

## The impact of Zika in Minas Gerais, Brazil: epidemiological profile and spatial diffusion of the disease, 2015-2019

### O impacto do Zika em Minas Gerais, Brasil: perfil epidemiológico e difusão espacial da doença, 2015-2019

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#### ABSTRACT:

**Objective:** To overview the epidemiological profile for Zika in MG and map its spatial diffusion from 2015 (onset of the outbreak) to 2019. **Method:** this is a descriptive observational study based on three secondary databases: Disease Notification System (SINAN), the Brazilian Institute of Geography and Statistics (IBGE) and the Health Surveillance Secretariat of Minas Gerais State (SVS-SES/MG). The spatial diffusion of the confirmed cases was georeferenced with Geographic Information Systems (GIS) and Geographic Database (BDG), using ArcGIS 10.3 software. **Results:** in Minas Gerais, the spread of Zika was similar to other regions of Brazil. The first cases were recorded in 2015, reaching all 13 regions in 2016, declining in 2017 and 2018, increasing again in 2019. 10,465 cases were confirmed. Almost 80% of the reported cases were female and of these, 26.5% were pregnant women. **Final considerations:** in addition to socio-economic inequalities in Minas Gerais, it can be argued that women who are young, mixed-race, with low-education and from vulnerable areas are more likely to be affected by the disease. Analysis of disease epidemiology and mapping enhance the assessment of the impact of disease, thus contributing to more adequate public health policies and planning.

**KEYWORDS:** Zika virus; Epidemiology; Medical and Health Geography.

#### RESUMO:

**Objetivo:** Traçar um panorama do perfil epidemiológico do Zika em Minas Gerais e mapear sua difusão espacial de 2015 (início do surto) até 2019. **Métodos:** Este é um estudo observacional descritivo baseado em três bases de dados secundárias: Sistema de Notificação de Doenças (SINAN), Instituto Brasileiro de Geografia e Estatística (IBGE) e Secretaria de Vigilância Sanitária de Minas Gerais (SVS-SES / MG). A difusão espacial dos casos confirmados foi georreferenciada com Sistemas de Informações Geográficas (SIG) e Banco de Dados Geográficos (BDG), utilizando o software ArcGIS 10.3. **Resultados:** Em Minas Gerais, a disseminação do Zika foi semelhante a outras regiões do Brasil. Os primeiros casos foram registrados em 2015, atingindo todas as 13 regiões em 2016, diminuindo em 2017 e 2018, voltando a aumentar em 2019. Foram confirmados 10.465 casos. Quase 80% dos casos notificados eram mulheres e destes, 26,5% eram gestantes. **Considerações finais:** além das desigualdades socioeconômicas em Minas Gerais, pode-se afirmar que as mulheres jovens, pardas, com baixa escolaridade e de áreas vulneráveis têm maior probabilidade de serem afetadas pela doença. A análise da epidemiologia e o mapeamento das doenças podem conferir melhor acesso ao impacto das doenças, contribuindo para um planejamento e políticas de saúde pública mais adequadas.

**PALAVRAS-CHAVE:** Zika vírus; Epidemiologia; Geografia médica e da saúde.

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## INTRODUCTION

A Zika virus (ZIKV) is an arbovirus belonging to the genus *Flavivirus*, family *Flaviviridae*. It was first isolated in 1947 from a monkey of the genus *Rhesus* from the Zika forest in Uganda<sup>1</sup>. Transmission of ZIKV between humans occurs mainly via the bite of female mosquitoes of the genus *Aedes*, the species *Aedes aegypti* being the main vector in tropical regions<sup>2</sup>. Sexual transmission<sup>3</sup> and transmission through blood transfusion<sup>4</sup> have also been demonstrated.

