

UNIVERSIDADE ESTADUAL DE MONTES CLAROS
PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS EM SAÚDE

ROSANNA LORRANE FRANCISCO DOS REIS MATOS

**ATIVIDADE LARVICIDA DO EXTRATO DE PLANTA DO CERRADO FRENTE
AO *Aedes Aegypti* E *Culex quinquefasciatus* E ANÁLISE TEMPORAL
DA DENGUE EM MUNICÍPIOS DO NORTE DE MINAS GERAIS (2017-2022) NO
CONTEXTO DE SAÚDE ÚNICA**

Montes Claros
2024

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Coorientador: Prof. Dr. Fredy Galvis Ovallos

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RESUMO

Os mosquitos *Aedes aegypti* e *Culex quinquefasciatus* são vetores importantes de arboviroses, como a dengue, que representam desafios significativos para a saúde e a gestão pública. Esses insetos adaptam-se facilmente a criadouros artificiais, facilitando o aumento populacional e a propagação de doenças. A dengue, transmitida pelo *Aedes aegypti*, é uma doença de alta incidência global e apresenta desafios graves devido à sua rápida disseminação. O primeiro artigo, já publicado, dos dois que compõem este trabalho, avaliou a atividade larvicida do extrato aquoso das folhas de *Mauritiella armata* em larvas de *Ae. aegypti* e *Cx. quinquefasciatus*. O extrato foi preparado com 500 mL de água para cada 50 g de material, aquecido a 40°C, filtrado e seco até peso constante. As concentrações testadas foram de 2,625 a 10,5 mg/mL para *Ae. aegypti* e de 2,25 a 21 mg/mL para *Cx. quinquefasciatus*. A concentração $\geq 7,87$ mg/mL foi 100% eficaz no controle de *Ae. aegypti*, enquanto a concentração de 21 mg/mL apresentou 88,7% de eficácia contra *Cx. quinquefasciatus*. O segundo artigo, submetido, descreveu a epidemiologia da dengue em 54 municípios do Norte de Minas Gerais entre 2017 e 2022, com base em dados do Sistema de Informação de Agravos de Notificação (SINAN). Foram registrados 55.389 casos de dengue, com maior incidência na faixa etária economicamente ativa e uma maior frequência de casos em 2019, seguido por uma redução em 2020 devido à pandemia. Os resultados da dissertação destacam a necessidade de integrar ações de vigilância entomológica com atenção primária à saúde, sob a perspectiva da saúde única. Essa abordagem coordenada facilita o controle dos vetores e melhora a prevenção, o diagnóstico precoce e o tratamento das doenças transmitidas por vetores. Assim, é possível fortalecer o sistema de saúde local e reduzir o impacto da dengue e outras arboviroses de maneira sustentável e integrada.

Palavras-chave: Arboviroses. Controle de vetores. Epidemiologia.

ABSTRACT

Mosquitoes *Aedes aegypti* and *Culex quinquefasciatus* are key vectors for arboviral diseases such as dengue, posing significant challenges to public health and management. These insects easily adapt to artificial breeding sites, leading to population growth and disease spread. Dengue, transmitted by *Ae. aegypti*, is a globally prevalent disease that presents serious challenges due to its rapid spread. The dissertation comprises two articles. The first, already published, assessed the larvicidal activity of aqueous extracts from *Mauritiella armata* leaves against *Ae. aegypti* and *Cx. quinquefasciatus* larvae. The extract was prepared using 500 mL of water for every 50 g of plant material, heated to 40°C, filtered, and dried to a constant weight. Tested concentrations ranged from 2.625 to 10.5 mg/mL for *Ae. aegypti* and from 2.25 to 21 mg/mL for *Cx. quinquefasciatus*. A concentration of ≥ 7.87 mg/mL achieved 100% efficacy in controlling *Ae. aegypti*, while a concentration of 21 mg/mL showed 88.7% efficacy against *Cx. quinquefasciatus*. The second article, which has been submitted, described the epidemiology of dengue in 54 municipalities in Northern Minas Gerais from 2017 to 2022 using data from the Notifiable Diseases Information System (SINAN). A total of 55,389 dengues cases were reported, with the highest incidence in the economically active age group and a peak in cases in 2019, followed by a decline in 2020 due to the pandemic. The findings underscore the need for integrating entomological surveillance with primary health care from a One Health perspective. This coordinated approach facilitates vector control and enhances prevention, early diagnosis, and treatment of vector-borne diseases. By doing so, it is possible to strengthen the local health system and reduce the impact of dengue and other arboviral diseases in a sustainable and integrated manner.

Keywords: Arboviruses. Vector control. Epidemiology.

LISTA DE ABREVIATURAS E SIGLAS

AE – Extrato aquoso

CL – Concentração letal

DEN – Dengue

DENV-1 – Dengue virus serotype 1 (Sorotipo 1 do Vírus da dengue)

DENV-2 – Dengue virus serotype 2 (Sorotipo 2 do Vírus da dengue)

DENV-3 – Dengue virus serotype 3 (Sorotipo 3 do Vírus da dengue)

DENV-4 – Dengue virus serotype 4 (Sorotipo 4 do Vírus da dengue)

DTNs – Doenças tropicais negligenciadas

IBGE – Instituto Brasileiro de Geografia e Estatística

IIP – Índice de Infestação Predial

LIRAA – Levantamento Rápido de Índices para *Aedes aegypti*

MG – Minas Gerais

OMS – Organização Mundial da Saúde

PAHO – Pan American Health Organization

PEAA – Plano de Erradicação do *Aedes aegypti*

PIACD – Plano de Intensificação das Ações de Controle da Dengue

PNCD – Plano Nacional de Controle da Dengue

RT – Tempo de retenção

WHO – World Health Organization

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1 INTRODUÇÃO

1.1 Saúde única

O aumento da circulação global de pessoas, animais e mercadorias, a degradação dos ecossistemas, a expansão da monocultura e a pressão demográfica são fatores cruciais que intensificam as epidemias no século XXI (Karesh *et al.*, 2012). Esses elementos contribuem para a crescente relevância das doenças zoonóticas, uma vez que, no passado, a separação geográfica e os meios de transporte menos eficientes ajudavam a conter a propagação de doenças (Silvestrini *et al.*, 2020).

O conceito de Saúde Única destaca a interconexão entre a saúde humana, a saúde animal e o meio ambiente, reconhecendo a necessidade de um ecossistema equilibrado para garantir a saúde de forma abrangente. Adotar uma abordagem integrada, que envolva profissionais de diferentes áreas da saúde, é essencial para a prevenção e o controle eficaz de doenças (CFMV, 2015). A falta de equilíbrio entre essas esferas pode resultar em graves problemas de saúde pública, como evidenciado pelas doenças transmitidas, como a dengue (Zonetti *et al.*, 2018).

Nesse contexto, o conceito de Saúde Única é particularmente relevante para a abordagem das arboviroses e para o estudo de extratos vegetais como agentes larvicidas. Esses extratos oferecem uma solução ambientalmente segura e sustentável para o controle de vetores.

1.2 Doença tropical transmitida por vetores

As Doenças Tropicais Negligenciadas (DTNs) afetam majoritariamente as populações pobres dos continentes tropicais e subtropicais. Atualmente, a Organização Mundial da Saúde (OMS) classifica 20 doenças crônicas como DTNs, incluindo a dengue e as leishmanioses (WHO, 2023).

Muitas das DTNs são transmitidas por vetores, cujos agentes etiológicos têm distintos reservatórios animais e ciclos de vida complexos (WHO, 2023). As doenças transmitidas por vetores englobam uma ampla gama de enfermidades causadas por vírus, bactérias ou parasitas, que são propagadas aos seres humanos por meio de diversos invertebrados, pertencentes aos grupos de artrópodes e moluscos (Neves, 2005; Rey, 2011). A propagação de doenças por vetores constitui mais de 17% de todas as doenças infecciosas, causando um número alarmante de mortes, estimado em mais de um milhão de óbitos por ano.

Nessa perspectiva, ressalta-se a importância de compreender e combater efetivamente as doenças transmitidas por vetores, a fim de reduzir seu impacto na saúde pública (OMS, 2017).

