● **Original article**

AN OVERVIEW OF DENGUE IN THE SOUTHERN REGION OF BRAZIL FROM 2001 TO 2017*

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Objective: To record cases reported as classical dengue fever and deaths in the southern region of Brazil between 2001 and 2017. **Method:** Descriptive-retrospective study using secondary data from DATASUS/ SINAN and State Departments, analyzed through descriptive statistics. **Results:** An increase in the percentage of cases of the disease in the three states was observed in the three Brazilian southern states: in Paraná (PR) the percentage of autochthonous cases reached 94% in the last four years; in Santa Catarina (SC), the percentage was 95%, and in Rio Grande do Sul (RS), 83%, respectively, in 2015 and 2016. There was an increase in the number of deaths by severe dengue (dengue hemorrhagic fever), mainly in PR; in 2016, the first death caused by dengue was observed in SC; and an increase of more than 90% in the cases of dengue among adults in the last two years in Rio Grande do Sul. **Conclusion:** Despite the fact the Southern region of Brazil has the lowest incidence of dengue, special attention should be paid by health agencies to the situation in the southern states due to the increase in the number of cases and deaths caused by dengue.
KEYWORDS: Disease reporting; Mortality; Morbidity; Epidemics; Arbovirus.

PANORAMA DA DENGUE NA REGIÃO SUL DO BRASIL DE 2001 A 2017*

Objetivo: inventariar casos notificados por dengue clássica e óbitos na região Sul do Brasil entre 2001 e 2017. **Método:** estudo descritivo-retrospectivo a partir de dados secundários do DATASUS/SINAN e das Secretarias de Saúde, analisados através de estatística descritiva. **Resultados:** observou-se aumento dos casos nos três estados: Paraná (PR) elevou casos autóctones para 94% nos últimos quatro anos, Santa Catarina (SC) para 95%, e Rio Grande do Sul (RS) para 83%, respectivamente, em 2015 e 2016. Observou-se crescente aumento de óbitos por dengue hemorrágica, principalmente no PR; em 2016, o primeiro óbito em SC; e aumento nos últimos dois anos no RS, mais de 90% em adultos. **Conclusão:** a região requer atenção dos órgãos de saúde, devido ao aumento de casos e óbitos por dengue, embora apresente a menor incidência da doença do país. Este estudo contribuiu para o conhecimento do cenário atual e da evolução da dengue na região Sul do Brasil.
DESCRITORES: Notificação de doenças; Mortalidade; Morbidade; Epidemias; Arbovírus.

PANORAMA DE LA DENGUE EN LA REGIÓN SUR DE BRASIL DE 2001 A 2017

Objetivo: inventariar casos notificados por dengue clásica y óbitos en la región Sur de Brasil entre 2001 y 2017. **Método:** estudio descriptivo retrospectivo con base en datos secundarios del DATASUS/SINAN y de las Secretarías de Salud, analizados por medio de estadística descriptiva. **Resultados:** se observó crecimiento de los casos en los tres estados: Paraná (PR) tuvo elevación de casos autóctonos para 94% en los últimos cuatro años, Santa Catarina (SC) para 95%, y Rio Grande do Sul (RS) para 83%, respectivamente, en 2015 y 2016. Se observó todavía creciente aumento de óbitos por dengue hemorrágico, principalmente en PR; en 2016; el primero óbito en SC; y crecimiento en los últimos dos años en RS, más de 90% en adultos. **Conclusión:** la región necesita atención de los organismos de salud, a causa del crecimiento de casos y óbitos por dengue, a pesar de presentar la menor incidencia de la enfermedad del país. Este estudio contribuyó para el conocimiento del escenario actual y de la evolución de la dengue en la región Sur de Brasil.
DESCRIPTORES: Notificación de enfermedades; Mortalidad; Morbilidad; Epidemias; Arbovirus.

