

Chikungunya: time to change the paradigm of a non-fatal disease

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According to recent advances in mortality trends interpretation, there is no doubt that chikungunya may be a major cause of death, of great magnitude [1-3] including for previously healthy and young patients [4].

So, why is there so much resistance to admitting that chikungunya can lead the patient to death?

We believe that the difficulties in assuming that chikungunya is a cause of death are maintained by the official ECDC (European Center for Disease Prevention and Control) documents, we quote here the Fact Sheet about Chikungunya which states that "Despite it being considered as a non-fatal disease, deaths have been partly (authors' emphasis) attributed to the virus" [5]. In addition, the World Health Organization states in Fact Sheet about chikungunya in april 2017 that "Serious complications are not common, but in older people, the disease can contribute (authors' emphasis) to the cause of death" [6].

However, together with hospital-based studies, several analyses of mortality trends have already shown excess mortality associated with chikungunya epidemics in Ahmedabad (India, 2944 deaths), Republic of Mauritius (Africa, 743 deaths) [7,8]. In the Americas, alongside the French Antilles (Guadeloupe and Martinique), excess mortality associated with chikungunya epidemics has also been demonstrated in different countries, such as Brazil (7,500 deaths), Jamaica (2,499 deaths), Dominican Republic (4,952 deaths) and Puerto Rico 1,310 deaths) [9-13].

During the 2014 chikungunya epidemic in Guadeloupe and Martinique (French Antilles), there were 74 deaths attributed to the virus in four public hospitals that were confirmed by consensus between biologists and medical infectologists [3]. Death certificates totaled 160 mentions of chikungunya [14], which was unexpectedly high for the two islands that total less than 800,000

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inhabitants. A study, which analyzed the excess of deaths stratified by age, made it possible to estimate that the number of deaths attributable to chikungunya was fourfold higher (639 deaths) than those indicated on death certificates [13], corresponding to an overall mortality of 81.4 deaths per 100,000 inhabitants. In this study, there was also a strong correlation ($R^2 = 0.81$) between the monthly excess of deaths and the number of chikungunya cases [12].

Syndromic surveillance is a very important tool to identify changes in the pattern of occurrence of diseases and deaths that may be related to massive events. This type of surveillance may raise explanatory hypotheses for events not yet well known. But when it is already known that certain events are potentially responsible for a large number of deaths, the surveillance of excess deaths should be considered complementary to the surveillance of specific diseases and be integrated with that for a better evaluation of the dimension of the phenomenon. In this case, if there is a fact that can cause death and at the same time there is no other phenomena of great magnitude that causes deaths, the mortality estimated by the excess of deaths must then be attributed to the phenomenon that is already known. Thus, the mortality associated with infectious causes, such as seasonal and pandemic influenza, is estimated, ditto for non-infectious causes such as heat wave [15]. Considering the specific case of mortality associated with the 2014 chikungunya epidemic in the French Antilles the body of evidence that this virus causes an excess of deaths and the absence of another natural or human phenomenon in that locality should be sufficient to attribute this excess of deaths to the chikungunya [12].

On the other hand, recent studies [15,16] that showed excess deaths not associated with other causes, even with robust evidence of this finding, still have difficulty accepting this phenomenon that chikugunya can lead the patient to death. Yasmine Baghdadi and colleagues had report as a limitation that in this latter event, "the causal relationship between the chikungunya epidemic and the excess mortality was not formally established". The

authors attribute this difficulty to the lack of cause of death notification in the SurSaUD® surveillance system "when an excess death is detected outside the occurrence of known public health events influencing mortality", as to the widespread opinion that chikungunya was not considered life-threatening, despite the previous experience of an excess mortality during the 2005-06 Réunion island chikungunya outbreak" [15].

This set of studies demonstrates that the mortality observed in epidemics is not a casual finding. Instead, it emphasizes that the pattern of chikungunya epidemics is to cause a large number of deaths that in some situations are almost entirely captured by epidemiological surveillance, as in the Reunion Island, and in other situations are not captured individually but appear in the analyzes of mortality trends from time series, as in SurSaUD®. It is thus of paramount importance that the official guidelines for communicable disease surveillance be refined and recognize chikungunya as a major cause of excess deaths so that this disease is better understood, studied and new investments are made in research to improve its management and prevent related deaths. In addition, the surveillance of excess deaths may be used in conjunction with disease-specific epidemiological surveillance to better measure the impact of chikungunya and thus define investments in vaccines and other forms of protection. Risk communication to the population should also be improved. Rather than chikungunya being known only as a cause of chronic incapacitating joint pain, it should be known as a virus causing excess deaths, allowing the population to take the necessary countermeasures.

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