A falta de acesso a condições sanitárias adequadas, a ausência de educação em saúde, o baixo investimento em novos fármacos, a falta de vacinas e de testes diagnósticos contribuem para a proliferação das doenças infecciosas (WHO, 2017; Luna; Campos, 2020; Rocha *et al.*, 2020). Estima-se que aproximadamente 1,7 bilhão de pessoas em todo o mundo seja alvo, anualmente, de atividades de prevenção e tratamento de pelo menos uma das DTNs (WHO, 2023). No entanto, ainda são necessários desenvolvimentos de pesquisas para melhorias no controle e na prevenção das doenças transmitidas por vetores, visto que essas são fundamentais para reduzir a sua propagação. Diante desse panorama, é crucial fortalecer as pesquisas e implementar medidas eficazes para reduzir o impacto dessas doenças na saúde pública global. Nesse contexto, pesquisas sobre o uso de extratos vegetais, como o da *Mauritiella armata*, surgem como uma alternativa sustentável e promissora para o controle de vetores. Esta dissertação concentra-se na avaliação da atividade larvicida do extrato de *Mauritiella armata* contra *Aedes aegypti* e *Culex quinquefasciatus*, além de analisar a epidemiologia da dengue no Norte de Minas Gerais.

1.3 *Aedes aegypti*

O *Aedes aegypti* (Linnaeus, 1762), conhecido como mosquito da dengue, é um vetor importante de arboviroses como dengue, febre amarela urbana, chikungunya, zika e mayaro (Terra *et al.*, 2017). Com um ciclo de vida de cerca de 10 dias, o mosquito se adapta bem a criadouros artificiais, como pneus e vasos, e apresenta uma alta capacidade de transmissão de doenças devido aos hábitos alimentares das fêmeas (Zara *et al.*, 2016).

A dengue, causada pelo vírus *Flavivirus*, é endêmica em regiões tropicais e subtropicais e tem quatro sorotipos. No Brasil, o DENV-2 é o mais comum. O aumento da dengue está ligado à urbanização desordenada, à falta de saneamento e à globalização (Guzman *et al.*, 2010; Sinclair; Asgari, 2020; Huang *et al.*, 2021). A incidência tem crescido nas últimas décadas, com milhões de casos registrados anualmente e uma mortalidade que pode ser reduzida com detecção precoce e tratamento adequado (Texeira *et al.*, 1999; Ribeiro *et al.*, 2006; Almeida, 2010; OPAS, 2023).

Prevenir e controlar a dengue envolve eliminar criadouros do mosquito e aumentar a conscientização pública. Medidas eficazes de controle de vetores e a colaboração das autoridades de saúde são essenciais para reduzir a propagação da doença. A pesquisa sobre a

atividade larvícida do extrato de *Mauritiella armata* é vital para desenvolver novas estratégias de controle, especialmente em regiões como o Norte de Minas Gerais, onde a dengue é endêmica.

1.4 *Culex quinquefasciatus*

O *Culex quinquefasciatus* (Say, 1823), popularmente conhecido como muriçoca, carapanã ou pernilongo doméstico, é um mosquito cosmopolita que se encontra em regiões tropicais e subtropicais. Esse inseto é um vetor significativo de doenças como filariose linfática, febre do Oeste do Nilo Ocidental, febre do Vale Rift e encefalite de Saint Louis (Shaikevich *et al.*, 2016). Sua abundância é frequentemente associada a áreas urbanas com deficiências em saneamento, onde há proliferação de criadouros em água contaminada e rica em matéria orgânica (Consoli; Oliveira, 1994).

O *Culex quinquefasciatus* é morfológicamente identificado por sua coloração marrom-clara, tarsos escuros e escudo marrom coberto por escamas amarelo-douradas (Consoli; Oliveira, 1994). Com hábitos noturnos, esse mosquito é conhecido pelo zumbido desconfortável e por picadas que podem causar reações alérgicas (Cardoso *et al.*, 2010). Machos e fêmeas se alimentam de seiva de plantas, mas as fêmeas, já inseminadas, precisam de sangue para maturar seus ovos. Elas podem se alimentar de vários vertebrados, incluindo humanos, aumentando o risco de transmissão de patógenos zoonóticos (Consoli; Oliveira, 1994; Bhattacharya; Basu, 2016).

Os mosquitos do gênero *Culex* têm um ciclo de vida holometábólico, que inclui os estágios de ovo, larva (com quatro instares), pupa e adulto alado. Ao contrário do *Aedes aegypti*, as formas imaturas do *Culex* se desenvolvem em habitats variados, incluindo águas poluídas e esgotos.

Dada a importância do *Culex quinquefasciatus* como vetor de doenças e sua proliferação em áreas urbanas com saneamento inadequado, estudar a eficácia do extrato de *Mauritiella armata* contra esse mosquito pode oferecer uma solução sustentável e eficaz para reduzir a incidência de doenças associadas.

1.5 Controle vetorial

Entre 1958 e 1973, o *Aedes aegypti* foi erradicado duas vezes no Brasil (Soper, 1965). No entanto, o vetor foi reintroduzido em 1976 devido a falhas na vigilância e ao rápido crescimento populacional (Zara *et al.*, 2016). Em 1996, o Ministério da Saúde lançou o Plano de Erradicação do *Aedes aegypti* (PEAa) para reduzir casos de dengue hemorrágica, mas o

plano falhou em erradicar o vetor devido à expansão da infestação e ao aumento dos casos de dengue (Braga; Valle, 2007).

Em 2001, o governo implementou o Plano de Intensificação das Ações de Controle da Dengue (PIACD) em municípios com altos índices de transmissão. Contudo, em 2002, foi criado o Plano Nacional de Controle da Dengue (PNCD), que ainda está em vigor. Esse plano é fundamentado na gravidade dos casos de dengue e na introdução do terceiro sorotipo no Brasil (Braga; Valle, 2007; Figueiró *et al.*, 2010). O PNCD utiliza indicadores epidemiológicos para identificar áreas vulneráveis e adapta suas ações com base no nível de infestação (Brasil, 2002). No entanto, o uso de larvicidas químicos tem causado resistência nos mosquitos e impactos ambientais e à saúde humana (Gambarra *et al.*, 2013; Zara *et al.*, 2016).

Ao contrário do *Aedes aegypti*, não há um programa nacional de controle para o *Culex quinquefasciatus* (Amorim, 2013). A busca por alternativas de controle mais econômicas e ambientalmente amigáveis é essencial para a saúde pública. Nesse sentido, os extratos vegetais têm emergido como uma alternativa promissora. Os bioinseticidas, derivados de plantas, têm mostrado eficácia no controle de mosquitos, especialmente em populações resistentes aos inseticidas químicos. Esses compostos naturais têm propriedades ovicidas, larvicidas, pupicidas, adulticidas e repelentes, oferecendo uma solução sustentável para o controle de *Aedes spp.*, *Anopheles spp.* e *Culex spp.* (Fernández *et al.*, 2011; Louise, 2014; Duprat *et al.*, 2015; Gomes *et al.*, 2016).

Além disso, novas tecnologias, como o uso de larvicidas bacterianos, fúngicos e vegetais, têm se mostrado eficazes no controle do *Aedes aegypti*. Estudos indicam que larvicidas de origem bacteriana (Garcez *et al.*, 2013), fúngica (Gomes *et al.*, 2015) e vegetais, como óleos essenciais (Oliveira *et al.*, 2013; Ferreira *et al.*, 2015) e extratos vegetais (Garcez *et al.*, 2013; Porto *et al.*, 2017), são promissores.

Outra abordagem relevante é o controle biológico utilizando a bactéria entomopatogênica *Wolbachia*. Essa bactéria, que não é prejudicial para humanos e animais domésticos, reduz a longevidade dos mosquitos e induz incompatibilidade citoplasmática, resultando em progênie estéril (McMeniman *et al.*, 2009; Yeap *et al.*, 2011). A pesquisa contínua é fundamental para aprimorar o controle e a prevenção de vetores. A estratégia de prevenção deve incluir a eliminação de criadouros, a conscientização pública e a cooperação das autoridades de saúde.

2 OBJETIVOS

2.1 Objetivo geral

- Avaliar atividade larvicida da *Mauritiella armata* sobre larvas de *Aedes aegypti* e *Culex quinquefasciatus* e descrever a epidemiologia da dengue em 54 municípios do Norte de Minas Gerais, nos anos de 2017 a 2022.

2.2 Objetivos específicos

- Testar a atividade larvicida do extrato aquoso das folhas de *Mauritiella armata* para o controle de *Aedes aegypti* e *Culex quinquefasciatus*.
- Investigar o perfil epidemiológico das pessoas notificadas com dengue, de 2017 a 2022, em 54 municípios do Norte de Minas Gerais, Brasil.
- Associar a ocorrência de casos de dengue e a densidade vetorial, de 2017 a 2022, em 54 municípios do Norte de Minas Gerais, Brasil.

