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Review Paper

Chikungunya virus infection prevalence in Africa: a contemporaneous systematic review and meta-analysis

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ABSTRACT

Objectives: The (re)emergence of chikungunya virus (CHIKV) in Africa requires better knowledge on the epidemiology of CHIKV infection in the continent for efficient public health strategies. We aimed to describe the epidemiology of CHIKV infection in Africa, a neglected tropical disease (NTD).

Study design: This was a systematic review with meta-analysis of studies reporting CHIKV infection prevalence. We searched Embase, PubMed, Africa Journal Online and Global Index Medicus to identify observational studies published from January 2000 to September 2017.

Methods: We used a random-effect model to pool the prevalence of CHIKV infections reported with their 95% confidence interval (CI). Heterogeneity was assessed via the Chi-squared test on Cochran's Q statistic. Review registration is in PROSPERO CRD42017080395.

Results: A total of 39 studies (37,881 participants; 18 countries) were included. No study was reported from Southern Africa. Thirty-two (82.0%), seven (18.0%) and no studies had low, moderate and high risk of bias, respectively. Outside outbreak periods, the pooled immunoglobulin M (IgM) and immunoglobulin G (IgG) seroprevalence was 9.7% (95% CI 3.0–19.6; 16 studies) and 16.4% (95% CI 9.1–25.2; 23 studies), respectively. The IgM seroprevalence was lower in Northern Africa, and there was no difference for IgG prevalence across regions in Africa. The IgM and IgG seroprevalences were not different between acute and

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non-acute febrile participants. The seroprevalence was not associated with GPS coordinates (latitude, longitude and altitude).
Conclusions: Although considered a NTD, we find high prevalence of CHIKV infection in Africa. As such, chikungunya fever should deserve more attention from healthcare providers, researchers, policymakers and stakeholders from many sectors.

Introduction

Chikungunya fever, an arboviral infection caused by chikungunya virus (CHIKV), is a mosquito-transmitted *Alphavirus* (family Togaviridae) disease, with *Aedes aegypti* and *Aedes albopictus* being the main urban vectors.[1,2] This virus was first isolated in Tanzania in 1953 during a large outbreak.[3] Its clinical presentation includes non-specific signs and symptoms such as acute fever, headache, nausea, vomiting, myalgia, arthralgia and rash.[1,2] One can note that symptomatic CHIKV infection shares some clinical signs with dengue, malaria and Zika virus diseases, which can lead to misdiagnosis in areas where these diseases coexist. To date, there is no specific treatment or effective vaccine for this neglected tropical disease (NTD). The treatment is essentially symptomatic. The location of mosquito larval sites close to homes is a serious risk factor for chikungunya fever. The disease is found in Africa and Asia. A major outbreak, however, began in 2013, eventually affecting most tropical and subtropical regions of the Americas.[4] In Africa, CHIKV also circulates in an enzootic cycle involving forest dwelling mosquitoes and non-human primates (NHP).[1]

Vector-borne diseases account for more than 17% of all infectious diseases, causing more than 700,000 deaths annually.[5] Since 1953, there is rapid increasing of number of countries reporting CHIKV outbreaks (over 60).[6] The World Health Organization (WHO) encourages countries to build and maintain the capacity to detect and confirm arboviral disease cases, to treat patients and to implement social communication strategies to reduce the presence of mosquito vectors.[4] To curb the burden of disease related to CHIKV infection, it is necessary to have accurate data for efficient and effectiveness strategies as recommended by the WHO. On the basis of published and unpublished data, a systematic review without meta-analysis carried out by Humphrey and colleagues showed that anti-CHIKV antibodies or reports of autochthonous transmission in acute febrile populations were identified from 10 of 23 countries in the Middle East and North Africa region, with median seroprevalence of 1.0% (range 0–43%) and 9.8% (range 0–30%), respectively.[7] Although half of countries with identified CHIKV infection are located in Africa, to the best of our knowledge, there are no data on the epidemiology of CHIKV infection in Africa. With the recent introduction of the vector *A. albopictus* into Africa, which can increase the dissemination of the virus, better knowledge on the epidemiology of CHIKV infection in the continent is major public health need. Therefore, we conducted the present systematic review with meta-analysis to determine the prevalence of CHIKV infection in Africa, including seroprevalence based on immunoglobulin M (IgM) and immunoglobulin G (IgG), and prevalence based on the presence of CHIKV ribonucleic acid (RNA). The aim of this work was to provide accurate data to guide health policymakers and to identify potential information gaps that could orientate future research.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines served as the template for reporting the present review (Supplementary Table 1). This review is registered in the PROSPERO International Prospective Register of Systematic Reviews, registration number CRD42017080395.