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INTRODUCTION

Dengue is a mosquito-borne viral disease that has rapidly spread in many world regions, and thus, has become an important public health issue. The dengue virus (DENV), transmitted by female mosquitoes of the *Culicidae* family, consists of a single-stranded RNA genome and 4 distinct serotypes (DENV 1, 2, 3 and 4) belonging to genus *Flavivirus* and *Flaviviridae* family.[1] The virus can cause an acute febrile disease, and symptoms will show 3-14 days after the mosquito bite. A wide spectrum of illness can be observed, ranging from unapparent asymptomatic disease, called dengue fever (FD) to a severe hemorrhagic fever (DHF) that can progress to death. [1]

To date, there is no specific treatment for dengue,[2] and this illness has emerged as one of the most infectious diseases of the 21st century [1,3], with an incidence about three times higher than estimated by the World Health Organization (WHO). Dengue is ubiquitous throughout the tropics, with the highest risk zones in the Americas and Asia.[4]

The growing global threat of dengue outbreaks requires an effective management of these events. [2] According to the WHO, 50 million people are infected with the virus each year and about one third of the world's population lives in risk zones. [1] Estimates show that Brazil contributed the highest number of cases in the Americas (2.1 million; i.e., 39% of the total number of cases) in the 2000-2007 period. [5]

In Brazil, the first reports of dengue occurred in the late nineteenth and early twentieth century in the cities of Curitiba (PR) and Niterói (RJ). At the beginning of the twentieth century, the mosquito had already become a major health problem, but because it was a vector of yellow fever, not dengue. In 1955, the A. *aegypti* was eradicated, but in 1960 the vector was reintroduced in Brazil. [6] The first dengue outbreak in Brazil occurred in the 1980s, in Boa Vista (Roraima), where serotypes DEN-1 and DEN-4 were isolated. [7] In 1986, there were dengue epidemic outbreaks in Rio de Janeiro (RJ) and in some capitals in the Northeastearn region of Brazil. Currently, the mosquito vector of dengue and cases of the disease occur in all Brazilian states. [6,8]

Climate conditions, such as high rainfall rates, hot and humid climate in most of the Brazilian territory, favor the proliferation and distribution of *Culicidae*, vectors that are determinant for the maintenance of the complex cycle of infection of the arboviruses and change in the incidence of dengue cases [8-9], although the southern region is characterized by the occurrence of alternating cold and warm periods. Cases of dengue have been recorded in urban populations, where high population density and the dispersion of the mosquito over relatively short distances favor viral transmission. [10]

Thus, the present study aimed to identify the number of reported cases and deaths from dengue hemorrhagic fever that occurred annually in the states of southern Brazil (PR, SC and RS) from January 2001 to November 2017, given the lower incidence rate of the disease in the southern region (according to a study carried out in the 2002-2012 period) compared to other regions of the country. [11]

METHOD

Descriptive-retrospective study using secondary data obtained from records of notification of cases of classical dengue fever and deaths from dengue hemorrhagic fever in the three southern Brazilian states: Paraná (PR), Santa Catarina (SC) and Rio Grande do Sul (RS).

Data was collected from December 2016 to February 2017 and updated in November 2017. Data on the incidence of classical dengue fever were obtained using the International Code of Disease (ICD A90) and for dengue hemorrhagic fever (ICD A91).

In the 2001-2016 period, the total number of annual cases of classical dengue fever was obtained from the epidemiological situation described in the spreadsheet "Dengue Cases. Brazil, Major Regions and States, 1990 to 2016 "made available at SUS health portal, Ministry of Health (SINAN: a national system of information on notifiable diseases and events), which informs the total number of dengue cases in the country. [12-13]

In 2017, the number of notifications for classical dengue fever was extracted from the epidemiological bulletins available in the health department of each state, ,[14-16] due to the lack of updated data in the SUS health portal...[12] Additional data such as gender (male and female), age group (grouped: <1 year, 1 to 4 years, 5 to 19 years, 20 to 59 years,> 60 years) and number of autochthonous cases were extracted from the DATASUS database (Department of Information technology of the Unified Health System – (TABNET health information: epidemiology and morbidities), collected using option "SINAN Notification Diseases and Injuries, 2001 to 2006 and 2007 onwards, where information is available up to 2012. [13]

Other data were obtained in epidemiological bulletins, as well as information from the website of the Health Department of each state. [14-16] I The number of autochthonous cases in 2017 could not be estimated because of the lack of data.

The number of cases of dengue hemorrhagic fever was extracted from the database DATASUS - SUS Information Technology (17), which includes information until 2015. Recent records (from 2016 to November 2017) were obtained from a specific site of the Health Department of each one of the states, using the TABNET option or epidemiological bulletins,[14-16]. The data were then extracted, stored and analyzed with the aid of Excel spreadsheets. The following variables were organized and analyzed: state (PR, SC and RS), annual period, age group, gender, autochthonous cases, classical dengue fever and deaths caused by dengue. Based on the quantification for each set of variables, the absolute numbers and corresponding percentages were obtained.