3 MÉTODOS

Esta dissertação é composta por dois produtos principais (artigos científicos), que abordam metodologias distintas para responder aos objetivos propostos.

O primeiro artigo, intitulado “Larvicidal Activity of Leaf Extract From *Mauritiella armata* (Aceraceae) on *Aedes aegypti* and *Culex quinquefasciatus* (Culicidae)”, foi publicado na *Journal of Agricultural Science* (Qualis periódico: B1 – Interdisciplinar). Trata-se de um estudo experimental que teve como objetivo avaliar a eficácia da atividade larvícida do extrato aquoso da folha de *Mauritiella armata* no controle dos vetores de arboviroses *Aedes aegypti* e *Culex quinquefasciatus*. O artigo foi formatado segundo as normas de publicação disponíveis em: <https://ccsenet.org/journal/index.php/jas/article/view/0/46596>.

O segundo artigo, intitulado “Epidemiologia da Dengue em Municípios do Norte de Minas Gerais, Brasil, de 2017 a 2022”, foi submetido à *Revista Acta Tropica* (Qualis periódico: A2 – Interdisciplinar). Trata-se de um estudo epidemiológico descritivo, quantitativo e retrospectivo, com análise de série temporal, que aborda o perfil epidemiológico das pessoas notificadas com dengue e a associação entre a ocorrência de casos de dengue e a densidade vetorial. A pesquisa abrange o período de janeiro de 2017 a dezembro de 2022, em 54 municípios do Norte de Minas Gerais, Brasil. O artigo foi formatado segundo as normas de publicação disponíveis em: <https://www.sciencedirect.com/journal/acta-tropica/publish/guide-for-authors>.

Demais informações sobre os métodos empregados estão descritas nas seções “Métodos” e “Materiais e Métodos” de cada produto apresentado a seguir.

4 PRODUTOS TÉCNICO-CIENTÍFICOS GERADOS

4.1 Produto 1: MATOS, Rosanna Lorrane Francisco dos Reis *et al.* Larvicidal Activity of Leaf Extract from *Mauritiella armata* (Aceraceae) on *Aedes aegypti* and *Culex quinquefasciatus* (Culicidae). *Journal of Agricultural Science*, v. 14, n. 2, p. 63-69, 2022.

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Larvicidal Activity of Leaf Extract From *Mauritiella armata* (Aceraceae) on *Aedes aegypti* and *Culex quinquefasciatus* (Culicidae)

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Abstract

The mosquitoes *Aedes aegypti* and *Culex quinquefasciatus* (Diptera: Culicidae) are important vectors of several arboviruses, and are relevant public health problems. Conventional control, using chemical larvicides have selected resistant Culicidae populations and caused negative effects on the environment and human health. However, the use of plant extracts has represented a sustainable alternative for insect control. Popularly known as Xiriri, *Mauritiella armata* (Mart.) Burret (Aceraceae) is an abundant palm tree in Vereda ecosystems and has economic and social importance. In this study, the aim was to evaluate the larvicidal activity of the aqueous extract (AE) leaves of this plant on *Ae. aegypti* and *Cx. quinquefasciatus* larvae. The mortalities of larvae were analyzed after treatment with four concentrations of the extract, comparing with a negative control

using mineral water. The AE promoted 100% efficacy against *Ae. aegypti* larvae at 7.9 mg/mL. The lethal concentration to promote 90% mortality of *Cx. quinquefasciatus* larvae was estimated at 30.57 mg/mL. After chromatographic analyses, flavonoids, catechin and carbohydrates were detected. AE from *M. armata* leaves presented high larvicidal activity against *Ae. aegypti* and *Cx. quinquefasciatus*, and represents a promising alternative to be used in vector control.

Keywords: arboviruses, plant extract, palm tree and unique health

1. Introduction

Vector-borne diseases account for 17% of the estimated global burden of all infectious diseases (WHO, 2018). *Aedes aegypti* (Linnaeus, 1762) and *Culex quinquefasciatus* (Say, 1823) are vectors of several arboviruses, which are considered a public health problem due to their increasing territorial dispersion, high capacity to adapt to artificial ecotopes and difficulty to be controlled (Donalisio, Freitas, & Zuben, 2017).

Vector control is the main form of prevention, and the elimination of breeding sites is the most effective method; however, conventional treatments with chemical larvicides select resistant populations of Culicidae (Gray *et al.*, 2018; Atyame *et al.*, 2019; Lopes *et al.*, 2019). As a result, the use of plant extracts appears as a promising alternative, ecologically and environmentally safe, and biodegradable, contributing to the reduction of negative effects on the environment and public health (Hwang *et al.*, 2017; Hari & Mathew, 2018).

Mauritiella armata (Mart.) Burret belongs to the Arecaceae family and is popularly known as Xiriri. It is a palm tree widely distributed in the Brazilian territory, in the Vereda areas and has economic and social importance for the Vereda communities (Andrew Henderson, 1995; Martins, 2012). Although some studies have shown that plants of the Arecaceae family have a larvicidal effect against Culicidae larvae (Tayler *et al.*, 2019, Koc *et al.*, 2016), the phytochemical composition of *M. armata* extracts and the potential of metabolites in the control of insects however, are not known. In this perspective, the study proposed to evaluate the larvicidal activity of aqueous extract of *Mauritiella armata* leaves on *Aedes aegypti* and *Culex quinquefasciatus*.

2. Methods

2.1 Plant Material

The plant material was composed of leaves of *Mauritiella armata*, from the Almescla vereda of the Pandeiros Environmental Protection Area, located in northwestern Minas Gerais, Brazil (15°22'50"S and 44°55'28"W). The desiccated leaves were deposited at the Montes Claros Herbarium: MCMG and identified as *Mauritiella armata* (Mart.) Burret (xiriri), receipt n° 5778a.

2.2 Production of Extract

Leaves of *M. armata* were selected and washed in running water, and damaged or deteriorated were discarded. Afterwards, they were dehydrated in a greenhouse with forced air circulation at 40 °C for 72 hours and ground in a feed mill. The resulting material was placed in paper bags, free from the incidence of light.

The aqueous extract (AE) was prepared by adding 500 mL of distilled water to 50 g of raw powder of the plant species, being heated in a water bath at 40 °C for 60 min. After this period, the extracts were hot filtered in a funnel with gauze and cotton and later sent to a greenhouse with forced air circulation at 40 °C until constant weight was obtained (Nery *et al.*, 2010, Morais-Costa *et al.*, 2015).

The subsamples of the extracts were submitted to dry matter determination at 105 °C, to calculate the tested concentrations (Patricia Cunniff, 1995). After determining the dry matter weight, the extracts were adjusted to the concentrations to be tested.

2.3 Chromatographic Analysis of the Extract

Quotas (1.0 mg) of the plant extract was measured in a conical glass and then dissolved in 60 µL of pyridine and 100 µL of BSTFA (N,O-bis(trimethylsilyl) = trifluoroacetamide) containing 1% of chlorotrimethylsilane. The reaction mixture was heated at 60 °C for 30 min. Of the solution obtained, only 1 µL was injected into the CG-MS, and the procedure was performed in triplicate.

Chromatographic analyses were performed in an Agilent Technologies gas chromatograph (GC 7890A) equipped with an electron impact ionization detector (CG-MS) and a DB-5MS capillary column (Agilent Technologies, 30 m long × 0.25 mm internal diameter × 0.25 µm film thickness). Helium (99.9999% purity) was used as the trailing gas at a rate of 1 mL min⁻¹. Using an autoinjector (CTC combiPaL), 1 µL of the sample was injected into the chromatograph at a split ratio of 1:10. The split/splitless injector was kept at 290 °C. The chromatographic column, initially at 80 °C, isothermal for 5 min, was heated at a rate of 4 °C min⁻¹ to 260 °C

for 10 min. After separating the compounds, the temperature was raised to 300 °C and maintained for 2 min (after running). The interface temperature was maintained at 280 °C and the ionization performed by impact of 70 eV. The m/z sweep range was from 30 to 600 Da.

2.4 Origin of Insects

Native larvae of *Culex quinquefasciatus* were provided by the Montes Claros Zoonoses Control Center (Centro de Controle de Zoonoses-CCZ) and identified in accordance with the *Cx. quinquefasciatus* surveillance guide (Ministério da Saúde, 2011). The eggs of *Aedes aegypti* came from the F4 and F5 generations of the already established closed colony, provided by the insectarium of the Insect Behavior Laboratory of the Federal Institute of Northern Minas-Campus Salinas.

