Review Article

Seropositivity of Chikungunya in Hospital Setting, India: A Systematic Review and Meta-Analysis

Ramya Nagarajan, Lavanya Ayyasamy, Parasuraman Ganeshkumar, Saravanakumar Velusamy[1], Manoj Murhekar[1]

Division of Non-Communicable Disease, [1]Division of Infectious Disease and Epidemiology, Indian Council of Medical Research- National Institute of Epidemiology, Chennai, Tamil Nadu, India

Abstract

Backround: Information about the chikungunya disease burden by age groups and geographic distribution is necessary to guide appropriate control measures. With this, we conducted a systematic review and meta-analysis to estimate the disease burden of chikungunya fever in India. **Material and Methods:** We conducted this systematic review according to the Cochrane Collaboration guidelines. We retrieved relevant articles from PubMed and a free online search. Two investigators screened titles and abstracts and extracted data from the relevant articles. Our primary outcome is the proportion of laboratory-confirmed Chikungunya fever among clinically suspected patients. We used a random effect model to estimate the pooled proportion of Chikungunya fever. **Result:** A total of 20 articles were included in the quantitative syntheses. The pooled proportion of laboratory-confirmed chikungunya fever from 20 studies estimated using the random effects model is 24% (95%CI: 15-34%). We found the pooled proportion in the southern region was 35% (95%CI: 4-66%), 28% (95%CI: 3-58%) in the western region, 24% (95%CI: 1-48%) in the eastern region, 20% (95%CI: 12-29%) in the northern region, and 4% (95%CI: 1-6%) in North-eastern region. **Conclusion:** This review emphasizes the need to strengthen the surveillance of disease burden using multiple diagnostic tests and the need for an appropriate molecular diagnostic for early detection of the chikungunya virus.

Keywords: Chikungunya, meta-analysis, proportion, sero-positivity, systematic review

Introduction

Chikungunya is a mosquito-borne viral disease transmitted by an infected female mosquito of *Aedes aegypti and Aedes albopictus* species. Clinically, Chikungunya is an abrupt onset of fever frequently accompanied by joint pain. Chikungunya has been reported in over 60 countries in Asia, Africa, Europe, and the Americas.[1] To date, no vaccine is available to practice to prevent chikungunya virus infection or disease.[2] Ocular problems such as retinitis or uveitis, myocarditis, nephritis, cranial nerve palsies, Guillain-Barre Syndrome, and renal and neurological disorders are all caused by Chikungunya.[2] In rare cases, a high viral load causes the virus to stay in minor joints during the acute stage, resulting in persistent arthritis.[2]

In India, several Chikungunya outbreaks were reported during 1963-1973.[3] No reports were published about the CHIKV outbreak during 1974-2004.[4] Chikungunya re-emerged in India in 2005 with large-scale attacks in Southern India.[5] During the 2006 epidemic, it was approximated that 25,588 disability-adjusted life years (DALYs) were forfeited, resulting in an aggregate burden of 45.26 DALYs per million population.[4] Chikungunya's burden varied among the states of India (0.01-265.62 DALYs per million population).[4] According to the National Vector-borne Disease Control Program (NVBDCP), more than 40,000 clinically suspected cases were reported in India in 2020.[6] The case fatality rate (28 days) of Chikungunya was 9.5%.[7] Furthermore, a specific mortality rate of 11.9% was observed in Ahmedabad, indicating the case-fatality rate in that region.[8]

Control and preventive measures for Chikungunya infection are being implemented under a national program, the NVBDCP.[9] NVBDCP's facility-based sentinel surveillance

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Address for correspondence: Dr. Parasuraman Ganeshkumar, Scientist-E, Indian Council of Medical Research- National Institute of Epidemiology, Ayappakkam, Chennai - 600 077, Tamil Nadu, India.
E-mail: ganeshkumardr@gmail.com

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for Chikungunya is conducted in 707 sites across India.[9] Data regarding the burden, prevalence, incidence, and geographical distribution of Chikungunya disease is crucial for formulating, determining, and executing essential control strategies within the NVBDCP framework. Thus, we intended to estimate the pooled proportion of confirmed Chikungunya infection among the suspected Chikungunya fever cases in the hospital setting since 2006 across India. These burden estimates would inform the policymakers for program planning, implementation, and public health preparedness.

Methods

Reporting guidelines and search strategy

We conducted this systematic review according to the Cochrane Collaboration guidelines,[10] and the findings were compiled following the "Preferred Reporting Items for Systematic Reviews and Meta-analyses" (PRISMA) guidelines. Protocol was registered in PROSPERO [Prospero registration number: CRD42017065625]. This study employed an extensive search strategy utilizing the search terms outlined in Supplementary Table 1_Supplementary data. With this approach, we systematically combed through the PubMed and Embase databases for studies documenting the prevalence of Chikungunya infection among suspected cases reported in hospital or laboratory-based surveillance. Additionally, a comprehensive free-text search was conducted to identify relevant articles. This search encompassed Medical Subject Headings (MeSH) terms related to Chikungunya infection, alongside free-text words with appropriate truncations, wildcards, and proximity. We employed Boolean operators ("OR" and "AND") to combine the outcomes of individual searches. Furthermore, the search was restricted to articles published in English.

Eligibility criteria

We have included the studies based on the following criteria:

A) Published studies from India reported a proportion of laboratory-confirmed chikungunya fever cases from 2006 to 2023.
B) Published studies from India on clinically suspected chikungunya cases and confirmed the cases based on the WHO diagnostic algorithm.[11] Diagnostic tests include immunoglobulin G (IgM) against the chikungunya virus, real-time polymerase chain reaction (RT-PCR) positivity or virus isolation.
C) Published studies conducted in hospital or laboratory settings. We excluded studies reporting outbreak investigations of Chikungunya fever.
D) We have incorporated accessible studies for full-text review. For those eligible but inaccessible studies, we have reached out to the corresponding authors via email, requesting the full text and included them in the review.

Study selection process

We adopted three stages in the study selection process:

Phase 1- Initial screening: After importing all retrieved studies from the databases into the Mendeley reference management software, duplicates were removed to compile a list of selected studies for screening. Two independent investigators (LA and RN) assessed the titles, abstracts, and keywords of the identified citations. Full-text articles were obtained from the shortlisted studies.

Phase 2- Subsequent screening: Following the eligibility criteria of our review, full-text articles from the primary screening were evaluated by the same two reviewers (LA and RN). Studies that did not meet the eligibility criteria were excluded, and reasons for exclusion were documented.