Eligibility criteria

We considered observational studies (cross-sectional, case–control and cohort). In the case of duplicate reports, the most comprehensive/complete and up-to-date version was included. We considered studies conducted during outbreak periods and out of outbreak periods. Case series or studies in which CHIKV infections were imported were excluded. Our population of interest was people living in Africa. The primary outcome of our study was the prevalence of CHIKV infection in Africa. To be included, the search for CHIKV aetiology had to be conducted systematically or by sampling of the population residing in Africa and CHIKV detection by polymerase chain reaction technique, enzyme-linked immunosorbent assay or plate reduction neutralization test on any samples. Sample analysis should detect CHIKV RNA, IgM or IgG. Studies lacking or with no extractable primary data, and/or explicit methods description, were excluded. In the case of missing data, we contacted authors of the article. When an article was not published in French, English, or Spanish, we used Google Translate.

Search strategy

We performed a comprehensive and exhaustive search of MEDLINE through PubMed, Excerpta Medica Database, Africa Journals Online and Global Index Medicus to identify all relevant articles published on CHIKV in Africa from January 1, 2000 until September 18, 2017 regardless of language of publication. We limited to 2000 to have contemporaneous epidemiology and therefore better guide health policymakers. Both text words and medical subject heading terms were used. The following terms and their variants were used for CHIKV:

'CHIKV', 'chikungunya virus' and 'chikungunya'. Individual names of African countries and subregions were also used as additional key search terms for more abstracts on the subject. African country names were introduced both in English and languages relevant to each country. Titles and abstracts of all eligible articles were reviewed and full texts of articles were accessed. The search strategy conducted in PubMed, shown in Supplementary Table 2, was adapted to fit other databases. The search in electronic databases was conducted on September 18, 2017. Reference lists of eligible articles and other relevant review articles were scanned to identify other eligible papers.

Study selection

Two investigators (F.B.N.S and S.K) independently screened records for eligibility based on titles and abstracts. Full texts of articles deemed potentially eligible were retrieved. Further, these investigators independently assessed the full text of each study for eligibility and consensually retained studies to be included. Disagreements were solved through a discussion or by an arbitration of a third investigator (J.J.B).

Data extraction and management

Data were extracted using a preconceived and tested data abstraction form. In the case of missing data, authors were directly contacted. Two investigators (F.B.N.S and S.K) independently extracted data including name of the first author, publication year, study design, setting, sampling method, period of inclusion of participants, timing of data analysis, site of recruitment location (country, city, latitude and longitude), clinical presentation, number of participants screened, number of patients infected with CHIKV, diagnostic techniques used, proportion of male participants and whether study was conducted during an acute febrile illness outbreak period. We assigned a United Nations Statistics Division (UNSD) African region (Central, Eastern, Northern, Southern and Western) to each study regarding the country of recruitment.[8] Using the Google Global Positioning System, we assigned latitude and longitude based on the city and country of recruitment.[9] Disagreements were solved by the arbitration of a third investigator (J.J.B).

Two investigators (J.J.B and E.A.W) evaluated risk of bias in included studies using an adapted version of the tool designed by Hoy and colleagues.[10] The total score was determined on a scale of 0–9 as follows: 7–9, 'low risk of bias'; 4–6, 'moderate risk' and 0–3, 'high risk'. Disagreements were solved through discussion and consensus.

Data synthesis and analysis

Data were analysed using the '*meta*' packages of the statistical software R (version 3.3.3; The R Foundation for Statistical Computing, Vienna, Austria). Unadjusted prevalence of CHIKV infection was recalculated based on crude numerators and denominators provided by individual studies. To minimize the effect of studies with extremely small or extremely large prevalence estimates, the variance of the study-specific prevalence was stabilized with the Freeman–Tukey double arcsine transformation before pooling the data within a random-effect meta-analysis model.[11] Symmetry of the funnel plot and Egger's test served to assess the presence of publication bias.[12] A P-value < 0.10 on the Egger test was considered indicative of statistically significant publication bias. We also conducted a trim-and-fill adjusted analysis to take into account asymmetry in the published articles, recomputing the prevalence at each iteration until the funnel plot was symmetrical about the (new) prevalence.[13]

Heterogeneity was evaluated by the Chi-squared test on Cochrane's Q statistic,[14] which was quantified by H and I^2 values. The I^2 statistic estimates the percentage of total variation across studies because of true between-study differences rather than chance. In general, I^2 values greater than 60%–70% indicate the presence of substantial heterogeneity.[15] Univariable and multivariable metaregressions were used to test for an effect of study and participants' characteristics. For multivariable metaregression analysis, we planned to use stepwise manual backward selection if P value > 0.25. For categorical variables, the global P value was considered for the inclusion in multivariable models. A P-value < 0.05 was considered statistically significant. Following crude overall prevalence, a sensitivity analysis was conducted considering only studies with a low risk of bias. Subgroup analyses were performed for UNSD region of Africa and clinical presentation (acute febrile versus non-febrile participants).