2.5 Bioassays and Data Analysis

The bioassays were carried out according to the methodology described by the WHO (1981). Final third instar or early fourth instar larvae were transferred to disposable plastic containers containing 30 mL of AE or negative control containing mineral water. Tests were performed in triplicate; 20 larvae of *Ae. aegypti* and 15 *Cx. quinquefasciatus* larvae were added to each container, and the final concentrations evaluated were 10.5; 7.875; 5.25 and 2.625 mg/ml and 21.0; 15.25; 10.5 and 5.25 mg/mL, respectively. After a period of 24 and 48 hours, the tests were evaluated, which included counting the dead larvae and observing the occurrence of morphological deformations by optical microscopy.

The experiments were carried out in a completely design (treatments defined randomized split-plot as concentrations and periods as subplots). The data were subjected to analysis of variance and the means were compared using the Scott-Knott test ($p > 0.05$), using the SAEG 9.1 statistical package (2007). The concentration capable of promoting 90% larval mortality was determined by probit regression analysis ($p > 0.05$) in the same statistical program.

3. Results

3.1 Effect of Tested Aqueous Extract on Culicidae Larvae

The bioassays performed showed a significant interaction between the periods and concentrations tested ($p < 0.001$) against *Ae. aegypti* and *Cx. quinquefasciatus*, obtaining greater efficacy after 48 hours of treatment. During this period, the AE of *M. armata* leaves showed 100% efficacy in the mortality of *Ae. aegypti* larvae at ≥ 7.87 mg/mL and efficacy of 88.7% against *Cx. quinquefasciatus* larvae at 21 mg/mL (Table 1).

Table 1. Mortality of *Aedes aegypti* and *Culex quinquefasciatus* in larvae treated with *Mauritiella armata* leaves after two periods aqueous extract of

Treatments (mg/mL)	24h	48h
<i>Ae. Aegypti</i>		
10.5	93.33Aa	100.00Aa
7.88	60.00Bb	100.00Aa
5.25	20.00Bc	85.00Ab
2.625	6.67Bd	21.67Ac
Mineral water	0.00Ae	0.00Ae
.....		
<i>Cx. quinquefasciatus</i>		
21.00	48.67Ba	89.00Aa
15.25	37.67Bb	75.67Ab
10.50	26.67Bc	55.67Ac
5.25	11.00Bd	48.67Ad
Mineral water	0.00Ae	0.00Ae

Note. Distinct lowercase letters in columns indicate differences between treatments, and distinct uppercase letters in rows indicate differences between periods at ($p < 0.05$).

After 24 h of incubation, larvae subjected to AE of *M. armata* leaves showed deterioration and induction of intestinal content elimination in both vectors (Figure 1).



Figure 1. *Aedes aegypti* larva exposed to distilled water (A); *Ae. aegypti* larvae exposed for 48 hours to the aqueous extract of *Mauritiella Armata* (A1); Larvae of *Culex. quinquefasciatus* from the control group (B) and exposed to the extract (B1). Expansion by 400 $\times$ (objective lens: 40 $\times$, down: 10 $\times$) For the larvae of *Ae. aegypti* it was not possible to estimate the CL₉₀, as it showed 100% mortality a concentrations; however, the CL₉₀ for *Cx.quinquefasciatus* larvae was estimated to be 30.57 mg/mL (25.57 - 9.10 mg/mL) (Figure 2).

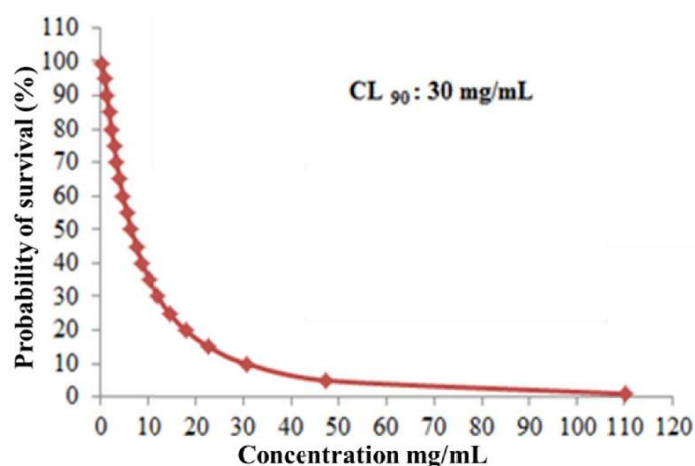


Figure 2. Probability of survival of *Culex. quinquefasciatus* larvae after 48 h of treatment with aqueous extract of *Mauritiella armata* leaves

3.2 Phytochemical Analysis

In the phytochemical analysis, carbohydrates, tannins, and acids were identified in the AE of *M. armata* leaves. The largest classes according to the size of their áreas were carbohydrate- β -D-glucopyranose (18.46% carbohydrate-thalose (10.33%); in addition, the presence of catechin (0.05%) was observed.

Table 2. Compounds identified by gas chromatography in *Mauritiella armata* leaf extracts and their area (%) in the chromatographic profile

Aqueous extract			
N	RT	Compounds (Area%)	N
1	7.312	2-hydroxypropanoic acid	0.18
3	8.805	L-alanine	0.06
4	9.766	Glyconic acid	0.16
11	17.909	Phosphate	1.35
12	15.035	Glycerol	0.82
13	16.381	Butanedioic acid	0.06
18	22.116	2-hydroxybutanedioic acid	0.39
28	31.343	Carbohydrate- β -D-Glycopyranosis	18.46
34	33.129	Carbohydrate- β -D-Glycopyranosis	10.68
35	33.288	Carbohydrate-galactopyranose	5.95
43	35.530	Carbohydrate-talose	10.33
47	37.420	Carbohydrate- β -D-Galactofuranosis	1.62
48	37.900	Carbohydrate-Inositol	5.34
62	54.551	Catechin	0.05

Note. RT: Retention time (min.); N.I.: 1.

4. Discussion

Aqueous extracts from leaves appear as an alternative for vector control. In the literature, extracts of *Annona glabra*, *Bougainvillea spectabilis*, and *Saraca asoca* with larvicidal activity in larvae of *Ae. aegypti* and *Aedes*, and *Ae. Albopictus*, with LC₅₀ of 5.29 mg/L and 3.02 mg/L respectively (Amarasinghe *et al.*, 2020; Sharma *et al.*, 2019) stand out. Likewise, for *Cx. quinquefasciatus* AE from leaves of *Cassia didymobotrya* and *Cayratia trifolia* showed 100% mortality efficacy (Nagappan, 2012; Chakraborty *et al.*, 2013).

The results obtained demonstrate that the AE of *M. armata* leaves presented larvicidal potential at the evaluated concentrations. In 48 h, there was a higher mortality of larvae in both insects. This fact corroborates the results of Hari and Mathew (2018), who in the same period, observed higher larval mortality of *Ae. aegypti* and *Cx. quinquefasciatus* through a combination of plant extracts. According to Santos *et al.* (2015), the longer the exposure time of larvae to the AE, the higher the mortality percentages, due to the absorption of toxic substances.

The control larvae of both insects showed high mobility and quick reaction to any touch. In contrast, larvae submitted to AE showed loss of mobility and morphological changes after 24 h of treatment. According to Barreto *et al.* (2007), the first sign of the extract's larvicidal action is the reduction of larval mobility.

Additionally, the AE from the leaves of *M. armata* caused deterioration and induction of elimination of the intestinal contents of the larvae of both vectors (Figure 2). Procopio *et al.* (2015), observed a similar effect on *A. aegypti* larvae exposed to the leaf extract of *Schinus terebinthifolius* (Anacardiaceae). This behavior has been reported as a defense mechanism of mosquito larvae in order to expel substances that are toxic to them (Gusmão *et al.*, 2002). Although the larvae present this defense mechanism, our results showed that this was not enough to avoid the harmful effects of the extract, since the larvae survival rate decreased after the larvicide test.

Assessing the chemical composition of *M. armata*, Royo *et al.* (2019) detected significant flavonoid content in its leaves, petiole and root. Flavonoids are a diverse and abundant group among secondary metabolites in

different plants (Filho, Antonio Carlos Pereira; Castro, 2019). In the study by Tayler *et al.* (2019), EA from leaves of *Cocos nucifera* (Arecaceae) showed antiparasitic activity against the malaria protozoan, due to the synergistic action of flavonoids with other compounds.