Regarding ethical aspects, the study was based on secondary data from public domain sites, and, thus, did not involve ethical issues. Hence, authorization from ethics committees was not required.

● RESULTS

Classical dengue fever and deaths related to the dengue virus

The results for classical dengue fever cases can be seen in Figures 1, 2 and 3 and show the number of reported cases of dengue fever and the number of autochthonous cases in the three southern states of Brazil.

Regarding the state of Paraná (Fig. 1), on average 71% of the records were considered autochthonous (transmission in the state of PR from 2007 to 2012). However, in the last 4 years (except for 2017) autochthonous cases accounted for 94% of the total cases.

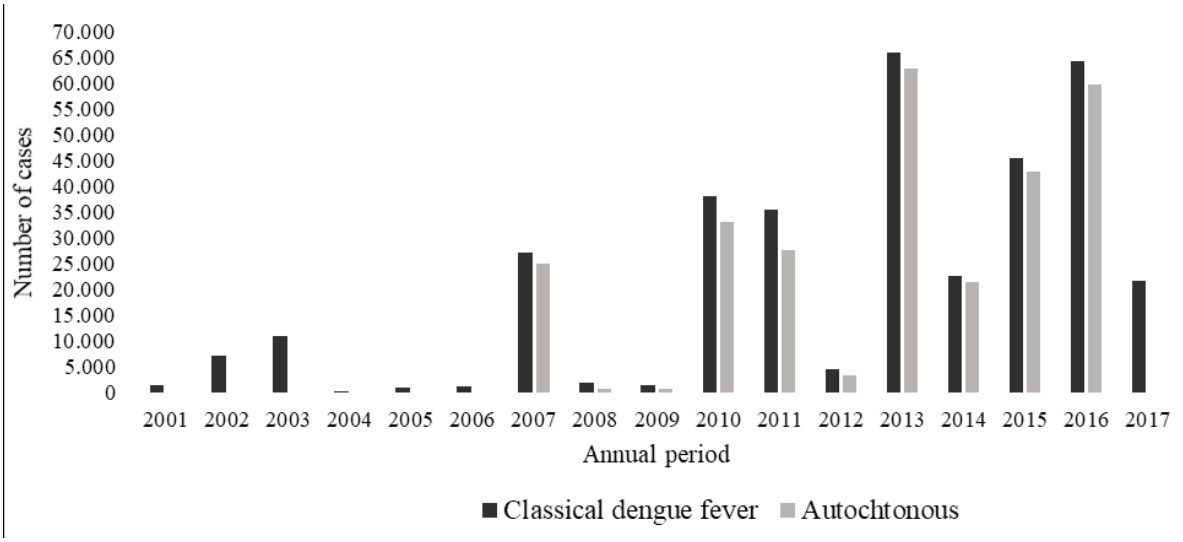

Figure 1 - Total number of notified cases of classical dengue fever and autochthonous records in PR between 2001 and November 2017. Paraná, Brazil, 2017

For the state of Santa Catarina (Fig. 2), in the 2007-2014 period, there was a low number of autochthonous cases (average of 4%). However, there was an increase in the last two years in the number of cases, and the average rose to 95% (except for 2017). There was also an increase in the number of cases, particularly in 2015 and 2016, almost reaching 5,000 cases per year, while the maximum number of cases in any of the other previous annual periods was 300 cases.

