermectin, available in formulations of 6 and 100 µg/kg, which can be administered monthly for monthly prophylaxis. According to the American Heartworm Society, annual prevention is recommended in all regions with large temperature variations throughout the year. The main preventive substances used in dogs are diethylcarbamazine and macrocyclic lactone.

Macrocyclic lactones act by potentiating the neuronal inhibitory action mediated by gamma-aminobutyric acid (GABA), promoting hyperpolarization of the neuron and, therefore, inhibiting nervous transmission. Furthermore, diethylcarbamazine alters the metabolism of arachidonic acid in both microfilariae and host endothelial cells. These modifications can induce vasoconstriction, which amplifies endothelial adhesion, favoring the immobilization of the circulating parasite. Moreover, this process increases the adherence and cytotoxic activity of the host's platelets and

granulocytes. These events may represent an activation of the innate immune system, of a non-specific nature, occurring independently of the specific adaptive immune response to the antigen.

4. Biological Vector Associated

4.1. *Aedes Aegypti* and its participation as an obligatory vector of Dengue Virus and intermediate host of Heartworm Disease.

Dengue is caused by the DENV virus belonging to the *Flavivirus* genus with a single-stranded RNA genome that encodes three structural proteins, namely capsid, rpM/M and seven non-structural proteins that are present during the replication cycle, being one of the most important infectious diseases in the world and considered an endemic viral disease, with four distinct serotypes, DENV-1, DENV-2, DENV-3 and DENV-4 [1, 26].

Heartworm disease is caused by a filarial nematode that, to complete its cycle, requires intermediate vectors, such as *Culex spp*., *Aedes spp*. and *Anopheles spp*. Its definitive hosts are canines, felines and non-human primates. Males and females live in the tissues or organic cavities of definitive hosts [27]. In the wild, adult *D. immitis* worms are generally in subcutaneous tissues, but microfilariae will circulate in the bloodstream and can be ingested by the hematophagous vector, passing on transmission [28]. Infection in dogs is the main disseminator of human heartworm disease, microfilaremic dogs and wild felines are reservoirs of the emerging pathogen and normally when the parasite reaches humans, it is unable to reach its adult form [28].

Aedes Aegypti is the obligatory vector of the dengue virus and an intermediate vector of *Dirofilaria Immitis*. Therefore, when an animal infected with *D. immitis* is ingested, it will automatically be infected with microfilariae [29]. There have been already cases of events in humans, where the parasite that causes heartworm disease migrates to the lungs through mosquito bites [27]. It is affected by the appearance of a solitary pulmonary nodule that can lead to lung cancer (Figure 2) [30].