Diterpene extracted from *Copaifera reticulata*, and a fraction rich in catechetal tannins, extracted from *Magonia pubescens* caused the death of *Ae. aegypti* through cell destruction in the midgut (Volotto *et al.*, 2011). In the work by Elumalai *et al.* (2016), the catechin isolated from *Leucas aspera* showed 100% mortality in *Ae. aegypti*, *Anopheles stephensi* and *Cx. quinquefasciatus* at a concentration of 20 ppm. The catechin, which has insecticidal properties, was identified in the phytochemical analysis of the xiriri leaf.

The aqueous extract of the leaves of *Mauritiella armata* represents a promising alternative for the control of *Aedes aegypti* and *Culex quinquefasciatus*, due to its high larvicidal effect. In addition, this study presents a simple, clear, and low-cost methodology that contributes to the valuation of ecosystem services and the promotion of unique health.

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4.2 Produto 2: MATOS, Rosanna Lorrane Francisco dos Reis *et al.* Epidemiologia da Dengue em municípios do Norte de Minas Gerais, Brasil, de 2017 a 2022

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Epidemiology of Dengue in municipalities in the North of Minas Gerais, Brazil, from 2017 to 2022

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Abstract

Objectives: This is an epidemiological study that investigated the temporal distribution and epidemiological profile of the resident population, and the association between the occurrence of dengue cases and vector density, from 2017 to 2022, in 54 municipalities in the North of Minas Gerais, Brazil.

Method: A time series analysis was carried out using as a source secondary data obtained from the Notifiable Diseases Information System and the Rapid Index Survey for *Aedes aegypti* in the analyzed municipalities.

Results: 55,389 cases of dengue were reported, with 2019 having the highest number, followed by 2022, 2018, 2020, 2017 and 2021. Of this total, 49.27% were confirmed cases of the disease, 37.5% were discarded and 13.23 % were inconclusive. According to the incidence rate, the municipality of Porteirinha recorded the highest number of confirmed cases per 10 thousand inhabitants in 2017 and 2020, succeeding Janaúba in 2018, Padre Carvalho in 2019, Matias Cardoso in 2021 and Espinosa in 2022. The age group with the highest number of cases being 20 to 49 years old, with a higher frequency in females.

Conclusion: Thus, it was possible to observe a higher incidence in the economically active age group, a higher frequency of cases in 2019, following the decline in 2020, which corresponds to the pandemic period. Considering the results, we emphasize the need to improve surveillance, health education actions and frequent training of service professionals for rapid detection and care for affected people.

Keywords: *Aedes aegypti*; Arbovirus; Tropical Disease; Pandemic.

1. Introduction

Dengue is an arbovirus endemic in Brazil, caused by a virus with four different serotypes (DENV-1, DENV-2, DENV-3, and DENV-4), belonging to the *Flaviviridae* family and the *Flavivirus* genus (Guzman *et al.*, 2010; Snclair and Asgari, 2020). The disease presents itself in an epidemic form

with cyclical variations and is expanding geographically since approximately half of the world's population lives in transmission areas at risk of acquiring the infection. It is estimated that in the Americas, around 500 million people are at risk of becoming infected by one or more serotypes of the virus (PAHO, 2023).

The disease is considered by the World Health Organization (WHO) as one of the most serious public health problems in the world and presents a broad spectrum, which includes clinical manifestations from mild to severe (Harapan *et al.*, 2020), ranging from asymptomatic cases and severe conditions, which are classified as dengue, dengue with warning signs and severe dengue, which can progress to different phases: dengue hemorrhagic fever (DHF, Dengue Hemorrhagic Fever) and/or dengue shock syndrome (DSS, Dengue Shock Syndrome) (PAHO, 2023; Salle *et al.*, 2018).

The female mosquito *Ae. aegypti* (Diptera: Culicidae) is responsible for transmitting the four serotypes of the DENV virus during the blood meal process (Brady and Hay, 2020). The development and proliferation of *Ae. aegypti* are favored on intertropical continents, due to environmental and meteorological conditions (Instituto Oswaldo Cruz, 2023), as well as the result of structural determinants such as lack of basic sanitation, water supply, and precarious infrastructure, characteristic of neglected diseases. The mosquito has synanthropic and anthropophilic behavior, that is, it can easily adapt to artificial breeding sites and proliferate in urban areas (Teixeira *et al.*, 1999). Therefore, vector control is essential for the prevention of dengue (Simmons, 2012), however, there are still obstacles to the control, such as the resistance of vector populations to insecticides and the toxicity of these products to vertebrates (Zara *et al.*, 2016). Furthermore, dynamical and evolutionary processes have contributed to the adaptive selection of species, which directly interferes with the health conditions of the human population (Zara *et al.*, 2016).

Disorganized urbanization, population growth, and the irregular functioning of health systems are important determinants for the occurrence of infectious diseases, especially arboviruses, which constitute one of the main public health problems in the world (Teixeira *et al.*, 1999). Reported cases of arboviruses have increased in recent years, raising the risk of growth in the number of hospitalizations and deaths resulting from the disease (Medes *et al.*, 2020) which generates impacts on the social and economic aspects of affected populations. In this sense, epidemiological surveillance actions are important for understanding the dynamics of the disease, mainly through case notification systems (Bohm, 2016), which allow monitoring trends and improving decision-making.

In recent years, the state of Minas Gerais has presented a high incidence of dengue cases in municipalities, which has experienced four major epidemics, in 2010, 2013, 2016, and 2019 (PAHO, 2020; Brasil, 2019), in a way that last year it was the one that recorded the highest number of deaths in the country (Brasil, 2022).

In view of this, epidemiological studies contribute to understanding the characteristics of the affected population, living conditions, and the health-disease process, in addition to helping to develop health promotion strategies (Medes *et al.*, 2022). Thus, the present study aimed to analyze the temporal distribution and epidemiological profile of residents, as well as the association between the occurrence of dengue cases and vector density, from 2017 to 2022, in 54 municipalities in the North of Minas Gerais, Brazil.

2. Materials and methods

2.1 Study design

This is an epidemiological, quantitative, and retrospective study with time series analysis, covering the period from 2017 to 2022 in 54 municipalities in the North of Minas Gerais, Brazil.

2.2 Study area

The northern region of the state of Minas Gerais is located in the southeast of Brazil and made up of 89 municipalities, divided into seven microregions: Bocaiúva, Grão Mogol, Janaúba, Januária,

Montes Claros, Pirapora and Salinas. The region has a territorial extension of approximately 67,577.35 km², an estimated population of 1,125,986 inhabitants, and a demographic density of approximately 16.66 inhabitants/km² (IBGE, 2022). The North of Minas is characterized by low social indicators, notable social inequality, a mostly rural population, and distant municipalities (Damasceno and Cladeira, 2018).

2.3 Obtaining the data

The study was developed with data on dengue cases obtained from the Notifiable Diseases Information System (SINAN) (<https://portalsinan.saude.gov.br/>), made available by the Ministry of Health (MS). Notified cases from the 54 municipalities in the Northern region of Minas Gerais were included, referring to the period from January 2017 to December 2022. The data were composed of the number of reported and confirmed cases, distribution by age group, sex, disease classification, and evolution of cases (death or cure).

To evaluate the geographic distribution of dengue cases across municipalities in the North of Minas Gerais, the population estimate and the geographic grids such as the territorial limits of each municipality.

To analyze the association between the occurrence of reported cases of dengue fever and vector density from January 2017 to October 2021, data referring to the Building Infestation Index (Índice de Infestação Predial - IIP), which makes up the Rapid Index Survey for *Aedes aegypti* (Levantamento Rápido de Índices para *Aedes aegypti* - LIRAA), were obtained through the Health Department of the Northern Macroregion of Minas Gerais. LIRAA consists of the IIP, an indicator that measures the risk of the population becoming ill from diseases transmitted by *Ae. aegypti*, produced through the analysis of mosquito larvae collected in properties by Endemic Disease Control Agents (Agentes de Combate à Endemias - ACEs) and the calculation is carried out using: positive properties/researched properties x 100.

2.4 Spatial analysis

The geographic distribution of dengue cases across the 54 municipalities in the North of Minas Gerais was done using the Qgis® program (https://qgis.org/pt_BR/site/), version 3.28.2. A description of the occurrence of cases was prepared, categorizing the number of cases per municipality according to the number of notifications and represented on the geographic map according to the magnitude of colors: red (above 4,001 reported cases), orange (between 3,001 and 4,000 reported cases), yellow (between 2,001 and 3,000 reported cases), pink (between 1,001 and 2,000 reported cases) and gray (less than 1,000 reported cases).

