Epidemiology of dengue in Portugal – a portrait

Epidemiologia da dengue em Portugal – um retrato

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INTRODUCTION

Dengue is a systemic infectious disease of viral etiology transmitted through the bite of female hematophagous mosquitoes of the genus *Aedes*, with *Aedes aegypti* and Aedes albopictus *being the* most competent species for its transmission [1-4]. Dengue virus (VDEN) taxonomically belongs to the family *Flaviviridae* and the genus *flavivirus* [5-8]. To date, four antigenically differentiated serotypes - VDEN-1, VDEN-2, VDEN-3 and VDEN-4 - have been reported based on biological, immunological and molecular criteria [8,9].

Among all arboviruses, VDEN is by far the pathogen that most affects humans [10-13]. According to the World Health Organization (WHO) in the last 50 years the incidence of Dengue cases has increased by about 30 times, and it is estimated that there are currently between 50 and 100 million infections annually [10]. The disease is widespread in all tropical and subtropical regions of the planet, with a growing incidence in Asia, Africa, Latin America and the Pacific region [10,14]. It is estimated that approximately 2.5 billion people live at risk of contracting the disease in endemic countries [10,13]. Around 120 million people travel to affected areas each year, with travellers playing a key role in the geographical spread of the disease (the return of infected travellers from Dengue-endemic countries can establish autochthonous cycles of infection) [15,16, 17].

The last Dengue epidemic in Europe occurred in Greece in 1927-28, with an estimated 1 million cases [16]. In addition, some autochthonous cases have been detected in some areas of France (2012) and Croatia (2010) [16,18].

GOAL

This article aims to characterize the epidemiology of Dengue in Portugal, with the following objectives:

- Specify and analyse the epidemiological information available;
- Characterize the outbreak registered in the Autonomous Region of Madeira, discriminating the period and dispersion of cases;

- Predict the potential effects of globalization, climate change and the lack of effective mosquito population control programs on the introduction of Dengue vectors in mainland Portugal;

METHODOLOGY

The main methodology for collecting information was the search for scientific articles published in scientific journals and journals. This was carried out between January 2013 and May 2013 in the following electronic databases: Pubmed, ScienceDirect, Eurosurveillance, B-on, World Health Organization and CDC (Center for Disease Control and Prevention). It was used during the research the combination of the words Dengue, Dengue Fever, Aedes *aegypti, Aedes* albopictus*, Dengue in Portugal,* Dengue in the Autonomous Region of Madeira and Dengue in travelers. Documents, books and theses published on the subject were also used.

DEVELOPMENT

The geographical dispersion of Dengue is marked by the geographical expansion of the virus and vectors [13].

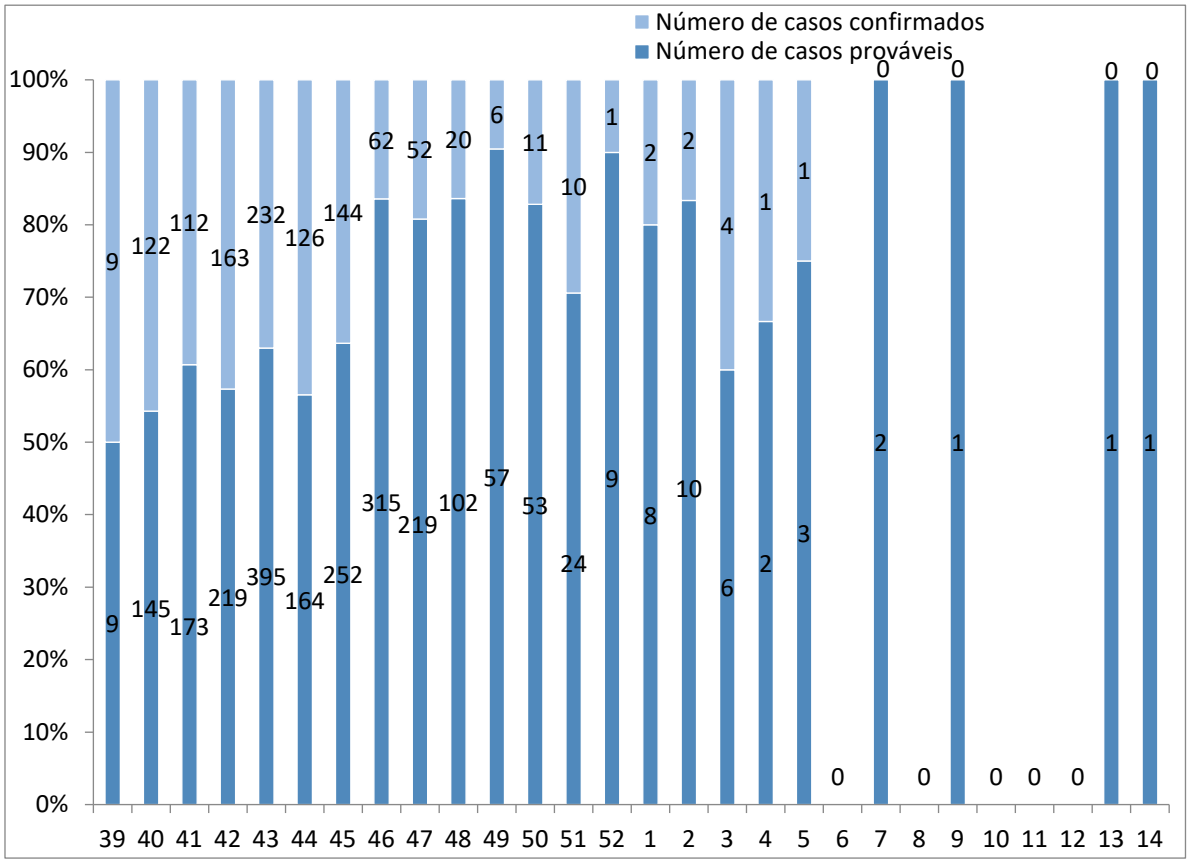
So far, no vectors of VDEN have been detected in mainland Portugal, a fact that explains the absence of autochthonous cases [11]. All cases of Dengue diagnosed to date in mainland Portugal correspond to cases imported from endemic regions [11], being identified annually at the level of the National Institute of Health Dr. Ricardo Jorge (INSA) about two dozen imported cases originating mainly in Brazil, Timor, India, Cape Verde, Mexico, Thailand, Angola, Pakistan and Vietnam [19-21].

