

PATHOPHYSIOLOGICAL RELATIONSHIP BETWEEN DENGUE VIRAL INFECTION AND ITS CARDIAC MANIFESTATIONS

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Abstract: Dengue is a Public Health problem with immense impact in tropical countries, which is characterized by being a visceral epidemic in the national territory since 1980, given the immense and growing deforestation and rampant urbanization, which fails the basic health criteria for ensure adequate and universal quality of life. Furthermore, with the advent of the COVID-19 pandemic, it had been neglected due to the exhaustion of beds, since these were directed to patients affected by SARS-CoV-2. However, infection by the dengue virus, DENV 1-4, does not is frivolous and requires public attention, it must be clarified that studies indicate that one of its manifestations is associated with the main causes of morbidity and mortality in Brazil: cardiac comorbidities. In this context, the objective of this study is to analyze and correlate the evolution of dengue and its consequences on the cardiac system, in order to systematize updated information and ensure broad knowledge and insight into the importance of integrated care, early diagnosis and monitoring, such as explained by the Inter-American Society of Cardiology (IASC). To this end, Scielo and PubMed will be used, selecting articles in English and Portuguese from the last 9 years. Furthermore, the keywords selected for data collection will be “dengue”, “cardiac manifestations”, “myocarditis”, “DENV” and “public health”. The dengue virus and its cardiac problems are two situations characterized as visceral Public Health problems in Brazilian territory. Therefore, its impact concerns awareness and improvement at the national level regarding the control and treatment of this non-contagious acute infectious disease, in addition to contributing to the scientific community with systematized information about the cardiac manifestations associated with the pathophysiology of DENV 1-4, which are essential for health professionals

and students, given that both use evidence-based information in their jobs and academic training.

Keywords: Dengue; Cardiac Manifestations; DENV; Epidemic; Public Health.

INTRODUCTION

Dengue is a febrile disease transmitted by the bite of the female *Aedes aegypti* mosquito. In the meantime, it is an arbovirus prevalent in Brazil since the 1980s, being characterized as a national epidemic of a visceral nature in Brazilian territory, given that its virus is transmitted by the mosquito of the genus *Aedes* mentioned above, which is endemic and seasonal, with notable increase in cases during the summer. Furthermore, the development of dengue occurs due to deforestation, global warming and unrestrained urbanization, which promote the colonization of the *Aedes aegypti* vector. With regard to heart problems, dengue infection is defined by the Inter-American Society of Cardiology (IASC) as a NET-Heart (Neglected Tropical Diseases and other Infectious Diseases involving the Heart), that is, as an infection in underdeveloped countries and in neglected development and which requires strategies to avoid cardiac compromise. Therefore, it is worth highlighting that during a dengue virus infection, cardiac complications are not uncommon, being transient, but may be associated with highly serious morbidities and even significant mortality, since myocarditis can lead to organic failure of the heart and, thus, potentiate refractory shock. Therefore, given the neglect of dengue in the midst of the COVID-19 pandemic, due to the public crisis and the high demands and exhaustion of elected officials, identify the evolution processes of the infection, from the initial phase of dehydration to the recovery period, passing through the critical period of plasma extravasation and hemorrhage,

and identifying risk factors are necessary public care for collective health and must be propagated and taught in primary health, through Family Health Teams (EqSF), in order to combat dengue epidemics, offer early diagnosis and treatment, in addition to reducing the number of hospitalizations resulting from cardiac manifestations.

METHODOLOGY

This systematic review used the digital databases SciELO and PubMed, with the purpose of selecting scientific articles in Portuguese and English from the last 9 years. The descriptors were: “dengue”, “cardiac manifestations”, “myocarditis”, “DENV” and “public health”.

In this scenario, 639 articles were found, which went through a strict selection filter in order to distinguish those with the greatest scientific relevance to be reviewed and analyzed. The exclusion criteria were those articles without full access, with repeated texts, outside the proposed period (2015 - 2023) and/or unrelated to the topic raised, with a total of 18 reviewed works prevailing.

RESULTS

Dengue, as presented in the study by Schaefer et al. (2022), is caused by a single-stranded RNA virus of the Flavivirus genus and caused by serotypes DENV1-4, which are composed of three structural proteins, seven non-structural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5), simple positive-strand RNA of 10.7 kb and a lipid envelope, in addition to being around 50 nanometers. This viral infection affects tropical regions, essentially countries in Africa, Asia and Latin America, thanks to the hot climate and rainy season prevalent in these regions, which favors the proliferation of its vector. In this sense, the dengue arbovirus is transmitted by mosquitoes of the genus *Aedes*, which has

been endemic in Brazil since 1980. However, due to environmental changes, low hygienic-sanitary conditions and rampant urbanization, there has been an increase in serious cases and colonization of the *Aedes aegypti* vector in the national territory. Considering dengue infection, the IASC defines it as a NET-Heart; infection prevalent in underdeveloped countries neglected by the health agenda and which requires strategies for better diagnoses and treatments in order to avoid heart problems in countries that are already economically deficient. Therefore, during infection with the dengue virus, cardiac manifestations may occur and may even present a clinical progression to myocarditis, one of the most serious cases that leads to cardiac organic failure and refractory shock, characterized by cold and mottled skin, abnormal levels of consciousness, jugular distension, dyspnea, rales and death, as referenced by Shivanthan et al. (2015).