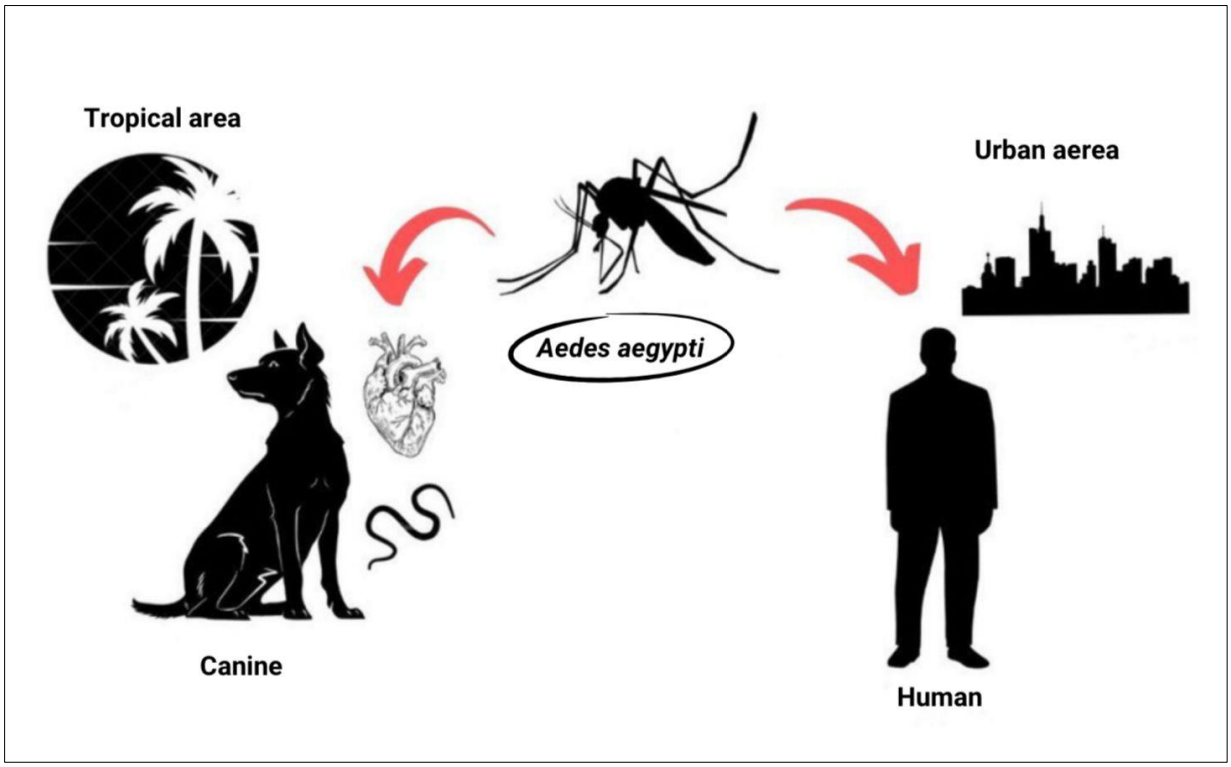

Figure 2 Biological Vector Associated: Aedes Aegypti and its participation as an obligatory vector of Dengue Virus and intermediate host of Heartworm Disease (design by the authors)

5. Perspectives: Challenges for global public health.

5.1. Dengue and Heartworm Disease

Heartworm disease affects dogs and humans around the world. It is considered an emerging disease in Southern, Northern and Central Europe, such as Switzerland, Netherlands, Germany, Czech Republic, Slovenia, Lithuania, Russia and Serbia, with both forms of heartworm disease, being considered an endemic country [31].

In Brazil, accurate and updated mapping of *D. immitis* can result from public health and veterinary work, but some research is rarely carried out throughout Latin America [32]. The first report of the infection in South America was in 1878. At that time there were few publications on the subject as they were very laborious and therefore valuable information [33]. In the Lábrea municipalities, increased recurrence levels of *D. immitis* were found in rural locations in the Amazonas State than in urban centers [32]. In the Northeast region of Brazil, heartworm disease is carried by its main vector *Aedes Aegypti*, showing in experimental infection from dogs infected with *D. immitis* and *Aedes Aegypti* [27].

There are reports of *Dirofilaria spp*. in the United States from people who became infected with *D.immitis*. which it is considered the more important of the two species of the *Dirofilaria spp*. in the United States. Its importance for public health is linked to the severity of the radiographic findings of a lesion in the size of a coin, rather than being associated with a clinical disease [34].

Dengue is an infection considered the most potent and important in the world. Estimates are 390 million people are infected per year and 96 million manifest the disease. With the increase in population and climate changes involved in the spread of viral and vector dissemination, it has been stipulated that the risk of transmission potential is 6.1 billion cases by 2080 [1]. In Brazil, in the first three months of 2022, there were records of more than 63 new municipalities transmitting dengue. Most in the South of the country in past periods, however it was pointed out that in the states of Santa Catarina and Rio Grande do Sul there was an increase in cases of one to two per year, to ten cases in 2022 [11].

The epidemiological expansion of this vector is spreading, and based on the data obtained, it is likely that the dengue virus (DENV1) will spread further. Therefore, it is worth highlighting that an individual can be exposed several times to this agent throughout their life [1]. There are three most defined dengue borders in Brazil, being the South, North and Northeast of the country. Climate change together with the impact of urbanization has seen that the South is better suited for the reproduction of the *Aedes Aegypti* mosquito and potential in Argentina and Paraguay [11]. Over the last three centuries, the occurrence of dengue fever has been documented in different parts of the planet. There are historical records that dengue was the producer of pandemics and isolated epidemics, affecting countries in Africa, Europe, Australia and Asia [35, 36].

6. Conclusion

The epidemiological expansion of this vector is spreading by climate change together with the impact of urbanization has been a high issue combating zoonotic diseases for global public health. There have been recent advances in the development of therapeutic drugs, and vaccines that are currently being pursued at several phases of preclinical and clinical development. The preventive measures of dengue virus transmission associated Heartworm Disease by *Aedes aegypti* mosquitoes and challenging the epidemiological surveillance of the zoonotic diseases are the key role to control the spread this vector through of the improve the health promotion campaigns in water supply, personal protection, biological and mechanism vector approaches.