Results

The review process

We identified 1573 records; after elimination of duplicates, 1091 remained. After screening titles and abstracts, we retained and assessed 65 full-text articles for eligibility. Finally, 39 full texts were included (Fig. 1).[16–54] The inter-rater agreement for study selection was high ($\kappa = 0.89$). Nineteen, 25 and 12 studies identified CHIKV infection using IgM;[16,17,19,20,22,24,26,27,29,30,33,34,43–50,53]; IgG;[17,18,21,22,24,26–32,35,36,38,39,42,43,45,47–49,52,53]; and CHIKV RNA,[23,25,34,37,39–41,45,46,50,51,54], respectively.

Characteristics of included studies

Table 1 summarizes characteristics of included studies. Thirty-two (82.0%), seven (18.0%) and no studies had low, moderate and high risk of bias, respectively. Eight studies were conducted during an outbreak period,[23,27,37,39,41,44,46,51] and the others were not associated with an outbreak.[16–22,24–26,28–36,38,40,42,43,45,47–50,52–54]. Most studies were prospective, used consecutive samples, and were conducted in the eastern region of Africa. Based on UNSD of Africa, no study was from the southern region of Africa. Studies were from 18 countries; Central Africa (Cameroon [n = 4],[27,30,35,45] Gabon [n = 4],[23,31,37,41] Democratic Republic of Congo,[44] Republic of Congo[39]), Eastern Africa (Comoros,[26] Djibouti,[18] Kenya [n = 8],[36,38,40,42,48,52–54] Madagascar [n = 2],[46,47] Mayotte,[49] Mozambique,[32] La Reunion,[51] Tanzania [n = 3][24,25,34]), Northern Africa (Sudan [n = 3][16,28,29]) and Western Africa (Benin,[22] Guinea,[33] Nigeria [n = 4],[17,20,21,43] Senegal,[50] Sierra Leone[19])

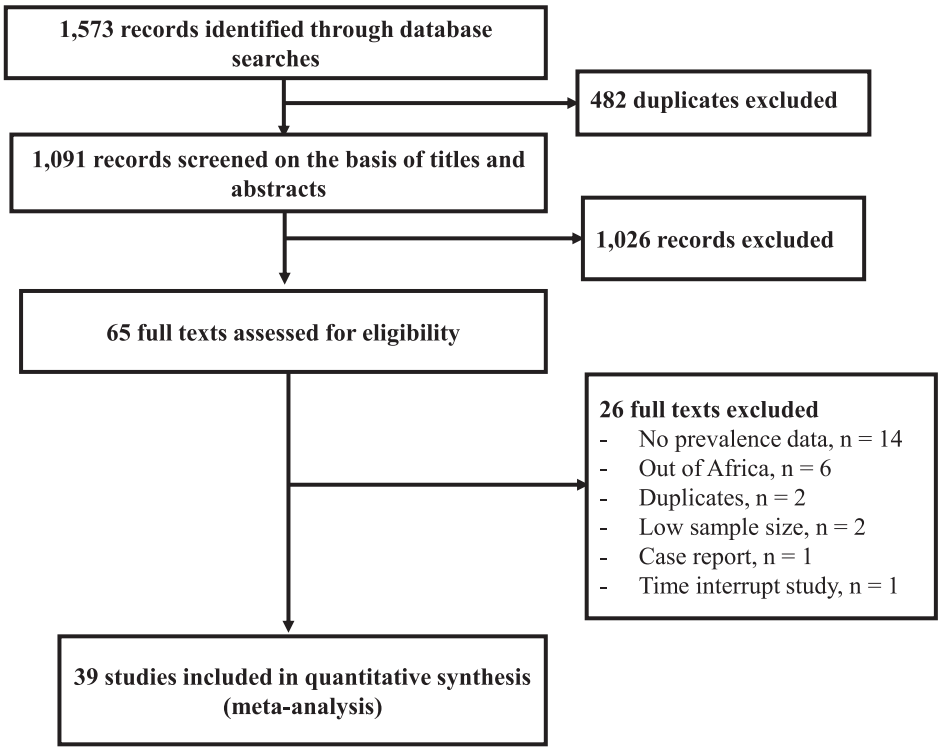

Fig. 1 – Study selection.

Individual characteristics of included studies are presented in Supplementary Table 3.

