Climate Variability and the Outbreaks of Cholera in Zanzibar, East Africa: A Time Series Analysis

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Abstract. Global cholera incidence is increasing, particularly in sub-Saharan Africa. We examined the impact of climate and ocean environmental variability on cholera outbreaks, and developed a forecasting model for outbreaks in Zanzibar. Routine cholera surveillance reports between 1997 and 2006 were correlated with remotely and locally sensed environmental data. A seasonal autoregressive integrated moving average (SARIMA) model determined the impact of climate and environmental variability on cholera. The SARIMA model shows temporal clustering of cholera. A 1°C increase in temperature at 4 months lag resulted in a 2-fold increase of cholera cases, and an increase of 200 mm of rainfall at 2 months lag resulted in a 1.6-fold increase of cholera cases. Temperature and rainfall interaction yielded a significantly positive association ($P < 0.04$) with cholera at a 1-month lag. These results may be applied to forecast cholera outbreaks, and guide public health resources in controlling cholera in Zanzibar.

INTRODUCTION

Since the beginning of the millennium, global cholera incidence has increased steadily with 24% more cases reported between 2004 and 2008 compared with 2000 and 2004.[1] In the last 30 years, the burden of cholera has shifted from Asia to Africa, which is currently the source of over 94% of reported global cases.[1,2] *Vibrio cholerae* O1 El Tor strain is the causative agent for the large majority of these cases.[2] In Africa, cholera cases tend to occur sporadically or as small outbreaks, with a constant threat for more explosive epidemics, as illustrated in the recent Zimbabwe epidemic with 98,592 reported cases and 4,288 deaths in 11 months.[3]

Cholera outbreaks exhibit strong seasonality, tending to occur after increased rainfall and warm temperatures. This seasonality has been observed for centuries but it was not until the late 1970s that the environmental habitat of *V. cholerae* was discovered.[4] Pathogenic *Vibrios* inhabit coastal and estuarine ecosystems, commensal with algae and the roots of aquatic plants, phytoplankton, zooplankton, and in particular copepods. A single copepod has been shown to host up to 10^3–10^5 *Vibrios,* attached to the gut wall and so ingestion of just a few copepods can have the potency to deliver an infective dose of *V. cholerae*.[5,6] The significance of copepods as a transmission vector was demonstrated in Bangladesh where water filtration through sari cloth removed 99% of *V. cholerae*, i.e., those cells attached to the plankton.[6]

During periods between epidemics *V. cholerae* is able to adopt a viable but non-culturable state in response to nutrient deprivation, allowing *Vibrios* to persist in their natural aquatic habitat for long periods in a dormant state. Reversion back to the culturable, infectious phase is triggered by favorable environmental factors such as increased water temperature, pH, seawater nutrients, and decrease in salinity.[7–9] The same environmental factors facilitate proliferation of copepods and free-living *V. cholerae* populations, resulting in large and sudden increases in environmental *Vibrio* numbers.[8–11]

Three marine environmental variables, sea surface height (SSH), sea surface temperature (SST), and ocean chlorophyll concentration (OCC), have shown to be predictive of cholera outbreaks in Kolkata, India; Matlab, Bangladesh; and Hue, Vietnam.[10,12,13] The first of these studies, conducted in 2000 by Lobitz and others,[10] used satellite imagery to derive the values for ocean parameters and linked these with cholera incidence. The SST was positively associated with cholera cases, affirming the hypothesis that a rise in SST encourages phytoplankton populations to bloom, which is directly associated with greater zooplankton populations and *V. cholerae*.[10] The positive association of SSH with cholera cases was attributed to increased human to aquatic *Vibrio* contact.[10,14] The indirect measurement of OCC in Kolkata showed a positive association with cholera, it is thought that the rise in OCC allows copepod populations to grow and thus *V. cholerae*.[12] Measurement of OCC is difficult, however, and possibly problematic for making predictions because of its variability across small areas.[5]

