REVIEW ARTICLE



How climate change can affect cholera incidence and prevalence? A systematic review

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Received: 29 February 2020 / Accepted: 1 July 2020 / Published online: 14 July 2020 © Springer-Verlag GmbH Germany, part of Springer Nature 2020

Abstract

Although the number of cholera infection decreased universally, climate change can potentially affect both incidence and prevalence rates of disease in endemic regions. There is considerable consistent evidence, explaining the associations between cholera and climatic variables. However, it is essentially required to compare and interpret these relationships globally. The aim of the present study was to carry out a systematic review in order to identify and appraise the literature concerning the relationship between nonanthropogenic climatic variabilities such as extreme weather- and ocean-related variables and cholera infection rates. The systematic literature review of studies was conducted by using determined search terms via four major electronic databases (PubMed, Web of Science, Embase, and Scopus) according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) approach. This search focused on published articles in English-language up to December 31, 2018. A total of 43 full-text studies that met our criteria have been identified and included in our analysis. The reviewed studies demonstrated that cholera incidence is highly attributed to climatic variables, especially rainfall, temperature, sea surface temperature (SST) and El Niño Southern Oscillation (ENSO). The association between cholera incidence and climatic variables has been investigated by a variety of data analysis methodologies, most commonly time series analysis, generalized linear model (GLM), regression analysis, and spatial/GIS. The results of this study assist the policy-makers who provide the efforts for planning and prevention actions in the face of changing global climatic variables.

Keywords Climate change · Cholera · Rainfall · Air temperature

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Responsible Editor: Lotfi Aleya

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s11356-020-09992-7) contains supplementary material, which is available to authorized users.

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Introduction

Environmental factors are likely to be affected by climate change as the result of direct and indirect impacts. The rise in mean global temperature due to anthropogenic activities and increased fossil fuel consumption and CO2 emissions can lead to melting of glaciers, rising sea levels, and increased risk of extreme weather (floods, storms, and heat waves) which can indirectly cause long-term drought, food shortages, natural disasters, and health risks. The rate of infectious diseases such as malaria, diarrhea, and cholera could be changed by changing climatic conditions which together lead to more than 3 million deaths per year (Campbell-Lendrum et al. 2007). Cholera is known as an acute diarrheal disease caused by a free-living, nonspore, and gram-negative bacterium called Vibrio cholerae (V. cholerae). Its natural milieu is both fresh- and saltwater environments (Colwell 1996; Nkoko et al. 2011), and the best environmental conditions are water temperature of 30 °C, 15% salinity, and pH = 8.5 (alkaline environments) (Chowdhury et al. 2017). It was reported that there are nearly 1.3 to 4.0 million cholera cases and 21,000 to 143,000 deaths globally every year (Weekly Epidemiological Record 2017). The total number of cases reported to WHO in 2017 was 179,835, 13,818, and 1,034,123 for Africa, the USA, and Asia, respectively. Therefore, cholera has been remaining as one of the most important global health threats, especially in low-income and developing countries (Weekly Epidemiological Record 2018). The disease can be transmitted person-to-person, especially by the food and waterborne mode which is highly associated with insufficient access to sanitation, poor hygiene, inadequate safe water supplies, and food contamination. In other words, this disease is known as an indicator of deprivation and absence of social development (Taylor et al. 2015).

It was indicated that the transmission and incidence of cholera are significantly influenced by environmental parameters such as seasonality (Hashizume et al. 2010; Pascual et al. 2002), temperature (Luque Fernández et al. 2009; Olago et al. 2007), rainfall (Hashizume et al. 2008; Ruiz-Moreno et al. 2007b), sea surface temperatures (SST) (Bouma and Pascual 2001), and the El Niño Southern Oscillation (ENSO) events (Nkoko et al. 2011; Pascual et al. 2002; Ramírez 2014). Periodic variation in the sea surface temperature (El Niño) and the air pressure of the atmosphere (Southern Oscillation) in the equatorial Pacific Ocean is known as ENSO which has environmental and socio-economic effects globally (McPhaden et al. 2006; NOAA n.d.). The reviewed papers showed the most cholera endemic regions are Bangladesh, India, Haiti, Nigeria, Ethiopia, the Democratic Republic of the Congo (DRC), Tanzania, and Kenya with more than 100,000 cases per year (Ali et al. 2015). It was reported by WHO that Yemen with more than one million suspected cases per year followed by DRC and Somalia with 56,190 and

75,414 cases, respectively, had the highest numbers of cholera cases in their recent history (Weekly Epidemiological Record 2018, b). On the continent of Africa, in Kenya, changing in rainfall patterns and inadequate health equipment were recognized as the most important parameters in the incidence of cholera disease (Stoltzfus et al. 2014). However, in some regions of Africa, there was found a complex relationship between the incidences of cholera and rainfall. So that, increasing in rainfall during El Niño time periods led to rise in the number of cholera, while decreasing in rainfall end to increase the number of cholera cases in other regions (Moore et al. 2017). This pattern of rainfall could happen in the same region. The dual pattern of rainfall on cholera can be attributed to "dilution" impact of rainfall on pathogen concentration in the environment and then increasing its effect on secondary transition during rainfall extreme events (Ruiz-Moreno et al. 2007a). It also was reported that a significant correlation between the high temperature and the incidence of cholera in Tanzania and Zanzibar (Reyburn et al. 2011; Trærup et al. 2011). The similar results were observed in Bangladesh to report the relationship between aforementioned climatic parameters and the incidence of cholera (Hashizume et al. 2008; Hashizume et al. 2010; Islam et al. 2009). Droughts, floods, and their related factors such as river discharge, changing in rainfall, and monsoon patterns can influence on not only the concentration of pathogens in water bodies but also the nutrient concentration, salinity, pH, and finally on the survival of the bacterium. As the consequent, human exposure and susceptibility to cholera infection can also be increased by changing these phenomena and subsequently decreasing the sanitary conditions levels (Jutla et al. 2011; Pascual et al. 2002). As the relationship between cholera incidence and climatic variables has been investigated by a variety of data analysis methodologies in different regions around the world, it is critically important to combine and compare the results of these studies to assist national and international policy-makers which provide the redouble efforts for planning and prevention actions in the face of changing global climatic variables. Therefore, the main aims of our study were to summarize and assess the existing universal findings of previous studies that reporting climate variability, extreme weather, ocean related variables, and their effects on the incidence of cholera.

Methods

Search strategy and study selection

We applied the strategies of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol (PRISMA) and MOOSE guidelines to conduct the systematic search (Shamseer et al. 2015; Stroup et al. 2000). We searched original research studies published in English language with no restriction on year or country up to December 31, 2018. The searched databases were EMBASE, Scopus, Web of Science, and PubMed databases. Combinations of search terms from two categories (climate change keywords AND cholera keywords) were applied to search for the relevant literature. Search terms related to climate change were "Climate Change" OR "Climate" OR "Global warming" OR "Weather" OR "Precipitation" OR "Heat" OR "Rain*" OR "Drought*" OR "Temperature" OR "Humidity" OR "Flood*" OR "Season*" OR "Runoff" OR "variability" OR "ENSO" OR "El Nino" OR "sea surface temperature," and cholera keywords were "Cholera" OR "Vibrio cholera" OR "Diarrhea" OR "Water-borne disease" OR "Water-related disease." The EndNote X7.4 (Thomson Reuters, New York, USA) was used to manage the imported citations, and duplicated papers were checked and removed. In the case of unavailable papers, however, the full texts were requested from the authors by e-mail. We applied only the abstracts (if it contained enough information) while the author did not answer our e-mail, or finally, papers were excluded from our study.

The original research studies were included, but reviews, letters, non-English language papers, conference abstracts, short communications, news articles, and posters were excluded from our study. The articles included if (1) they published in peer-reviewed journals, (2) the outcome measures were incidence or the number of cholera cases, (3) they included methods to assess the effect of climatic variables on incidence of cholera, and (4) they reported at least one continuous year data. The search strategy is presented in Fig. 1.

Screening and data extraction

Included articles were screened according to the title and abstract information by evaluation of two independent reviewers (ZA and AB). The two reviewers have compared their results and resolved differences by consulting the other authors (MG and HM). In the second step, the full text of qualified studies was assessed by authors (ZA, AB, SN, MK, and YM). The extraction of data was done using a standardized form to determine the eligible studies. The specific questions in the content of methods and applicability were determined and are presented in S1. The required data from scientific papers were recorded in the summary tables based on the specific questions and applied factors, including the name of the first author, year of publication, country, study outcome, study design, main results, and limitations. We did not include exposure/outcomes and significant quantitative summary statistics because of heterogeneity in the designing of systematic review study. Furthermore, quality analysis of the included studies was not undertaken.

Results

Overall, 13,083 articles were identified by designated literature search on the four abovementioned databases. After excluding duplicates, 10,900 articles were evaluated based on title and abstract. In the screening step, 10,841 were unrelated to the purpose of our study and were excluded. Finally, the remaining 59 studies were reviewed for eligibility evaluation which at the end, 43 full-text articles met the inclusion criteria (Fig. 1). Methodology, exposure, results, and assessed lag time were eligible for the systematic review and are summarized in Table 1. The analysis of the findings is summarized below.