Phase 3- Final study selection: Any conflicts in the selection of studies between the two investigators were resolved during the screening process. The final selection of studies was made through consensus with a third reviewer (PG).

Outcomes

The main focus of this review was to determine the percentage of laboratory-confirmed cases of chikungunya fever among patients clinically suspected of the disease in a hospital setting. We described the pooled proportion by region and year. Data will also be collected in the study setting, year of reporting, region of reporting, symptoms reported, and type of laboratory test used to confirm the diagnosis.

Risk of bias

We utilized a modified Joanna Briggs Institute appraisal checklist designed for prevalence studies to evaluate the potential bias in the studies included in our analysis.[12] The checklist has several domains for evaluating the risk of bias, including participants, testing methods, case definition, and outcome variables.

Statistical methods

The meta-analysis was conducted using the R software with the final set of selected studies.[13] The random effects model was used to estimate pooled burden outcomes of Chikungunya fever. Burden estimates, such as the proportion of laboratory-confirmed Chikungunya among suspected case-patients, were summarized as pooled proportions with a 95% confidence interval. We used the Arcsine transformed proportion method for pooling the proportion. The pooled estimates were visually represented through forest plots. We performed additional analyses, such as subgroup analysis by region and study setting, since high heterogeneity was anticipated in our research. Heterogeneity was assessed using both the Chi-square test and the I2 statistic.[14] A Chi-square test with a *P* value less than 0.10 suggests significant heterogeneity, while the I2 statistic quantifies the degree of heterogeneity. Since we anticipated significant heterogeneity in our analysis, a meta-regression analysis was performed to find out the influencing parameter. The potential covariates considered for conducting meta-regression included age, publication year, region, positivity rate, and study quality. Multivariate meta-regression analysis was carried out by including the factors that had a *P* value less than 0.20 in the

univariate model. We assessed publication bias using Egger's test ($P < 0.10$) and LFK index and by visually inspecting the Doi plot and funnel plot.[15] We considered the LFK index value between −1 and +1 as an indicator of the absence of publication bias. Additionally, sensitivity analysis was performed to check for the consistency of pooled estimates.

Results

Study selection process

The study adhered to the guidelines outlined in the "Preferred Reporting Items for Systematic Reviews and Meta-analyses" (PRISMA). [Supplementary Table 2_ Supplementary data]. We found 427 published studies in PubMed, Embase, and a Free online search based on the search strategy. After listing it in the reference software, we eliminated 12 duplicate entries, resulting in a total of 406 studies for title and abstract screening. Subsequently, 118 studies underwent full-text retrieval and further evaluation after the title and abstract screening process. We found 20 studies deemed to be eligible as per the criteria.[16–35] These 20 studies represented a sample of 69,646 participants and were included in our final quantitative syntheses [Figure 1].

Characteristics of studies included

Among the 20 articles reporting laboratory-confirmed Chikungunya infection among reported in India, ten were conducted in the northern region, five studies were conducted in the Southern region, two studies were conducted in the Eastern and Western regions each, and one in the north-eastern region of India. Of 20 articles, 18 studies reported Chikungunya confirmation by ELISA IgM antibodies, and two studies reported confirmation by reverse transcriptase – polymerase chain reaction (RT-PCR). Among the 20 articles, 13 were

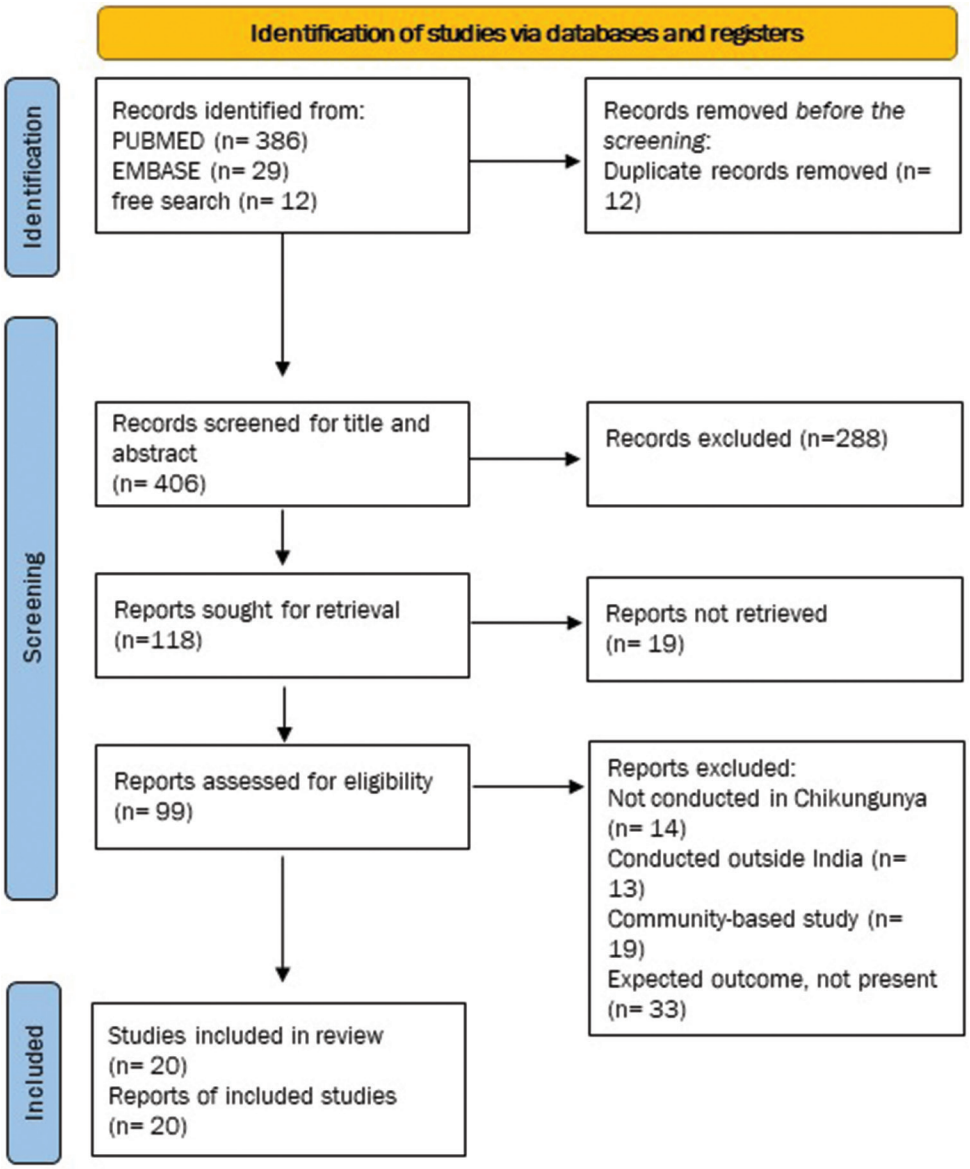

Figure 1: PRISMA flowchart ($n = 20$)

