

Economic assessments for Chikungunya: a narrative review

Avaliações econômicas para Chikungunya: uma revisão narrativa

DOI:10.34119/bjhrv6n4-057

Recebimento dos originais: 13/06/2023

Aceitação para publicação: 11/07/2023

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ABSTRACT

Chikungunya is an important and growing public health problem that causes high morbidity. Despite the high social and economic impact generated by the disease, few economic evaluations have focused on the disease. The objective of the present study was to perform a narrative review of economic evaluations related to Chikungunya. A review of the scientific literature was performed using the PubMed and Lilacs databases. All identified articles were reviewed by two researchers. The literature search identified 24 articles related to the topic, and after analysis, six studies were included in the present review. These articles were published between 2011 and 2019 and were conducted in the United States, Colombia, France, Mexico and Brazil. All of these studies reported the economic and/or social burden of Chikungunya for patients and/or health services. The main items described in the studies were direct costs related to diagnostic tests, consultations, hospitalizations, medications and rehabilitation, and indirect costs resulting from the loss of patient productivity, years lived with a disability and disability-adjusted life years lost. The results show that economic evaluations related to Chikungunya are recent and limited, and the results are difficult to extrapolate. In this context, more economic studies focusing on Chikungunya are needed.

Keywords: economic evaluations, Chikungunya, diagnostic, treatment.

RESUMO

A chikungunya é um problema de saúde pública importante e crescente que causa alta morbidade. Apesar do alto impacto social e econômico gerado pela doença, poucas avaliações econômicas se concentraram na doença. O objetivo do presente estudo foi realizar uma revisão narrativa das avaliações econômicas relacionadas à Chikungunya. Foi realizada uma revisão da literatura científica usando os bancos de dados PubMed e Lilacs. Todos os artigos identificados foram revisados por dois pesquisadores. A pesquisa bibliográfica identificou 24 artigos relacionados ao tópico e, após análise, seis estudos foram incluídos na presente revisão. Esses artigos foram publicados entre 2011 e 2019 e foram realizados nos Estados Unidos, Colômbia, França, México e Brasil. Todos esses estudos relataram a carga econômica e/ou social da Chikungunya para pacientes e/ou serviços de saúde. Os principais itens descritos nos estudos foram os custos diretos relacionados a testes de diagnóstico, consultas, hospitalizações, medicamentos e reabilitação, e os custos indiretos resultantes da perda de produtividade do paciente, anos vividos com uma deficiência e anos de vida ajustados por deficiência perdidos. Os resultados mostram que as avaliações econômicas relacionadas à Chikungunya são recentes e limitadas, e os resultados são difíceis de extrapolar. Nesse contexto, são necessários mais estudos econômicos com foco na Chikungunya.

Palavras-chave: avaliação econômica, Chikungunya, diagnóstico, tratamento.

1 INTRODUCTION

Chikungunya is an arbovirus disease caused by an Alphavirus of the family *Togaviridae* and transmitted to humans by mosquitoes of the genus *Aedes*, mainly *Aedes aegypti* and *Aedes albopictus* species in Africa, Asia and the Americas, where more than 2 million cases have been reported since 2005. Sporadic outbreaks also occur in other regions of the world¹. It is an important, emerging and growing public health problem in tropical countries, where it presents epidemic behavior². No antiviral treatment or vaccine is available for the disease³.

Chikungunya symptoms usually appear between 4 and 7 days after the patient has been bitten by the vector and are characterized by sudden fever accompanied by joint pain¹. Other common manifestations include muscle pain, headache, tiredness and skin rashes. Although Chikungunya is not associated with high mortality, it is associated with high morbidity because a considerable number of patients present symptoms that persist for several months, including rheumatological manifestations⁴.

The clinical presentation of Chikungunya affects the quality of life of patients and causes significant social and economic impacts for the patient and for the health system⁵. Despite the economic burden brought by the disease, there are few economic studies focusing on Chikungunya. Economic evaluations focusing on tropical diseases are particularly important because they affect poor and vulnerable populations living in remote regions of the planet, where resources are scarce. The results of these evaluations can guide the decision-making of

health managers, indicating the need for investment in new technologies or the improvement of existing technologies and services⁶.

The objective of the present study was to perform a narrative review of economic evaluations related to Chikungunya and described in the literature.

2 MATERIALS AND METHODS

A review of the scientific literature was performed using the PubMed and Lilacs databases. The search strategy used in PubMed was "Cost of Illness"[MeSH] AND "Chikungunya Fever"[MeSH], and the search strategy used in Lilacs was Chikungunya and cost. Articles in Portuguese, English and Spanish were read in full by two researchers independently. In the present review, partial and complete economic evaluations related to any topic within Chikungunya were included.