Where were the included studies investigated and for which time periods?

The majority of the reviewed studies (67%) were performed in Bangladesh and several countries in Africa which about more than one-third of the total studies belong to Bangladesh (n =17). No scientific articles were reported upon in the developed countries in Europe and North America except one in Sweden (Table 2). Almost all of the reviewed studies were conducted in underdeveloped and developing countries. Eight publications were investigated at the national and state scale (Constantin de Magny et al. 2006; Gil et al. 2004; Ngwa et al. 2016; Ramirez and Grady 2016; Ramirez et al. 2013; Semenza et al. 2017; Stoltzfus et al. 2014; Trærup et al. 2011), twenty-eight studies provided effect estimates at the district level (Akanda et al. 2011; Akanda et al. 2009; Cash et al. 2014; Constantin de Magny et al. 2012; Eisenberg et al. 2013; Emch et al. 2010; Hashizume et al. 2008; Hashizume et al. 2013; Hashizume et al. 2010; Islam et al. 2009; Jutla et al. 2011; Koelle et al. 2005; Lama et al. 2004; Lobitz et al. 2000; Luque Fernández et al. 2009; Ohtomo et al. 2010; Pascual et al. 2000; Pezeshki et al. 2012; Rajendran et al. 2011; Ramírez 2014; Reyburn et al. 2011; Rodo et al. 2002; Ruiz-Moreno et al. 2007a; Sebastian et al. 2015; Speelmon et al. 2000; Wu et al. 2018; Xu et al. 2014), three studies were done at the several national and district scale (Constantin de Magny et al. 2008; Emch et al. 2008; Jutla et al. 2013), and five papers were at the continental scale (Constantin de Magny et al. 2007; Moore et al. 2017; Olago et al. 2007; Paz 2009; Rieckmann et al. 2018). All articles were published from 2000 to 2018.

It can be estimated that almost 95% of all published reviewed papers were reported that the cholera incidence was investigated over extended periods of time from 1960 to 2016. However, two papers were performed in India and Haiti which investigated the effect of weather variables on the cholera incidence from 1901 to 1940 and 1875 to 1900, respectively (Fig. 2). The greatest number of included papers used the time unit of months (almost 63%, n = 27) while daily,

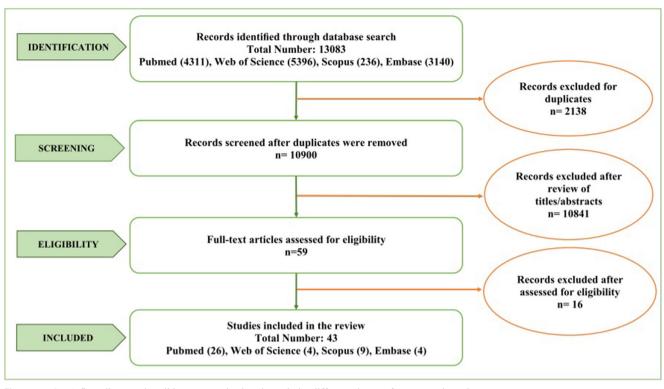


Fig. 1 PRISMA flow diagram describing paper selection through the different phases of a systematic review

weekly, seasonality, and yearly units were allocated in 11.63%, 18.60%, 2.32%, and 4.65% of studies, respectively (Fig. 3).

Which climate variables were affected cholera incidence and what were their effects?

The climate variables which have been considered in the reviewed studies included rainfall, air temperature, ENSO indices, relative humidity (RH), SST, sea surface height (SSH), river discharge, flood, drought, Indian Ocean Index (IOI)/ Indian Ocean Dipole (IOD), and chlorophyll variables (Fig. 4). Each study recognized one or more climatic variables that contributed to the cholera incidence and had a role in the transmission of the disease. Among these factors, rainfall, SST/SSH, temperature, and ENSO were the most important variables in all studies. A smaller portion of papers included other environmental variables (e.g., RH, solar activity, chlorophyll).

Rainfall More than 58% (n = 25) of the articles described the relationship between cholera incidence and rainfall, and in most of them, rainfall had an important role in cholera epidemics. A strong positive association between rainfall patterns and cholera epidemics was determined in Ghana (Constantin de Magny et al. 2006); Kolkata, India (Constantin de Magny et al. 2008); Tanzania (Reyburn et al. 2011); Ghana, Togo,

Benin, and Nigeria (west of Africa) (Constantin de Magny et al. 2007); Cameron (Ngwa et al. 2016); and Zambia (Luque Fernández et al. 2009). Furthermore, the analysis of cholera incidence in Peru between 1997 and 1998 (Ramírez 2014) and 1996 to 1999 (Ramirez and Grady 2016), with the consideration of the 1997-1998 El Niño, demonstrated that rainfall was strongly correlated with the cholera incidence, but there was no evidence of an El Niño-cholera association in the earlier part of the decade (Ramirez and Grady 2016). The daily record of the cholera cases between May and December 2005 over the 11 regions of Senegal emphasized that the dynamics of cholera disease are linked strongly with heavy rainfall during the winter season (Constantin de Magny et al. 2012). In India (Bengal), cholera cases between 1996 and 2008 were significantly correlated with moderate to highest (>7 cm) rainfall as an ideal condition for V. cholerae infection (Rajendran et al. 2011). In addition, the increased risk of cholera in Haiti (Eisenberg et al. 2013) and Peru (Ramirez et al. 2013) was associated with heavy rainfall as the most significant influenced factor. Contrary to above discussed studies, cholera incidence was negatively correlated with India rainfall at a long period in Bangladesh (Koelle et al. 2005); it was related to below average rainfall in India/Pakistan (Jutla et al. 2013), and also, it was significantly related to lower precipitation from July to December in Iran (Pezeshki et al. 2012). Several articles were found both negative and positive correlations between the cholera incidence

Table 1 Stud	lies meeting the inclusic	on criteria for	Studies meeting the inclusion criteria for systematic review (sequence based on the published year)	ice based on the pr	ublished year)		
Ref.	Author (YOP)	Study period	Country	Exposure*	Method	Effect measure**	Assessed lag
Lobitz et al.	Brad Lobitz (2000)	1980–1995	Bangladesh	SST and SSH	Unknown	I	1
Pascual et al. (2000)	Mercedes Pascual (2000)	1980–1998	1980–1998 Bangladesh	ENSO	Nonlinear time series models	r	ENSO: 11 months
Speelmon et al. (2000)	E. C. Speelmon (2000)	1997–1998 Peru	Peru	Temperature	Regression analysis	I	Temperature: 3 weeks
Rodo et al. (2002)	Xavier Rodo (2002)	1980-2001	1980–2001 Bangladesh	ENSO	Singular spectrum analysis (SSA), maximum entropy method (MEM). time series analysis	r	ENSO: 8 months
Gil et al. (2004)	Ana I. Gil (2004)	1997–2000	Peru	SST	Linear regression models	I	Ι
Lama et al. (2004)	Javier R. Lama (2004)	1991–1998	Peru	ENSO, temperature	Multiple regression analysis	r	1
Koelle et al. (2005)	Katia Koelle (2005)	1966–2002	Bangladesh	Rainfall, ENSO, SST	Time series analysis	L	(Long period) Rainfall = 14 months@@(Sh- ort period) SST = 10 months, ENSO = 9 months
Constantin de Magny et al. (2006)	Guillaume Constantin de Magny (2006)	1975–1995 Ghana	Ghana	LSTA, rainfall, IOI	Incidence time series (wavelet analysis)	IRR	Rainfall = -0.75 months, LSTA = 5.7 months
Constantin de Magny et al. (2007)	Guillaume Constantin de Magny (2007)	1975–2002	1975–2002 West Africa	Rainfall, IOI	Wavelet analysis and derived methods	I	1
Olago et al. (2007)	Daniel Olago (2007)	1978–1999 East Africa	East Africa	ENSO, temperature, flood, streamflow	Kendall's tau-b correlations	×	1
Ruiz-Moreno et al. (2007a)	Diego Ruiz-Moreno (2007a)	1901–1940 India	India	Rainfall	Cluster analysis/spatial correlation analysis	Moran's index	Rainfall: zero lag
Constantin de Magny et al. (2008)	Guillaume Constantin de Magny (2008)	1998–2006	1998–2006 India@@Bangladesh	Rainfall, SST, CHL	A generalized linear model (GLM) (ordinary linear re- gression) with a Poisson distribution, self-controlled case series method	β coefficient	CHL: 1 month
Emch et al. (2008)	Michael Emch (2008)	1983–2003	1983–2003 Bangladesh@@Vietnam Rainfall, SST, CHL, temperature and river discharge	Rainfall, SST, CHL, temperature, and river	Bivariate and multivariate statistical models	I	CHL: 2 months in Bangladesh@@Rainfall: 2 months in Vietnam
Hashizume et al.	MasahiroHashizu (2008)	1996–2002	1996–2002 Bangladesh	Rainfall	Poisson regression models		