Prevalence of chikungunya virus infection in Africa

A total of 37,881 individuals were included in meta-analyses. Outside of recognized outbreaks, the crude overall IgM seroprevalence was 9.7% (95% confidence interval [CI] 3.0–19.6; range: 0.1–39.0) (Fig. 2), 16.4% (95% CI 9.1–25.2; range: 0.3–71.5) for IgG seroprevalence (Fig. 3) and 2.8% (95% CI 0.1–8.1; range: 0.1–8.4) for viral RNA prevalence (Fig. 4). These crude prevalences did not differ compared with the sensitive prevalence that included only low risk of bias studies or compared with trim-and-fill adjusted analysis (Table 2). The funnel plot for IgM seroprevalence and viral RNA prevalence but not for IgG seroprevalence suggested publication bias (Supplementary Figures 1-3, respectively). These findings were confirmed by the Egger test (Table 2). Substantial heterogeneity was present for overall and within all subgroups except for IgG seroprevalence during the outbreak (Table 2, Supplementary Table 4).

In subgroup analyses (Table 3), the IgM seroprevalence was lower in Northern Africa. The viral RNA prevalence was lower in Western Africa than Central and Eastern Africa. The IgG seroprevalence was not different among regions for exposure to CHIKV. There was no difference between people with and without fever for seroprevalence. In metaregression analyses (Supplementary Table 5), studies' and participants' characteristics were not associated with IgM seroprevalence. The IgG seroprevalence decreased with year of publication only (Supplementary Table 6).

During outbreaks, the overall IgM and IgG seroprevalence and CHIKV RNA prevalence were 36.7% (95% CI 9.8–68.9), 35.1% (95% CI 31.4–39.0) and 28.5% (95% CI 15.4–43.9), respectively (Table 2).

Discussion

Accurate data on the prevalence of CHIKV infection in Africa are needed to formulate effective disease control policies. This systematic review and meta-analysis of 39 studies involving 37,881 individuals yielded to a pooled prevalence of CHIKV infection of 9.7%, 16.4% and 2.8% for IgM, IgG and CHIKV RNA, respectively. During outbreaks, the prevalence was not surprisingly high. The IgM seroprevalence was lower in Northern Africa. There was no difference for IgG seroprevalence across UNSD regions. The prevalences were not different between acute febrile and non-febrile individuals.

The seroprevalence found in this review was in the range of that found in one systematic review conducted for urban areas in the Middle East and North Africa (0–43%) with a median of 1% in studies from 1970 to 2015.[7] However, it is difficult to make a comparison because the latter study did not include a meta-analysis and not differentiated different types of prevalence. Our review focused on all UNSD African countries reporting data from 18 countries of the continent and also reported CHIKV viral RNA prevalence. The prevalence from other parts of the world varies widely (4–75%)[55–61] as in our study. This variability may be due to heterogeneity among study populations (clinical presentation), environments favouring nearby enzootic circulation or the abundance of

Table 1 – Characteristics of included studies.

Characteristics	N = 39
Year of publication (range)	2004–2017
Period of inclusion of participants (range)	1999–2016
Age range, years	1–90
% Male	0–75.1
Timing of data collection	
Prospective	32 (82.1)
Retrospective	7 (17.9)
Area	
Rural	5 (12.8)
Urban	4 (10.3)
Rural and Urban	1 (2.6)
Undefined	29 (74.4)
United Nations Africa subregions	
Eastern	19 (48.7)
Central	10 (25.6)
Western	7 (18.0)
Northern	3 (7.7)
Southern	0 (0.0)
Sampling	
Consecutive	34 (87.1)
Random	3 (7.7)
Multistage	1 (2.6)
Stratified	1 (2.6)
Diagnostic with IgM	19 (48.7)
Diagnostic with IgG	25 (64.1)
Diagnostic based on viral RNA	12 (30.8)
Presentation	
Acute febrile illness	12 (37.8)
General population	27 (69.2)
Outbreak period	
Yes	8 (20.5)
No	31 (79.5)
Median Latitude (range)	−0.02 (−21.11; 14.50)
Median Longitude (range)	30.218 (−14.45; 55.54)

Data are n (%) or median (range).
IgM: immunoglobulin M; IgG: immunoglobulin G; RNA: ribonucleic acid.

urban vectors that mediate human-to-human transmission (*A. aegypti* and *A. albopictus*), vector infection rates and study methodological characteristics. In addition to the seroprevalence, our review reported and differentiated prevalence based on a more sensitive and specific method, the detection of viral RNA. The prevalence of viral RNA was clearly lower than the seroprevalence. IgM and IgG antibodies are highly sensitive, but specificity can be low because of cross reactivity with other arboviruses such as Semliki Forest and o'nyong–nyong viruses.[62,63] Therefore, some positive serologic analyses may not be attributable to CHIKV infection. The high IgG prevalence may also be explained by the fact that this antibody class appears in sera approximately 15 days after infection and remains for many years up to decades compared with the presence of CHIKV RNA that reflects the viremia during the acute phase of only up to seven days after infection.[64]