Table 1: Characteristics of the included studies (*n*=20)

Author name	Year	Setting	State	Region	Suspected cases	Laboratory-confirmed cases	Laboratory test name	Quality Of Study
Afreen 2014	2014	Hospital-based surveillance	New-Delhi	North	87	25	Reverse transcriptase–polymerase chain reaction	Moderate
Arvind 2018	2018	Hospital-based surveillance	Karnataka	South	432	23	IgM antibodies	Moderate
Bhagwati 2013	2013	Hospital-based surveillance	Gujarat	West	193	84	IgM antibodies	High
Dinker 2018	2018	Hospital-based surveillance	Uttar Pradesh	North	186	23	IgM antibodies	High
Dutta 2011	2011	Hospital-based surveillance	Hospital	North-East	280	10	IgM antibodies	Moderate
Galate 2018	2018	Hospital-based surveillance	Maharashtra	West	200	25	IgM antibodies	High
Joshi 2020	2020	Laboratory-based surveillance	Maharashtra	North	4019	494	Reverse transcriptase–polymerase chain reaction	Moderate
Kumar 2019	2019	Hospital-based surveillance	New Delhi	North	200	77	IgM antibodies	Moderate
Lakshmi 2008	2008	Hospital-based surveillance	Andhra Pradesh	South	296	144	IgM antibodies	High
Murhekar 2019	2019	Laboratory-based surveillance	New Delhi	South	49380	10124	IgM antibodies	Moderate
Nayak 2020	2020	Hospital-based surveillance	Delhi	North	434	184	IgM antibodies	Moderate
Ozair 2020	2020	Laboratory-based surveillance	Uttar Pradesh	North	3240	771	IgM antibodies	Moderate
Patil 2020	2020	Laboratory-based surveillance	Maharashtra	North	87	6	IgM antibodies	Moderate
Paul 2011	2011	Hospital-based surveillance	Kerala	South	134	122	IgM antibodies	High
Pooja 2020	2020	Hospital-based surveillance	Maharashtra	North	711	90	IgM antibodies	Moderate
Saswat 2015	2015	Hospital-based surveillance	Orissa	East	222	28	IgM antibodies	Moderate
Sengupta 2020	2020	Hospital-based surveillance	West Bengal	North	641	158	IgM antibodies	Moderate
Shaikh 2014	2014	Hospital-based surveillance	Karnataka	South	6554	622	IgM antibodies	High
Singh 2018	2018	Hospital-based surveillance	Uttar Pradesh	North	1800	6	IgM antibodies	Moderate
Tharaphdar 2012	2012	Hospital-based surveillance	West Bengal	East	550	199	IgM antibodies	High

deemed to have a moderate risk of bias, while seven were considered to have a low risk of bias [Table 1].

Seropositivity of chikungunya in hospital-based surveillance

The pooled proportion of laboratory-confirmed chikungunya fever from 20 studies estimated using the random effects model is 24% (95%CI: 15-34%). However, we found substantial heterogeneity among the studies (I^2 = 99%; Chi-square test for heterogeneity, $P < 0.001$) [Figure 2]. This shows that 24% of the suspected cases are confirmed for Chikungunya by laboratory tests in hospital-based surveillance. We performed Egger's test, funnel plot, and LFK index with Doi plot to identify publication bias. The *P* value in Egger's test is 0.024, and the LFK index is 5.69 [Figure 3], which signifies the presence of publication bias. The funnel and Doi plot visually demonstrate publication bias in our review [Supplementary Figure 1]. This intended for us to perform sub-group analysis by year of the study, region, and laboratory investigation used to confirm the diagnosis.

While performing sub-group analysis by region, we found the pooled proportion in the southern region was 35% (95%CI: 4-66%), 28% (95%CI: 3-58%) in the western region, 24% (95%CI: 1-48%) in the eastern region, 20% (95%CI: 12-29%) in the northern region, and 4% (95%CI: 1-6%) in North-eastern region [Supplementary Figure 2_Supplementary data]. The pooled proportion of

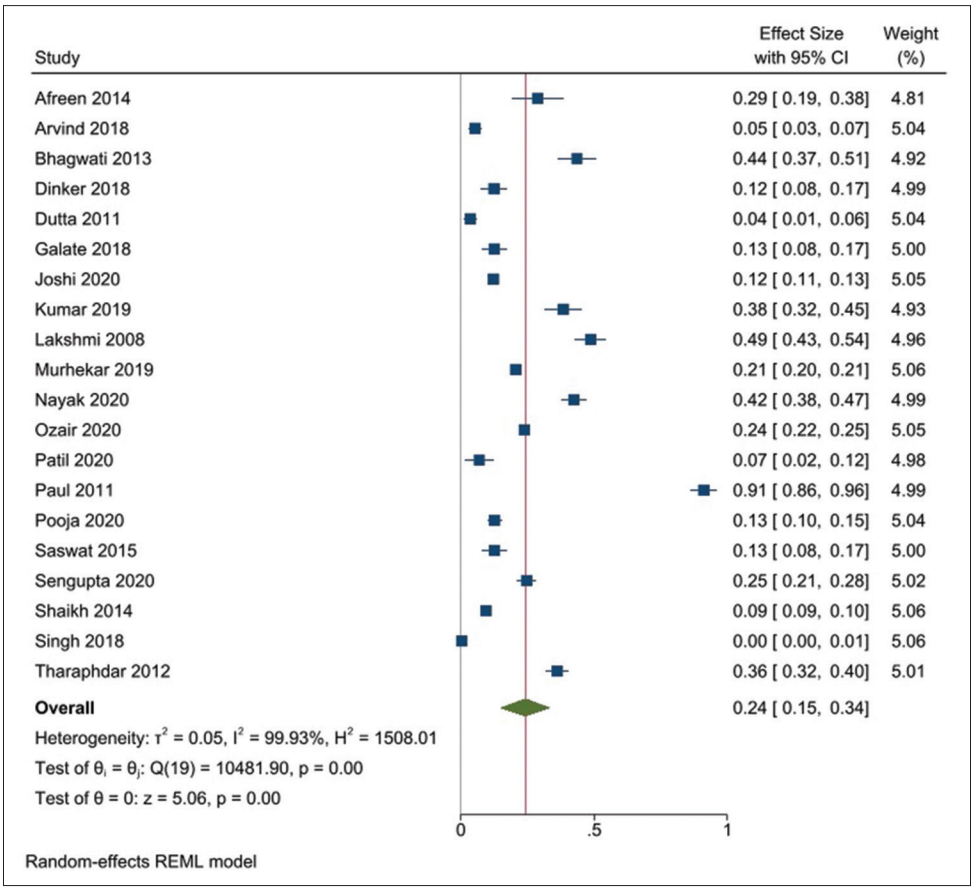

Figure 2: Forest plot showing the proportion of lab-confirmed chikungunya cases among the suspected cases in hospital-based surveillance, India, 2006-2023 (n = 20)