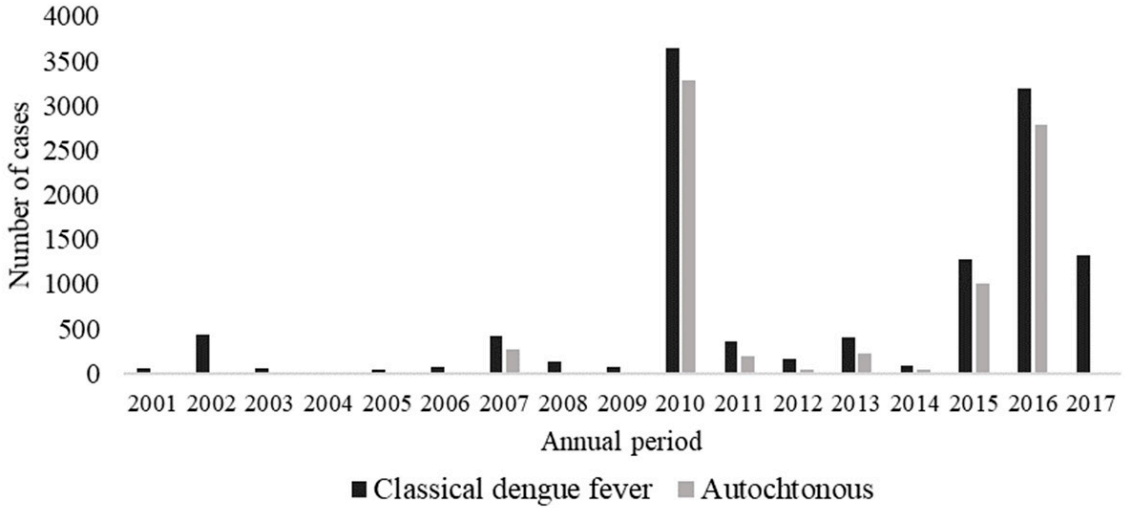

Figure 2 – Total number of notified cases of classical dengue fever and autochthonous records in SC between 2001 and November 2017. Santa Catarina, Brazil, 2017

In Rio Grande do Sul (Fig. 3), on average (2007-2014 period) the rate of autochthonous cases reached 43%, and in the last two years the rate of autochthonous rose to 83% (except for 2017). The highest number of cases of dengue occurred in 2010 (more than 3,500), and in 2016 with 3,195 notifications.

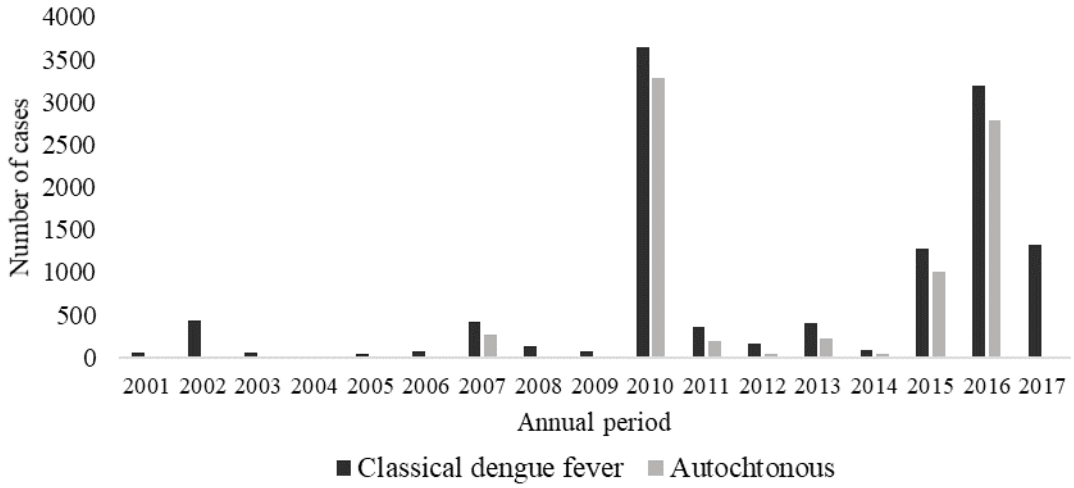

Figure 3 – Total number of notified cases of classical dengue fever and autochthonous records in RS between January 2001 and October 2017. Rio Grande do Sul, Brazil, 2017

Figure 4 represents the cases of classical dengue fever in the different age groups in the three Southern states. In 80% of the cases, adult individuals were affected, and the age group 20-59 years was the most affected by classical dengue fever (70%). In contrast, the age group that was least affected by the disease was that of children under 1 year old (1%).