The *Aedes aegypti vector* was detected in the Autonomous Region of Madeira in 2005, and the mosquito population continues to expand today on the island [20, 26]. The ecological success of this vector in Madeira is attributed to the combination of diverse natural and urban conditions that are favorable to it [22-25]. Thus, the existence of densely populated residential areas, green areas containing abundant subtropical vegetation and the presence of numerous artificial breeding sites, associated with the meteorological profile of the island, make Madeira an area conducive to colonization by the vector [25].

On 3 October 2012, the first two autochthonous cases of Dengue Fever were reported on the island of Madeira [20, 25-27]. Although vectors of the infection were identified on the Island in 2005, there have never been autochthonous cases to date [20, 23]. Both cases were confirmed by serology and one of the cases allowed the detection of the circulating serotype by RT-PCR, and VDEN-1 was identified as the responsible etiological agent [21,27]. Subsequently, the sequential analysis of the identified viral genome revealed 99% of similarities with the VDEN-1 that circulated in Venezuela (2006-2007), Colombia (2006-2009) and Roraima, northern Brazil (2010), thus calculating that the VDEN-1 detected in Madeira originated

in Latin America [21]. By 7 April 2013, 28 weeks after the first autochthonous case was identified, 2170 probable cases of Dengue Fever were reported on Madeira Island from hospital records and primary health care, of which 1080 were laboratory-confirmed [22, 28]. It should also be noted the detection of 11 cases in mainland Portugal and 71 cases in thirteen other European countries, all in travelers returning from Madeira Island [22].

Figure 1 - Number of cases reported per week on the island of Madeira from 3 October 2012 to 7 April 2013 [22,28]



The dengue outbreak recorded in 2012-13 in the Autonomous Region of Madeira is the first of its kind in Europe since 1928 [16]. Although the introduction of VDEN on the island was expected (considering the spread of the virus in the last 50 years, the vector density present on the Island and the high number of travellers who travel annually to the Region [25, 27]), this outbreak was a significant episode for the health of the local population and for that of the travellers who came to the island.

The entry of VDEN in Madeira is not yet fully clarified, formulating two possible theories:

- Cycle of infection induced by a traveler infected by VDEN combined with the strong vector density present in the Region [15,25];
- Transport of VDEN-infected eggs that ended up incubating weeks/months later in breeding sites in the Region and inducing the infection cycle [4,25];

2170 probable cases of Dengue fever have been reported on Madeira Island since the outbreak began on 3 October 2012, of which 1080 have been laboratory-confirmed [22,28]. In addition, 11 other cases were reported in mainland Portugal and 71 in thirteen other European countries, all in travelers returning from the island [22]. Weeks 43 and 46 corresponded to the weeks with the highest number of recorded cases, with 395 and 315 cases, respectively. At week 47, 219 cases were reported, representing a change of -30% from the previous week. The downward trend in the number of recorded cases continued the following week, in which 102 new cases were reported (change of -54% from the previous week). The number of cases decreased in December 2012, although in the following months there were still some cases in residents and tourists [22, 25]. However, since 4 February 2013 there have been no laboratory-confirmed autochthonous cases [22].