In subgroup analyses, we found that the IgM seroprevalence was lower in Northern Africa. The CHIKV RNA prevalence was lower in Western Africa than in Central and Eastern Africa. The IgG seroprevalence did not differ among regions. These findings should be interpreted with caution because there was a small number of studies in certain subgroups, and certain geographical regions were not represented (especially Southern Africa in all subgroup analyses). Therefore, future findings could significantly modify these differences. In the multivariable metaregression analyses for IgM and IgG seroprevalence, there was no difference among regions. In addition, we did not find any association of CHIKV seroprevalence with (absolute) latitude, longitude or altitude, suggesting that geographic position does not influence the distribution of CHIKV throughout the African continent. Although the distribution of African vectors is nearly ubiquitous, the overall density of vectors decreases with the distance from the equator; and it is less present in the northern part of the continent.[65] This may explain why we found lower IgM seroprevalence in the northern region. Although the distribution of the CHIKV vectors in Africa is nearly ubiquitous, there are other local geographical factors (weather, humidity and enzootic interaction) that are different within subregions and countries which may also influence the density of CHIKV vectors.

Data describing the distribution of the prevalence of CHIKV infection among vectors in the continent are lacking and may better explain the distribution of CHIKV infection in humans across African regions. Human infection by CHIKV in Africa is known to occur through two mechanisms: direct exposure to the enzootic cycle (NHP-mosquito-human) via several sylvatic vectors,[66,67] and the urban cycle (human-mosquito-human), historically via *A. aegypti* and recently via *A. albopictus*. There is evidence of the former mechanism from few locations, mainly South Africa,[67,68] Cameroon[69] and eastern Senegal[66] where enzootic amplification occurs periodically, presumably when NHP herd immunity falls to a level permissive for efficient circulation. Urban transmission has also been documented in only a few locations including the first described outbreak from 1952 to 1953 in Tanzania,[70] more recently in Senegal[71] and Central Africa via *A. aegypti* and recently *A. albopictus*.[69,72] Better surveillance to identify locations of enzootic circulation and potential urban transmission is needed to more fully understand human exposure to CHIKV in Africa.

We found that there was no difference between acute and non-acute febrile populations in seroprevalence. The fever due to CHIKV usually appears between 4 and 7 days after infection and lasts less than one week. IgG appears approximately 15 days after infection and typically remains for years. IgM typically appears approximately 5 days after infection and remains up to several months. Logically, this demonstrates that there may be a long period of time during which one can have detectable antibodies following the cessation of clinical signs and symptoms including fever. Therefore, if an active surveillance focus for detecting CHIKV infection cases is based on clinical signs and symptoms including febrile illness, some cases with subclinical infection can be missed.

This review depicted a high prevalence of CHIKV infection in Africa, especially during outbreak periods. Chikungunya has been identified in nearly 40 countries including half of them from Africa.[73] To date, there is no specific treatment for the disease and no effective vaccine to prevent it. In areas of urban CHIKV transmission by *A. aegypti* and *A. albopictus*,