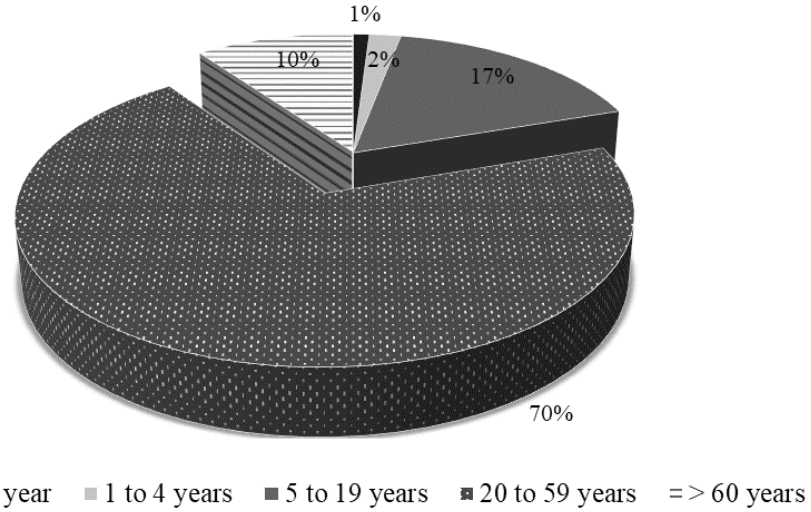

Figure 4 –Average percentage (%) of cases of classical dengue fever by age group in the three states (PR, SC and RS) between 2001 and 2016. Brazil, 2016

Figure 5 shows the number of deaths in the different age groups due to haemorrhagic dengue fever in the three states. In 2017, there is no record of deaths due to dengue hemorrhagic fever (ICD A91) up to November, according to information obtained from the websites of the departments of health of Paraná and Santa Catarina (TABNET) and in epidemiological bulletins of Rio Grande do Sul.

Regarding fatalities related to dengue hemorrhagic fever, there were 72 deaths from 2001 to November 2017. The state of Paraná had the highest number of deaths: 67 (93%) followed by Rio Grande do Sul, with 4 deaths (5.6%) and Santa Cataria, with one death (1.4%).

The state of Paraná has been recording death cases since 2003, particularly in 2013, where there were 14 deaths due to the disease, and in 2016, 20 deaths (year with the highest number of notifications of classical dengue fever). In Rio Grande do Sul there was one death in 2001 and 3 deaths between 2015 and 2016, while in Santa Catarina the first death was notified in the first half of 2016. Such data depict a serious public health issue, especially Paraná that led the number of deaths, and also Santa Catarina that recently recorded its first death, and Rio Grande do Sul where there was an increase in the number of fatalities in the last two years. The non-existence of a record of deaths due to dengue hemorrhagic fever until November 2017 is a positive sign from the point of view of public health.

According to figure 5, there was no record of deaths of children under 1 year of age due to dengue in the three states. However, Paraná reported 7% of deaths in individuals aged 5-19 years and 1% of deaths in children aged 1-5 years.

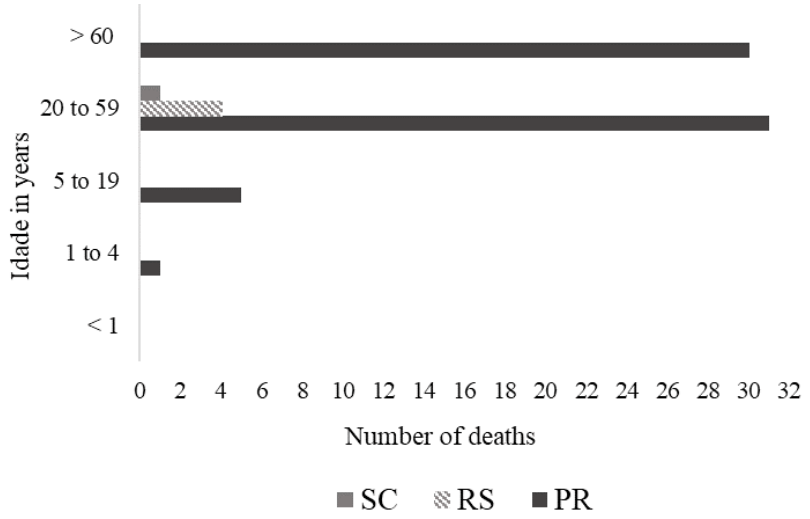

Figure 5 – Total number of deaths due to dengue hemorrhagic fever (ICD A91) in the different age groups for PR, SC, RS, between 2001 and November 2017. Brazil, 2017

● DISCUSSION

There was no difference in the incidence of classical dengue, which was equal (50%) for both genders in the three states and throughout the study period.

