Burden of Illness (BOI) and Paucity of Treatment of the Mosquito-Borne Chikungunya Virus (CHIKV)

Poster
EPH160

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Introduction

Disease background:

- CHIKV is a re-emerging arbovirus transmitted by mosquitos. Infection is characterized by an acute phase commonly presenting with fever, severe polyarthralgia, and myalgia, which can progress to chronic sequelae resulting in productivity losses and a significant reduction in health-related quality-of-life (HRQoL). Clinical manifestations are not specific and are difficult to differentiate from similar arboviruses (1).
- It is important to understand the impact of chikungunya and its health burden to contextualize the value of future preventive measures

Objectives:

- To investigate the available evidence on the disease burden and treatments associated with chikungunya, we conducted a systematic literature review (SLR) of the clinical evidence and a targeted literature review (TLR) on the burden of CHIKV.

Method

Systematic review of clinical evidence

- The SLR of clinical evidence was conducted in the Medline and Embase databases (no date restriction) and congress abstract repositories (2019–2021). The search adhered to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Targeted review on the burden of illness of chikungunya

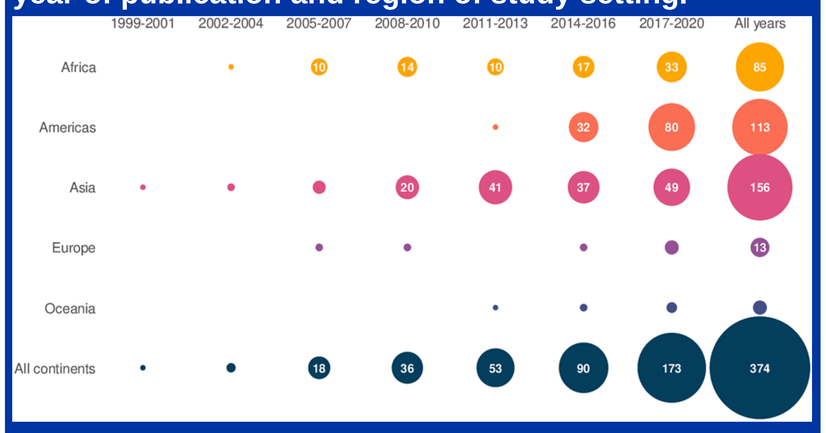
- A database search and additional targeted grey literature search was performed to identify evidence on the burden of chikungunya.

Results

Literature reviews

- Of 13,285 records identified in the searches, 246 studies were included in the SLR. Of these, 17 (6.91%) were interventional studies.
- The TLR included 101 studies.
- In general, studies lacked standardization in data and used different methodologies for CHIKV diagnosis.

Figure 1. Number of references reporting on CHIKV per year of publication and region of study setting.

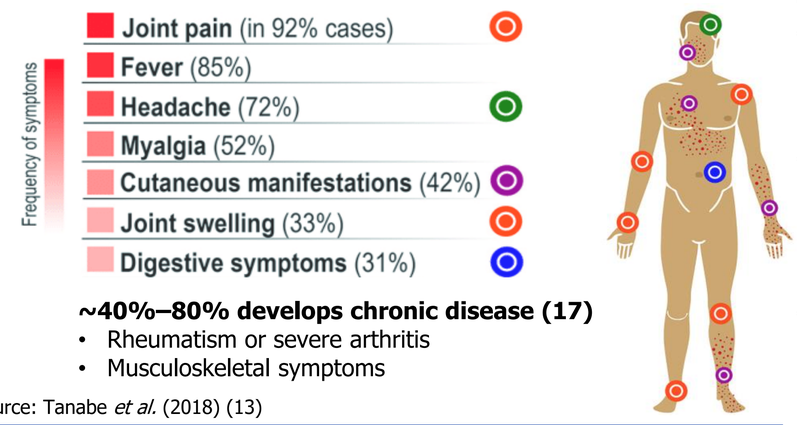


Note: Circles are proportional to the number of studies. Circles with values lower than 10 are not labelled. Three references reported research in more than one region. Source Bettis *et al.* (2)