2.5 Statistical analysis

The case incidence coefficient was calculated using the formula: number of confirmed cases/resident population of the municipality x 10,000. The lethality rate was also calculated, which considers the ratio between the number of deaths/number of cases of the disease x 100 (Marques *et al.*, 2020).

To test the variation in the number of dengue cases between years and in function of IIP, Generalized Linear Models (GLM) were constructed. The incidence of dengue cases was inserted as a response variable, while years and IIP were considered explanatory variables. The models were subjected to residual analysis to determine the fit of the error distribution. The complete model was built with Quasi-Poisson error distribution, with Log (y) link function and simplified step by step, in which non-significant variables were removed. Each of the models used was subjected to analysis of variance (ANOVA) to check significance ($p < 0.05$). All model analyses were conducted using RStudio software, version 4.3.3 (R Development Core Team, 2020).

2.6 Ethical considerations

As it is freely accessible secondary data, the study was exempt from consideration by the Research Ethics Committee.

3. Results

A total of 55,389 dengue cases were reported between January 2017 and December 2022 in the 54 Northern Minas Gerais municipalities. From these total, 49.3% were confirmed cases, 37.5% were discarded and 13.2% were inconclusive. Most cases progressed into cure and nine (0.02%) resulted in death.

During the period evaluated, the municipality of Montes Claros was responsible for 41% of reported cases. Followed by the municipalities of Janaúba, Bocaiuva, Espinosa, and Porteirinha, which presented between 3% and 11% of cases, while the municipality of Berizal presented only 0.01% (n=5) of the reported cases (Figure 1).

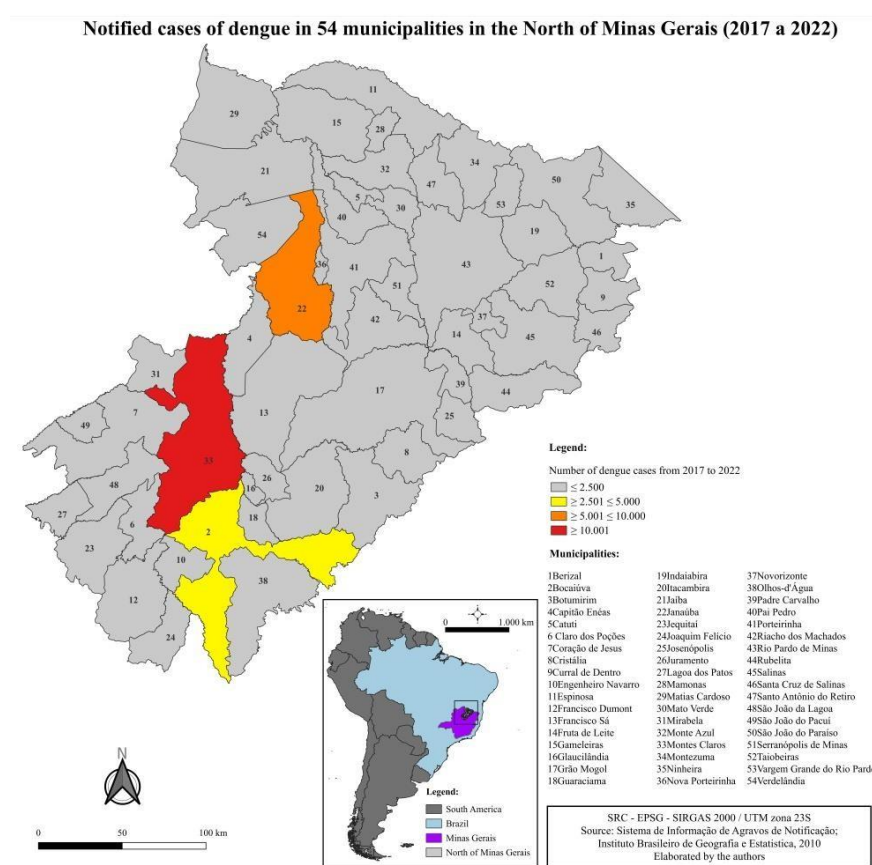


Figure 1. Distribution of reported dengue cases in 54 municipalities in the North of Minas Gerais, Brazil, from January 2017 to December 2022 (n=55,389).

The year 2019 presented 45.1% of reported cases. Regarding the average number of dengue cases per 10,000 inhabitants, the year 2019 was 153.14, followed by 2022 (38.64), 2018 (26.57), 2020 (8.20), 2021 (4.74) and 2017 (7.58). The highest number of deaths (n=6) was recorded in 2022 and the highest fatality rate (0.18%) was in 2021. The more detailed description is available in the supplementary material.

A higher frequency of dengue cases was observed in the group of people aged between 20 and 49 years old (53.1%); the least affected age group was from those over 80 years old (0.9%). Regarding gender, there was a predominance of the female (55.7%) in the reported cases. A more detailed description is available in the supplementary material.

According to the incidence coefficient, the municipality of Porteirinha was the one with the highest number of confirmed cases per 10,000 inhabitants in 2017 and 2020, while in 2018 it was the city of Janaúba, followed by Padre Carvalho in 2019, Matias Cardoso in 2021 and Espinosa in 2022. In the latter, it was possible to observe an alarming increase in cases, as well as the municipality of Janaúba, which, after two years of its highest incidence (2020 and 2021), again registered a worrying increase in 2022. Furthermore, it is noteworthy that seven municipalities evaluated (Berizal, Curral de Dentro, Josenópolis, Ninheira, Olhos-d'Água, Santo Antônio do Retiro and Vargem Grande do Rio Pardo) had no recorded incidence in four non-consecutive years, during the six years analyzed (Table 1).

Municipality / Year	2017	2018	2019	2020	2021	2022
Berizal	0	0	0	4,76	0	0
Bocaiuva	4,58	84,72	5,51	28,93	2,08	19,98
Botumirim	0	0	13,81	1,72	0	3,45
Captão Aeneas	0,7	12,76	1,36	11,34	7,08	10,63
Catuti	37,98	88,62	3,01	0	0	204,68
Claro dos Poções	0	8,37	3,29	6,97	2,79	6,97
Coração de Jesus	0	4,33	3,34	0,78	1,57	6,3
Cristália	0	19,52	5,07	5,85	0	1,95
Corral de Dentro	0	0	0	0	0	2,7
Engenheiro Navarro	0	0	2,78	17,31	9,44	34,62
Espinosa	0	0	3,28	0	34,81	341,29
Francisco Dumont	0	2,22	2,9	0	0	11,1
Francisco Sa	9,79	18,31	205,7	10,22	4,68	101,38
Fruta de Leite	0	0	191,5	8,6	0	6,45
Gameleiras	0	108,49	390,1	4,17	58,41	33,38
Glaucilândia	3,41	34,15	54,6	6,83	13,66	30,73
Grão Mogol	0	0	6,76	0	0	0,71
Guaraciama	7,91	158,38	2,59	3,95	3,95	15,83
Indaiabira	1,57	0	23,63	0	0	3,15
Itacambira	0	0	9,4	0	0	2,35
Jaíba	0,26	0	4	19,64	4,77	41,15

Janaúba	28,85	216,69	233,94	11,31	6,93	205,94
Jequitai	9,25	0	255,1	0	0	0
Joaquim Felício	0	0	2,49	2,59	5,18	31,13
Josenópolis	0	0	297,5	55,09	0	0
Juramento	0	0	209,6	0	0	5,3
Lagoa dos Patos	3,01	0	166	12,07	0	0
Mamonas	3,33	148,4	91,71	13,34	8,33	81,7
Matias Cardoso	2,24	3,37	67,4	5,62	131,53	14,61
Mato Verde	4,98	13,29	3,32	4,98	0	68,94
Mirabela	0,73	158,96	494,4	11,72	10,25	8,05
Monte Azul	0,98	8,85	49,19	5,41	8,36	3,44
Montes Claros	2,05	5,6	202,34	1,71	0,65	4,87
Montezuma	0	0	82,75	4,35	1,45	8,71
Ninheira	0	0,94	0	0	0	0
Nova Porteirinha	2,98	131,22	17,89	0	4,47	175,96
Novorizonte	0	0	2,18	13,12	0	2,18
Olhos-d'Água	0	3,71	159,7	0	0	0
Padre Carvalho	0	0	597,07	37,56	0	1,97
Pai Pedro	9	36,02	108,08	41,43	0	115,29
Porteirinha	125,8	21,36	59,56	67,84	17,36	51,81
Riacho dos Machados	0	1,14	13,7	3,42	11,42	189,58
Rio Pardo de Minas	0	0,35	6,72	0	0	56,82
Rubelita	0	1,76	38,7	29,93	0	19,36
Salinas	0,24	0	16,42	10,7	1,74	9,7
Santa Cruz de Salinas	0	0	48,59	12,78	2,55	0
Santo Antônio do Retiro	0	0	64,86	1,5	0	0
São João da Lagoa	8,29	12,44	120,28	0	0	2,07
São João do Pacuí	0	22,65	56,23	20,14	0	0
São João do Paraíso	0	0,83	1,25	1,25	0,41	20,49
Serranópolis de Minas	0	6,81	0,9	2,27	2,27	25,11
Taiobeiras	0,6	1,21	62,33	12,4	1,81	21,06
Vargem Grande do Rio Pardo	0	0	6,47	0	0	8,63

Verdelândia	2,6	31,28	35,19	1,3	20,85	0
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Table 1. Incidence of dengue cases in the 54 municipalities in the North of Minas Gerais, from January 2017 to December 2022. Data collection carried out in Montes Claros, Minas Gerais, Brazil, January 2023.