Locally measured variables such as temperature and rainfall have been positively associated with increased cholera incidence in multiple studies. One of which was in Zambia, located in the same geographic region as Zanzibar, but lack of cholera case data between epidemics prevented the development of an appropriate predictive model.[15] Environmental variables are linked to cholera outbreaks through the fluctuation of environmental *Vibrio* populations. Lagged dynamics are typically seen because of the time required between the change in the environment and environmental *Vibrio* reaching sufficient numbers for ingestion of an infectious dose.[4] We hypothesize that ambient temperature is linked to SST and at its optimum for *Vibrio* growth, a lagged increase in cholera cases will occur.

Understanding environmental drivers of cholera outbreaks could facilitate a degree of outbreak prediction, allowing governments to prepare and respond early to potential outbreaks through actions such as employing vaccines. In addition, it offers insight into the local etiology of cholera, which would be helpful in planning prevention strategies. This study examines the association between climate variability and cholera outbreaks, and develops a climate-based forecasting model for cholera in Zanzibar using a time series analysis.

METHODS

Study area. Zanzibar, an archipelago ~50 km off the eastern coast of Tanzania mainland, consists of two main islands,

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FIGURE 1. Study area: Zanzibar, East Africa.

Unguja and Pemba (Figure 1). The total population is about 1.1 million, of which 17% are < 5 years of age, 28% are 5 to 15 years of age, and 56% are > 15 years of age.[16] Life expectancy is 57 years of age.[16] The economy of the islands depends largely on agriculture, tourism, and fishing. The mean temperature varies between 21°C/70°F and 33°C/91°F with monthly rainfall between 25 mm/0.1 in. and 434 mm/1.7 in.[17] The long rains and short rains typically occur between March and May, and from October to December, respectively. We restricted our study to Unguja where we collected data on the temporal distribution of cholera. The study omitted Pemba as the cholera data available was not enough to conduct a time series analysis. It is likely that the identified environmental predictors would apply to both islands as they are geographically, environmentally, and socioeconomically similar other than one area of Unguja, which is more urbanized than any part of Pemba.

Source data. *Environmental data.* Table 1 summarizes the source information for the environmental data. Mean monthly SST, SSH, and OCC were derived from satellite imagery. The satellite data for the SST variables are available from the beginning of January 1985, and are distributed by NASA's Jet Propulsion Laboratory. The Advanced Very High Resolution Radiometer (AVHRR), a space-borne sensor of the National Oceanic and Atmospheric Administration's (NOAA) family

of polar orbiting platforms, collects data on 4-km areas. The SSH, a measure used to detect sea-level anomalies, is derived through satellite altimetry, and is available from 1992 from the TOPEX/Poseidon sensor, and available from 2002 from the Jason-1 sensor. Starting in 1997, OCC data were available from SeaWiFS and MODIS (MODerate resolution Imaging Spectroradiometer) sensors at a spatial resolution of 9 and 1 km, respectively. Approximately the same area is used to compile data for the satellite-derived, monthly environmental variables collected by all four sensors. Climate data from *in situ* sources include monthly minimum temperature, maximum temperature, rainfall, and humidity, which are collected by the Meteorological Department of the Zanzibar Government.

Population and cholera data. The population data were obtained from the national census of Zanzibar. Case reports for cholera were based on the Zanzibar Ministry of Health and Social Welfare's (MoHSW) cholera surveillance records. Reporting was based on the recommended World Health Organization (WHO) guidelines of acute watery diarrhea with microbiological confirmation; or after microbiological confirmation of the first 10 cases in an outbreak, and clinical criteria of severe watery diarrhea.[18,19] All available local surveillance records and WHO country reports for Tanzania were reviewed for consistency, but only local reports were used