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest.

References

[1] Kala, M. P., St. John, A. L., & Rathore, A. P. S. (2023). Dengue: Update on Clinically Relevant Therapeutic Strategies and Vaccines. Current Treatment Options in Infectious Diseases. DOI: DOI 10.1007/s40506-023-00263-w.

[2] Vasilakis N., Cardosa J., Diallo M., et al. Sylvatic dengue viruses share the pathogenic potential of urban/endemic dengue viruses. J Virol. 2010;84(7):3726–8. https://doi.org/10.1128/JVI.02640-09.

[3] Lindenbach B., Rice C. Flaviviridae: the viruses and their replication. In: Knipe DM, Howley PM, editors. Fields' Virology. 4th ed. Lippincott Williams & Wilkins; 2001. p. 991–1041.

[4] Schlesinger, R. W. Dengue viruses. Wien, Springer-Verlag, 1980.

[5] Martinez, E. M. Dengue hemorrágico en niños. Habana: Ed. José Marti; 1990.

[6] Halstead, S. B. Dengue hemorrhagic fevera public health problem and a field for research. Bull. WHO, 58 (1): 1-21, 1980.

[7] Hammon, W. D. Dengue hemorrhagie fever. Do we know its causes? Am. J. Trop. Med. Hyg., 22 (1): 82-91, 1973.

[8] Nimannitya, S. Dengue hemorrhagic fever. Pediatric Practice, Thailandia (155-161).

[9] Braga, I. A; Valle, D. Aedes aegypti: histórico do controle no Brasil. Epidemiologia e serviços de saúde, 16 (2): 113-118, 2007.

[10] Roy, S. K., & Bhattacharjee, S. (2021). Dengue virus: Epidemiology, biology, and disease aetiology. Canadian Journal of Microbiology. DOI: dx.doi.org/10.1139/cjm-2020-0572.

[11] Codocco, C.T, Oliveira, S. S., & Ferreira, D. A. C et al (2022). Fast expansion of dengue in Brazil. The Lancet Regional Health - Americas. DOI: https://doi.org/10.1016/j.lana.2022.100274.

[12] de Almeida I.F., Lana R.M, Codeco, C.T (2022). How heterogeneous is the dengue transmission profile in Brazil? A study in six Brazilian states. PLoS Negl Trop Dis 16(9): e0010746. https://doi.org/10.1371/journal. pntd.0010746

[13] Lenharo, M. (2023). Massive mosquito factory in Brazil aims to halt dengue. Nature.

[14] Nature 2023 Apr;616(7958):637-638. doi: 10.1038/d41586-023-01266-9.

[15] Simmons, C.P., Farrar, J.J., Vinh Chau, N., Wills, B. Clinical Management of Dengue Infection. N Engl J Med 2012; 366:1423-1432, DOI: 10.1056/NEJMra111026

[16] Vasconcelos, J.L.M et al. Perspectivas emergentes no diagnóstico e manejo da dengue: Uma revisão sistemática. Brazilian Journal of Implantology and Health Sciences, 6 (2): 1808-1814, 2024. DOI: https://doi.org/10.36557/2674-8169.2024v6n2p1808-1814.

[17] Singhi, S; Kissoon, N; Bansal, A. Dengue e dengue hemorrágica: aspectos o manejo na unidade de terapia intensiva. Jornal de Pediatria. São Paulo, 83 (2): S32, 2007. DOI: https://doi.org/10.1590/S0021-75572007000300004

[18] Oliveira, A. M. F. Avaliação dos efeitos da Dirofilariose Cardiopulmonar sobre os parâmetros de função cardíaca e hemodinâmicos em cães na Ilha da Madeira. 2023. Dissertação (Mestrado em Medicina Veterinária) – Universidade de Évora, Évora, 2023.

[19] Simón F, Siles-Lucas M, Morchón R, González-Miguel J, Mellado I, Carretón E, Montoya-Alonso JA (2012). Human and animal Dirofilariasis: the emergence of a zoonotic mosaic. In Clinical Microbiology Reviews.

[20] Da Silva, J. S. M. Caracterização clínica e epidemiológica da dirofilariose cardiopulmonar canina no concelho de Benavente, Portugal. 2018. Dissertação de Mestrado. Universidade de Lisboa (Portugal).