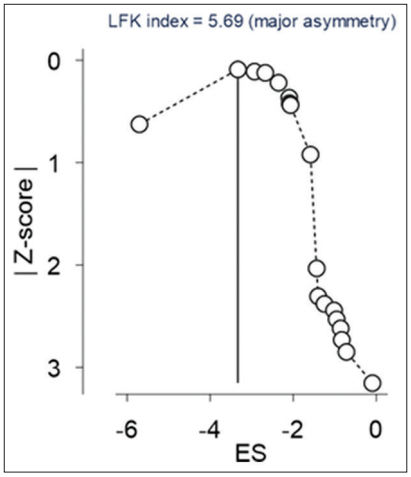

Figure 3: Doi plot and LFK index to demonstrate publication bias

laboratory-confirmed chikungunya cases during the years 2006-2010 was 49% (95%CI: 43-54%), during 2011-2015, it was 32% (95%CI: 10-54%) and it was 18% (95%CI: 10-25%) during the year of 2016-2023 [Supplementary Figure 3_ Supplementary data]. The pooled proportion of fever confirmed by IgM was 25% (95%CI: 14-35%), and it was 20% (95%CI: 4-36%) for fever confirmed by RTPCR [Supplementary Figure 4_Supplementary data]. The pooled proportion of laboratory-confirmed chikungunya cases among hospital-based surveillance was 26% (95%CI: 15-38%), and laboratory-based surveillance was 16% (95%CI: 9-23%) [Supplementary Figure 5_Supplementary data].

In addition, we conducted a univariate meta-regression analysis with outcome variables such as age, region, type of laboratory test performed, study setting, year of publication, and quality of the study. None of them were found to be significant. However, we could include variables such as quality of study and year of publication in a multivariate meta-regression analysis, but none were found to be significant [Supplementary Table 3_ Supplementary data]. Sensitivity analysis showed that none of the studies influenced the overall effect estimate of the pooled proportion [Supplementary Figure 6_Supplementary data].

Discussion

Our systematic review assessed the prevalence of chikungunya fever using published literature from India covering two decades. Notably, there were no community-based epidemiological studies documenting the incidence of Chikungunya.[6] However, according to NCVBDC, the incidence of Chikungunya cases among suspected cases in India stood at 9.54% from 2018 to 2023.[6] Also, according to the World Health Organization, the incidence of chikungunya

cases in tropical regions such as Brazil, Belize and Paraguay were 14.2 cases, 10.4 cases, and 1103.4 cases per 1,00,000 population, respectively.[36] Our analysis indicated that about a quarter of the suspected case-patients had laboratory-confirmed CHIKV infection — the burden of chikungunya fever varied by year of the study and geographical location across India. Among regions of India, the southern, western, and eastern regions reported a high burden of Chikungunya fever. Also, the percentage positive for chikungunya fever was higher during 2011-2015, and cases drastically decreased during 2016-2023.[37,38] The decline in chikungunya cases may be credited to advancements in surveillance and diagnostics, particularly Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR), enabling rapid and accurate detection of the virus in patient samples. This facilitates prompt treatment, isolation of infected individuals, and implementation of control measures, curbing virus spread. The hospital-based multicentric study conducted by Ray *et al*. 2012[39] on Chikungunya fever found high test positivity among cases reported from western and southern regions of India. As per the 2017 report from the Manipal Centre for Viral Research, out of 27,586 reported cases of acute febrile illness, 371 were confirmed positive for Chikungunya.[40] This corroborates our review findings. According to National Vector Borne Disease Control program reports, between January 2015 and July 2021, more cases were reported in the western and southern regions of India.[6] Similar to our review findings, Kumar *et al*. 2018[41] reported seroprevalence of Chikungunya fever was high in the south and low in the north-eastern regions of India.

Strength and limitation

Our review included studies reported from various regions, which is one of the significant strengths of our thinking. This made us report burden estimates by region and year of the study, which would help policymaking for public health programs. On performing sensitivity analysis, we found none of the studies influenced the overall effect estimate. Thus, our overall effect estimate reflects the prevalence of Chikungunya fever in India. In addition, we also performed a meta-regression to find whether any factors influence the overall effect estimate. In our review, we observed high heterogeneity among the included studies. This would limit the interpretation of the overall effect estimate. Methodological differences among the included studies may contribute to such heterogeneity. However, using a random effects model handled this limitation. Next, we observed very few studies reporting mortality data for Chikungunya fever. We couldn't perform quantitative synthesis (meta-analysis). This would limit the interpretation of the mortality of Chikungunya fever in India. Another limitation we observed in our review is the presence of significant publication bias. Probably this may be due to the absence of published literature on outbreaks, community-based studies, and the non-inclusion of surveillance data.

Conclusion

Our systematic review reveals a concerning proportion of confirmed Chikungunya fever cases among suspected cases, indicating a substantial disease burden. Particularly noteworthy is the higher prevalence observed in the southern region of India, suggesting regional disparities in disease incidence. To address this, we advocate for enhanced reporting of India's most prevalent neglected tropical disease through both published literature and robust surveillance systems. This comprehensive approach is crucial for gaining a more accurate understanding of the true burden of this vector-borne illness. Additionally, we recommend the establishment of community-based surveillance programs for Chikungunya fever to capture and monitor incidence trends effectively, ultimately aiding in targeted intervention strategies and disease management efforts.