Table 1 (continued)	tinued)						
Ref.	Author (YOP)	Study period	Country	Exposure*	Method	Effect measure**	Assessed lag
(2008)						eta coefficient	Increasing rainfall: 0 to 8 weeks.@@Decreasing rainfall: 0 to 16 weeks.
Akanda et al. (2009)	Ali Shafqat Akanda (2009)	1980–2000 Bangladesh	Bangladesh	Seasonal flow, drought, flood, and river	Pearson and Kendall's tau-b correlations	<i>.</i> .	I
Fernandez et al. (2009)	Miguel Ángel Luque Fernández (2009)	2003–2006 Zambia	Zambia	unscutatinge Rainfall and temperature	Poisson auto-regressive model	RR	Temperature: 6 weeks, rainfall: 3 weeks
Islam et al. (2009)	M.S. Islam (2009)	1989— 2005	Bangladesh	Temperature, RH, rainfall, and sunshine hours	Classification and regression tree@ @Principal component analysis (PCA)	I	1
Paz (2009)	Shlomit Paz (2009)	1971–2006	Southeastern Africa	Temperature and SST	Poisson regression model	eta coeffi- cient	I
Emch et al. (2010)	Michael Emch (2010)	2003-2007 Bangladesh	Bangladesh	SST, SSH, and CHL	Generalized estimating equations (GEE)	OR	I
Hashizume et al. (2010)	MasahiroHashizume (2010)	1983–2008 Bangladesh	Bangladesh	Temperature, high, and low rainfall	Poisson regression model	AF	High rainfall: 0–8 weeks@@Low rainfall: 0–16 weeks@@Temperature: 0–4 weeks
Ohtomo et al. (2010)	K. OHTOMO (2010) 1980–1998 Bangladesh	1980–1998	Bangladesh	SST, solar activity	Time series analysis, singular spectrum analysis (SSA), maximum entropy method (MEM), nonlinear least converse method (7 CM)		-
Akanda et al. (2011)	Ali Shafqat Akanda (2011)	1980–2007 Bangladesh	Bangladesh	SST, CHL, streamflow, flood	Linear multivariate regression analysis	~	I
Jutla et al. (2011)	Antarpreet Jutla (2011)	1997–2009	1997–2009 Bangladesh	SST	Wavelet analysis	r	I
Rajendran et al. (2011)	dran (2011)	1996–2008 India	India	RH, temperature, and rainfall	Seasonal auto-regressive integrated moving average (SARIMA) model	r	I
Reyburn et al. (2011)	Reyburn et al. RitaReyburn (2011) (2011)	1997–2006 Tanzania	Tanzania	RH, temperature, rainfall, SST, SSH, CHL	Seasonal auto-regressive integrated moving average (SARIMA) model		Minimum temperature: 2-4 months@@Maximum temperature: 2 months@@RH: 5 months@@Rainfall: 1 month
Trærup et al. (2011)	Sara L. M. Trærup (2011)	1998–2004 Tanzania	Tanzania	Temperature and rainfall	Negative binomial regression	RR	Temperature: 1 month

Table 1 (cont	(continued)						
Ref.	Author (YOP)	Study period	Country	Exposure*	Method	Effect measure**	Assessed lag
Constantin de Magny et al. (2012)	Guillaume Constantin de Magny (2012)	2005	Senegal	Rainfall	Cross-correlation analysis	IR	Rainfall: 23 days
Pezeshki et al. (2012)	Z Pezeshki (2012)	1997–2006 Iran	Iran	Temperature, rainfall, RH	Binominal multivariate binary logistic regression and bivariate correlation	eta coefficient	1
Eisenberg et al. (2013)	Marisa C. Eisenberg (2013)	2010–2011 Haiti	Haiti	Rainfall	Distributed lag nonlinear models, "SIWR" model	OR	Heavy rainfall:6-7 days
Hashizume et al. (2013)	Masahiro Hashizume 1983–2008 Bangladesh (2013)	1983–2008	Bangladesh	ENSO, IOD	Cross-wavelet coherency analysis	r	1
Jutla et al. (2013)	Antarpreet Jutla (2013)	1875–1900	1875–1900 India, Pakistan, Haiti	Temperature, rainfall	Time series analysis	r, OR	Rainfall: 6 days@@Temperature: 2 months
Ramirez et al. (2013)	Iva'n J. Ramirez (2013)	1990–1992	Peru	SST, rainfall, ENSO	Time series analysis, Pearson analysis	r	I
Cash et al. (2014)	Benjamin A. Cash (2014)	1979–1995	Bangladesh	SST, ENSO	Spearman rank correlations	r	I
Ramírez (2014)	Iva'n J. Ramírez (2014)	1997–1998 Peru	Peru	SST, rainfall, temperature, ENSO	Ordinary least squares (OLS) regression	L	SST: 0–1 month@@Rainfall: 1 month@@Mean and maximum temperatures: 5 months
Stoltzfus et al. (2014)	James D Stoltzfus (2014)	1999–2009 Kenya	Kenya	Rainfall	Multivariate analysis	RR	I
Xu et al. (2014)	Min Xu (2014)	1999–2008	China	SST, SSH, CHL	Nonparametric Spearman correlation	r	SST: 2 months@@SSH: 1 month@@CHL: 2 months
Sebastian et al. (2015)	Tunny Sebastian (2015)	2000–2010 India	India	Rainfall, temperature, RH	Time series models (auto-regressive model, seasonal auto-regressive integrated moving average model (SARIMA), segmented regression model, and har- monic regression mode)		I
Ngwa et al. (2016)	Moise C. Ngwa (2016)	2000–2012	Cameroon	Rainfall, temperature	Spatiotemporal auto-regressive Poisson regression model and spatial cluster analysis	IRR	Rainfall: 2 weeks@@Temperature: 2 weeks
Ramirez and Grady (2016)	Ivan J. Ramirez (2016)	1991–2001 Peru	Peru	SST, ENSO, rainfall, air temperature, and river discharge	Cross-wavelet coherency analysis (continuous wavelet transforms (CWT), cross-wavelet transform (XWT) and wavelet coherence (WTC), and mediating analysis) and ordinary least squares (OLS) regression	β coefficient	Rainfall: 1 month@@SST: 4-6 months@@Temperature: 6 months@@River discharge: 0 month
Moore et al. (2017)	Sean M. Moore (2017)	2000–2014 Africa	Africa	ENSO, rainfall	Linear regression models	I	1

Table 1 (continued)	tinued)						
Ref.	Author (YOP)	Study period	Country	Exposure*	Method	Effect measure**	Assessed lag
Semenza et al. (2017)	Jan C. Semenza (2017)	2006–2014 Swedish	Swedish	SST	Conditional logistic regression model	RR	SST: 2 weeks
Rieckmann et al. (2018)	Andreas Rieckmann 1990–2010 Sub-Saharan Africa (2018)	1990–2010	Sub-Saharan Africa	Droughts and floods	Self-controlled case series (SCCS)	IR	I
Wu et al. (2018)	Jianyong Wu (2018) 1983-2009 Bangladesh	1983–2009	Bangladesh	Rainfall	Conditional logistic regression models	OR	Rainfall: 2 days
*Sea surface te Ocean Index (]	*Sea surface temperature (SST), sea surface hei Ocean Index (IOI), Indian Ocean Dipole (IOD)	urface height (ble (IOD)	(SSH), El Niño/Southern C	Dscillation (ENSO)	*Sea surface temperature (SST), sea surface height (SSH), El Niño/Southern Oscillation (ENSO), CHL (chlorophyll), relative humidity (RH), LSTA (land and sea surface temperature anomalies), Indian Ocean Index (IOI), Indian Ocean Dipole (IOD)	and sea surfa	ce temperature anomalies), Indian

**Risk ratio (RR), incidence rate ratio (Memish et al. 2014), odds ratio (OR), attributable fraction (AF), incidence rate (IR)

and rainfall because of complex rainfall-cholera relationship and also spatial and temporal variations. In India, a negative correlation was observed between cholera and rainfall in the southern region of Madras, while a positive association was found in the northeast cluster (Ruiz-Moreno et al. 2007a). In Dhaka, Bangladesh, the number of cholera cases was increased from 14 to 24% for each 10 mm increase and decrease in rainfall above and below the threshold (45 mm), respectively (Hashizume et al. 2008). In another study in Bangladesh, at the end of the monsoon, increasing rainfall caused a peak in cholera disease, while in the spring, decreasing rainfall predicted growth in the number of cholera cases (Hashizume et al. 2010). Cholera in Kenya had a negative association with rainfall from April to June, but it was changed to a positive relationship between October and December (Stoltzfus et al. 2014). During El Niño periods in the regions of East Africa, the higher cholera disease rates were observed during the peak of rainfall months, while in some regions, there was a negative association between rainfall and cholera occurrence (Moore et al. 2017). In some cases, no significant association was detected between cholera incidence and rainfall (Islam et al. 2009; Trærup et al. 2011; Wu et al. 2018). The results of a study on Cholera in Bangladesh and Vietnam illustrated that rainfall was not associated with cholera in Bangladesh, while rainfall decrease the possibility of cholera outbreaks by 4-7% in Hue, Vietnam, and increase the probability of cholera by 10% in Nha Trang, Vietnam (Emch et al. 2008). In India, there was a significant positive correlation between rainfall and the number of cholera cases during 2000-2004, but there was not found any correlation between 2005 and 2010 (Sebastian et al. 2015). Similar findings of these disconnected connections were also found in Peru (Ramirez and Grady 2016). This highlights the nonstationarity of climate and cholera link. In some regions, rainfall was influenced by ENSO events and the intermittent warming of surface waters in the equatorial Pacific Ocean which are discussed in the next section.