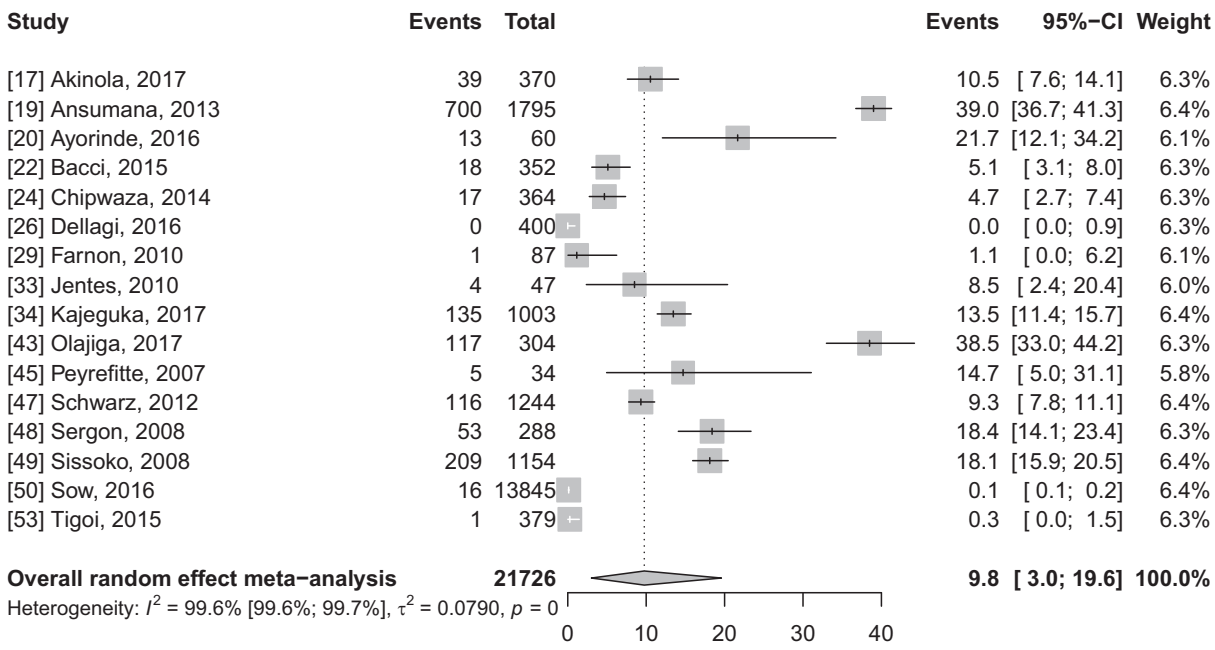

Fig. 2 – Meta-analysis prevalence of Chikungunya immunoglobulins M infection among adults living in Africa.

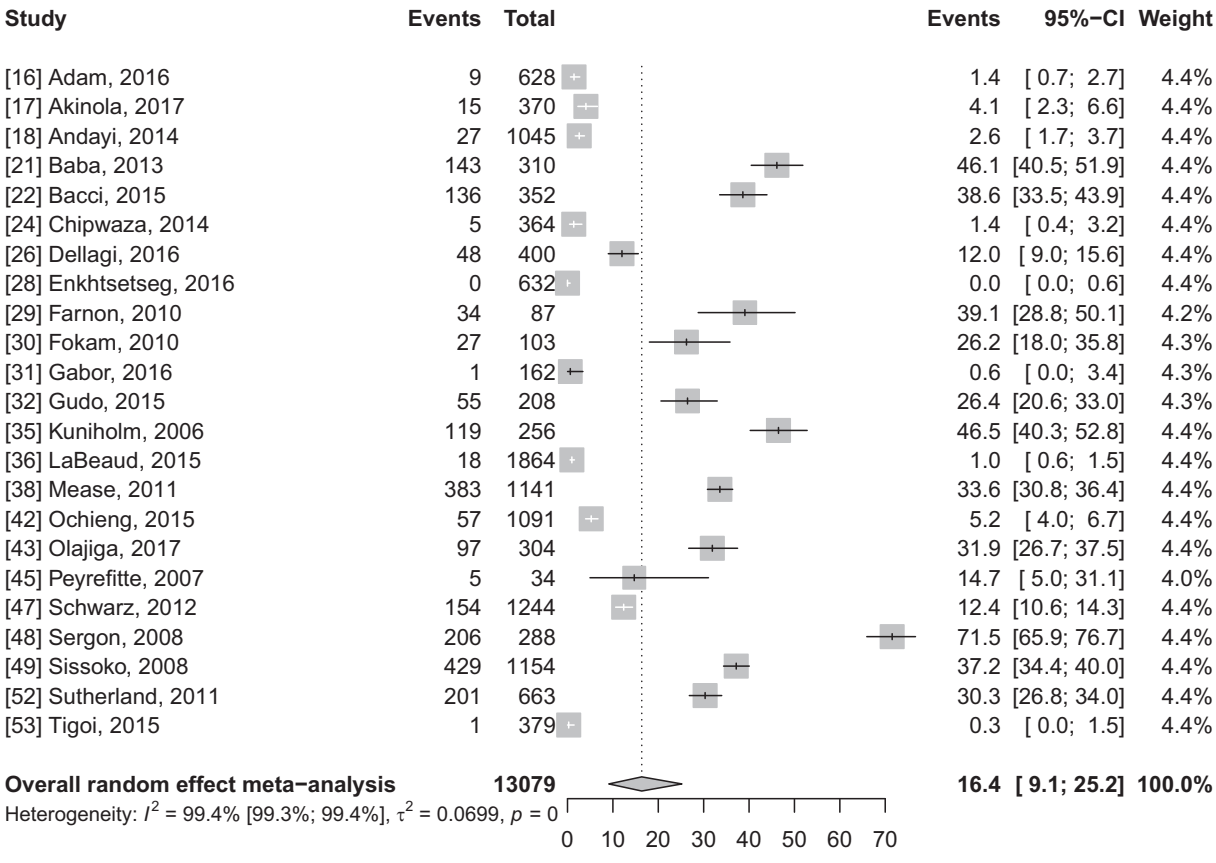

Fig. 3 – Meta-analysis prevalence of Chikungunya immunoglobulins G infection among adults living in Africa.

vector prevention and control can be combined with dengue control efforts.[74] WHO strategies for curbing the CHIKV-related burden of disease include integrated vector management (IVM) to control mosquito vectors. IVM aims at improving efficacy, cost effectiveness, ecological soundness and sustainability by safe use of insecticides; individual and household protection and eviction of confined larval habitats, both man-made and natural.[74]