Despite the serious implications arising from the complications of dengue fever, there was neglect with this viral infection amid the COVID-19 pandemic, a Homeric infection by the SARS-CoV-2 virus that generated international concern during 2020 and 2021. This pandemic was characterized by a crisis public, essentially, in Brazil and generated huge impacts on the Unified Health System (SUS) thanks to the high demands and exhaustion of elected officials, as these were directed to patients with COVID-19. In the midst of this health crisis, dengue was marginalized and left in the background, generating a large increase in the number of cases. In this context, between January 2 and March 12, 2022, one hundred and sixty-one thousand six hundred and five (161,605) notifications of probable infected people were made, reaching a significant increase of 43.9% (<https://datasus.saude.gov.br/aceso-a-informacao/doencas-e-agravos-de-notificacao-de-2007-em-diante-sinan>).

This increase in dengue cases is worrying when we analyze its relationship with one of the biggest cases of morbidity and mortality in Brazil: cardiovascular diseases. In this panorama, according to Araiza-Garaygordobil et al. (2021), the specific pathophysiological mechanisms that link dengue fever and cardiac complications have not been completely described and are associated with varied manifestations, which may include palpitations, hypotension, pleurisy, chest pain, pulmonary edema and clinical signs of cardiogenic shock, with hypoperfusion, reduced level of consciousness, hypoxia and fluid overload.

These aforementioned complications are the result of the evolution of viral infection by the dengue virus, which is marked by three phases: initial phase, critical phase and final phase, as stated by Giri et al. (2022). Thus, in the critical phase of the disease, there is intense viral replication in infected cells, for example, cardiomyocytes. This process requires an increase in the individual's immunological response, which is marked by higher levels of inflammatory mediators found in the plasma of the patient affected by the disease, as stated by Ribeiro et al. (2017). According to Roy and Bhattacharjee (2021), dengue is defined as an infection of unique pathogenic complexity, which causes an immunological increase in the host in relation to innate immunity, with intense production of interferons (IFN), and adaptive, which is acquired after six approximately days of infection and consists of TCD8+ and TCD4+ lymphocytes, which recognize, respectively, non-structural and structural proteins preferentially. Therefore, the increase in vascular permeability, characteristic of the critical phase, in which there is an increase in interleukins 6, 13 and 18 and serum tumor necrosis factor, tends to bleeding and circulatory shock. Consequently, the most common

mechanisms of cardiac injury in dengue are the production of inflammation mediators, as well as an immune response mediated by cytokines, and the direct action of DENV virus subtypes on cardiomyocytes. In the case of patient recovery, fluid overload has been related to increased morbidity resulting from myopericarditis triggered by dengue, which, through viral action, potentiates an infection of the myocardium and pericardium. Other immunological factors responsible for the pathophysiology of cardiac complications are nitric oxide and the cytokines IFN-alpha and IFN-beta, TNF-alpha and IL-6, as analyzed by Gonçalves et al. (2017).

As there is no specific treatment for myocardial diseases associated with dengue, thanks to the presence of varied manifestations, it is essential to carry out an early diagnosis in affected patients. Thus, according to Farias et al. (2019), NS1, a non-structural protein secreted by DENV-infected cells, such as infected cardiomyocytes, must be quickly dosed, since rapid support is capable of controlling and avoiding shock or additional loss of cardiac function. As explained by Arora and Patil (2016), cardiac complications arising from arboviruses can develop into a chronic condition, such as T wave changes on the ECG and heart failure, which will last throughout the patient's life.

Therefore, dengue is a risk factor for rhythm disturbances and myocarditis in severe cases. To this end, providing cardiac monitoring for patients with altered ECG is essential, since, as explained by Oliveira et al. (2022), cardiomyopathies and heart failure are important and visceral public health problems in Brazil, as is dengue fever.

Furthermore, the economic burden of

cardiac disorders is high for the State, as it generates costs to guarantee hospitalization and monitoring. It is important to highlight that these costs could be reversed, since dengue is capable of being addressed in Primary Health Care, through epidemiological surveillance and the Family Health Program, as explained by Gomes et al (2015), since that the basic health team is effective in raising awareness among the population about the problems caused by dengue and about ways to prevent the spread of the mosquito vector.

CONCLUSION

The study highlights aspects of dengue virus infection and its intimate relationship with heart problems, two situations characterized as major public health problems rooted in Brazilian territory. Therefore, its impact concerns awareness and improvement at the national level regarding the control of this infectious disease, in order to avoid an exacerbation of cardiac dysfunctions in Brazil. Furthermore, there is a contribution to the scientific community through systematized and current information about cardiac manifestations associated with the pathophysiology of DENV, which are crucial for health professionals and students, given that both require evidence-based information to treat and understand the pathophysiology of two diseases that are so common in the country. Within the results found, it is clear that the dengue viral infection has a pathophysiological relationship with cardiac problems and both scenarios are Public Health problems, which rely on basic surveillance actions to prevent cardiac manifestations arising from dengue and, thus, reduce the hospitalization and mortality burden.

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