3 RESULTS

The literature search identified 17 PubMed articles related to the topic of interest, and after reading them, five studies were included in the present review. In Lilacs, seven articles were identified, of which one study was included in the present review. These articles were published in 2011, 2015, 2016, 2017, 2018 and 2019 in the following countries: United States (1), Colombia (2), France (1), Mexico (1) and Brazil (1), respectively. The description of the studies is presented below.

In the United States, in an outbreak of Chikungunya that occurred in the US Virgin Islands between 2014 and 2015, Feldstein et al.⁵ estimated direct medical costs, indirect costs and years lived with disability– (YLD) as a result of the disease. The costs per individual and total were estimated taking into account suspected cases that sought care at local health services with fever ≥ 38 °C, severe arthralgia or arthralgia of undefined origin. Of all the suspected cases that could be tested, either by detection of virus RNA or anti-IgM antibodies, 30% were negative. All suspects, regardless of laboratory confirmation, were contacted by telephone and invited to participate in the study. Those who agreed to participate answered a questionnaire providing data on costs incurred as a result of the disease at three times: 1-2, 6 and 12 months after the acute phase.

Indirect costs were estimated based on the period of absenteeism from work due to the infection and were calculated based on a standard 40-hour work week and the average salary for each island. One to two months after the onset of illness, 89% of subjects reported having been absent from work due to illness for an average of 6 days, 33% reported having sought

additional medical care, and 9% reported having been hospitalized due to Chikungunya. Six months after the onset of the disease, 88% reported having missed work for an average of two days due to illness, and after 12 months, 9% reported having missed work for an average of one day. The mean cost of illness-related absenteeism per person at 1 to 2 months, 6 months and 12 months after symptom onset ranged from US\$713 to US\$825, US\$275 to US\$318 and US\$148 to US\$172, respectively, depending on the island of residence. The total estimated cost of absenteeism associated with acute and long-term illness was US\$1.76 million.

The direct medical costs were estimated for the acute and chronic phases using two data sources: charges made by two hospitals where the patients were admitted and the average cost of hospitalizations and outpatient consultations among reported cases. The mean cost of an outpatient visit for a case during the acute phase of the disease was estimated at US\$1,526, and the mean cost of hospitalization was estimated at US\$16,982. In the present study, 1,929 suspected cases were reported, of which 1,850 required outpatient consultations and 79 were hospitalized. Thus, the estimated total cost of outpatient visits and hospitalizations associated with suspected cases during the acute phase was US\$2.9 million, with hospitalizations representing 48% of the total cost. After 12 months, the total cost of additional outpatient visits was estimated at US\$620,400. The total estimated direct cost associated with the Chikungunya outbreak ranged from US\$3,536,000 to US\$3,696,700, depending on the degree of underreporting of the use of health services.

The calculation of years lived with disability was performed using data from the 2013 Global Burden of Disease, and the assumed weights were those determined for osteoarthritis and rheumatoid arthritis. This measure allowed the estimation of the amount of time, capacity and activity lost due to persistent Chikungunya arthralgia. The study showed that the years lived with disability associated with Chikungunya ranged from 599 to 1,322. In the present study, the authors concluded that the disease burden caused by Chikungunya was significant, as up to 1% of the islands' gross domestic product (GDP) was lost due to the disease outbreak.

In Colombia, Cardona-Ospina et al.⁷ estimated disability-adjusted life years (DALYs) lost by patients with Chikungunya in 2014, considering both the disability observed in the acute and chronic phases of the disease. In addition, the authors also estimated the direct and indirect costs related to the clinical management and sequelae caused by the disease in patients treated at three Colombian hospitals.

In the present study, a case was considered clinically confirmed when the patient lived in a municipality where there was previous confirmation of Chikungunya and presented with fever, severe arthralgia or arthritis and sudden-onset skin rash. A laboratory-confirmed case

was defined by viral isolation, RT–PCR, IgM serology or a fourfold increase in IgG in paired samples 15 days apart. During the Chikungunya outbreak studied, a total of 106,592 cases were reported (104,141 clinically confirmed, 3,890 laboratory confirmed and 1,439 clinically and laboratory confirmed), with incidences ranging from 0 to 1,837.3 cases/100,000 population.

The burden of disease/DALYs was calculated according to Murray⁸. In the acute phase of Chikungunya, 1.52 to 1.86 DALYs were lost per 100,000 population, and in the chronic phase, approximately 39 to 43 DALYs were lost per 100,000 population. In total, 40.44 to 45.14 DALYs were lost per 100,000 population.

The costs per individual and total were estimated from the perspective of the payer. The cost estimates included direct costs attributed to hospital care and treatments, such as hospitalization procedures, rehabilitation, medication and diagnostic tests. Indirect costs were calculated based on the sick leave taken by patients during the acute phase of the disease. From an economic point of view, care for one patient costs between US\$ 1,438.74 and US\$ 3,396.57 in the first year of the disease. The chronic phase was responsible for at least 95% of the total estimated costs, with the most expensive item being medication. Overall, the estimated cost for the 2014 outbreak ranged from US\$73.6 million (conservative scenario) to US\$185.5 million (worst-case scenario).