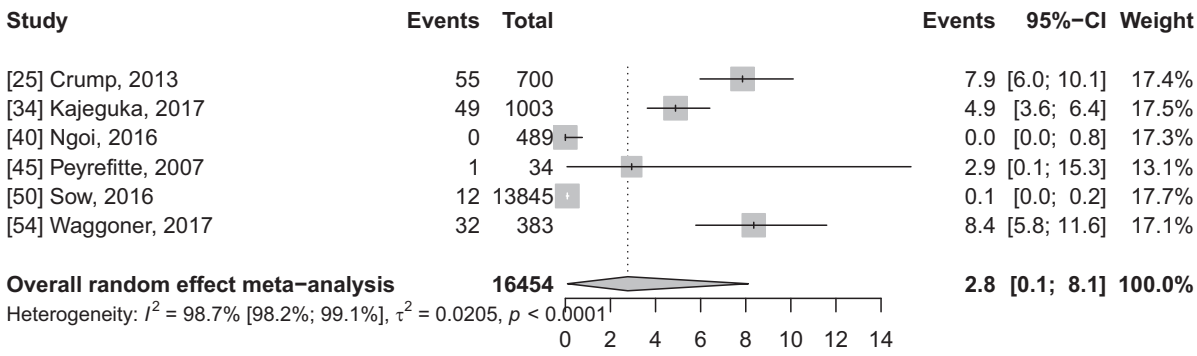

Fig. 4 – Meta-analysis prevalence of Chikungunya ribonucleic acid infection among adults living in Africa.

Table 2 – Summary statistics of chikungunya viral infection prevalence in Africa.

Chikungunya biomarkers	Number of studies	Number of participants	Prevalence (95% CI)	I^2 (95% CI)	H (95% CI)	P, heterogeneity	P, Egger test
Overall							
IgM seroprevalence	16	21,726	9.7 (3.0–19.6)	99.6 (99.6–99.7)	16.3 (15.3–17.4)	<0.0001	0.046
Trim-and-fill adjusted analysis	24	NA	9.8 (0.0–23.0)	99.8 (99.7–99.8)	20.2 (19.3–21.2)	<0.0001	0.711
IgG seroprevalence	23	13,079	16.4 (9.1–25.2)	99.4 (99.3–99.4)	12.5 (11.7–13.3)	<0.0001	0.220
Viral RNA prevalence	6	16,464	2.8 (0.1–8.1)	98.7 (98.2–99.1)	8.8 (7.4–10.5)	<0.0001	0.097
Trim-and-fill adjusted analysis	9	NA	4.5 (0.0–15.5)	99.1 (98.8–99.3)	10.5 (9.3–11.9)	<0.0001	0.943
Low risk of bias studies							
IgM seroprevalence	16	21,726	9.7 (3.0–19.6)	99.6 (99.6–99.7)	16.3 (15.3–17.4)	<0.0001	0.046
IgG seroprevalence	16	7926	21.5 (12.4–32.2)	99.1 (99.0–99.3)	10.7 (9.8–11.7)	<0.0001	0.980
Viral RNA prevalence	6	16,464	2.8 (0.1–8.1)	98.7 (98.2–99.1)	8.8 (7.4–10.5)	<0.0001	0.097
Outbreak							
IgM seroprevalence	3	236	36.7 (9.8–68.9)	96.0 (91.5–98.1)	5.0 (3.4–7.3)	<0.0001	0.413
IgG seroprevalence	2	622	35.1 (31.4–39.0)	0.0	1.0	0.362	NA
Viral RNA prevalence	6	6229	28.5 (15.4–43.9)	99.0 (98.6–99.3)	10.0 (8.6–11.7)	<0.0001	0.550

CI, confidence interval; IgM: immunoglobulin M; IgG: immunoglobulin G; NA, not applicable; RNA: ribonucleic acid.

Results from this study should be interpreted with caution in the context of its limitations. First, we found substantial heterogeneity in the estimation of the prevalence of CHIKV infection. Although we identified some sources of heterogeneity, there may still be others not investigated including distribution of CHIKV infection in vectors, different genotypes of CHIKV and ecosystem. However, we were unable to assess these factors because they were not reported in primary included studies. Climate change is likely to continue to facilitate the spread of mosquitoes capable of transmitting CHIKV.[23] Second, countries and UNSD African regions were not uniformly represented, partly owing to difficult retrieval of African medical literature, especially for older articles and those published in local journals. In addition, there was no identified study from Southern Africa. This can limit the generalizability of findings to the entire continent. Third, we found publication bias in some analyses, suggesting that published/retrieved studies could not alter the findings of these studies. However, the findings from trim-and-fill adjusted analysis were not different to that of crude analysis. Fourth, the review is also limited by scarcity of data in the continent highlighting the need for research. Despite these possible limitations, this study is, to the best of our knowledge, the first systematic review and meta-analysis on prevalence of CHIKV infection in Africa. Strengths also include a comprehensive search strategy and involvement of two independent investigators in all stages of the review process. Almost 80% of the studies were assessed as having low risk of bias in their methodological quality, suggesting that we can be confident in the quality of our findings. In addition, the sensitivity analysis including only studies with low risk yielded a very close prevalence to that estimated in the crude analysis. A multivariable metaregression analysis was conducted helping to control potential confounders of source of variation of prevalence.