Air temperature We assessed 17 articles that examined the association between air temperature and cholera infection rates. Although, different definitions were applied by these articles, including minimum, mean, and maximum temperatures over yearly, monthly, weekly, and daily periods. The analysis results in different studies demonstrated that temperature rising positively affects the variability of the cholera incidence in Peru (Speelmon et al. 2000), several countries in East Africa (Kenya, Tanzania, Uganda) (Olago et al. 2007), Zambia (Luque Fernández et al. 2009), Bangladesh (Islam et al. 2009), Cameron (Ngwa et al. 2016), and also Iran (Pezeshki et al. 2012). After the strong El Niño 1997-1998 and rising the environmental temperature in Lima, Peru, the reported cholera cases were increased compared to the entire decade (Lama et al. 2004). In Southeastern Africa countries, including Uganda, Kenya, Rwanda, Burundi, Tanzania,

Africa		Asia		Americas		Europe	
Country	Number	Country	Number	Country	Number	Country	Number
Africa*	5	Bangladesh	17	Peru	6	Sweden	1
Tanzania	2	India	5	Haiti	2		
Kenya	1	Iran	1				
Cameron	1	Pakistan	1				
Senegal	1	China	1				
Zambia	1	Vietnam	1				
Ghana	1						
Total	12	Total	26	Total	8	Total	1

Table 2 Number of scientific articles included in the systematic review according to the cholera outcome in each country

*Scientific articles which have done in several counties in Africa

Malawi, Zambia, and Mozambique, cholera cases between 1971 and 2006 were multiplied by 1.87 with increasing in annual mean air temperature by 0.1 °C (Paz 2009). Lower incidence of cholera in 1983–2008 was related to lower temperatures in the first 15 weeks of the year in Bangladesh (Hashizume et al. 2010), and also, cholera cases detected between 1998 and 2004 in Tanzania had a significant positive correlation with maximum and minimum temperature

(Trærup et al. 2011). In 1875–1900, the chances of cholera epidemic in India and Pakistan increased sixfold by increasing the temperature above the average. They demonstrated that almost 50% of the cholera outbreaks happened when the air temperature is higher than 31 °C (Jutla et al. 2013). A higher number of cholera cases in the latter half of the 1990s were reported by two different studies in Piura which was correlated significantly with the mean and maximum of air temperatures

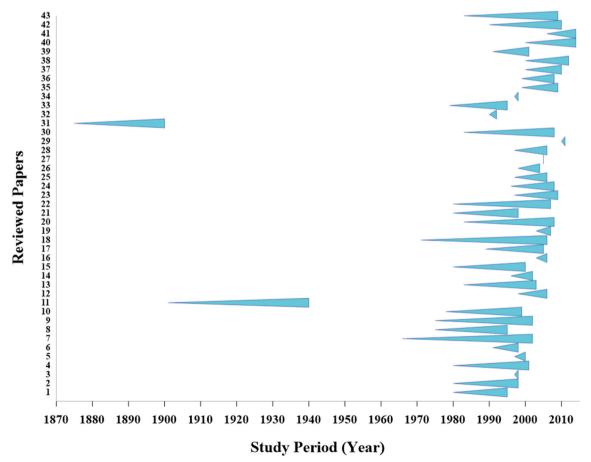


Fig. 2 The study period of scientific articles included in the systematic review

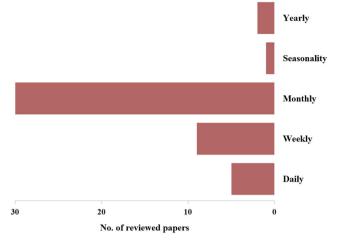


Fig. 3 Time units used in all studies included in the systematic review

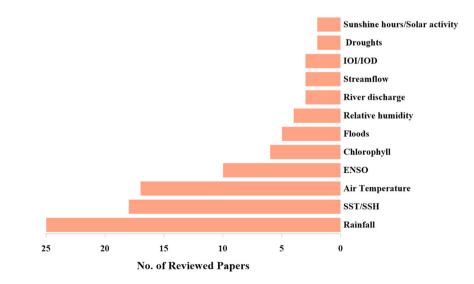
after El Niño 1997–1998 (Ramírez 2014; Ramirez and Grady 2016). There was no significant association between monthly cholera cases and temperature in Bengal and Vellore, India (Rajendran et al. 2011; Sebastian et al. 2015), and also in Bangladesh and Vietnam (Emch et al. 2008). However, the results of a study in Tanzania showed that cholera incidence had a positive and negative correlation with the minimum and the maximum temperature, respectively (Reyburn et al. 2011).

SST/SSH Cholera transmission has sometimes been influenced by SST or SSH. Out of the reviewed studies that met our quantitative inclusion criteria, 14 articles were evaluated this association with just SST, while four papers were examined the effect of both SST and SSH and cholera disease transmission. According to the reviewed studies, cholera incidence in local coastal of Bangladesh (Akanda et al. 2011; Cash et al. 2014; Koelle et al. 2005; Lobitz et al. 2000; Ohtomo et al. 2010), Peru (Gil et al. 2004; Ramírez 2014; Ramirez and Grady 2016; Ramirez et al. 2013), Swedish (Semenza et al. 2017), and China (Xu et al. 2014) were positively correlated

Fig. 4 The climate variables included in the reviewed papers

with SST/SSH. In Ghana, during a 20-year study period (1975–1995), there was a strong association between land and sea surface temperature anomalies (LSTAs) and cholera case incidence (Constantin de Magny et al. 2006). Between 1971 and 2006, in the southeastern African countries, including Uganda, Kenya, Rwanda, Burundi, Tanzania, Malawi, Zambia, and Mozambique, the cholera rates multiplied by 1.31 with 0.1 °C increase in the SST (Paz 2009). Increases in SST were the most influential on cholera outbreaks in Hue, Vietnam, whereas in Nha Trang, SSH had significant correlation with cholera incidence (Emch et al. 2008). There was not reported a significant relationship between cholera incidence and seasonal SST in Bangladesh (Emch et al. 2008; Emch et al. 2010; Jutla et al. 2011). Although, Emch et al. was found a negative significant correlation between cholera incidence and SSH during the pre-monsoon period (Emch et al. 2010). Reyburn et al. did not detect any effect of SST and SSH on cholera disease in Tanzania (Reyburn et al. 2011), and Constantin de Magny et al. removed the factor of SST from their applied model in Bangladesh because of an anomaly in the single grid point or the 5° grid box mean (Constantin de Magny et al. 2008).

ENSO More than 23% of reviewed studies examined the observed or the modeled ENSO in their analysis in which half of them were conducted in Bangladesh (n = 5). Although, most of the studies examined the warm phase of ENSO, El Niño. Analysis of monthly cholera between 1980 and 1998 in Bangladesh by Pascual et al., as the first to quantify the ENSO–cholera link, showed that changes in the atmospheric circulation of south Asia led to regional temperature anomalies and subsequently the influence of ENSO on cholera incidence (Pascual et al. 2000). This observation was confirmed by another study that analyzed the cholera cases in Bangladesh from 1980 to 2001 and found a strong association between cholera and ENSO events in the last 20 years (1980–



2001) (Rodo et al. 2002). However, cholera cases which had been detected between 1991 and 1998 in Peru were not linked with ENSO (Lama et al. 2004). Cholera transmission demonstrated an obvious interannual variation with the strong correlation by SST in the Bay of Bengal and ENSO in a short period of time (under 7 years), during 1966-2002 in Bangladesh (Koelle et al. 2005). In addition, the relationship between cholera hospitalizations and the ENSO did not remain constant during 25 years (1983-2008) in Bangladesh and 5-6-year long coherent cycles between ENSO and cholera rates were indicated (Hashizume et al. 2013). The results of another study in Bangladesh have shown that the increasing in monsoon rainfall and SST corresponded to ENSO event and led to an increase in the post-monsoon cholera outbreaks (Cash et al. 2014). Two different studies were performed in Peru: first, of the period 1990–1992, the cholera emergence contributed to ENSO neutral (La Niño) conditions rather than El Niño (Ramirez et al. 2013) and, in the second one, it was reported that a strong link existed between El Niño and cholera cases in the latter part of the 1990s while no correlation was found in the earlier part of the decade (Ramirez and Grady 2016). In another study in Peru, climate anomalies during the 1997-1998 El Niño such as the rising in sea surface level and air temperatures (by several months) and also increasing the amount of rainfall and decreasing the maximum temperature (concurrent) caused a rise in cholera infection in 1998 (Ramírez 2014). Essentially, the ENSO link was mediated or facilitated by rainfall, demonstrating a connection between global and local climate. SST rising change rainfall pattern inland in coastal Peru and other regions which can effect on cholera incidence (Ramirez and Grady 2016). The analysis of cholera incidence in East Africa between 1978 and 1999 (Olago et al. 2007) and 2000-2014 (Moore et al. 2017) indicated that El Niño events and related rainfall had close positive association with cholera disease outbreak.