The circulation of ZIKV was limited among people of the African and Asian continents until an outbreak was detected on Yap Island in Micronesia in 2007<sup>5</sup>. Between the years 2013-2014, other outbreaks were reported on several Pacific islands, including French Polynesia<sup>5</sup>. In Brazil, its first detection through laboratory diagnosis occurred in some states of the Northeast region in 2015<sup>6</sup>. ZIKV cases were concurrent with an unexpected increase in the number of live births with microcephaly in the state of Pernambuco<sup>7</sup> and later in Rio Grande do Norte<sup>8</sup>. This pattern of increase in microcephaly and other neurological complications expanded to other states in the Northeast region<sup>7</sup>, leading the Brazilian Health Ministry to establish the compulsory notification of microcephaly. In November 2015 the Ministry declared the epidemic a Public Health Emergency of National Concern (PHENC)<sup>9</sup>. In February 2016 the World Health Organization (WHO) declared it an Public Health Emergency of International Concern (PHEIC)<sup>10</sup>. In 2016, the relationship between ZIKV, microcephaly and other neurological complications became known as the Congenital Zika Syndrome (CZS)<sup>11</sup>.

In less than a year after its introduction in Brazil, ZIKV spread throughout the country in an uneven manner, with a greater number of cases in the Northeast and Southeast regions. Nonetheless, five years after the onset of the outbreak, the real impact of Zika is still difficult to assess. The number of studies that have specifically analyzed the spatial diffusion of Zika in Brazil is limited. Studies have considered the distribution of the disease in municipalities in such states as Bahia<sup>12</sup>, São Paulo, Rio de Janeiro<sup>13</sup>, Rio Grande do Norte<sup>14</sup> and Amazonas; some of these studies compare Zika data to other arboviruses<sup>15</sup>. This scarcity is even more glaring when it comes to the analysis of the disease for the state of Minas Gerais (MG). Vega *et al.*<sup>16</sup> have compared the emergence of chikungunya and Zika in the municipality of Santa Luzia, but there are no comprehensive studies of the disease's temporal and spatial distribution for the whole state, from the onset of the outbreak in 2015 until the present day.

It is of the utmost importance to understand the epidemiological profile, the temporal and spatial diffusion of Zika in MG. Over the past few decades, the region has repeatedly experienced severe arboviral epidemics, presenting some of the highest cases numbers for arboviruses in the country. In the case of the 2016-2017 urban Yellow Fever outbreak, the state has also been characterized as a possible gateway of disease and *Aedes* distribution between the Northern and Southern regions of Brazil. The analysis of the MG case can thus provide important clues for the analysis of the diffusion of Zika in Brazil as a whole.

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Seeking to address this important gap, we provide an analysis of the epidemiological profile for Zika in the state of MG, mapping the spatial diffusion of the disease from 2015 (since the onset of the outbreak) until 2019. This analysis speaks to an assessment of the impact of the disease, thus contributing to more adequate public health control policies and planning.

## METHOD

The present study was submitted to, and approved by, the research ethics committee of the Instituto René Rachou, under ethical assessment certificate number 65695916.5.0000.5091.

### ***Study Area***

Minas Gerais has an estimated population of 21,168,791 inhabitants and a territory of 586,521.123 km<sup>2</sup>, making it the second most populated and the fourth largest in Brazil. The state has the highest number of municipalities (853) in the country, grouped into 13 health macro-regions and 76 health micro-regions.

### ***Study Characterization***

This is a descriptive, observational study based on secondary databases. Data were obtained from: the Disease Notification System (Sistema de Informação de Agravos de Notificação - SINAN); the Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística, IBGE); and the Health Surveillance Secretariat of Minas Gerais State (Subsecretaria de Vigilância à Saúde - Secretaria de Estado de Saúde de Minas Gerais, SVS-SES/MG). We also analyzed data available from the Epidemiological Bulletins and other publications of the Brazilian Health Ministry.

### ***Data Analysis***

We analyzed and described the temporal and spatial distribution of confirmed Zika cases in MG from 2015 to 2019. The sociodemographic characteristics of the population (municipality, age, sex, race, pregnancy, region of origin, educational level) were also described. Disease diagnosis and confirmation criteria were referenced. Exclusively for women, the age-group according to reproductive age was observed, considering pregnancy and its stages. A database was created and all data was analyzed using Sigma-plot 8.0.2 software (Ser 9539094), which was also used to make the figures.