Author's contribution

RN − designing the study, screening, data extraction and analysis, manuscript writing; LA − designing the study, screening, data extraction and analysis, manuscript writing; PG − designing the study, screening, data extraction and analysis, manuscript writing; SV − designing the study, data analysis, manuscript review; MM − designing the study, manuscript review.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Search strategy:
Pubmed Search

S.No	Search Terms	Results
#1	(Chikungunya-Fever) OR (Chikungunya-virus) Sort by: Most Recent	6428
	"chikungunya fever"[MeSH Terms] OR ("chikungunya"[All Fields] AND "fever"[All Fields]) OR "chikungunya fever"[All Fields] OR ("chikungunya virus"[MeSH Terms] OR ("chikungunya"[All Fields] AND "virus"[All Fields]) OR "chikungunya virus"[All Fields])	
#2	((((hospital-based surveillance) OR (hospital surveillance)) OR (laboratory-based surveillance)) OR (laboratory surveillance)) OR (surveillance) Sort by: Most Recent	3052054
	("hospital-based"[All Fields] AND ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "surveillance"[All Fields] OR "epidemiology"[MeSH Terms] OR "surveilance"[All Fields] OR "surveillances"[All Fields] OR "surveilled"[All Fields] OR "surveillence"[All Fields])) OR (("hospital s"[All Fields] OR "hospitalisation"[All Fields] OR "hospitalization"[MeSH Terms] OR "hospitalization"[All Fields] OR "hospitalising"[All Fields] OR "hospitality"[All Fields] OR "hospitalisations"[All Fields] OR "hospitalised"[All Fields] OR "hospitalizations"[All Fields] OR "hospitalized"[All Fields] OR "hospitalize"[All Fields] OR "hospitalizing"[All Fields] OR "hospitals"[MeSH Terms] OR "hospitals"[All Fields] OR "hospital"[All Fields]) AND ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "surveillance"[All Fields] OR "epidemiology"[MeSH Terms] OR "surveilance"[All Fields] OR "surveillances"[All Fields] OR "surveilled"[All Fields] OR "surveillence"[All Fields])) OR ("laboratory-based"[All Fields] AND ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "surveillance"[All Fields] OR "epidemiology"[MeSH Terms] OR "surveilance"[All Fields] OR "surveillances"[All Fields] OR "surveilled"[All Fields] OR "surveillence"[All Fields])) OR (("laboratorial"[All Fields] OR "laboratories"[MeSH Terms] OR "laboratories"[All Fields] OR "laboratory"[All Fields] OR "laboratory s"[All Fields]) AND ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "surveillance"[All Fields] OR "epidemiology"[MeSH Terms] OR "surveilance"[All Fields] OR "surveillances"[All Fields] OR "surveilled"[All Fields] OR "surveillence"[All Fields])) OR ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "surveillance"[All Fields] OR "epidemiology"[MeSH Terms] OR "surveilance"[All Fields] OR "surveillances"[All Fields] OR "surveilled"[All Fields] OR "surveillence"[All Fields])	
#3	(((((Seropositivity) OR (proportion)) OR (prevalence)) OR (cross-sectional study)) OR (descriptive study)) OR (analytical study) Sort by: Most Recent	4415849
	"seroepidemiologic studies"[MeSH Terms] OR ("seroepidemiologic"[All Fields] AND "studies"[All Fields]) OR "seroepidemiologic studies"[All Fields] OR "Seropositivity"[All Fields] OR "Seropositivitys"[All Fields] OR "seroprevalance"[All Fields] OR "seroprevalances"[All Fields] OR "seroprevalency"[All Fields] OR "seroprevalent"[All Fields] OR ("proportion"[All Fields] OR "proportions"[All Fields]) OR ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "prevalence"[All Fields] OR "prevalence"[MeSH Terms] OR "prevalance"[All Fields] OR "prevalences"[All Fields] OR "prevalence s"[All Fields] OR "prevalent"[All Fields] OR "prevalently"[All Fields] OR "prevalents"[All Fields]) OR ("cross sectional studies"[MeSH Terms] OR ("cross sectional"[All Fields] AND "studies"[All Fields]) OR "cross sectional studies"[All Fields] OR ("cross"[All Fields] AND "sectional"[All Fields] AND "study"[All Fields]) OR "cross sectional study"[All Fields]) OR (("description"[All Fields] OR "descriptions"[All Fields] OR "descriptive"[All Fields] OR "descriptively"[All Fields] OR "descriptives"[All Fields]) AND ("studies"[All Fields] OR "study"[All Fields] OR "study s"[All Fields] OR "studying"[All Fields] OR "studys"[All Fields])) OR (("analyte"[All Fields] OR "analyte s"[All Fields] OR "analytes"[All Fields] OR "analytic"[All Fields] OR "analytical"[All Fields] OR "analytically"[All Fields] OR "analyticity"[All Fields] OR "analytics"[All Fields]) AND ("studies"[All Fields] OR "study"[All Fields] OR "study s"[All Fields] OR "studying"[All Fields] OR "studys"[All Fields]))	
#4	Search: India Sort by: Most Recent	713209
	"india"[MeSH Terms] OR "india"[All Fields] OR "india s"[All Fields] OR "indias"[All Fields]	
#5	#1 AND #2 AND #3 AND #4	386

Embase Search

S.No	Search terms	Results
#1	'chikungunya'/exp OR 'chikungunya'	10244
#2	'monitoring'/exp OR 'monitoring' OR 'hospital based' AND surveillance OR 'laboratory based surveillance'	1544394
#3	'seropositivity'/exp OR 'prevalence'/exp	915864
#4	'india'/exp OR 'india'	1302551
#5	#1 AND #2 AND #3 AND #4	29

Supplementary Table 2: PRISMA Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
		Title	
Title	1	Identify the report as a systematic review.	1
		Abstract	
Abstract	2	See the PRISMA 2020 for the Abstracts checklist.	2, 3
		Introduction	
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	4, 5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	4, 5
		Methods	
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5, 6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix- Supplementary table 1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g., for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	6
	10b	List and define all other variables for which data were sought (e.g., participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	6
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	7
Effect measures	12	Specify for each outcome the effect measure(s) (e.g., risk ratio, mean difference) used in the synthesis or presentation of results.	7
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g., tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	7
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	7
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	7
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	7
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g., subgroup analysis, meta-regression).	7
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	7
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	7
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	7

Contd...