TABLE 1
Climate and environmental variables and data sources

Variable	Data source and availability
In situ climate variables	
Temperature	Meteorological department, Zanzibar Government: Unguja airport weather station (2002–2008)
Rainfall	Meteorological department, Zanzibar Government: Unguja airport weather station (2002–2008)
Humidity	Meteorological department, Zanzibar Government: Unguja airport weather station (2002–2008)
Satellite-derived environmental variables	
Sea surface temperature	AVHRR (2002–2008) Source: http://poet.jpl.nasa.gov/
Sea surface height	TOPEX/Poseidon (2002–2008) Jason-1 (2002–2003), Source: http://www.aviso.oceanobs.com/
Ocean chlorophyll concentration	MODIS (2002–2008), Source: SeaWiFS (2002–2008), Source: http://oceancolor.gsfc.nasa.gov/

for this study, which were available from 2002 to 2008. The large majority of cases were clinically diagnosed cholera with a smaller proportion of laboratory-confirmed cases, consistent with the WHO international guidelines. Both clinical- and laboratory-confirmed cases were included in the analysis.

Ethics. The analysis was based on cholera reports collected routinely by the MoHSW Zanzibar, from whom we obtained the data for analysis. The reports did not include individual patient identifiers, thus no Institutional Review Board approval was sought for this study. Individual consent was not obtained for this study, because this was a retrospective analysis of existing data collected by MoHSW, hence, it was not necessary or possible to obtain consent from participants. Environmental data were obtained from open access sources.

Data analysis. We analyzed the data by month, producing 84 time points during the study period (2002–2008). Univariate analysis was conducted for each of the climate and ocean environment variables with cross-correlation analysis to assess associations between cholera cases and covariates over a range of time lags.[20,21] The time lags chosen for the final model were outcomes of the cross-correlation analysis using seasonal

differencing of the data. A multivariate seasonal autoregressive integrated moving average (SARIMA) model was used to examine the independent contribution of the cholera transmission covariates, because its integrated functions for controlling seasonal variation, autocorrelation, and long-term trends make it the most appropriate model for this time series analysis.[22] The numbers of terms in the SARIMA model were determined by autocorrelation function (ACF) and partial autocorrelation function (PACF). The outcome variable (number of cases) was transformed into a square root, as recommended by Johnson and Wichern,[23] to address issues with zero-inflated count data.

To create an appropriate stationary time series for the analysis, all dependent and independent variables were seasonally differenced with regard to yearly periodicity. We determined the need for differencing the monthly cholera cases by checking stationarity (trends in the mean and variance), and the order of both seasonal and non-seasonal autoregressive and moving average indicators by using the ACF and PACF. The model used in this study was $SARIMA(p,d,q)(P,D,Q)s$, where p is the order of autoregression; d, the degree of difference; q, the order of moving average; P, the seasonal autoregression; D, the seasonal integration; Q, the seasonal moving average; and s, the length of the seasonal period. We used the stepwise SARIMA method to select covariates associated with cholera cases at $P < 0.1$. Our main criterion for judging the superiority of the model against other models was based on the lowest value in the Akaike's information criterion (AIC), a measure of the goodness-of-fit of an estimated statistical model.[24] The goodness-of-fit of the models were determined for appropriate modeling, using both ACF and PACF of residuals, and checking the normality of the residuals.

Data from 2002 to 2008 were used for parameter estimations. For validation of the model, we used the data from 2002 to 2007 as the training period, and the data from 2008 as the validation period. Finally, the data from 2008 was used to test the forecasting ability of the method using the root mean square (RMS) error criterion. The smaller the RMS error, the better the model is for forecasting. All analyses were carried out using SAS version 9.1 (SAS Institute, Inc., Cary, NC).