Chlorophyll Out of the reviewed studies that met our quantitative inclusion criteria, 6 papers were evaluated the correlation between chlorophyll concentration and cholera disease. The cholera incidence in India (Kolkata) and also in Bangladesh (Matlab) of the period of 1998-2006 had a statistically significant relationship with chlorophyll concentration (Constantin de Magny et al. 2008) which was similar to the relationship of chlorophyll values and cholera prevalence in Bangladesh (Akanda et al. 2011; Emch et al. 2008). However, these relationships were not seen in Tanzania (1997-2006) (Reyburn et al. 2011) and Vietnam (1983–2003) (Emch et al. 2008). In another study in Matlab, Bangladesh, ocean chlorophyll concentration was positively correlated with cholera during the pre-monsoon period, while there was no relationship during the post-monsoon period (Emch et al. 2010). Although the simultaneous ocean concentration of chlorophyll had no significant association with the cholera incidence in China, the correlation became stronger as time was delayed (Xu et al. 2014).

River discharge, flood, drought, and streamflow Correlation of the cholera incidence with flood (n = 5), river discharge (n = 3), drought (n = 2), and streamflow (n = 3) was assessed in some studies. In a 20-year study period (1990-2010) performed in sub-Saharan Africa, the cholera outbreak happened in one of every 15 floods and one of every three droughts. Floods and droughts were known as the most notable factors associated with cholera outbreaks; however, due to long durations of drought, the prevalence of cholera outbreaks was higher during this phenomenon (Rieckmann et al. 2018). During cholera outbreaks in Bangladesh between 1890 and 2000, spring cholera outbreaks were negatively related to streamflow, but cholera rates in autumn were positively correlated to streamflow. In contrast, the highest cholera cases in spring were observed during the strong drought years, while the most autumn number of cholera cases was detected in high flood years (Akanda et al. 2009). In a study that was conducted in three African countries (Kenya, Tanzania, and Uganda), cholera incidence in long rains season occurred during flood and streamflow, while throughout El Niño years, it was coincided with high streamflow peaks in September, October, November, and December. This pronouncement emphasizes on the significant relationship between cholera rates and flooding during these months (Olago et al. 2007). According to the results of cholera outbreaks analysis (1980-2007) in Bangladesh, streamflow and flood in July, August, September, and October months had a remarkable positive effect on the cholera incidence in summer and fall seasons, but this relationship was not detected during wet season (Akanda et al. 2011). The analysis results of a study in Peru demonstrated that river discharge was strongly correlated with cholera incidence (Ramirez and Grady 2016). This relationship was negative in Bangladesh (Akanda et al. 2009; Emch et al. 2008), while river discharge had a positive effect on cholera in Nha Trang, Vietnam (Emch et al. 2008).

Other environmental variables A small proportion of reviewed papers assessed the function of other environmental factors such as RH (n = 4), IOI/IOD (n = 3), and solar activity (n = 2) on the cholera occurrence (Fig. 4). The cholera incidence was negatively correlated with solar activity from 1980 to 1998 in Bangladesh (Ohtomo et al. 2010), while further studies have revealed that monthly cholera occurrence was positively associated with sunshine hours (Islam et al. 2009). Moreover, no significant correlation was found between mean of relative humidity and cholera cases in India (2000–2010) (Sebastian et al. 2015). Conversely, in another study in India that examined the cholera outbreaks during 1996–2008, monthly average of relative humidity was related to increases in the cases of cholera disease during monsoon season

(Rajendran et al. 2011). In addition, a similar relationship was found in Tanzania between 1997 and 2006 (Reyburn et al. 2011). The cholera incidence in India (Kolkata) and also in Bangladesh (Matlab) between 1998 and 2006 had a statistically significant relationship with chlorophyll concentration (Constantin de Magny et al. 2008) which was similar to the relationship of chlorophyll values and cholera prevalence in Bengal Delta region of Bangladesh (Akanda et al. 2011). However, these relationships were not seen in Tanzania (1997-2006) (Reyburn et al. 2011). Although the simultaneous ocean concentration of chlorophyll had no significant association with the cholera incidence in China, the correlation became stronger as time was delayed (Xu et al. 2014). The investigated relationship between cholera cases and Indian Ocean Dipole index in Dhaka and Matlab, Bangladesh (1983–2008), showed that cholera outbreaks were associated with the strength of the IOD (Hashizume et al. 2013). In two different studies that were conducted in various country in Africa, IOI was significantly correlated with cholera incidence during the early 1990s in the 2- to 4-year periodic band (Constantin de Magny et al. 2007) and in the 2-3vear periodic band from 1989 to 1995 (Constantin de Magny et al. 2006).

What methods and effect measures have been used in the reviewed studies?

As demonstrated in Fig. 5, the most commonly used methods in the reviewed studies were time series analysis, generalized linear model (GLM), regression analysis, and spatial/GIS. As can be seen from Fig. 6, the applied effect measures were shown in the reviewed papers. Almost 44% of studies have used coefficient of correlation (r) to assess the association between the cholera incidence and climatic variables. The rest of studies were reported outcome measures by using beta coefficient (β), risk ratio (RR), incidence rate ratio (Memish et al. 2014), odds ratio (OR), attributable fraction (AF), incidence rate (IR), and Moran's Index.

Out of the selected studies, seven of them have used the time series models to investigate the effect of climate factors on the cholera incidence. These models was applied to analyze time series data and extract significant statistics and other characteristics of the data (Rangaswamy et al. 2013). A non-linear time series approach was fitted by Pascual et al. to evaluate the specific functions of the underlying factors such as ENSO in the cholera incidence in Bangladesh by reporting r as the effect measure (Pascual et al. 2000). In another study in Bangladesh, three different techniques were used to demonstrate the correlation between cholera rates and ENSO event during 21 years (1980–2001) including, singular spectrum analysis (SSA) for isolation of the interannual variability data, maximum entropy method (MEM) for determination of frequencies in the interannual patterns, and the time series

analysis for quantification the strength of the relationship between cholera and ENSO with the effect measure of r (Rodo et al. 2002). Koelle et al. (2005), Jutla et al. (2013), and Ramirez et al. (2013) also applied a time series method to determine the association between local climatic variables and cholera by using the coefficient of correlation (r) and OR. The time series analysis method was used to investigate the extensive periodic structure of cholera cases as well as the association between cholera rate, solar activity, and El Niño. This method was exerted alongside with spectral analysis based on maximum entropy method (MEM) as a nonlinear least squares (LSM) method. They used Kendall's τb and Spearman's ρ as correlation coefficients (Ohtomo et al. 2010). Similarly, of the period 2000-2010 in Peru, different methods of time series models such as Seasonal Auto-Regressive Integrated Moving Average (SARIMA) model, segmented regression model, auto-regressive model, and harmonic regression model were used (Sebastian et al. 2015).

The generalized linear model (GLM) is a flexible generalization of linear regression which can be applied to find highest likelihood estimation of parameters with observations (Nelder and Wedderburn 1972). The GLM with different distribution models, i.e., negative binomial and Poisson regression models, was applied in seven studies. Poisson regression models have been used to determine the possible correlation between cholera disease and climatic variables. In a study assessing the cholera outbreaks in sub-Saharan Africa, selfcontrolled case series method was used as a sensitivity analysis by adjusting the time-fixed confounding between countries. This method was inspired by the case crossover design applying Poisson regression of the countries with just cholera outbreaks (Constantin de Magny et al. 2008). In another study in southeastern Africa, the possible relationship between cholera and the annual variability of SST and air temperature of the period 1971-2006 was estimated by Poisson Regression Model (Paz 2009). The effect measure in both aforementioned studies was standardized by coefficients or β coefficients. Hashizume et al. conducted two different studies to investigate the correlation between weather factors and cholera cases using Poisson regression models over the period of 1996 to 2002 (Hashizume et al. 2008) and 1983-2008 (Hashizume et al. 2010) in Bangladesh; moreover, the effect measures were β coefficients and AF, respectively. This method also was applied to assess the significant associations between cholera and climatic factors in Zambia (RR) (Luque Fernández et al. 2009), Tanzania (RR) (Trærup et al. 2011), and Cameron (Memish et al. 2014; Ngwa et al. 2016).

