

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

Since the initial description of the first human cases the chikungunya has been considered as a non-lethal virus. Since the emergence of the global virus in 2005, it has become increasingly common in the scientific literature to describe many cases of death, including in young people without preexisting diseases. In addition, it has been observed that in settings where, for some reason, death cases are not properly reported for epidemiological surveillance, it is possible to identify mortality due to chikungunya through the excess of deaths occurring during the period of chikungunya epidemics. Even so, international public health bodies still do not recognize in their official documents the importance of chikungunya as the cause of death. We believe it is necessary to review these positions and to increase investment in research to improve knowledge about the pathophysiology of severe forms and to review investment priorities in vaccines and other forms of chikungunya prevention.

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Yasmine Baghdadi and colleagues had published a paper about of the French reactive mortality surveillance system supporting decision making which give a good evaluation of the attributes and qualities of the French syndromic surveillance system (SurSaUD®) focusing on the mortality subsystem(Baghdadi et al., 2018).

SurSaUD®, the French syndromic surveillance system, was an important construction developed after the consequences of the 2003 heat wave in France that led to a re-evaluation of former surveillance systems that were almost exclusively based on disease notifications declarations by physicians. The objective was to develop the capacity to detect new threats to public health, as diverse as environmental catastrophes or emerging infectious disease outbreaks. The authors conclude that “The ability of the SurSaUD® to detect and follow mortality outbreaks in the whole territory has been demonstrated”, and that it is a useful tool for the early evaluation of the impact of threats on mortality and decision makers to adapt control measures(Baghdadi et al., 2018).

Among other achievements, the authors endorse the usefulness of SurSaUD® to identify excess deaths during influenza epidemics, heat waves and the 2014 chikungunya epidemic in Guadeloupe. However, they 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”(Baghdadi et al., 2018). Another document produced in the context of SurSaUD® that discusses the excess mortality identified in Guadeloupe in 2014 attributes the same limitation to the system “Difficulty in attributing the excess of mortality observed solely to the chikungunya epidemic”(Daudens-Vaysse et al., 2014).

We wish to comment on this specific aspect. In our opinion, it is particularly strange not to recognize that this excess of death has a direct causal relationship with the chikungunya epidemic, even without the cause of death being reported in the SurSaUD® system. There is enough evidence in the literature to mount that chikungunya is a disease that can lead to the death of a large number of patients. In 2005-2006 the French overseas territory of La Réunion was hit by a chikungunya epidemic with a high mortality rate, this high mortality was identified by the surveillance of excess deaths, by the surveillance of death certificates (with mention of chikungunya as the basic cause or associated) and by the hospital-based diseases surveillance simultaneously and independently (Josseran et al., 2006; Renault et al., 2007, 2008; Economopoulou et al., 2009). The result of this integrated surveillance was consistent, the number of deaths obtained from death certificates was 255, the estimated excess deaths were 260 (33.1 per 100,000 inhabitants), reinforcing the utility of surveillance of excess deaths as a tool to measure the impact of the chikungunya. The Reunionionese experience could have been harnessed and fully utilized during the response to the chikungunya epidemic in the French Caribbean and extended to other countries affected by this virus, including continental Europe which has a real risk of new introductions of this virus, as occurred in Italy in 2017.

We believe that the difficulties in assuming that chikungunya is a cause of excess deaths, and that, thereby, this indicator could be useful for disease surveillance, are maintained by the official documents ECDC (European Center for Disease Prevention and Control) , 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”(European Centre for Disease Prevention and Control, 2017). 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”(World Health Organization, 2017). According to the scientific evidence currently available, there is no more room for doubt that chikungunya may be a major cause of death, of great magnitude(Josseran et al., 2006; Renault et al., 2007, 2008) including for previously healthy and young patients(Economopoulou et al., 2009; Dorleans et al., 2018) contrary to the statements in the official WHO and ECDC documents.

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(Dorleans et al., 2018). Death certificates totaled 160

mentions of chikungunya(CIRE - Cellule de le Intitut de Veille Sanitaire en région - Antilles Guyane, 2015), which was unexpectedly high for the two islands that total less than 800,000 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 (Freitas, Alarcón-Elbal & Donalisio, 2018), 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 (Freitas, Alarcón-Elbal & Donalisio, 2018). In support, there were no other climatic, seismic or epidemiological events on those islands that could explain this excess of deaths. The information gathered from this epidemic suggests that the mortality associated with the chikungunya epidemic in the French Antilles was higher than that observed in La Réunion island, which is coherent with the age profile of these Caribbean islands, where the proportion of elderly people is higher.

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(Baghdadi et al., 2018). 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 (Freitas, Alarcón-Elbal & Donalisio, 2018).

Different studies have already shown excess mortality associated with chikungunya epidemics in the different countries of Ahmedabad (India, 2944 deaths), Republic of Mauritius (Africa, 743 deaths)(Beesoon et al., 2008; Mavalankar et al., 2008). In the Americas, besides 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) (Freitas et al., 2017, 2018, 2019; Freitas, Donalisio & Alarcón-Elbal, 2018). 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 Islands, and in other situations are not captured individually but appear in the analyzed time series, as in SurSaUD®, as excess deaths.

It is thus of paramount importance that the official guidelines for communicable disease surveillance be refined and recognize chikungunya as a 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.

Conflict of interest statement

The authors declare that there is no conflict of interest regarding the publication of this article.

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