As for the spatial diffusion, the mapping of the disease incidence in the health macro-regions was carried out for each year under scrutiny. Confirmed Zika cases were filtered as notified in SINAN. Residential addresses for each case were georeferenced to generate spatial data through geoprocessing techniques, such as Geographic Information Systems

(GIS) and Geographic Database (BDG), using the ArcGIS 10.3 software. This software was used in the Cartography Laboratory of the Undergraduate Course in Geography of the Institute of Human Sciences in Pontificia Universidade Católica de Minas Gerais (PUC /MG).

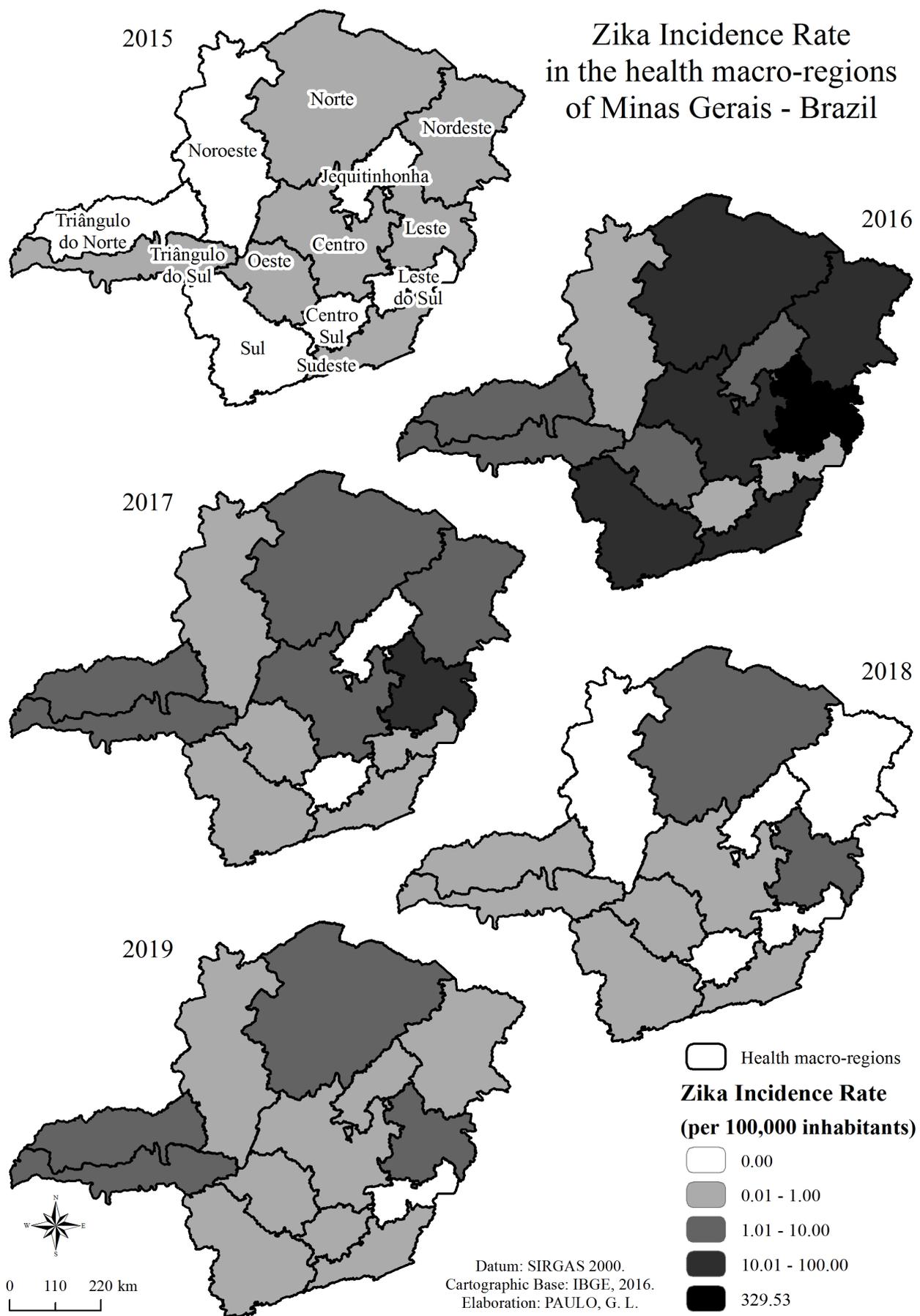
By cross-referencing patients' place of residence (municipality and health macro-region), it was possible to spatialize the data, which was then connected to the digital cartographic base (shapefile) of the Municipal network. Based on the municipality's shapefile and on the PDR/MG, the shapefile of the health macro-regions was established. For the spatial and temporal distribution of the disease, choropleth maps for Zika incidence in the health macro-regions of MG were also created.