In statistical modeling, regression analysis is used to evaluate the relationships between a dependent variable and one or more independent variables. It also widely used for prediction and forecasting a phenomena. Linear regression is the most common form of regression analysis which the correlations are modeled by linear predictor functions (Freedman 2009).

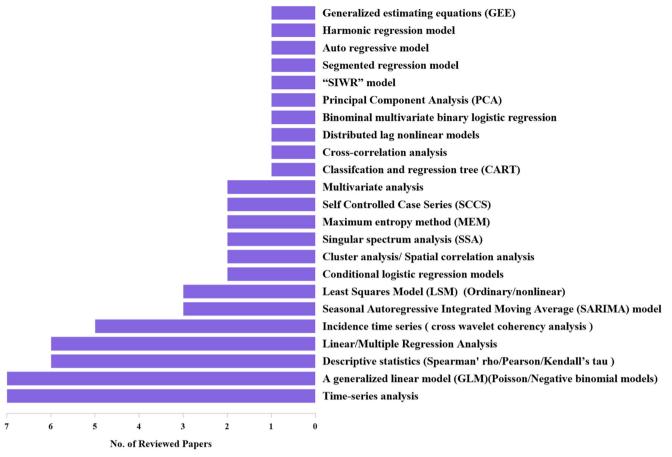


Fig. 5 The used data analysis methods included in the review papers

Lama et al. used multiple linear regression models to assess the associations between ENSO and temperature and also cholera incidence in Peru for the years of 1991–1998 (Lama et al. 2004). In another study in Peru, regression analysis was applied to assess the impact of higher air temperatures associated with the 1997–1998 El Niño event on the increasing of environmental *V. cholerae* and 1998 cholera outbreak (Speelmon et al. 2000). Statistical analysis with linear regression demonstrated that cholera outbreaks occurred in the summer of 1998 were associated with the SST peak (Gil et al.

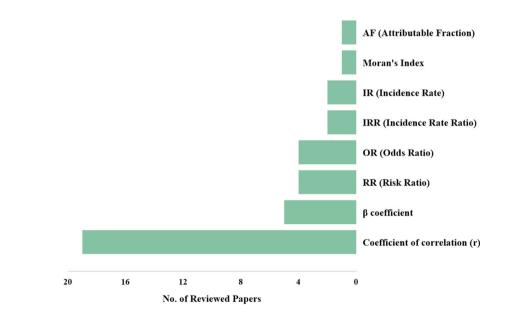


Fig. 6 The applied effect measure included in the reviewed papers

2004). Linear multivariate regression analysis was applied to describe the influences of hydroclimatic on cholera transmission cycles (1980–2007) in Bangladesh (Akanda et al. 2011). Linear regression model also was applied to estimate the effects of ENSO, rainfall, and flood related changes in cholera incidence in Africa from 2000 to 2014 (Moore et al. 2017). Five reviewed studies have exerted descriptive statistics such as quantitative measures of dependence included Spearman' rho (Cash et al. 2014; Xu et al. 2014), Pearson (Akanda et al. 2009; Ramirez et al. 2013), and Kendall's tau (Akanda et al. 2009; Olago et al. 2007) to assess the impact of climate variables on cholera incidence.

Cluster/spatial correlation analysis was also applied in studies that investigated in India (with an effect measure of Moran's Index) (Ruiz-Moreno et al. 2007a) and Cameron (Ngwa et al. 2016) to report cholera cases during 1901–1940 and 2010-2011, respectively. Conditional logistic regression model and also correlations were used to investigate climatic triggers, causing cholera disease in Sweden during 2006-2014 (Semenza et al. 2017) and in Bangladesh of the period 1983–2009 (Wu et al. 2018), as well as the correlations were estimated with effect measures of RR and OR, respectively. Cross-wavelet coherency analysis, as a data analysis technique (geological time series), is a helpful mathematical tool to detect the evolution of the nonstationarity series (with the periodic behavior) and allow quantification of periodicity associations between time series. In addition, this method has been used to investigate the ecological and epidemiological spatial as well as temporal dynamics of disease (Constantin de Magny et al. 2007; Rohani et al. 2003). This technique was applied to examine the effect of climate variability on cholera treats in Ghana during 1975-1995 (Memish et al. 2014; Constantin de Magny et al. 2006) and on cholera dynamics in Bangladesh between 1983 and 2008 (r) (Hashizume et al. 2013) and 1997 to 2009 (r) (Jutla et al. 2011) and in Peru for the period 1991–2001 (β coefficients) (Ramirez and Grady 2016). The wavelet analyses were applied to assess the association of cholera incidence across the five West African countries with IOI and rainfall (Constantin de Magny et al. 2007). In modeling seasonal time series with nonstationary statistics for a specified season across the years, SARIMA model is helpful (Abraham and Ledolter 2008). Out of the studies, two different studies in India applied SARIMA model to examine the effect of rainfall, temperature, and relative humidity on cholera disease during 1996–2008 in Bengal (r)(Rajendran et al. 2011) and between 2000 and 2010 in Vellore (r) (Sebastian et al. 2015). Reyburn et al. were investigated the relationship between relative humidity, temperature, rainfall, SST/SSH, and CHL on cholera outbreaks between 1997 and 2006 in Tanzania (Reyburn et al. 2011) by reporting r as the effect measure. Thirteen of forty-three reviewed articles used less commonly analytical methods which included least squares models (LSM) (r) (Ohtomo et al. 2010; Ramírez 2014; Ramirez and Grady 2016); generalized estimating equations (GEE) (Emch et al. 2010); singular spectrum analysis (SSA) and maximum entropy method (MEM) (r) (Ohtomo et al. 2010; Rodo et al. 2002); self-controlled case series (SCCS) (IR and β) (Constantin de Magny et al. 2008; Rieckmann et al. 2018); classification and regression tree (Stoltzfus et al. 2014); principal component analysis (PCA) (Islam et al. 2009); cross-correlation analysis (IR) (Constantin de Magny et al. 2012); distributed lag nonlinear models, "SIWR" model (OR) (Eisenberg et al. 2013); binominal multivariate binary logistic regression (β) (Pezeshki et al. 2012); segmented regression model, auto-regressive model, Harmonic regression model (r) (Sebastian et al. 2015); bivariate and multivariate statistical models (Emch et al. 2008); and multivariate analysis (RR) (Stoltzfus et al. 2014).

How long the temporal lag has been identified in the reviewed studies?

More than 50% of reviewed studies quantified the temporal lag for the happening/changing the weather conditions to the cholera disease detection. The lag timings assessed in variation periods by published papers for different climatic variables in spite of the same disease. Monthly scales highlighted as the importance of lag time in many studies. The analyzed lag times effects in cholera rates varied extensively by weather conditions and region (e.g., region with dry weather or abundant rain). Therefore, the lags of rainfall effects were varied between 0 and 14 months in India (Ruiz-Moreno et al. 2007a) and Bangladesh (Koelle et al. 2005). Moreover, in two different studies in Haiti, there was a rainfall-cholera relationship at a lag of 6 days (Eisenberg et al. 2013; Jutla et al. 2013). A time lag of 15-30 days was observed between rainfall and cholera incidence in Cameron (Ngwa et al. 2016), Senegal (Constantin de Magny et al. 2012), Zambia (Luque Fernández et al. 2009), Ghana (Constantin de Magny et al. 2006), and Tanzania (Reyburn et al. 2011). There was also a delay effect of 0 to 8 weeks for increase rainfall above the threshold (45 mm) and a time lag of 0 to 16 weeks for decrease rainfall below the same threshold in Bangladesh during cholera outbreaks in 1996-2002 (Hashizume et al. 2008). In other cholera investigations in Bangladesh, low rainfall caused a cholera peak in spring with 0-16 weeks lag and high rainfall led to a peak at the end of the monsoon with 0-8 weeks (Hashizume et al. 2010). In Piura, coastal area in northern Peru, a time lag of 1 month was observed between rainfall and cholera incidence during the 1997-1998 El Niño (Ramírez 2014; Ramirez and Grady 2016), While the lag effect of rainfall on cholera incidence in Vietnam was estimated at 2 months (Emch et al. 2008).