Epidemiology

- Since first being identified in Tanzania in 1952, CHIKV has spread across the globe. Large-scale outbreaks have been seen in South and Middle America, Africa, and Asia (3).
- There are now three major CHIKV genetic lineages: West African (WA); East–Central–South African (ECSA); and Asian (3). The emergence of a novel ECSA mutation in 2015 showed the influence of travelling in South Asia on CHIKV distribution (4).
- Global warming and the spread of the mosquito vector has led to the rapid geographical expansion of CHIKV distribution and outbreaks globally. There have been at least 5 million cases of CHIKV infection over the last 15 years, signifying the virus as an emerging global health threat (5,6).
- Travellers returning from at-risk areas are sentinels of the rapidly changing epidemiology of CHIKV (1).The global traveller infection rate (TIR) was 1.8 cases / 100,000 travellers between 2012 and 2018. Travel-related CHIKV infections have been identified in 13 European countries which originated in 59 countries with infection (7).
- Figure 1 shows the increasing number of studies reporting on CHIKV in recent years, and the spread of reports to other continents (2).

Figure 2. Symptoms acute phase of CHIKV infection

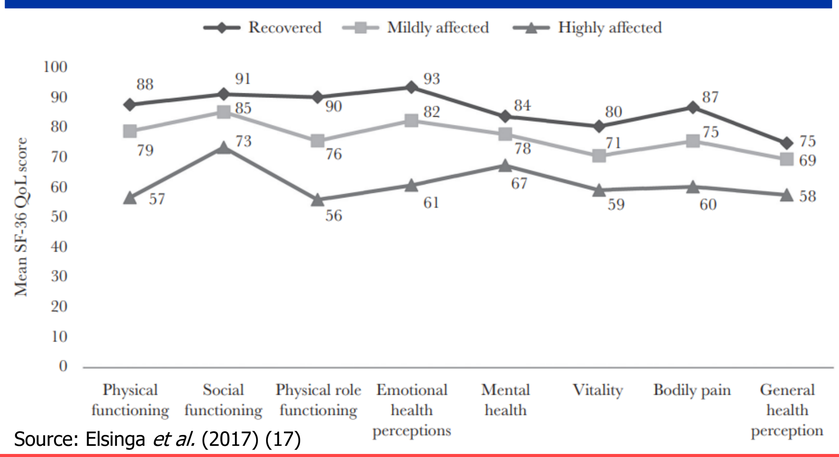


~40%–80% develops chronic disease (17)

- Rheumatism or severe arthritis
- Musculoskeletal symptoms

Source: Tanabe *et al.* (2018) (13)

Figure 3. Influence of chronic chikungunya on HRQoL



Source: Elsinga *et al.* (2017) (17)

Standard of Care

- There is currently no antiviral treatment for chikungunya. Treatment for CHIKV infection aims to palliate acute and chronic symptoms and soften the impact of the BOI (9).
- Table 1 provides an overview of pharmaceutical and non-pharmaceutical interventions in the pipeline identified in the review.
- Assessment of CHIKV disease incidence is often inaccurate due to misdiagnosis as other circulating febrile diseases, the lack of serological confirmation, and asymptomatic manifestations of CHIKV (10).
- Early diagnosis of CHIKV should support effective management, especially in reducing the frequency of misdiagnosis and mistreatment with antibiotics or antimalarial drugs (11).

Table 1. Identified interventions in the pipeline

Pharmaceutical interventions			
VLA1553	LA	Phase 3	Completed
MMR-vaccine	LA	Phase 2	Completed
TSI-GSD-218	LA	Phase 2	Terminated
V184	LA / MV	Phase 2	Completed
MV-CHIK	MV	Phase 2	Completed
PXVX0317	VLP-based	Phase 3	Recruiting
VRC-CHKVLP059-00-VP	VLP-based	Phase 2	Completed
BBV87	Inactivated	Phase 1	Completed
ChAdOx1 Chik	Chimpanzee AV vaccine	Phase 1	Completed
VAL-181388	mRNA-based	Phase 1	Completed
Ribavirin	Nucleoside analogue	NA	NA
(Hydroxy) Chloroquine	Antimalarial / amebicide	Phase 3	Terminated
CHIKIVIG-01	Immunoglobulins	Phase 1/2	Unknown
mRNA-1944	IgG mAb	Phase 1	Completed
SAR440894	IgG1 mAb	Phase 1	Recruiting
Methotrexate	Folate antagonist	Phase 3	Completed
NSAIDs	Anti inflammatory	NA	Completed
Steroids	Anti inflammatory	NA	Completed
Non-pharmaceutical interventions			
Auriculotherapy	Acupuncture	NA	Completed
Resistance exercise	Physical	Phase 1	Active
Yoga for chronic CHIK	Physical	Phase 3	Terminated
tDCS	Physical	NA	Completed
Wolbachia infection	Mosquito control	Phase 2	Recruiting
TIRS	Mosquito control	Phase 3	Active
Transfluthrin	Mosquito control	NA	Completed