## RESULTS

### *Temporal and spatial distribution of cases in MG*

During the study period, 26,809 suspected cases of Zika were reported. Of these, 10,465 cases (39%) were confirmed, and 11,510 cases (43%) were excluded as they did not meet the clinical, epidemiological and/or laboratory criteria. The remaining cases, 4,834 (18%), were left blank or the diagnosis confirmation field of the notification form had no information. Among the suspected cases which were excluded, 7,413 (64,4%) were by epidemiological criteria; 4,033 (35%) by laboratory criteria; and in 64 (0,6%) cases the relevant fields in notification forms were not completed. In what concerns confirmed cases, 8,821 (84,3%) were confirmed by epidemiological criteria and 1616 (15,4%) by means of laboratory criteria and 28 (0,3) were left blank. The onset of confirmed Zika cases in MG occurred from May 2015 and quickly spread to 10 municipalities, distributed among seven of the state's health macro-regions (Figure 1). In 2015, the incidence rate in each region was less than 1/100,000 inhabitants.

In 2016, the disease was reported in 171 municipalities, distributed throughout all 13 regions (Figure 1). The Centro Sul, Leste do Sul and Noroeste regions, which in 2015 had no incidence of Zika, had the lowest rates in 2016 (<1/100,000 inhabitants). The Jequitinhonha and Triângulo do Norte regions, which also did not have any incidence in the previous year, now appeared in the class interval between 1 and 10 confirmed cases per 100,000 inhabitants in 2016, along with the Oeste and the Triângulo do Sul regions, which saw an increase, approximately 57 and 27-fold respectively, of their number of confirmed Zika cases. The other macro-region without confirmed Zika cases in 2015 was Sul. However, in 2016 this region had the fourth highest incidence of the arbovirus infection, joining the Centro, Nordeste, Norte and Sudeste regions in the range of 10 to 100 confirmed cases per 100,000 inhabitants. The highest incidence rate of Zika in 2016 was in the macro-region Leste, with about 330/100,000 inhabitants.



**Figure 1:** Zika incidence rate in Minas Gerais state between 2015 and 2019.

In 2017 the disease was only found in 58 municipalities in MG, present in all but two health macro-regions (Centro Sul e Jequitinhonha). There was a reduction in the incidence rate of Zika in all regions of the state. As in 2016, Leste was the macro-region with the highest incidence of the disease – showing, nonetheless, a reduction of approximately 95%.

Following the 2017 trend, in 2018 the number of municipalities with confirmed Zika notifications continued to decrease, reaching 33. The macro-regions Centro Sul and Jequitinhonha continued without confirmation of cases of the disease. This also happened with Leste do Sul, Nordeste and Noroeste. The Leste macro-region continued the reduction and reached a Zika incidence rate of 1.7/100,000 inhabitants. The Norte region also continued to have an incidence rate slightly higher than 1/100,000 inhabitants, but less than the rate of the Leste region. The remaining health macro-regions (Centro, Oeste, Sudeste, Sul, Triângulo do Norte e Triângulo do Sul) had a disease incidence rate of less than 1/100,000 inhabitants.