The lag effect of air temperature on cholera incidence was evaluated in eight reviewed studies. The lowest lag time was attributed to a study in Cameron with 2 weeks (Ngwa et al. 2016) and followed by Peru with 3 weeks (Speelmon et al. 2000). It was also estimated 0-4 weeks in Bangladesh (Hashizume et al. 2010), 4 weeks in Tanzania (Trærup et al. 2011), 6 weeks in Zambia (Luque Fernández et al. 2009), and 8 weeks in India (Jutla et al. 2013). The results of air temperature-cholera correlation in Tanzania have shown that cholera cases were negatively associated with maximum temperature with 2 months lag and positively associated with minimum temperature with 2-4 months (Reyburn et al. 2011). The highest lag time between air temperature and cholera incidence was observed in Peru with 6 months during 1991–2001 (Ramirez and Grady 2016), while it was 5 months for the mean and the maximum temperatures in the same region between 1997 and 1998 (Ramírez 2014). The lag effect of ENSO on cholera incidence estimated in three studies in Bangladesh with 11 months (Pascual et al. 2000), 8 months (Rodo et al. 2002), and 9 months (Koelle et al. 2005). The lag effect of RH was assessed in only one paper, in which the results demonstrated that cholera outbreaks were positively correlated with humidity at a lag of 5 months (Reyburn et al. 2011). Chlorophyll also was evaluated in India/Bangladesh (Constantin de Magny et al. 2008) with 5 months lag and in China (Xu et al. 2014) and Bangladesh (Emch et al. 2008) with 2 months lag. The lag effect of SST/SSH on cholera outbreaks was in the minimum with 2 weeks in Swedish (Semenza et al. 2017), while it was in the maximum in Bangladesh with 10 months (Koelle et al. 2005). In two studies in Peru, significant associations were observed between SST and cholera transmission at lag 0–1 month (1997–1998) (Ramírez 2014) and 4-6 months (1991-2001) (Ramirez and Grady 2016). There was also a delay effect of 2 months for SST and 1 month for SSH during cholera incidence between 1999 and 2008 in China (Xu et al. 2014) and 5.7 months lag between LSTA and cholera incidence in 2-3 periodic band during 1989-1995 in Ghana (Constantin de Magny et al. 2006).

Discussion

This review has recognized forty-three analytical research studies to identify the climate change effects as the biggest health threat on cholera disease rate. Our study included only systematic review which investigated the relationship between cholera incidences accrued during widely time period in the different regions of the world to climate change factors in reviewed published papers. Rebaudet et al. evaluated the effects of the environmental determinants on cholera epidemics as a systematic review in just inland Africa (Rebaudet et al. 2013). We endeavor to provide a comprehensive evaluation of the cholera incidence/prevalence related to climate change and also report the knowledge gaps of relevant current published papers.

It was depicted that most cholera cases recorded in coastal areas such as Bangladesh, India, and Southeastern Africa countries. It could be related to the natural presence of the bacterium V. cholerae in coastal, riverine, and estuarine ecosystems in which climatic changes alter its distribution and occurrence (Constantin de Magny et al. 2008). Five impressive features that have altered the outbreak patterns of infectious disease, including cholera, are river basins, agriculture, tourism, coastal systems, and human health. The changes in climate change variables can extremely change these five factors. However, the disease patterns are different in some regions of the world. For instance, European countries are exposed to the climatic change effects, but cholera is not an important public health problem (Deen et al. 2020). According to previous literature, there are several important similarities such as the risk factors, the transmission routes, and the dynamics of cholera in areas worldwide where the infection happens, but there are also vital differences in the rate of disease. In Eastern Asia, cholera infection has seasonal recurrence. In Yemen, cholera infection outbreak is unexampled and is still continuing. Some areas of sub-Saharan Africa have become endemic for the infection, while other parts have apparently unforeseeable outbreaks. For several years, the cholera is absent in the Americas but the infection has now become endemic in some parts like Haiti. All in all, the worldwide cholera picture continues to develop and will likely change in the ongoing years. However, it seems that in the coming time, cholera infection will continue to affect pauperized populations without proper access to safe and adequate water and also sanitation (Ciscar et al. 2011; Deen et al. 2020).

In the tropical Indian Ocean, variability in interannual climate could lead to sea level anomalies, changes in rainfall patterns and flooding (Hashizume et al. 2013). In other words, elevated rainfall and flooding were known as the intermediate factors between SST anomalies and cholera incidence (Cash et al. 2008; Cash et al. 2010; Ramirez and Grady 2016). During four monsoon months, heavy rainfall led to flooding and opened mixing of water between rivers, sewers, drains, and water reservoirs which caused contamination of water bodies on the submerged areas with V. cholerae (Akanda et al. 2011; Akanda et al. 2009; Jutla et al. 2013). Heavy rains also can cause nutrient runoff, leading to plankton bloom changes in coastal areas (Ramirez et al. 2013). This enables that the bacteria's survival may increase with washing away of predators of V. cholerae during heavy rainfall, enhancing potentially the exposure rates. (Ramirez and Grady 2016). Furthermore, the destruction of sanitation facilities such as water and wastewater systems during flooding facilitated the mixing of sewage with surface and ground waters and increased the risk of population exposure with contaminated water by V. cholerae especially in a society with poor availability to safe water (Curriero et al. 2001; Jutla et al. 2013). The rainfall with complex pathways can have a dual role in cholera transmission. Cholera incidence can reduce organism concentrations due to a dilution effect of rainfall or increase contamination of water supplies by flooding (Ramirez and Grady 2016). In another way, during low rainfall periods or in the dry seasons, limited access to safe and sufficient water and thereby lack of hygiene and adequate sanitation concerns led to increasing the risk of cholera disease outbreak in the exposed population (Hashizume et al. 2010; Rieckmann et al. 2018). Indeed, water scarcity in the dry seasons because of the reduced volume of streamflow resulted in the intrusion of salinity front followed by planktons moving toward the inland freshwater and finally provides a proper condition for V. cholerae growth (Akanda et al. 2011; Hashizume et al. 2013). Although, several studies have shown that both increased and decreased rainfalls in the same region and same time period are determining factors in rising the cholera incidence (Hashizume et al. 2008; Hashizume et al. 2010; Moore et al. 2017; Ruiz-Moreno et al. 2007a; Stoltzfus et al. 2014). Overall, floods and droughts could affect the bacterium concentration in the human surrounding environment, the survival of the organisms (through effects on nutrient availability, salinity and pH), human exposure to the bacterial pathogen, sanitary environment, and susceptibility to the infection (Hashizume et al. 2008). Moreover, within regions where these climate parameters existed to maintain cholera transmission, seasonal variations in these factors could be the main determinants of the intensity and duration of transmission (Hashizume et al. 2010; Pascual et al. 2000; Sebastian et al. 2015).

Changing in the environmental factors could influence sea surface temperature (SST), rainfall, nutrient availability, salinity, and sea surface height (Xu et al. 2014). Warm phase of ENSO, El Niño, also has potential impact on cholera transmission through sea and air temperatures with their effects on the phytoplankton bloom (Pascual et al. 2000). Evidence had accrued to emphasize the correlation between ambient temperature and cholera incidence (Lama et al. 2004; Luque Fernández et al. 2009; Pezeshki et al. 2012; Ramirez and Grady 2016). This correlation could be due to the acceleration to the growth and multiplication of V. cholerae, which influences the abundance and also toxicity of V. cholerae in the aquatic milieu. Indeed, warm water promotes plant or algal growth and subsequent change in pH levels of aquatic environments. It also influences on plankton blooms formation. All changes provide favorable conditions for the multiplication of V. cholerae and increase the incidence risk of cholera disease in the population (Constantin de Magny et al. 2008; Wu et al. 2018). Two remote drivers of interannual climate variability, ENSO events and SST anomalies, were known as the effective factors on cholera transmission in several investigations located on the coastal part which subsequently could increase the nutrient concentration and also phytoplankton bloom (Akanda et al. 2011; Griffith et al. 2006; Lipp et al.

2002: Lobitz et al. 2000: Ramirez and Grady 2016). During El Niño, below average air pressure and convective activity conduct warmer temperatures and heavy rains from the western end to the eastern end of the Pacific Ocean basin. Elevated sea surface temperature and height associated with El Niño can lead to the promotion of plankton blooms and proliferation of V. cholerae and also the transmission of contaminated waters to the coast (Ramírez 2014). Moreover, other pathways of SST impact on cholera incidence may have occurred via local air temperature and rainfall as mediated (Ramirez and Grady 2016). One of the other climate models that lead to interannual climate variations in the tropical Indian Ocean was the Indian Ocean Dipole (IOD) which occurs by ocean-atmosphere interactions and affect regional ocean climate (Yamagata et al. 2004). This event could strongly change the sea level variations which consequently can have an impact on rainfall, flooding, and outbreaks of cholera (Constantin de Magny et al. 2006; Constantin de Magny et al. 2007; Hashizume et al. 2013). Favorable conditions such as raising temperature in marine and estuarine environments with a large number of phytoplankton and zooplankton, as a main marine reservoir of V. cholerae, can influence the ecology of V. cholerae which increase the transmission of the cholera disease to the human population using untreated water (Constantin de Magny et al. 2008; Xu et al. 2014). Although, according to Jutla et al. report, the impact of SST on cholera may be coincidental and high or low river discharge influences the association between SST and phytoplankton, so that nutrient runoff during heavy rains and river discharge which may happen during strong El Niños could affect the abundance of phytoplankton rather than SST (Jutla et al. 2011; Ramirez et al. 2013). The results of these studies were commonly consistent, indicating that the epidemics of cholera were influenced by climate in most regions. But despite finding a strong link between El Niño and cholera, it may be complex and nonstationary. ENSO effects can be "more sensitive" to the variability of ENSO characteristics overtime, different landscapes, human communities, and events (Constantin de Magny et al. 2007; Ramirez and Grady 2016; Rodo et al. 2002). Moreover, the characteristics of different ENSO events (e.g., effect on SST) should be assessed to find how it can impact the transmission of disease (Ramirez et al. 2013). It is important to note that the vital role of interaction between both extrinsic and intrinsic factors in determining infectious disease dynamics is demonstrated during refractory times. It was shown that when population susceptibility levels are decreased due to immunity, then the size of cholera outbreaks solely reflects climate forcing very weakly (Koelle et al. 2005).