In the present study, the authors reported that the costs of the outbreak observed in the most conservative scenario represented 0.8% of the total national health budget in 2014 and that the estimated 40 DALYs lost was higher than the burden reported in 2005 for traffic accidents and vascular and respiratory diseases. Finally, it is emphasized that disease control is a challenge and that surveillance requires constant improvement to seek effective management of resources.

In another study conducted in Colombia, Alvis-Zakzuk et al.⁹ estimated the economic impact of Chikungunya from a social perspective. The estimate of direct medical costs was retrospective and included data from the clinical records of patients treated at two private hospitals and two public hospitals between August 2014 and February 2015, a period in which the country experienced an outbreak of the disease. In turn, the estimate of indirect costs was prospective, and patients identified with the disease in an emergency room of one of the participating hospitals were invited to participate.

Direct medical costs included expenses for consultations, medications, diagnostic tests, procedures and hospitalization. Indirect costs considered the time lost from work due to the disease, expenses with transportation and purchase of medication. In the present study, 126 patients (67 children and 59 adults) with symptoms of the disease were studied. The mean direct

medical cost per pediatric patient was estimated at US\$ 257.9. In this group, the hospitalization category was responsible for 40% of the cost, followed by diagnostic tests with 36.4% and medications with 13.6%. The mean medical cost per adult patient was estimated at US\$ 66.6. In this group, the hospitalization category was also responsible for the largest share of the cost (38.1%), followed by diagnostic and imaging tests (34.7%) and consultations (14.8%). Most patients required consultation with a general practitioner (80%), and the remainder required consultation with specialist physicians (20%).

To estimate indirect costs, data from 15 patients with a mean age of 39.9 years were included. The mean family size was 6 people, and 90% of the patients reported having a family income of less than one minimum wage. Patients reported that they waited an average of 5 hours to receive the diagnosis of Chikungunya (range: 1-24 h). The mean duration of illness was 12 days (range: 3-30 days). On average, patients had to pay US\$ 0.8 for transportation and US\$ 4.2 for medication. The mean cost of lost productivity was estimated at US\$ 81.3 per adult patient.

The authors highlighted that the costs of Chikungunya sequelae were not estimated, which suggests that the costs related to the disease may be higher than those presented. In addition, the present study was conducted in only four hospitals, which is a limitation. In this context, the authors recommend conducting longitudinal studies with an economic focus to increase the external validity of the results.

In France, Soumahoro et al.¹⁰ estimated the cost of Chikungunya during an outbreak of the disease between 2005 and 2006 on the island of La Réunion. The study was conducted from the perspective of the third-party payer, in which the direct medical costs and indirect costs related to outpatient and inpatient cases were estimated. Direct medical costs of outpatients included consultations, diagnostic tests and medication, while inpatient costs included hospitalizations reported at regional hospitals. The indirect cost was estimated from the loss of productivity related to illness/absenteeism from work.

The number of consultations during the outbreak compared to nonepidemic periods was 470,000, reflecting a 25% increase and an average of two consultations per case. These consultations cost €12.4 million. The cost of diagnostic tests performed was estimated at €570,000, medicines at €5 million and hospitalizations at €8.5 million. During the epidemic, 12,800 patients were required to be absent from work for 112,400 days, resulting in an estimated loss of productivity of €17.4 million. In total, €43.9 million was invested in direct and indirect costs.

The authors highlighted that the cost of managing Chikungunya was high and emphasized that the results of the present study will be useful in evaluating the cost-effectiveness of the monitoring, prevention and control program of arboviruses both on the island of La Réunion and in other regions of the world.

In Mexico, Vázquez-Cruz et al.¹¹ estimated the indirect costs of Chikungunya, represented by disability caused by the disease, in patients treated at the Mexican Institute of Social Security in Guerreiro between January and April 2015. The cost of absenteeism was calculated by multiplying the estimated number of days subsidized by the current minimum salary in the municipality of Acapulco (Mex\$70.10/ /day).

During the study period, workers had to take time off work due to illness, of which 31.5% (38,271) had symptoms compatible with Chikungunya. For these patients, 41,197 days of leave were prescribed, of which 14,941 were subsidized, with an estimated cost of \$2,397,393.40. The authors reported that the costs of sick leave due to Chikungunya increased the costs of the health system in 2015, generating a significant economic impact from the labor point of view.