After two years of declining Zika cases in MG, in 2019 there was a rise in the reporting of the disease. The number of municipalities with confirmation of reported cases rose to 73, higher than in 2017. The Zika incidence rate increased in all the state's health macro-regions, except Leste do Sul. The disease reappeared in four regions (Centro Sul, Jequitinhonha, Nordeste e Noroeste) which did not have any confirmed cases in the previous year.

#### Demographic Profile

The 2015 and 2017, the highest number of confirmed cases occurred in individuals aged 30 -39, followed by the 20 -29 age-group (Table 1). In 2016, 2018 and 2019 the opposite occurred, with the most affected age-group being 20 -29, followed by 30 -39.

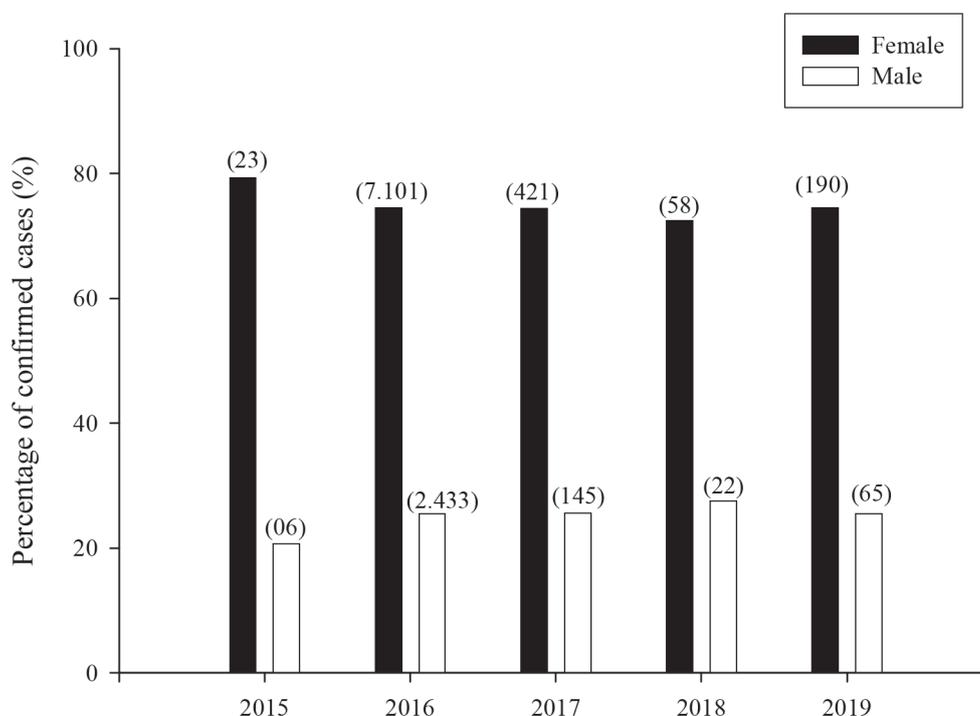
**Table 1:** Percentage of confirmed cases of Zika according to age-group in Minas Gerais.

Age group	Year (case percentage)				
	2015	2016	2017	2018	2019
0-12 months	0	1.6	1.8	8.8	3.1
0-9 years	3.5	6.2	8.1	3.6	11.4
10-19 years	0	12.2	16.0	13.8	15.0
20-29 years	20.7	23.2	21.0	25.0	25.2
30-39 years	37.9	21.9	22.4	20.0	20.1
40-49 years	17.2	16.1	12.0	10.0	9.1
50-59 years	13.8	11.0	11.1	11.3	7.8
More 60 years	7.8	7.8	7.6	7.5	8.3
<b>Total</b>	<b>100</b>	<b>100</b>	<b>100</b>	<b>100</b>	<b>100</b>