In the state of Paraná, the highest number of notified cases (approximately 66 thousand cases) occurred in 2013 contributing with the largest dengue outbreak in Brazil with approximately 2 million notifications. [18] Although there has been a decrease in the number of deaths reported from 2014 onwards compared to the previous year, there has been a gradual increase in the number of notified cases in the last three years, and in 2016, approximately 65 thousand new cases were reported, a figure similar to that of 2013.

Regarding the states of Santa Catarina and Rio Grande do Sul, there was an increase of 95% and 83%, respectively, in the notification of autochthonous cases in the last two years. Although Paraná had already a high rate of autochthonous cases notified in the 2007-2012 period (71%), such rate rose to 94% over the past four years. Thus, it can be seen that the three states are contributing to the increase in the number of notified cases of dengue in the region. The referred data indicate changes in the rates of dengue in the Southern region, which has the lowest rate of notification of cases of dengue in Brazil (1.2%), compared to the Northeastern and Southeastern regions, which have the highest rates (85% of the cases). On the other hand, in 2017 there was a significant reduction in the number of notifications for classical dengue fever, as follows: a decrease of 33%, 41% and 43%, respectively, for Paraná, Rio Grande do Sul and Santa Catarina, compared to 2016.

The increase in the number of autochthonous cases in the three states differs from the view that the climate of the Southern region with well-defined seasons and lower temperature, annual average lower than 20ºC, compared to the other Brazilian regions where the average temperature is higher than 20□C, ,[20] would not favor vector proliferation,[21], as it is known that a temperature lower than 20ºC interferes in the development and reproduction of the mosquito, thus reducing the number of dengue cases. [6]

The severity and frequency of dengue epidemic outbreaks, which are determinant factors of this growing trend, are strongly related to meteorological variables. Thus, seasonal variation of temperature and rainfall influence the vector dynamics and the incidence of the disease throughout the country, regardless of the climatic classification, [3, 9] as well as of factors related to the history of immunity, to the introduction of a new serotype or to demographic transitions that influence viral transmission. [1]

Therefore, in Brazil, according to the Ministry of Health, the transmission of dengue has been occurring since mid-1986, interspersed with the occurrence of epidemic outbreaks, often associated with the introduction of new serotypes in areas previously not affected by dengue or with the change of the predominant serotype. [18]

In the southern region of Brazil, all age groups were affected, though at different levels. While in the Southern region, in Brazil, and also in some regions of the Americas, adult individuals are predominantly affected by dengue, [21] in other regions of the world, such as Southeast Asia, children are the age group most affected by the disease. [22]

Moreover, in the state of Rio de Janeiro, during an epidemic outbreak in 2007, there was a change in the age distribution of the cases of dengue, with an increase in the number of children affected. [23] However, during the period assessed in this study, there was no increase in the incidence rate of dengue in children in the Southern region.

Thus, in an attempt to reduce the spread of the disease and its aggravating factors, recent national reports indicate that the state of Paraná has been a pioneer in the country in the immunization campaign against dengue in some municipalities since the second half of 2016. The introduction of an immunization program can be a strong ally in combating the disease, and may reduce the impact on public health in places where the disease is endemic. . [25], although vector control measures with the participation of citizens and public authorities should always be used to reduce the spread of the disease.

In order to estimate the impact of vaccination, researchers conducted a study in which they used different data from endemic countries in Asia and Latin America and reported significant reduction in the cases of dengue among the population after the introduction of vaccination during the first 10 years. . [25]

Thus, further studies should be conducted to provide data on post-vaccination impacts in different populations and regions where the immunization program is introduced, although the vaccine has already shown good safety and immunogenicity in pre-clinical tests in vitro and in vivo and in clinical trials. . [26]

After a long period of research, only in the second half of 2016 the first tetravalent vaccine was approved and released in Brazil and worldwide. The effective impact of the dengue vaccination program on public health is not known because the program is under in implementation phase.

It is important to highlight the lack of information (from autochthonous cases) in the DATASUS database (13) from 2001 to 2006. Therefore, the absence of information was a limitation, since the study could evaluate a longer period and with more representative data. It was not possible to assess cases of dengue in the period prior to 2001, since there is no record, according to the search performed on the DATASUS platform. . [13]

Nonetheless, we noticed an improvement in the information system in 2007, regarding the organization and availability of data, although there are some aspects that still need to be improved, especially regarding the entry of data in a faster and more consistent manner.