[21] Pegado, I. M. P. et al. Incidência de Dirofilaria immitis (LEIDY, 1856) por meio dos métodos de Knott modificado, Gota espessa e Imunocromatografia em cães atendidos no hospital veterinário Prof. Mário Dias Teixeira (HOVET-UFRA). 2019.

[22] American Heartworm Society 2014, Current Canine Guidelines for the diagnosis, prevention, and management of heartworm (Dirofilaria immitis) Infection in dogs (revised January, 2014). http://www.heartwormsociety.org/pdf/2014-AHS-Canine-Guidelines.pdf.

[23] De complicações, Baixo Risco. Dirofilariose Canina e Felina, uma Parasitose em Evolução (II)–Fisiopatologia, Diagnóstico e Terapêutica. Maio/2024.

[24] Ribeiro, M. F. Estudo da prevalência de dirofilariose cardiopulmonar canina na cidade de São Tomé, República Democrática de São Tomé e Príncipe. 2024. Dissertação (Mestrado em Medicina Veterinária) – Universidade de Lisboa, Lisboa, 2024.

[25] Silva, J. S. M. Caracterização clínica e epidemiológica da dirofilariose cardiopulmonar canina no concelho de Benavente, Portugal. 2018. Dissertação (Mestrado em Medicina Veterinária) – Universidade de Lisboa, Lisboa, 2018.

[26] Alho, A. M.; Meireles, J.; Belo, S.; Madeira de Carvalho, L. Dirofilariose Canina e Felina: uma parasitose em evolução. Prática Clínica, 2023.

[27] Shu, Pei-Yun; Chen, Li-Kuang; Chang, Shu-Fen et al. Dengue virus serotyping based on envelope and membrane and nonstructural protein NS1 serotype-specific capture immunoglobulin M enzyme-linked immunosorbent assays., Journal of Clinical Microbiology, v. 41, n. 6, p. 2489 - 2493, 2024. DOI: 10.1128/JCM.42.6.2489-2494.2004

[28] Silva, R. C.; Langori, H. Dirofilariose: zoonose emergente negligenciada. Ciência Rural, Santa Maria, v. 29, n. 5, p. 1614 - 1623, ago. https://doi.org/10.1590/S0103-84782009005000062

[29] Capelli, G; Genchi, C; Baneth; Gad et al. Recent advances on Dirofilaria repens in dogs and humans in Europe., Laboratory of Parasitology, Istituto Zooprofilattico Sperimentale delle Venezie, Itália. Parasites & Vectors, 11:2 - 21, 2018. https://doi.org/10.1186/s13071-018-3205-x

[30] AHID, Silvia MM; LOURENÇO-DE-OLIVEIRA, Ricardo. Mosquitos vetores potenciais de Dirofilariose canina na Região Nordeste do Brasil., Revista de Saúde Pública, Nordeste Brasil, 33 (6): 560-565, 1999. https://doi.org/10.1590/S0034-89101999000600007

[31] Cavallazzi, R. S; Cavallazzi, A. C; Souza, I. V et al. Dirofilariose pulmonar humana: relato de sete casos., Jornal Brasileiro de Pneumologia, São Paulo, v. 28, n. 2, p. 100- 102, 2002. https://doi.org/10.1590/s0102-35862002000200007

[32] Savic, S; Stosic, M. Z; Marcic, D et al., Seroepidemiological Study of Canine and Human Dirofilariasis in the Endemic Region of Northern Serbia., Frontiers in Veterinary Science, Intitutes in Slovakia and Belgium, v. 7, p. 1 - 5, 2020. Doi: 10.3389/fvets.2020.00571

[33] Barbosa, U. C; Nava, A. F. D; Neto, J. V. F et al., Dirofilaria immitis is endemic in rural areas of the Brazilian Amazonas State capital, Manual., v. 32, p. 1-6, 2023. DOI:10.1590/S1984-29612023018

[34] Bendas, A.J.R; Almeida, F. M. et al. Update on Dirofilaria immitis epidemiology in South America and Mexico: literature review., v. 54, n. 4, p. 319 - 329, 2017. DOI: 10.11606/issn.1678-4456

[35] Theis, J. H. Public Health aspects of dirofilariasis in the United States., Veterinary Parasitology, v. 133, p. 157-180, 2005. DOI: 10.1016/j.vetpar.2005.04.007

[36] Teixeira, M. G; Barreto, M. L et al., Epidemiolody and preventive measures of dengue., Instituto de Saúde Coletiva, v. 8, p. 5 - 33, 1999. DOI: 10.1007/s00105-017-4073-6