A range of diverse statistical methods has been applied to study the effect of climate variables on cholera diseases which included time series analysis, generalized linear model, and linear/multiple regression analysis (Table 1). Some of them were developing a prediction model for cholera according to climate relationships (Constantin de Magny et al. 2008; Eisenberg et al. 2013; Pascual et al. 2000). The time series analysis studies seek to directly investigate the relationship of disease trends over time on historical and concurrent weather. Epidemiological time series analyses of the nonstationarity correlation between exposure covariates and disease dynamics can evaluate with wavelet analysis. This method determines whether the specific periodic cycle of disease incidence corresponds to its exposure covariate (Hashizume et al. 2013). Standard GLMs such as negative binomial and Poisson models were the basic methods (short-term associations). The time series regression also was applied in studies that explore the dependence of disease cycle on medium- or long-term weather patterns such as ENSO (Imai et al. 2015; Imai and Hashizume 2014). The spatial methods often encompassed three main targets included: visual display of target data or descriptive (GIS/choropleth maps), evaluating global and local clustering by identified tests (spatial scan statistics/Moran's Index) and analyzing data to evaluate the intensity of spatial processes (splines/kriging) (Diggle 2013; Ostfeld et al. 2005). Time series regression with autoregressive model was applied in studies with forecasting approaches. In these studies, Box-Jenkins methods such as SARIMA often used and forecast target disease in the shortterm future according to the historical weather data as predictors (Iacono et al. 2017).

Many papers have assessed the importance of lag time between climatic factors and cholera incidence. This delayed effect could be explained by climatic variables which indirectly influenced the incidence of cholera. Sources of this lag compromise the time needed for the potential growth of V. cholerae population in their environment, dynamics of exposure, incubation period, and at the end delays in reporting (Iacono et al. 2017). Depending on the respective lag between the growth rate of microorganisms and the clinical symptoms, the lag between income and outcome data can differ. Understanding lag time could be helpful for an early notification system in public health. The time lag was shorter for maximum temperatures than minimum temperature (Reyburn et al. 2011), shorter for high rainfall than low rainfall (Hashizume et al. 2008; Hashizume et al. 2010), longer for temperature than rainfall (Jutla et al. 2013; Luque Fernández et al. 2009; Ramírez 2014; Ramirez and Grady 2016; Reyburn et al. 2011), and very long for ENSO and SST (Pascual et al. 2000; Ramirez and Grady 2016; Rodo et al. 2002). The wide variation in time lag by studies in spite of the same disease could be due to the mechanism of cholera manifestation such as incubation period and the transmission dynamics of V. cholerae which play a critical role in the causal pathway. Most of the reviewed studies used monthly data, but studies with daily data units were less. In some cases, when the time lags and incubation periods were short, using the longer time unit (monthly) can lead to an underestimation of risk factors. On the other way, studies conducted on vast geographic areas or long-time scales may be failed in demonstrating the relationships that happen in country level or daily or weekly periods (Imai and Hashizume 2014; Naish et al. 2014). Therefore, selection of the most biologically possible and robust time units was acceptable for analysis.

It is necessary to consider that the effects of climate variability on the burden of cholera disease are complex and depend on several factors from local socio-economic to environmental conditions. Different studies have shown that emerging infectious disease including cholera are associated with changing seasons, natural disasters, global travel, war, and several conditions that lead to inadequate sanitation, poverty, and social disruption. Due to mentioned factors, cholera infection has frequently reemerged over more than couple of centuries (Morens and Fauci 2013). Nowadays, despite remarkable improvement in development of diagnostic and therapeutic of cholera, the simplicity of world travel between different nations and increased globalization has added various layers of complexity to containing this infectious disease that affect both the health and the economic stability of distinct societies. This reemerging disease may cause public fear, economic loss, human toll, and other adverse outcomes (Deen et al. 2020; Nishiura et al. 2017).

Finally, it is important to note that according to the Intergovernmental Panel on Climate Change (IPCC) Fourth Assessment Report, the increase in fossil fuel consumption and the consequent increase in CO₂ emissions from anthropogenic activities caused more than half of the increase in global average temperatures from 1951 to 2010 and affect climate on the local and regional scale (Pachauri and Reisinger 2008). Based on climate model results using the representative concentration pathway (RCP) scenarios, global average temperature increases between 0.3 and 0.7 °C for the period 2016-2035 relative to 1986-2005 (similar for the four RCPs) (Pachauri et al. 2014). Changing average temperature of atmosphere and ocean could change the global hydrological systems, melting snow/ice, and changing precipitation patterns, which influence on quantity and quality of water resources. It also may cause rising in sea levels and the number of heavy precipitation events in some regions. The behavior of ENSO may influence by global climate change (Pachauri et al. 2014). In recent decades, the impacts of both natural and anthropogenic climate change caused severe effects on human and natural systems across the world which by the integration of technological, behavioral, and policy options in societies, and importantly, policy linkages among regional, national, and sub-national climate policies can develop potential climate change mitigation advantages.

Limitations of reviewed papers and the current study

Several limitations were elucidated by the authors of the different reviewed studies. Most of the studies were done in developing countries with more prevalent cholera disease, where water facilities, sanitation services, and hygiene infrastructure are not developed completely. Therefore, it is necessary to consider all these factors and determine their contribution to cholera incidence before climatic factors. Indeed, they were unable to merge socio-economic data into their analysis to investigate the possible effects of income and poverty on climate-cholera correlation. The other limitations in studies were lack of data, unavailability of data, or low reliability of data. The majority of cases were clinically recognized without any laboratory-confirmed (overestimate), or they were underreported because of refusing the clinical care; also, less severe cases did not include in the surveillance data (underestimate). In some remote and rural areas where access to health systems can be difficult, the surveillance system may not be consistent and many cases are not recorded. Moreover, in some regions, the cholera cases were reported by a passive surveillance system with low reliability. Other challenges of available data and methods consist of methodological barriers that resulted from the limited understanding of the complicated biophysical mechanisms, concurrent effects of correlated variables, poor evaluation of exposure and outcomes, unsuitable study design, weak adjustment of confounders, and poor quality and reporting bias of data.

There were some limitations in our study. First, some of the relevant literature has been missed due to the following: reviewing just in English language, papers which not peerreviewed, unpublished results, and not recognized by our search terms. Second, it is possible that we have missed related studies because of the failure of the online search engines. Third, there was not an assessment of the risk of bias in the reviewed papers. However, we designed our study according to the systematic review methods, so it was possible to decrease bias in our identification of studies.

Recommendations for future research

We recommend the following aspects for future research.

- Environmental factors, socio-economic demographics and interventions should be considered in examination of cholera determinants. This would help to better understand cholera epidemiology and recognize the most important predictors for the prediction of biological–climate relationships on cholera transmission.
- It needs to extend current scenarios according to socioeconomic and population growth development to minimize confounding effects population characteristics such

as tourism development, urbanization, and population growth.

- 3) All environmental factors with a possible role in the cholera incidence in the study area should be systematically applied in future studies. The present study would help for the selection of the most effective variables in the future studies. It should be necessary to consider units of measurement, time-scale, and lagged effects.
- 4) To enhance the comparability among studies and find the same approach for reporting the results, standardization of indicators would be required. Thus, confidence intervals and effect measures for all variables would be needed.
- 5) To develop cholera prevention and control programs, disease surveillance should be improved by awareness of inter-epidemic period as information on the cholera endemicity. Moreover, identification of prevalent bacterial serotypes in the study area during inter-epidemic periods and the introduction of another serotype would be helpful for control measures activity and prevention of the transmission of the organism.
- 6) In the evaluation of cholera-climate relationships, it would be useful to take precise attention to time lags, seasonal of long-term cholera trends, severe climatic events, and nonlinear effects.

Conclusion

Our synthesis of 43 studies indicated that changing rainfall patterns, rising temperatures, and subsequent effects due to global climate change can affect the risk of cholera diseases in endemic regions. The results of present study have implications that can be used toward the control of cholera incidence. This useful information can apply to develop accurate forecasting models which succor public health services for urgent decisions in providing lead time to manage a proactive and targeted response. In addition, we expect to enable public health investigators and policymakers to be conscious about regional, national, and sub-national impacts of climate change on cholera rates and to help assign research priorities and provide adequate equipment.

Acknowledgments We would like to appreciate all those researchers who helped us to conduct the present study.

Funding information This work was supported by Iran University of Medical Sciences, Tehran, Iran (Grant number: 1874).

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

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