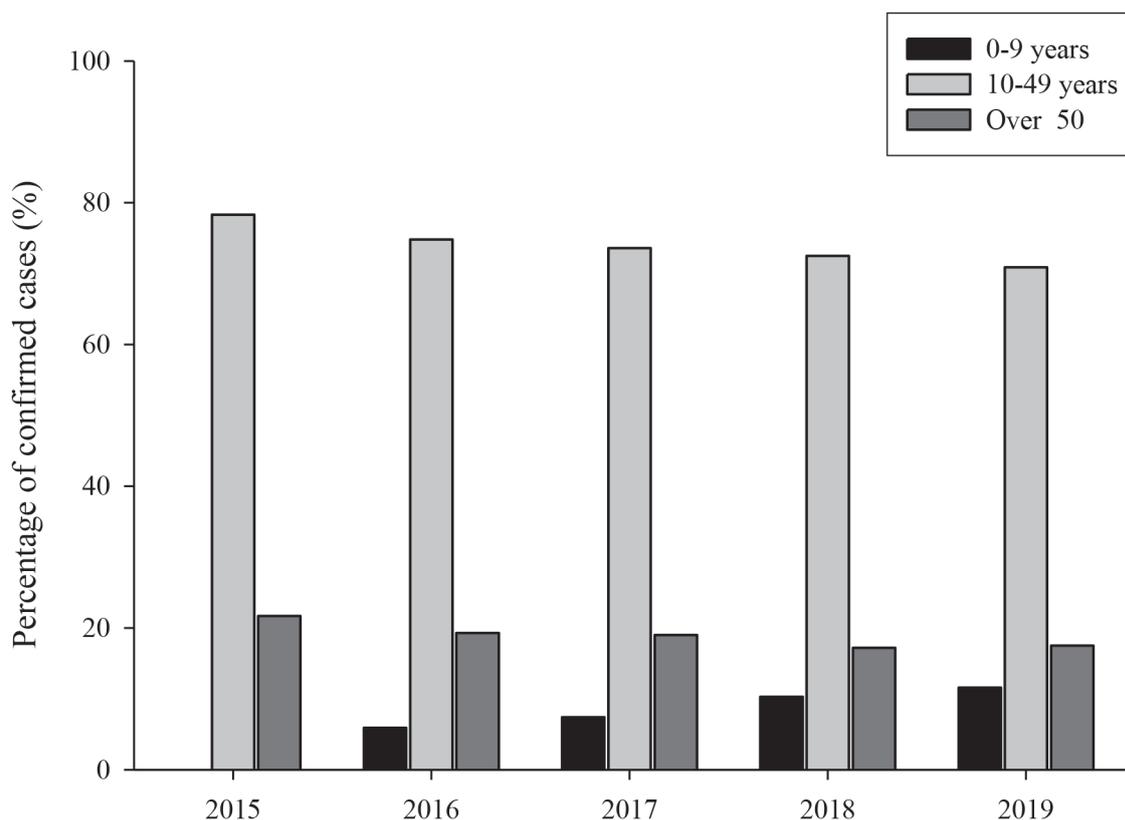
In what concerns race, for 2015 and 2018, more than 40% and 45% respectively of those infected declared that they were white. In 2016, 2017 and 2019, 40%, 50% and 55.7% respectively declared themselves to be mixed-race (“*pardo*”).

Schooling of those infected could not be analyzed since this field was left blank in most notification records.

In relation to gender, the number of confirmed Zika cases was disproportionately higher in females, reaching almost 80% over the five years studied (Figure 2). Almost 80% of the women infected with Zika were of childbearing age (Figure 3). In what pertains to pregnancy, the majority of women declared not to be pregnant (Table 2). Among pregnant women, 14.1% were between the ages of 10 and 19, 51.1% were between 20 and 29, 31.9% were between 30 and 39, and 2.9% were between 40 and 49. The schooling of women who were pregnant was left blank on 42% of the notification forms. In completed records, 36% reported high school level education (*Ensino médio*), 11% university education and 11% elementary education (*Ensino fundamental*).



**Figure 2:** Percentage of confirmed cases of Zika according to gender in Minas Gerais.



**Figure 3:** Percentage of confirmed cases of Zika in women according to age-group in Minas Gerais in the period from 2015 to 2019.