Key: AV, adenoviral-vectored; LA, live-attenuated; mAb, monoclonal antibody; MV, measles-vectored; NA, not applicable; tDCS, transcranial direct current stimulation; TIRS, targeted indoor residual spraying; VLP, virus-like particle. Source: ClinicalTrials.gov (8)

Burden of Disease

- Although fever, rash, and arthralgia associated with acute infection are usually self-limiting and last only 1 to 2 weeks, CHIKV infection can manifest typically and atypically, and atypical manifestations may result in death or necessitate aggressive medical interventions (12).
- Morbidity rates of 30%−70% are typical, and seroprevalence rates can be as high as 40% during outbreaks. The rates of symptomatic infections are high (Figure 2), and most symptomatic patients experience disability for weeks to months as a result of decreased dexterity, loss of mobility, and delayed reaction (14).
- ~40%−80% of patients develop chronic disease that can last from a few months to several years after infection (Figure 2) (15). The most reported risk factor for development of chronic chikungunya is the presence of comorbidities, such as hypertension, diabetes, and cardiovascular diseases (16).
- People with chikungunya often report long-term pain and limitation of mobility. This leads to physical and mental impairment as people experience limitations in performing their normal daily life activities, which also reduces emotional wellbeing (9). It also has a substantial health economic impact because it causes loss of productivity and incapacitation for work. With a higher duration of illness from the acute to chronic phase, the workdays and workhours lost increase (17)
- A cross-sectional survey of adults with confirmed CHIKV infection measured the influence of chronic chikungunya on HRQoL using the SF-35 questionnaire (Figure 3). The highly affected population showed worst scores on all HRQoL dimensions, followed by the mildly affected and the recovered populations (P ≤ 0.001) (18).
- The study by Watson *et al.* studied the impact of chikungunya on HRQoL and found an EQ-VAS Global Health Perception score of 68 (± 62) out of 100, for patients with chronic or long-term sequelae (19).

Conclusion

Clinical evidence

- The low number of interventional studies (i.e., 17) displays the paucity of available interventions for the treatment of CHIKV infection.
- The considerable number of identified studies in both reviews demonstrates a growing awareness of CHIKV.
- Studies used different and sometimes mediocre methodologies for chikungunya diagnosis, resulting in frequent misdiagnosis and misclassifications of CHIKV infection.
- Standardization of definitions and data collection would improve the quality of research.

Burden of Disease

- A combination of travel, CHIKV mutations, global warming, and the spread of the mosquito vector are all contributing to the rapid geographical expansion of CHIKV outbreaks and distribution.
- The spread of new epidemic strains has the potential to induce new subsets of clinical manifestations.
- The tools available to prevent and treat CHIKV infection are limited; vector control measures are suboptimal and challenging, and the only treatment that currently exists for chikungunya is symptomatic.
- No antiviral treatment exists for chikungunya. Preventive measures are needed to keep the disease, and the chronic polyarthralgia that it can cause, in check.
- CHIKV infection is associated with high morbidity rates, and the acute and sometimes long-term symptoms caused have a detrimental effect on HRQoL.

Due to the unpredictable nature of CHIKV spread and lack of treatment options, there is an immediate need for effective preventive measures such as vaccines

CHIKV is a serious threat to global public health and causes significant disease burden worldwide

Accurate diagnosis of CHIKV is important as misdiagnosis leads to underreporting and incorrect treatment and may underestimate the true burden of chikungunya

A prompt diagnosis and careful surveillance for the role of travellers in autochthonous disease transmission is required to keep track of the global spread of CHIKV

Rapid and appropriate diagnostic tools are needed to improve patient management and disease control measures

Increasing the awareness and knowledge of CHIKV could improve the effective usage of prevention strategies for CHIKV transmission and infection

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