The combination of the high vector density with the presence of numerous breeding sites (related to months of increased rainfall, for example), associated with the lack of immunity of the population, are factors that explain the size of the outbreak recorded [27].

The highest proportion of cases was recorded in residents of the parishes of Santa Luzia and Nazaré in the Municipality of Funchal, although a high number of cases have also been reported in Santa Cruz and Câmara de Lobos [20]. The high rate of cases recorded in these municipalities in the South of the Island probably results from the high population density present in these areas, as well as from the distribution of *Aedes aegypti* along the southern coast [20, 25].

Since the circulating serotype originated in Latin America and that all known serotypes (VDEN-1-4) currently circulate in this zone, it can be assumed that there is a risk of new introductions in Madeira Island [14]. This possibility may result in a serious public health problem, taking into account that the absence of long-term cross-immunity between the different serotypes allows the occurrence of multiple sequential infections with heterologous serotypes and the consequent occurrence of cases of greater severity [12, 27].

Considering the relationship between vector-borne diseases and climatic factors, and given the current evidence that the climate is changing, it is extremely important to determine what impact climate change may have on VDEN transmission in Portugal. Although the results obtained so far demonstrate that climate change is favorable to the proliferation of vector species and the establishment of other species that would normally only survive in tropical climates, this effect does not yet have an impact in terms of Public Health in mainland Portugal [35].

However, and taking into account the geographical extent recorded by *Aedes albopictus* in recent years, which has already been detected in 20 European countries, including Spain, several studies point to the possibility of a short-term establishment of this vector in Portugal, whose current climatic conditions are conducive to its establishment [19].

However, some projections point to a future decrease in the suitability of southern European countries, namely Portugal, Spain and the Mediterranean islands to *Aedes albopictus* from 2030 [36]. The climatic conditions simulated throughout the projections reveal that the extremely dry summers that will hit this region will constitute an obstacle to the dispersion of the vector through this zone, favoring the vector countries of Central-Western Europe [4,36].

Regarding *Aedes aegypti* there are no reasons that prevent its establishment in mainland Portugal, particularly in the South region (Algarve) where temperatures are higher. The large amount of traffic between Madeira and mainland Portugal also points to this possibility, since it can build the "bridge" that the vector needs for its importation [19].

FINAL CONSIDERATIONS

This review sought to compile information on the presence of Dengue in Portugal. Considering the lack of mosquitoes vectors of VDEN in mainland Portugal, the risk of the occurrence of autochthonous cases is for now removed. However, globalization, climate change and the lack of effective programs to control mosquito populations may favor a future establishment of the main vectors that transmit VDEN in mainland Portugal, which together with the growing number of cases recorded in recent years makes a future association between vector and virus in Portuguese territory expected.

The dengue outbreak recorded in 2012-13 in the Autonomous Region of Madeira is the first of its kind in Europe since 1928, with 2170 probable cases reported in the region, of which 1080 were laboratory-confirmed. The VDEN-1 serotype was identified as the etiologic agent responsible for the outbreak. Although there has been no laboratory-confirmed autochthonous case since February 4, 2013, the virus should persist on the island, taking into account that vertical transmission has already been documented between *Aedes aegypti* species. Considering the absence of long-term cross-immunity between the different serotypes and assuming that there is a risk of new introductions in the region, the occurrence of multiple sequential infections with heterologous serotypes may constitute a serious public health problem.

In this sense, the control and prevention of Dengue should be priorities of the National Public Health, being necessary an approach that encompasses all the possible protagonists of the transmission cycle. To deal with this possibility it is necessary to increase entomological surveillance in potential vector import areas, such as ports and airports, strengthen the monitoring of imported cases and alert the population to its role in mosquito control. Only with coordinated regional, national and international surveillance can the challenges posed by Dengue be addressed.