In Brazil, Teich et al.¹² evaluated public expenditures to combat the vector, direct medical costs related to disease management in the Unified Health System and indirect costs, both in the public and private spheres, associated with arboviruses, including Chikungunya in 2016. Vector control was R\$1.5 billion, and the reported cost for the acquisition of larvicides and insecticides was R\$78.6 million. The direct medical cost of all arboviruses was estimated at R\$374 million. Chikungunya generated the highest number of DALYs (0.036) when compared to the other arboviruses studied. The authors reported that arboviruses had a considerable economic and social impact on the country, and in 2016, 2% of the entire budget planned for health represented expenses for this group of diseases.

Table 1 presents a summary of the studies described above and their main results.

Table 1. Summary of articles found in the scientific literature related to economic evaluations focusing on Chikungunya

Study/country	Population	Main results
Feldstein et al. ⁵ /United States	Suspected Chikungunya subjects who sought assistance in local health services	<ul style="list-style-type: none"> Total direct medical costs: US\$ 3.536.000 to US\$ 3.696.700 Total indirect costs: US\$ 1.76 million Years of life with disability: 427 to 1,407
Cardona-Ospina et al. ⁷ /Colombia	Confirmed cases of Chikungunya registered with the Ministry of Health	<ul style="list-style-type: none"> 40.44 to 45.14 DALYs lost per 100,000 inhabitants Total direct and indirect costs: US\$ 73.6 million (conservative scenario) to US\$ 185.5 million

Alvis-Zakzuk et al. ⁹ /Colombia	Patients diagnosed with Chikungunya	with	• 257.9	<ul style="list-style-type: none"> • Mean direct medical cost per pediatric patient: US\$ • Mean direct medical cost per adult patient: US\$ 66.6 • Average indirect cost per adult: US\$ 81.3
Soumahoro et al. ¹⁰ /France	Patients diagnosed with Chikungunya	with	• million	Medical direct costs and total indirect costs: €43.9
Vázquez-Cruz et al. ¹¹ /Mexico	Patients diagnosed with Chikungunya	with	•	Total indirect cost: \$2,397,393.40
Teich et al. ¹² /Brazil	Patients diagnosed with Chikungunya	with	•	<ul style="list-style-type: none"> • Cost of combating the vector: R\$ 1.5 billion • Total indirect cost: R\$ 123,943.728 • DALYs: 0,036

DALY (Disability Adjusted Life Years): disability-adjusted life years lost

4 DISCUSSION

In 2022, the Pan American Health Organization (PAHO) recorded an increase in the number of cases and deaths due to Chikungunya above that recorded in previous years, and this trend has continued in the first months of 2023. This increase, together with the simultaneous circulation of other arboviruses, diseases such as dengue and Zika, is of great concern. In this context, PAHO recommended the intensification of actions to prepare health services to efficiently offer diagnostic tests and perform rapid clinical management of patients¹³.

The actions recommended by PAHO require strategic planning and financial investment. In this regard, the expenditures reported in the Chikungunya outbreak that occurred in the US Virgin Islands⁵ and Colombia⁹ in 2014 may help pinpoint investment priorities. For example, in these locations, the analysis of direct medical costs indicated that the hospitalization component represented 40% of the total estimated cost, followed by medications. In this regard, investment in hospital infrastructure and medication acquisition should be prioritized in areas where the disease is endemic.

Chikungunya is a disease that causes high morbidity, which is reflected in financial losses for both the patient and the health system. Feldstein et al.⁵ reported that 89% of patients evaluated in the acute phase of the disease, on average, needed to be away from work for six days, and at the time, the estimated total indirect cost was US\$ 1.76 million. In turn, Vázquez-Cruz et al.¹¹ reported that Mexican patients took a total of 41,197 days of leave due to the disease, of which 14,941 were subsidized by the Mexican Social Security Institute, at an estimated cost of US\$ 2,397,393.40.

The magnitude of the financial impact of the disease was reported by Feldstein et al.⁵, who highlighted that the outbreak in the US Virgin Islands caused a loss of up to 1% of GDP due to Chikungunya. In Brazil, Teich et al.¹² reported that approximately 2% of the entire

budget for health in 2016 already represented expenditures on arboviruses. These results demonstrate the burden of the disease in affected places or countries and point to the need for investment in disease prevention. Investing in prevention is an important control measure and has a direct impact on reducing the number of cases of the disease.

The present literature review showed that the economic evaluations available for Chikungunya are scarce and limited, and their results are difficult to extrapolate. Among the limitations, it should be noted that most studies did not evaluate costs related to the chronic phase of the disease, where persistent clinical manifestations can occur and generate a significant financial impact on patients and health systems⁵. Thus, conducting more economic evaluations focusing on Chikungunya is urgent.

AUTHORS' CONTRIBUTIONS

Data collection for this research was carried out by TSMA and ALFL. All authors contributed to data analysis and the writing of this article.

FUNDING

This work was supported by Fundação de Amparo à Pesquisa do Estado de Minas Gerais and Centro Federal de Educação Tecnológica de Minas Gerais. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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