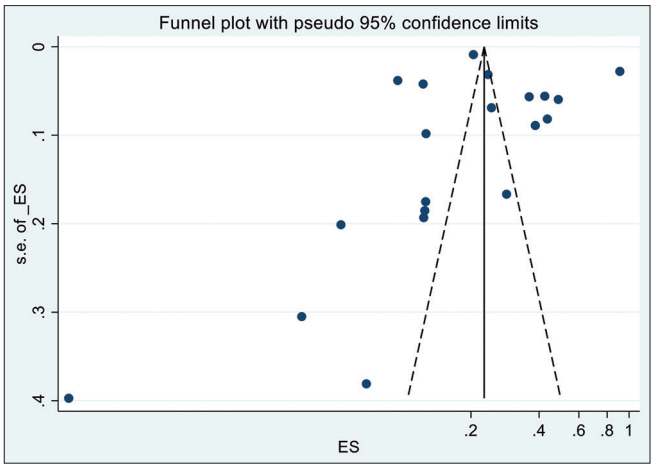
Supplementary Table 2: Contd...

		Results	
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	8
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	8
Study characteristics	17	Cite each included study and present its characteristics.	Table 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Table 1
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g., confidence/credible interval), ideally using structured tables or plots.	8
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	8, 9
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g., confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	8, 9
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	8, 9
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	8, 9
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	8, 9
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	8, 9
		Discussion	
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	10
	23b	Discuss any limitations of the evidence included in the review.	10
	23c	Discuss any limitations of the review processes used.	10
	23d	Discuss implications of the results for practice, policy, and future research.	10
		Other information	
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	5
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	5
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	5
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	11
Competing interests	26	Declare any competing interests of review authors.	11
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	11

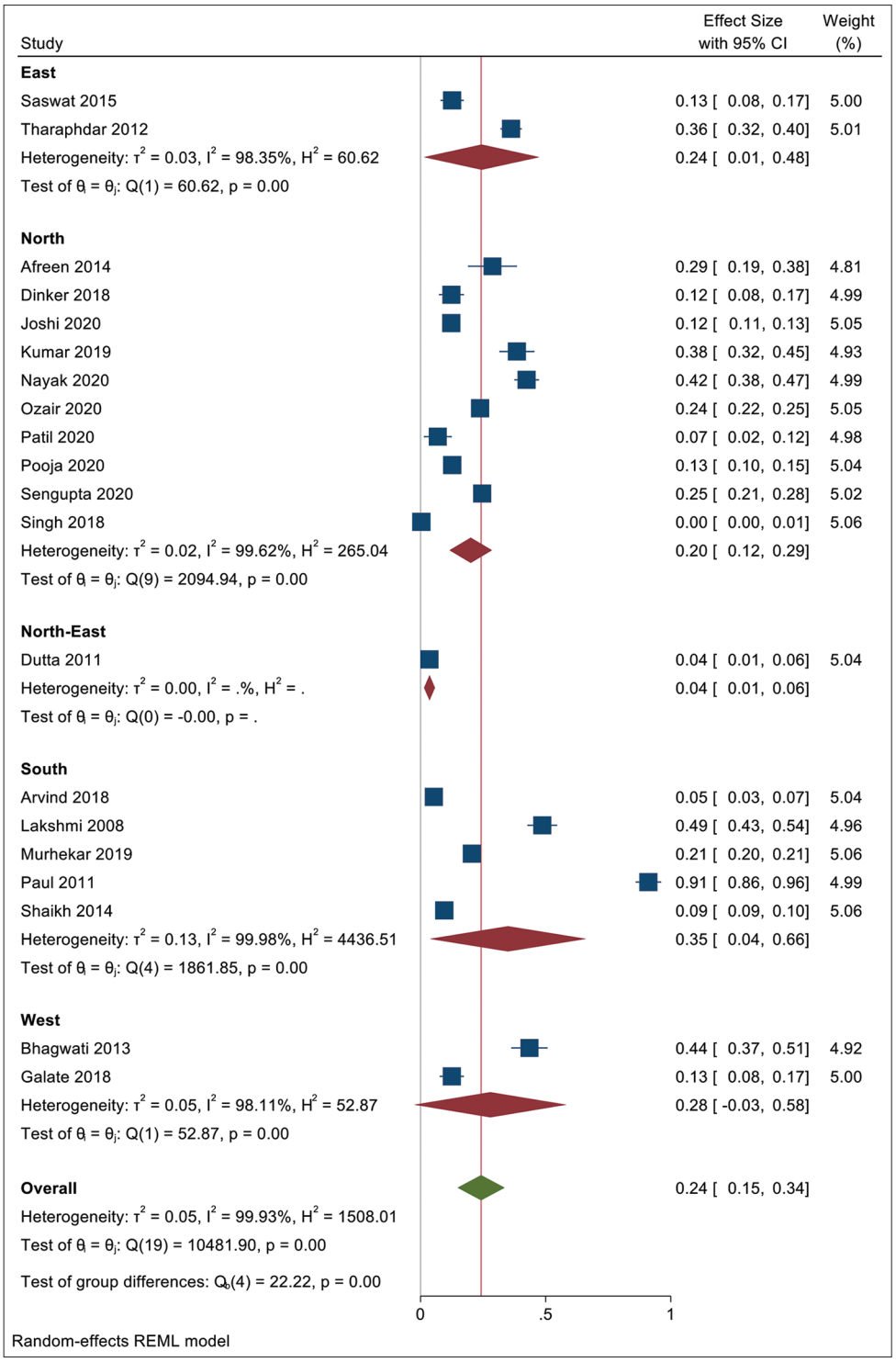
From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al*. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