Regarding the association of the IIP (from LIRAA carried out in the municipalities from 2017 to 2021) with the number of reported dengue cases per 10,000 inhabitants, no significant correlation was observed ($p=0.31$). This is probably due to the fact that the infestation rate in most municipalities is low when compared to the number of registered cases.

4. Discussion

The data analyzed from January 2017 to December 2022 from the North macro-region of Minas Gerais, in general, demonstrate a high number of dengue case notifications. Most of the reported cases progressed into cure, which demonstrates that the health services have adequate care conditions and also due to the fact that the disease has, for the most part, a mild clinical spectrum. However, the number of inconclusive cases is high, with approximately 13% of cases not having an accurate diagnosis, but this could mask the number of deaths or complications resulting from dengue and draw attention to the need to improve the diagnosis. (Figueiró *et al.*, 2011).

The number of deaths in this study was not considered high when compared to the number of cases. This may also be related to the endemicity and natural history of the disease, which has a history of low mortality, as early detection of the disease reduces mortality rates to below 1% (Yan *et al.*, 2020).

Given the natural history, the WHO classification of dengue underwent revisions due to rigidity and applicability limitations. Initially proposed in 1975 and revised in 1997, it included categories such as dengue fever (DF) and dengue hemorrhagic fever (DHF), with specific diagnostic criteria (PAHO, 2020). In 2009, a new classification was introduced, simplifying it into asymptomatic, symptomatic, non-severe dengue (without warning signs and with warning signs), and severe dengue. This review sought to make the criteria more practical and applicable, especially in regions with limited resources, allowing a more effective identification of severe dengue, covering complications previously not covered by previous criteria, such as encephalopathy and liver failure (Brasil, 2002; PAHO, 2020; Rocha *et al.*, 2011).

Additionally, increased investments in health promotion, educational campaigns, and prevention to combat dengue are factors that may be directly related to the reduction in the number of deaths, possibly due to the increase in diagnoses, with a consequent increase in case notifications. Furthermore, the number of deaths from dengue is an important aspect of public health, as it is a disease that is simple to diagnose and treat, but improvements in assistance and the flow of public health communications need to be highlighted to promote effective actions to combat dengue fever disease (Ramos *et al.*, 2021).

There is no distribution pattern of dengue cases across municipalities in the North of Minas Gerais with the number of cases varying between five and twenty two thousand. The municipality of Montes Claros was the one with the highest number of reported cases, which may be related to the fact that this municipality could be receiving cases from other municipalities since it has the best health infrastructure in the region (Moreira *et al.*, 2022).

Over the six years evaluated, no regularity was found in the epidemiological behavior, as in 2018 and 2020 the reported cases were similar, while there was an outbreak in 2019. This may be associated with the fact that dengue is a disease of compulsory notification so that all suspected or confirmed cases must be notified to the competent public health bodies and the notifications are passed on and made available on SINAN (Magalhães *et al.*, 2020).

According to the Pan American Health Organization - PAHO (2020), 2020 it was observed that in Brazil, there was a decrease in probable cases compared to 2019, possibly due to dengue presenting clinical similarities and laboratory tests with coronavirus (COVID-19) (Mascarenhas *et al.*, 2020). Additionally, the underreporting of cases may be related to the mobilization that state surveillance and healthcare teams carried out to combat the COVID-19 pandemic (Andrade *et al.*, 2021). In addition to underreporting by the individual (due to difficulty accessing the healthcare system or negligence), and/or association of symptoms with other diseases. The irregular pattern in cases reported in Brazil was also observed in the work of Andrade *et al.* (2021) and Rodrigues *et al.* (2016).

Dengue represents a serious public health problem in the world, as approximately 50% of the world's population is at risk of infection (Nealon, 2022; Cardoso Lucena, 2019). Furthermore, it is still considered a neglected disease, as it has a recurrent history of underreporting of cases in SINAN (Marques *et al.*, 2018). This situation, in addition to hindering the real knowledge of the epidemiology of arboviruses, makes data analysis difficult and compromises the taking of necessary measures for control (Ribeiro *et al.*, 2006). In view of this, it is essential to carry out epidemiological inspection of affected cases, in order to guide preventive actions and control effectively (Marques *et al.*, 2020).

Regarding the incidence of dengue cases by age and gender, it was observed that female individuals aged between 20 and 49 years are identified as the most affected by the disease. This case profile is also found in other studies (Fernandes and Gomes, 2018; Ferreira *et al.*, 2018). As for females, a possible justification is that women seek basic health services frequently and early, unlike men (Pinheiro *et al.*, 2013). Furthermore, females are commonly associated with domestic chores and, since *Ae. aegypti* is a mosquito with anthropophilic habits, the greater presence of women in homes may lead to an increase in infection in this group, compared to men (Ribeiro *et al.*, 2018). The age group corroborates the IBGE (2022) databases, with the state of Minas Gerais having more adults than elderly people and more women than men, which could also justify the high rate of cases in these population profiles.

Biological, sociodemographic, environmental, cultural, and economic factors can influence the occurrence and distribution of dengue cases. Furthermore, urbanization is one of the main factors for the disease, since the vector, *Ae. aegypti*, uses some specific locations for its reproduction, such as water tanks and containers with stagnant water, that is, the urban environment offers numerous resources for the formation of reproductive reservoirs, consequently, it helps in the establishment and dispersal of the vector (Nilson Aguiar and Moura *et al.*, 2022).

The calculation of the incidence coefficient revealed a high level of transmission of the disease in the municipalities of Minas Gerais. Notably, Padre Carvalho and Mirabela stand out, showing, in 2019, an incidence of confirmed dengue cases that surpassed the numbers recorded in the Americas in 2013 (PAHO, 2023). That year, the rate was 430.8 cases per 100,000 inhabitants; however, the municipalities in question exceeded this rate after six years, reaching approximately 597.07 and 494.4 cases per 10,000 inhabitants, respectively. This substantial increase highlights the urgency of effective measures to contain the spread of the disease in the region. Furthermore, seven municipalities did not record an incidence of dengue cases in four years, from 2017 to 2022, which highlights the diversity in the dynamics of the spread of the disease in the region, highlighting the importance of implementing specific adapted control and prevention strategies to the particularities of each location.

The IIP related to the number of cases reported per inhabitants, from 2017 to 2021, did not show any correlation. The municipalities with the highest infestation of *Ae. aegypti* had the highest number of reported cases, at the same time, those with the lowest infestation had the lowest number of reported cases. Furthermore, due to the lack of data, it was not possible to correlate the LIRAA with the dengue cases reported in 2022. Even though the data did not demonstrate a correlation, this methodology for measuring the IIP for *Ae. aegypti* is important for preventing and controlling the vector (Vernal *et al.*, 2021). According to Ramos and collaborators (Ramos *et al.*, 2021), one of the main difficulties found in their study was the population's disregard for combating the vector. Although the population knows about dengue, a large part still does not consider the disease to be serious.

Given the results, reported cases of dengue may be related to social, demographic, and environmental factors in the municipalities studied. However, the study by Vernal *et al.* (2021) demonstrated, from an analysis carried out in the state of São Paulo, that the profile of the disease is changing in its spatial risk model, mainly in the northern region of the state, showing that there are cases of dengue fever in areas with clusters well defined.