**Table 2:** Reproductive status of women with confirmed cases of Zika in Minas Gerais.

Status reproductive	Year				
	2015	2016	2017	2018	2019
1st trimester	0.3	3.8	6.7	12.1	6.9
2nd trimester	4.4	0	0	13.8	7.9
3rd trimester	21.7	7.1	7.8	13.8	9.0
Unknow pregnant gestation period	4.4	6.1	6.7	0	0
Not recorded	13.1	0.7	0.7	0	0
Not pregnant	21.7	52.2	53.2	48.2	50.8
Not applicable	4.4	13.8	16.1	12.1	23.8
Left blank	30.0	16.3	8.8	0	1.6
<b>Total</b>	<b>100</b>	<b>100</b>	<b>100</b>	<b>100</b>	<b>100</b>

In relation to the race of the pregnant women, 45.45% declared themselves to be mixed-race (*“pardo”*), 33.2% white, 7% black, 1% Asian (*“amarelo”*), 0.05% indigenous and in 13.3% of notification records this information was left blank.

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## DISCUSSION AND FINAL CONSIDERATIONS

Even though the Zika epidemic is no longer considered a public health emergency, it still impacts upon the lives of families and children across Brazil. As seen above, Zika is still a major public health problem in MG state.

The majority of Zika cases notified were confirmed by clinical tests. The diagnostics of Zika infection is complex given its similar symptoms and cross-reactivity with dengue fever. This hindered the assessment of the magnitude of the epidemic. Only in October 2016 did the Health Ministry announce the purchase of 3.5 million rapid tests for the identification of Zika virus and their distribution throughout all Brazilian states.

The trajectory of the epidemic in MG - with its onset in 2015, increasing incidence in 2016 and subsequent decrease in 2017 until 2019 - follows a trend of epidemiological dissemination similar to what occurred in other Brazilian states. As stated by Possas *et al.*<sup>17</sup>, the speed of the spread of the virus, in only nine months, from its emergence in the Brazilian Northeast until its propagation to other states and countries of Latin America, can be considered unprecedented. In MG, Zika cases presented a diffuse pattern since the onset of infections, quickly expanding to the whole state.

In MG, dengue and chikungunya had incidence rates of, respectively, 137 and 79.9 cases per 100,000 inhabitants in 2017, while Zika presented an incidence of 3.6 cases per 100,000 for the same period. In one of the few studies analysing the circulation of dengue, chikungunya and Zika in MG, with a focus on the city of Santa Luiza, Vega *et al.*<sup>16</sup>, concluded that given the similarities in initial clinical profiles in order to differentiate these arboviruses it is necessary to perform detailed clinical evaluation, laboratory diagnosis and patient follow-up.

As these arboviruses are transmitted by the same vector, the decrease in the number of Zika cases is not explained by the decrease in circulation of *Aedes aegypti* in the municipalities in question. However, it cannot be disregarded that the rate of asymptomatic Zika patients is 80%, and that underreporting of cases is common. Thus, Zika incidence may have been much higher than reported. In fact, it has been argued that the vast majority of Zika infections go undetected, and it is likely that this is due, in part, to the high similarity of case definitions for dengue, chikungunya and Zika virus, which co-circulate in Brazil<sup>18</sup>.

The higher incidence of Zika among young adults has been described in a previous study carried out in a municipality in the state of Bahia<sup>19</sup>, as well as in dengue surveys<sup>20</sup>. Seeking to explain this, Santos *et al.*<sup>20</sup> suggest that young adults are the most mobile segment of the population, moving through different environments, which exposes them to greater chances of getting into contact with infected mosquitoes.

In the study period, almost 80% of the Zika cases in MG were reported to be female. The epidemiological bulletin of the Ministry of Health pointed out that in 2016, 67.3% of Zika cases in Brazil were women<sup>21</sup>. Likewise, a study carried out in Camaçari (Bahia) showed that in the period of 2015-2017 75% of the registered cases were women<sup>19</sup>. For chikungunya,

there are also reports indicating the predominance of the disease in females<sup>22</sup>. For dengue, most of the reports described in the literature also show a higher incidence of the disease in women<sup>23</sup>. According to Magalhães and Morais<sup>19</sup> one possible hypothesis to explain the higher incidence of these arboviruses in women is their tendency to access health services in higher frequency, which increases notification.