In general, it was difficult to obtain the same information (exact quantification) in the different databases researched, especially regarding classical dengue fever. Thus, the present study draws attention to the need to improve and implement an information system that can provide updated and consistent data without the need to perform different searches within the currently available databases, which are time consuming and often provide inconsistent information.

In addition, in the current information system (DATASUS / SINAN) it is not possible to identify the viral serotype (DENV 1, 2, 3, 4), a key aspect of public health and research studies. The insertion of this information may facilitate the monitoring of the viral types that circulate in certain regions, as well as of the emergence of new serotypes, and, consequently, help tracking the evolution of the different viral types of dengue in each region.

In general, individuals of both genders died from dengue in southern Brazil, with a higher frequency for females (54%), which is similar to the findings of an epidemiological study in the state of São Paulo, (27) as well as in Rio Grande do Sul where all the cases of death (100%) were of female individuals. The

age group with the highest number of deaths was 20 and 59 years (50%) and over 60 years (42%), that is, adult individuals, accounting for more than 90% of the deaths, which is consistent with the previously mentioned data on classical dengue fever. Records of death cases in this region are similar to national data, where the incidence of dengue hemorrhagic fever (DHF) and complications (DCC), which are risk factors for death, has been higher in adults. .[23]

The non-existence of records of deaths caused by dengue in children under 1 year in all the three states is a positive sign from the point of view of public health, although Paraná has recorded in 2014, its first death in children between 1 and 5 years, and 5 deaths between 5 and 19 years of age, in 2007.

The occurrence of deaths caused by dengue in childhood and adolescence was also observed in the state of São Paulo, [27] where until 2007 there were no deaths recorded in individuals younger than 15 years. In 2008, an average rate of 13% was recorded in São Paulo, and in 2010 the first death caused by dengue was recorded in a child under 1 year of age in the referred state.

In 2008, there have been cases of dengue in younger age groups in the state of Rio de Janeiro. Although most notifications concerned the population aged 15-49 years (54%), the most severe cases were those of individuals aged 0 to 15 years, accounting for 48% of reports and hospitalizations and 42% of deaths. Such data is a warning about the increase of fatalities among these new age groups and reveal the growing number of deaths caused by dengue in the southern region, especially in the state of Paraná.

Dengue has a wide spectrum of clinical presentations, and there is no clear evidence that a particular viral serotype can trigger classical dengue fever or dengue hemorrhagic fever, or that any specific symptom is associated to a particular serotype. Evidence suggests that neutralizing antibodies and cross-reactions regulate dengue epidemics and disease severity. .[2, 22]

Thus, a study carried out in Latin American countries, over the past three decades, suggests that an earlier infection may lead to a more serious infection by a different serotype in later situations. .[29] Thus, dengue mortality, according to the WHO, can be reduced through the implementation of appropriate clinical management, laboratory diagnosis and adequate clinical management, training of human resources at all levels of the health system and hospital reorganization..[3]

● CONCLUSIONS

The present study provided greater insight on the occurrence and evolution of classical dengue fever and dengue hemorrhagic fever in the southern region of Brazil. There have been few studies on this issue in the referred region.

The study showed a growing trend in the number of autochthonous cases in the three states, especially in the last years (except for 2017), indicating that the region is requires more effective sanitary and environmental control measures to fight the vector.

The higher number of notifications of classical dengue fever, especially in recent years: in Paraná, in 2013; in Santa Catarina and Rio Grande do Sul, in 2015, reinforces the need for strict vector control and the implementation of strategies to reduce the incidence of the disease in this region.

The increasing number of deaths due to dengue hemorrhagic fever, especially in the state of Paraná, the record of the first death by dengue in Santa Catarina and the increase in the number of deaths by the disease in the last years in Rio Grande do Sul should receive more attention from the health bodies. Continued efforts have been made but have proven insufficient, in view of the increase in serious and lethal cases of dengue in the southern region, despite the fact that there have been no records of deaths by this disease until November 2017.

The present study exposed the need to improve the information system (DATASUS/SINAN), suggesting the implementation of a single platform with information on dengue mortality and morbidity, in each state. In addition, it is necessary to include data from viral serotypes (DENV 1, 2, 3, 4) and reduce the time taken to store data in the platform of the information system.

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