The present study demonstrated that dengue in the North of Minas Gerais, between 2017 and 2022, mainly affected the female population and adult individuals. The annual variability in incidence, with Montes Claros leading the cases, highlights the heterogeneity in the distribution of dengue in the region. The finding that cases remain active in consecutive years reinforces the premise that the region remains endemic for the disease. When considering the degree of infestation of the *Aedes aegypti* mosquito and the absence of drugs for all circulating serotypes, combating the disease requires the implementation of effective and robust strategies to raise awareness among the population, with the aim of eliminating the vector's breeding sites.

Furthermore, it is necessary to develop public policies through integrated efforts between epidemiological surveillance and primary care health teams, multidisciplinary researchers, and civil society, so that they can contribute to the advent of modified approaches to more effective and sustainable dengue control, consequently, greater strengthening of surveillance, in addition to adequate health treatments for the population, especially with prominent social vulnerability. Finally, the study can contribute to subsequent studies that are interested in this topic.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary Material

1. Characterization of individuals who reported dengue cases²

Numbers of dengue cases reported by gender and age group from January 2017 to December 2022. Data collection carried out in Montes Claros, Minas Gerais, Brazil, January 2023.

	2017	2018	2019	2020	2021	2022
Gender*	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Men	641 (44,18)	1952(41,67)	10541 (42,18)	1488 (41,86)	891(46,89)	7917(42,17)
Females	809 (55,75)	2732(58,33)	14446 (57,80)	2063 (58,03)	1038(53,11)	10839(57,73)
Age range						
<1 Years	29 (2,00)	94 (2,01)	486 (1,95)	97 (2,73)	53 (2,74)	250 (1,33)
1-9	83 (5,72)	356 (7,60)	2664 (10,66)	251 (7,06)	165 (8,54)	1598 (8,51)
10-19	273(18,81)	922 (19,68)	4890 (19,56)	540 (15,19)	231 (11,96)	2809 (14,97)
20-49	826 (56,92)	2590 (55,29)	12690 (50,78)	2053 (57,74)	1189 (61,64)	10059 (53,57)

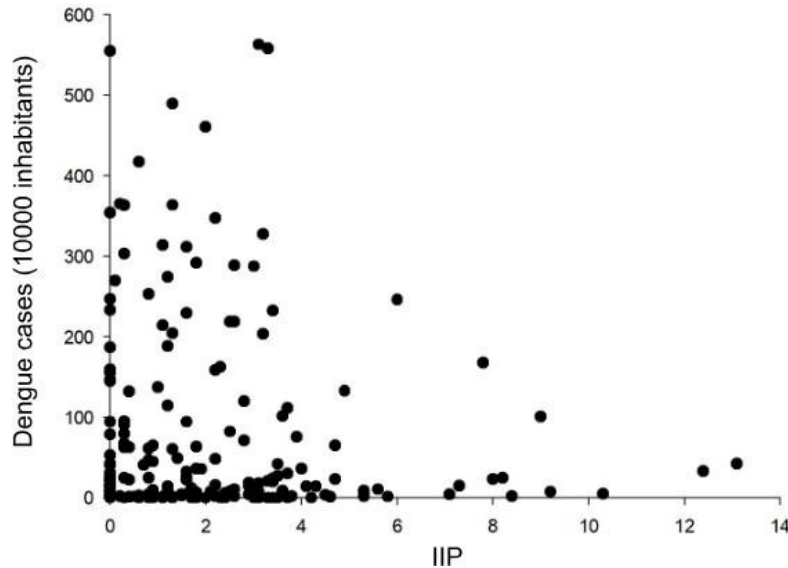
50-79	235 (16,20)	704 (15,03)	4078 (16,33)	585 (16,45)	283 (14,66)	3817 (20,33)
>80 Years	5 (0,35)	18 (0,39)	178 (0,72)	26 (0,74)	9 (0,46)	242 (1,29)

* Not declared: 2017: 1; 2018: 0; 2019: 7; 2020: 4; 2021: 1; 2022: 19. **Source:** Data obtained through SINAN.

2. Characterization of the Incidence of Dengue Related to the Building Infestation Rate in 54 Municipalities.

Notified cases of dengue per 10,000 inhabitants related to the IIP rate (positive properties/properties surveyed x 100) in 54 municipalities in the North of Minas Gerais, Brazil. Data collection carried out in Montes Claros, Minas Gerais, Brazil, January 2023.

Source: Prepared by the authors.



3. Analysis of the Incidence of Dengue in the 54 Municipalities in the North of Minas Gerais (2017-2022): Assessment of 55,389 Cases and Average per 10,000 Inhabitants

Number of dengue cases in the 54 municipalities in the North of Minas Gerais, Brazil, from January 2017 to December 2022 (n=55,389) and average number of cases per 10,000 inhabitants. Data collection carried out in Montes Claros, Minas Gerais, Brazil, January 2023.

Years	Number of cases reported	Number of confirmed cases	Average number of confirmed cases/10,000 inhabitants	Number of deaths from dengue	Fatality rate (%)
2017	1.451	866	7,58	1	0,12
2018	4.684	3.036	26,57	1	0,03
2019	24.994	17.494	153,14	0	0
2020	3.555	937	8,20	0	0
2021	1.930	542	4,74	1	0,18
2022	18.775	4.414	38,64	6	0,13

Source: Data obtained through SINAN.

5 CONSIDERAÇÕES FINAIS

O desenvolvimento dos produtos desempenha um papel crucial nos âmbitos científico, regional, social e pessoal. O primeiro estudo, que avaliou a atividade larvicida de *Mauritiella armata* sobre *Aedes aegypti* e *Culex quinquefasciatus*, demonstrou o potencial de um biolarvicida para o desenvolvimento da bioeconomia e a valorização do Cerrado. A utilização de extratos vegetais, isentos de toxicidade para o meio ambiente e para os seres humanos, pode ser uma alternativa promissora, de baixo custo e com menor impacto ambiental, para o controle mais eficaz dos vetores e, consequentemente, para a diminuição das arboviroses de forma sustentável.

O segundo estudo, que abordou a epidemiologia da dengue em 54 municípios do Norte de Minas Gerais, constatou que a região é endêmica e reemergente para a doença. Entre 2017 e 2022, a doença afetou majoritariamente a população do sexo feminino e indivíduos adultos. Além disso, as análises mostraram que o ano de 2019 foi o mais acometido pela doença e que o município de Montes Claros, Minas Gerais, apresentou o maior número de casos notificados. O estudo ressaltou que o combate à doença é indispensável e requer a integração das ações de vigilância entomológica e atenção primária, sob a perspectiva da saúde única. Essa abordagem demanda a implementação de estratégias efetivas e robustas de conscientização da população, visando eliminar os criadouros do vetor. Dessa forma, é possível fortalecer o sistema de saúde local e reduzir, de maneira sustentável e integrada, o impacto da dengue e outras arboviroses.

Em resumo, ambos os estudos contribuirão para o desenvolvimento de novas pesquisas sobre a mesma temática, já que ainda existem poucos estudos semelhantes na região Norte de Minas Gerais.

Portanto, eles oferecem insights valiosos para a saúde pública, enfatizando a importância da inovação científica e da implementação de políticas de saúde pública que integrem a vigilância e a atenção primária, adaptadas às condições locais, para enfrentar desafios contínuos relacionados às arboviroses. Os estudos também contribuíram para a formação pessoal dos autores, que adquiriram novos conhecimentos, técnicas de análise e aprimoraram seus métodos de pesquisa.

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Atividades de educação em saúde

Monitoraleish – Dia D Leishmaniose com Secretária Municipal de Saúde – Montes Claros (10 de agosto de 2023)

Implementa Chagas em Francisco Drumont em Escola da Zona Rural (6 de dezembro de 2022)

Implementa Chagas em Francisco Drumont na Praça Pública (16 de dezembro de 2022)

Curso de Boas Práticas de Manejo de Morcegos para Agentes de Controle Agropecuário e de Zoonoses em Montes Claros (9 e 10 novembro de 2023)

I Oficina sobre Novas Estratégias para o controle de Leishmaniose Visceral Canina em Montes Claros (13 de dezembro de 2023)

Monitoraleish



Dia D Leishmaniose com Secretária Municipal de Saúde – Montes Claros (10 de agosto de 2023)

Implementa SaMi-Trop em Francisco Drumont



Escola da zona rural (6 de dezembro de 2022) e em praça pública (16 de dezembro de 2022)

Curso de Boas Práticas de Manejo de Morcegos para Agentes de Controle Agropecuário e de Zoonoses em Montes Claros



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13 de dezembro de 2023