In 2016, the percentage of Zika cases in women of childbearing age in MG is similar to what was observed in the rest of the country. A survey conducted in 2016 showed that 72.8% of the probable Zika cases in women occurred in women of childbearing age, with 16.9% of pregnant women suspected of being infected with Zika<sup>21</sup>. In our study, this number reached 26.5% of confirmed cases between 2015 and 2019. It appears that in MG there were more women of child-bearing age affected by Zika than in other states in Brazil<sup>21</sup>. It is also noteworthy that some pregnant women did not know their gestation period, which indicates an absence of prenatal care. In addition, a significant number of notification records did not register whether the woman was pregnant or not. This is a concern, since the causal relationship between Zika infection and CZS has been firmly established<sup>7, 13</sup>.

Throughout the country, the vast majority of notification records did not record data related to schooling nor race of pregnant women suspected of having Zika virus<sup>21</sup>. In 2016, Vanderlei et al.<sup>24</sup> also reported that 61.9% of pregnant women in the municipality of Palmas declared themselves to be mixed-race. These reports are similar to the findings discussed here.

Due to deficiencies in vector control and in other interventions, especially in disease prevention and healthcare, which are compounded by existing socio-economic inequalities in MG, it can be argued that women who are young, mixed-race, with low-education and are from vulnerable areas are more likely to be affected by the consequences of ZCS. These vulnerabilities indicate the need and importance of intersectionality and of research on the determinants of health, specifically gender, for arbovirus prevention and control strategies<sup>25</sup>. Race, gender, economic class, age, sexual orientation and migratory status intersect in complex ways, reinforcing each other and acting together to shape the experiences of individuals<sup>25</sup>.

In our study, inconsistencies and absence of data for some of the fields in the Zika compulsory notification records – fields left blank, or incompletely filled – prevented the retrieval of important information, such as education level and occupation of affected individuals. Problems in the quality and completion of compulsory notification records have been discussed and pointed out by some authors<sup>20, 26</sup>.

One of the limitations of this study was the impossibility of correlating data of notified Zika cases with the data recorded in the Public Health Event Registration (PHER). Public data disclosed in the epidemiological bulletins of the State Health Secretariat and the Health Ministry do not provide raw data related to babies with congenital Z-STORCH syndrome<sup>27</sup>. Therefore, it is not possible to evaluate the percentage of pregnant women in MG which had babies with

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congenital malformations. In this sense, it is of extreme urgency to undertake studies that address this gap, mainly through subsidizing the municipal health network in its organization of user services.

Despite the limitations mentioned above, our findings are of relevance since they present an outline, still very scarce in the scientific literature, about the profile of women of reproductive age, especially pregnant women, affected by Zika. Knowledge of the profile of affected patients can contribute to the development of actions and control measures which may minimize the risk of transmission of the disease, especially in women. This knowledge can increase the chances of successful interventions in the future.

The Covid-19 pandemic added to the burden of other arbovirus epidemics in Brazil and in MG specifically. The situation could configure what some authors have characterized as a “syndemic”<sup>28</sup>, where dengue fever, chikungunya, Zika and now Covid-19 amplify each other’s impact on public health<sup>29</sup>. Before Covid-19, and recognizing the importance of a syndemic approach, the state of MG state put forth a contingency plan with emergency funding in order to contain the very serious triple epidemic of dengue, chikungunya and Zika<sup>25</sup>. However, in order to use the resources and strategic planning in the most effective way, it is fundamental that policymakers and health care workers understand the epidemiological profile, patterns and distribution of the disease in their territories<sup>30</sup>. Further studies are necessary to better assess disease impact and to enable more adequate arbovirus control policies and planning.

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## AUTHORS’ CONTRIBUTION

RF, MN & DNP conceived and designed the study. RF and GLP analyzed the data and developed the mapping. RF & DNP reviewed the literature and wrote the paper. JN, MN and DV reviewed the final draft.

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