Supplementary Table 3: Meta-regression analysis

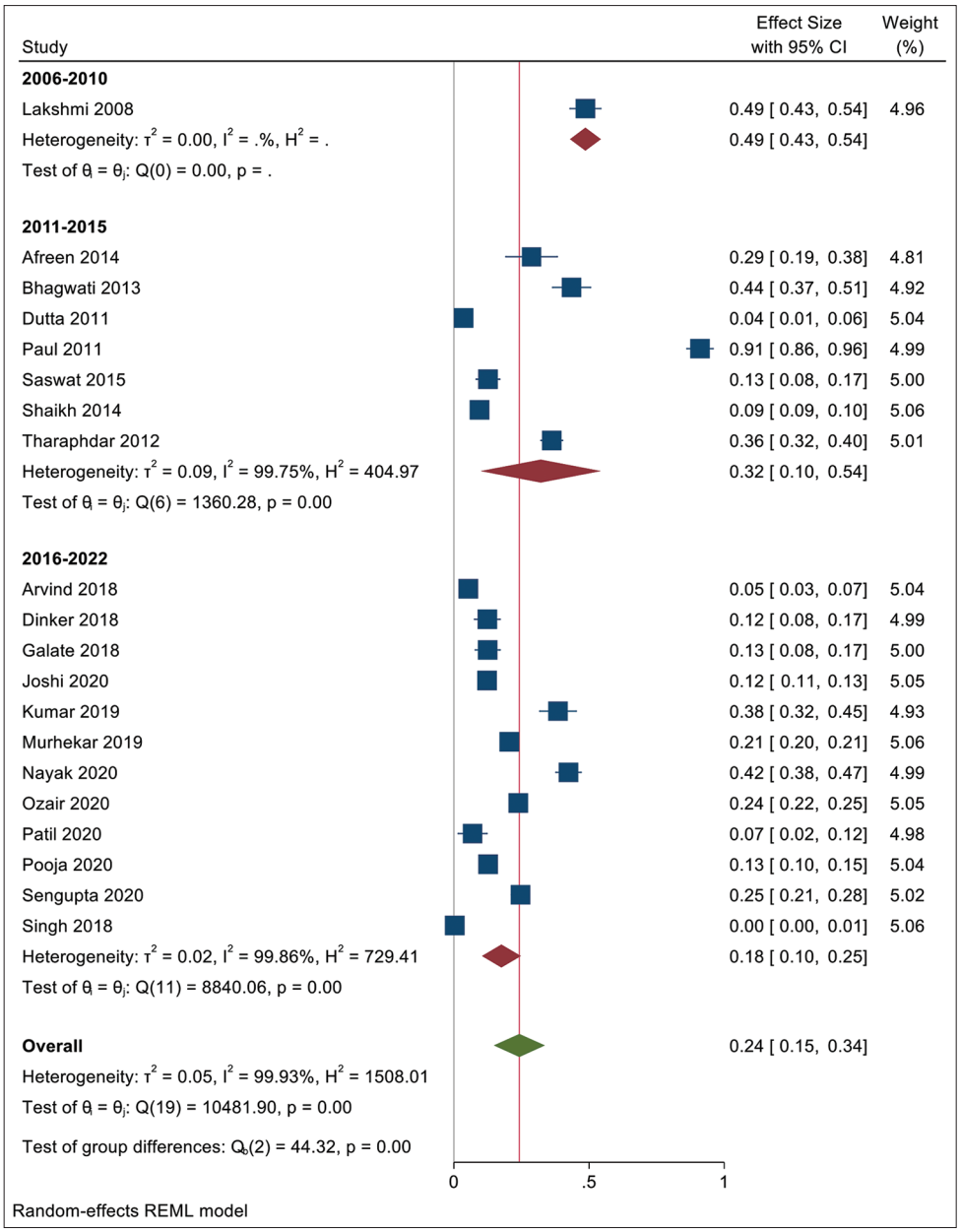
Variable	Univariate meta-regression		Multivariate meta-regression	
	Co-efficient	*P*	Co-efficient	*P*
Age	-0.20	0.139		
Year				
2006-2010	1			
2011-2015	-0.16	0.46	-0.11	0.61
2016-2022	-0.31	0.16	-0.20	0.38
Quality of study				
High	1			
Moderate	-0.18	0.06	-0.12	0.29



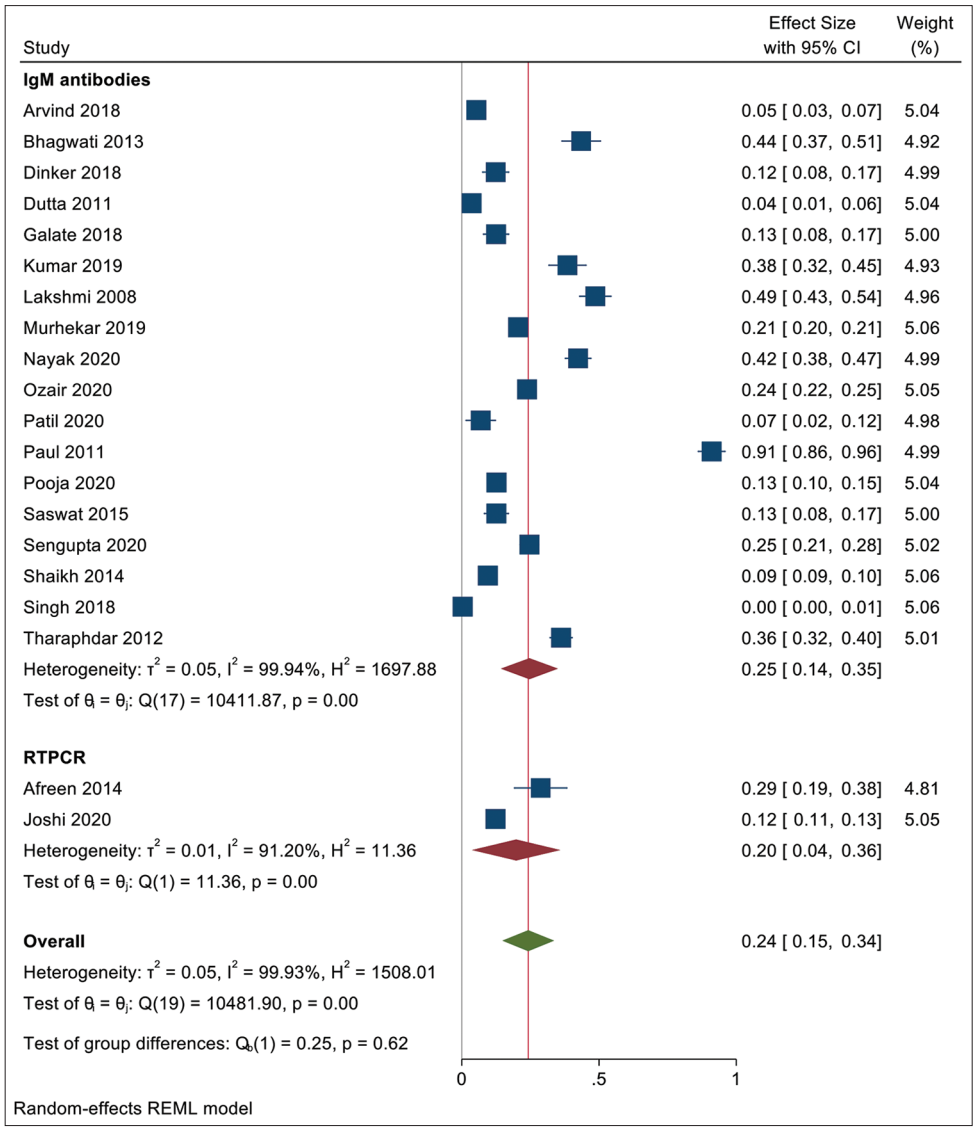
Supplementary Figure 1: Funnel Plot to demonstrate publication bias