RESULTS

In Unguja, 3,245 cholera cases were reported between 2002 and 2008, and the temporal patterns of cases are shown in Figure 2. The characteristics of the study data are shown in
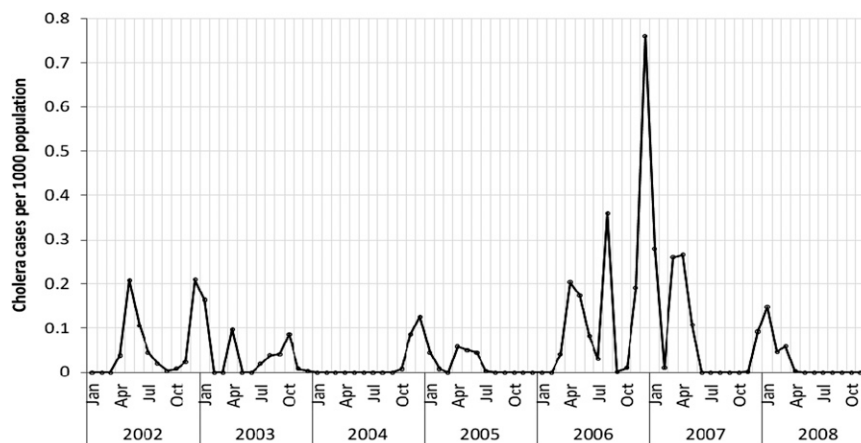

FIGURE 2. Monthly cholera incidence rates in Unguja, Zanzibar, 2002–2008.

Variables (monthly average)	N (months)	Mean	SD	Minimum	Maximum
Monthly cholera cases	84	38.63	77.17	0	534
Minimum temperature	84	23.15	1.37	20.2	25.3
Maximum temperature	84	30.68	1.47	28.2	33.8
Rainfall	84	141.35	156.36	3	705.4
Humidity	84	78.30	5.95	57	89
Sea surface temperature	79	27.64	1.44	25.065	29.894
Sea surface height	79	−0.17	3.96	−9.504	10.172
Ocean chlorophyll concentration from MODIS	78	0.13	0.05	0.068	0.353
Ocean chlorophyll concentration from Sea-Wifs	84	0.16	0.06	0.086	0.346

*The variables (except cholera cases) are monthly averages.

Table 2. We calculated 12 months of seasonally differenced values for each variable to ensure the time series of climate and environmental variables, and the square root transformed cholera outbreaks were stationary. The results of the cross-correlations using seasonal differencing of the data show that cholera outbreaks were significantly positively associated ($P < 0.05$) with minimum temperature at lags of 2 and 4 months, negatively associated with maximum temperature at a lag of 2 months, positively associated with humidity at a lag of 5 months, and positively associated with rainfall at a lag of 1 month. None of the ocean environmental variables show significant association with the cholera outbreaks (Table 3). Covariates indicating significant correlation are: minimum temperature with positive SST ($P < 0.01$), maximum temperature with negative rainfall ($P < 0.01$) and negative humidity ($P < 0.01$), rainfall with positive humidity ($P < 0.01$), humidity with negative SST ($P < 0.05$), and OCC from MODIS with positive OCC from SeaWiFS ($P < 0.01$) (Table 4). These variables were included separately in the models to avoid multi-collinearity. The seasonally differenced minimum temperature and rainfall, respectively, are positively associated with cholera outbreaks (Figure 3). However, a few cases did not line up well, because of the nature of the outbreak, reporting system, and lagged effects of climate and ocean environment variability.

SARIMA model. The best fit model without covariates (null model) was SARIMA($[1,0,0][0,1,1]_{12}$), and the best fit model with covariates (covariate model) was SARIMA($[1,4],[0,0][0,1,1]_{12}$) based on the AIC values. A backward elimination method selected variables most suitable for the model. The results of the null model showed temporal clustering of cholera at a 1-month lag. The patterns of the temporal clustering of cholera were modified by the climatic variables, as obtained in the covariate model, yielding clustering at a 1-month lag and at a 4-month lag (Table 5). The temporal lag relation of cholera and minimum temperature is 4 months, and the temporal lag relation of cholera and rainfall is 2 months. An increase of 1°C in minimum temperature at a 4-month lag resulted in a 2-fold increase of cholera cases; and an increase of 200 mm in rainfall at a 2-month lag resulted in a 1.6-fold increase of cholera cases. The interaction of temperature and rainfall yielded a significant association ($P = 0.04$) with cholera at a 1-month lag (Table 3). The goodness-of-fit analysis shows that there was no significant autocorrelation between residuals at different lags in the SARIMA model and the model fits the data well.