Although considered an NTD, we found a high prevalence of CHIKV infection in Africa. As such, chikungunya fever should deserve more attention from healthcare providers, researchers, policymakers and stakeholders from many sectors. Because there is no specific treatment and no effective vaccine, prevention should be based on vector control.

Author statements

Ethical approval

Not applicable. The current review is based on published data and as such, ethical approval is not a requirement.

Table 3 – Subgroup analysis of chikungunya viral infection out of outbreak prevalence in Africa.

Groups	Number of studies	Number of participants	Prevalence (95% CI)	I^2 (95% CI)	H (95% CI)	P, heterogeneity	P, Egger test	P, difference subgroups
United Nations African subregions analyses								
IgM seroprevalence								
Central	1	34	14.7 (4.4–28.9)	NA	NA	NA	NA	0.0235
Eastern	7	4832	7.0 (2.4–13.7)	98.3 (97.6–98.8)	7.6 (6.4–9.1)	<0.0001	0.183	
Northern	1	87	1.1 (0.0–4.9)	NA	NA	NA	NA	
Western	7	16,733	14.3 (0.74–39.5)	99.8 (99.8–99.8)	22.7 (21.0–24.7)	<0.0001	0.173	
Southern	0	NA	NA	NA	NA	NA	NA	
IgG seroprevalence								
Central	4	555	18.4 (0.7–50.0)	98.3 (97.2–98.9)	7.6 (6.0–9.7)	<0.0001	0.700	0.4170
Eastern	12	9841	15.1 (6.2–26.8)	99.5 (99.4–99.6)	14.5 (13.3–15.7)	<0.0001	0.410	
Northern	3	1347	6.7 (0.0–23.3)	98.5 (97.4–99.1)	8.2 (6.2–10.8)	<0.0001	0.203	
Western	4	1336	27.8 (9.3–51.4)	98.8 (98.1–99.2)	9.1 (7.3–11.3)	<0.0001	0.304	
Southern	0	NA	NA	NA	NA	NA	NA	
Viral RNA prevalence								
Central	1	34	2.9 (0.0–12.2)	NA	NA	NA	NA	0.0011
Eastern	4	2575	4.1 (0.8–9.8)	96.9 (94.4–98.3)	5.7 (4.2–7.6)	<0.0001	0.808	
Western	1	13,845	0.09 (0.04–0.14)	NA	NA	NA	NA	
Northern	0	NA	NA	NA	NA	NA	NA	
Southern	0	NA	NA	NA	NA	NA	NA	
Clinical presentation sub-group analyses								
IgM seroprevalence								
Febrile	12	18,953	9.5 (1.6–22.6)	99.7 (99.6–99.7)	17.5 (16.3–18.9)	<0.0001	0.110	0.8297
No febrile	4	2773	11.0 (5.5–18.0)	95.5 (91.4–97.7)	4.7 (3.4–6.5)	<0.0001	0.721	
IgG seroprevalence								
Febrile	12	3708	16.9 (16.0–30.0)	98.9 (98.6–99.1)	9.4 (8.4–10.5)	<0.0001	0.224	0.8771
No febrile	11	9371	15.7 (5.9–29.1)	99.6 (99.5–99.7)	15.6 (14.4–16.9)	<0.0001	0.421	
Viral RNA prevalence								
Febrile	6	16,464	2.8 (0.1–8.1)	98.7 (98.2–99.1)	8.8 (7.4–10.5)	<0.0001	0.097	NA
No febrile	0	NA	NA	NA	NA	NA	NA	

CI, confidence interval; IgM: immunoglobulin M; IgG: immunoglobulin G; NA, not applicable; RNA: ribonucleic acid.

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Competing interests

The authors declare no competing interest.

Data statement

All data used to generate findings of this study are included in the manuscript and supplementary files.

Contributors

F.B.N.S, J.J.B, S.K and M.D contributed in conception and design. J.J.B carried out the literature search and data synthesis and analysis. F.B.N.S, J.J.B and S.K contributed in study selection and prepared the first draft. F.B.N.S, S.K, E.A.W and J.J.B contributed in data extraction and management. F.B.N.S, S.K, E.A.W, J.J.B, S.C.W, P.F.M and M.D contributed in data interpretation. F.B.N.S, J.J.B, E.A.W, S.K, F.B.Y.S, S.C.W, P.F.M and MD contributed in critical revision of successive drafts of the article. M.D is the guarantor of the review. All authors approved the final version of the article.

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Appendix A. Supplementary data

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