REFERENCES

1. Doloi G, Mootezuma J, González V, Páez F, González B, Gas H. El dengue en México. Conocer para mejorar la calidad de la atención. Revista Médica del Instituto Mexicano del Seguro Social. 2012;50(6):631-9.
2. Higa Y. Dengue Vectors and their Spatial Distribution. Tropical Medicine and Health. 2011;39(4):17-27.
3. Guzman M, Halstead S, Artsob H, Buchy P, Farrar J, Gubler DJ, et al. Dengue: a continuing global threat. Nat Rev Microbiol. 2010;8(12): S7-16.
4. Fried JR, Gibbbons RV, Kalayanarooj S, Thomas SJ, Srikiatkhachom A, Yoon I-K, et al. Serotype-Specific Differences in the Risk of Dengue Hemorrhagic Fever: An Analysis of Data Collected in Bangkok, Thailand from 1994 to 2006. PLoS Negl Trop Dis. 2010;4(3): e617.
5. Ferreira GLC. Global dengue epidemiology trends. Rev Inst Med Trop Sao Paulo. 2012;54(Suppl. 18):S5-S6.
6. WHO. Dengue: Guidelines for diagnosis, treatment, prevention and control. New Edition. Geneva, Suiça: World Health Organization; 2009. 15-65
7. Tapia-Conyer R, Betancourt-Cravioto M, Méndez-Gálvan J. Dengue: an escalating public health problem in Latin America. Paediatrics and International Child Health. 2012;32(Suppl. 1):14
8. Wilder-Smith A. Dengue infections in travellers. Paediatrics and International Child Health. 2012;32(s1):28-32.
9. Marí RB, Peydró RJ. Re-Emergence of Malaria and Dengue in Europe, Current Topics in Tropical Medicine. 0. Espanha: InTech; 2012. 483-499
10. Larrieu S, Dehecq JS, Balleydier E, Jaffar MC, Michault A, Vilain P, et al. Re-emergence of dengue in Reunion, France, January to April 2012. Euro Surveill. 2012;17(20):pii: 20173.
11. DGS. Abordagem de casos de dengue. [homepage on the internet]. Portugal: DGS; 2012 copyright. [Acesso em 5 de abril de 2013]; Disponível em: http://www.dgs.pt/?f=3&id=23047
12. Alves M, Amaro F, Osório H, Luz T, Parreira P, Zé-Zé L. Diagnóstico laboratorial de dengue no Instituto Nacional de Saúde Doutor Ricardo Jorge: casos autóctones na Madeira. INSA: INSA; 2013. Disponível
13. Sousa CA, Clairouin M, Seixas G, Viveiros B, Novo MT, Silva AC, et al. Ongoing outbreak of dengue type 1 in the Autonomous Region of Madeira, Portugal: preliminary report. Euro Surveill. 2012;17(49):pii=20333.
14. Melím M. Da presença do Aedes aegypti ao aparecimento de dengue na Região Autónoma da Madeira. Madeira; 2009.
15. European Centre for Disease Prevention and Control. Dengue outbreak in Madeira, Portugal, October–November 2012. Stockholm: ECDC; 2013
16. Alves MJ, Fernandes PL, Amaro F, Osório H, Luz T, Parreira P, et al. Clinical presentation and laboratory findings for the first autochthonous cases of dengue fever in Madeira island, Portugal, October 2012. Euro Surveill. 2013;18(6):pii: 20398.
17. Almeida A, Gonçalves Y, Novo M, Sousa C, Melim M, Grácio A. Vector monitoring of Aedes aegypti in the Autonomous Region of Madeira, Portugal. Euro Surveill. 2007;17(46):pii=3311.
18. Alves MJ, Fernandes PL, Amaro F, Osório H, Luz T, Parreira P, et al. Clinical presentation and laboratory findings for the first autochthonous cases of dengue fever in Madeira island, Portugal, October 2012. Euro Surveill. 2013;18(6):pii: 20398.
19. DGS. Surto de dengue na Ilha da Madeira - situação em 7 de abril de 2013. [homepage on the internet]. Portugal: DGS; 2013 copyright. [Acesso em 29 de abril de 2013]; Disponível em: http://www.dgs.pt/?cn=683368347243
20. DGS. Surto de dengue na Ilha da Madeira - situação em 19 de maio de 2013. [homepage on the internet]. Portugal: DGS; 2013 copyright. [Acesso em 28 de maio de 2013]; Disponível em: http://www.dgs.pt/?cn=683368347243

21. Pawitan JA. Dengue virus infection: predictors for severe dengue. Acta Med Indones. 2011;43(2):129-35.
22. INSA. Alterações climáticas e estudo de vetores. [homepage on the internet]. Portugal: INSA; 2012 copyright. [Acesso em 11 de maio de 2013]; Disponível em: http://www.insa.pt/sites/INSA/Portugues/ComInf/Noticias/Paginas/EstudoVetores.aspx
23. Medlock JM, Hansford KM, Schaffner F, Versteirt V, Hendrickx G, Zeller H, et al. A review of the invasive mosquitoes in Europe: ecology, public health risks, and control options. Vector-Borne and Zoonotic Diseases. 2012;12(6):435-47.
24. Caminade C, Medlock JM, Ducheyne E, McIntyre KM, Leach S, Baylis M, et al. Suitability of European climate for the Asian tiger mosquito Aedes albopictus: recent trends and future scenarios. J R Soc Interface. 2012;9(75):2708-17.