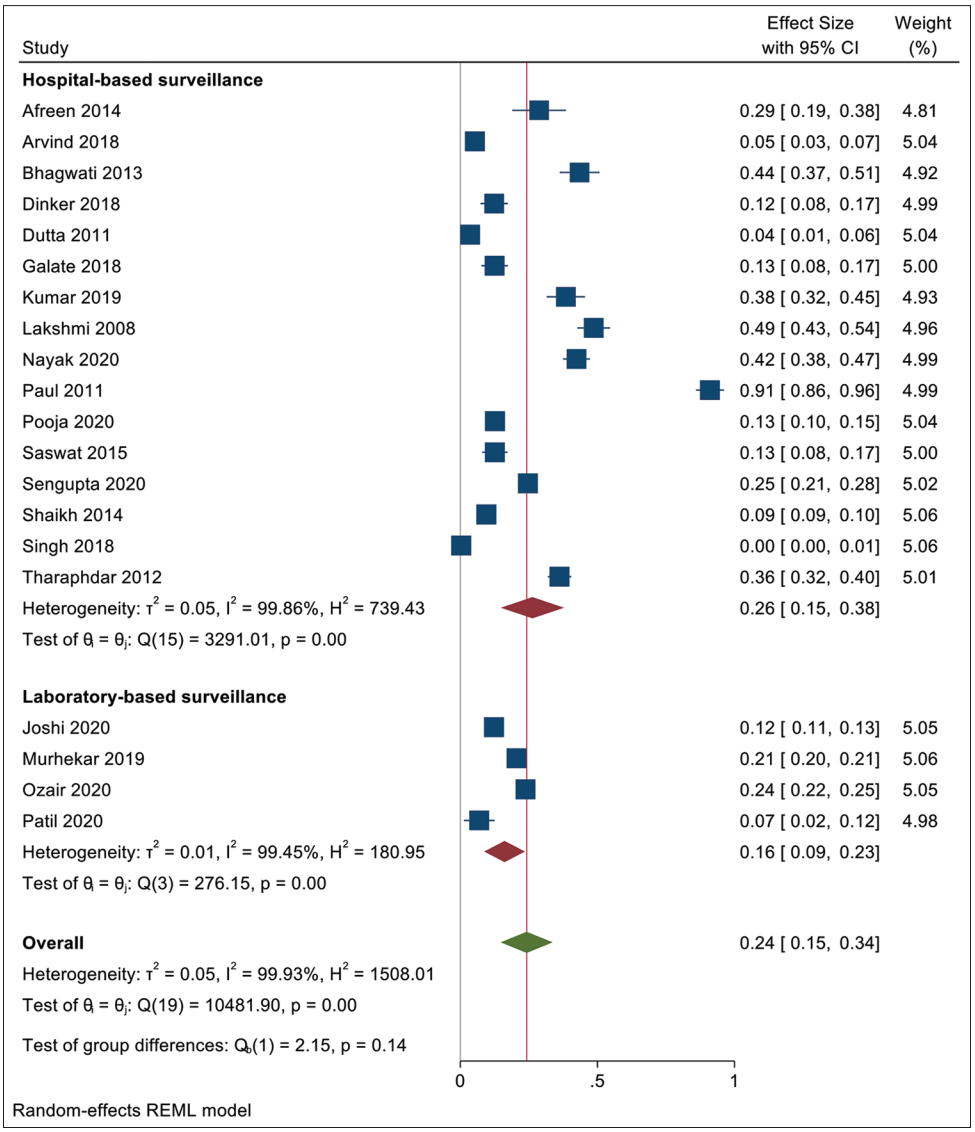
Supplementary Figure 2: Pooled sero-proportion of chikungunya in hosp/lab-based surveillance by region



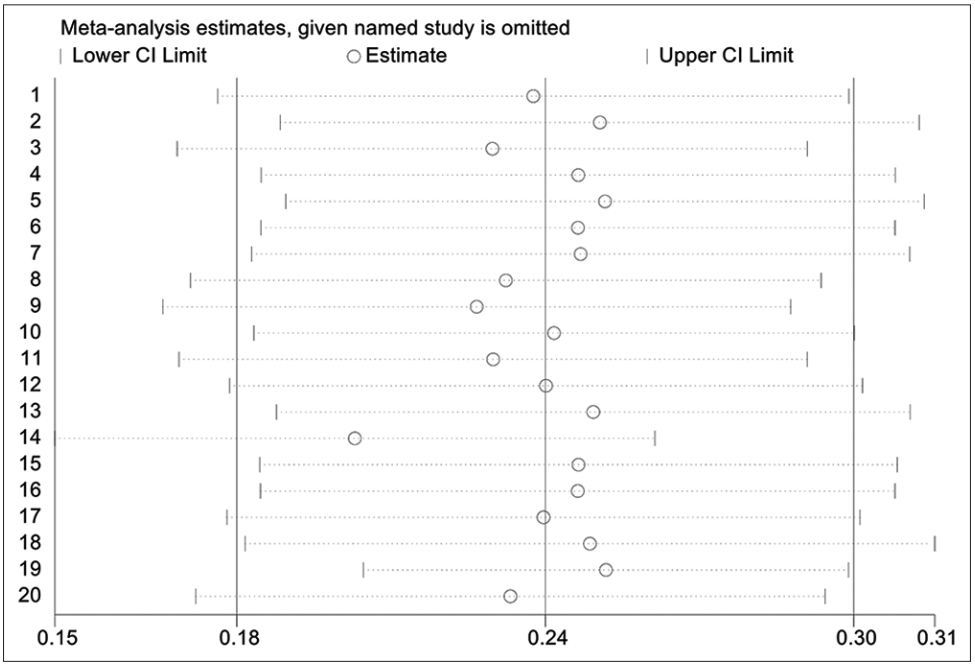
Supplementary Figure 3: Pooled sero-proportion of chikungunya in hosp/lab-based surveillance by year of conducting the study



Supplementary Figure 4: Pooled sero-proportion of chikungunya in hosp/lab-based surveillance by type of laboratory test used to confirm the diagnosis



Supplementary Figure 5: Pooled sero-proportion of chikungunya in hosp/lab-based surveillance by type of study setting



Supplementary Figure 6: Sensitivity analysis