Validation model. The model developed using the data for the 2002–2007 periods was used to predict cholera cases, and then validated using the data between January and December 2008. The validation results show the SARIMA model to be an appropriate model for forecasting cholera outbreaks in Zanzibar (RMS errors for both training and validation period are 3.92 and 4.50, respectively). In the training period, it had lower predicted values in August and December 2006, and in the validation period, it had a higher observed value in December 2008 (Figure 4). Except for these points, the predicted and observed cases were matched reasonably well, and there was consistency in the trend. The time series plot of cumulative sums of observed and predicted cholera cases showed only a small gap in August 2006, and that was retained during the rest of the study period (Figure 5).

DISCUSSION

This study provides reassuring evidence that rainfall and temperature, among various climate and ocean environmental variables are the key drivers of cholera outbreak, consistent

Variables	Lag (month)					
	0	1	2	3	4	5
Minimum temperature	0.00	0.08	0.25**	0.07	0.23**	−0.02
Maximum temperature	−0.11	−0.19*	−0.12	−0.05	0.07	−0.02
Rainfall	0.05	0.24**	0.19*	0.09	−0.01	0.00
Humidity	0.00	0.20*	0.08	−0.09	−0.04	0.22**
Sea surface temperature	−0.11	−0.01	−0.04	−0.17	−0.15	0.07
Sea surface height	0.07	0.04	0.16	−0.01	−0.06	−0.05
Ocean chlorophyll concentration from MODIS	0.08	0.00	0.06	−0.01	−0.07	−0.02
Ocean chlorophyll concentration from Sea-Wifs	−0.14	−0.12	0.18*	0.12	−0.17*	−0.01

* $P < 0.1$; ** $P < 0.05$.

TABLE 4
Inter-correlations between climate and environmental variables using 12-month seasonal differencing, Unguja, Zanzibar

Variables	Maximum temperature	Rainfall	Humidity	SST	SSH	OCC from MODIS	OCC from Sea-Wifs
Minimum temperature	0.16	0.20	0.01	0.35***	0.12	−0.15	0.01
Maximum temperature		−0.53***	−0.52***	0.22	0.14	0.01	0.16
Rainfall			0.48***	0.09	−0.001	0.14	−0.13
Humidity				−0.26**	0.001	0.06	−0.23*
SST					−0.12	−0.11	−0.01
SSH						−0.06	−0.09
OCC from Modis							0.69***

SST = sea surface temperature; SSH = sea surface height; OCC = ocean chlorophyll concentration.
* $P < 0.1$; ** $P < 0.05$; *** $P < 0.01$.

with results from other studies.[14] In Nha Trang, Viet Nam, Emch and coworkers[13] showed that the probability of outbreaks was higher with increased rainfall, river height, and discharge. In Bangladesh, Hashizume and coworkers[25] showed the risk of cholera increased with high rainfall, and conversely, with decreased rainfall suggesting that river level was on the causal pathway. Their findings illustrate the variability of environmental predictors across and within study sites, hence the importance of conducting thorough time series analysis by site if a plausible predictive model is to be reached. Consistent across the two studies was the attribution of the positive association of cholera with rainfall, to increased *Vibro* to human contact caused by flooding and an inundation effect where the environment is inundated with the bacteria.

Heavy rainfall and consequent flooding increases the risk of sewage contaminating the drinking water. In Zanzibar the most common toilet facility are pit latrines,[26] where the untreated waste water can overflow or seep through the ground into the drinking water found in wells or pipes. Many piped water lines contain leaks caused by age and lack of maintenance and
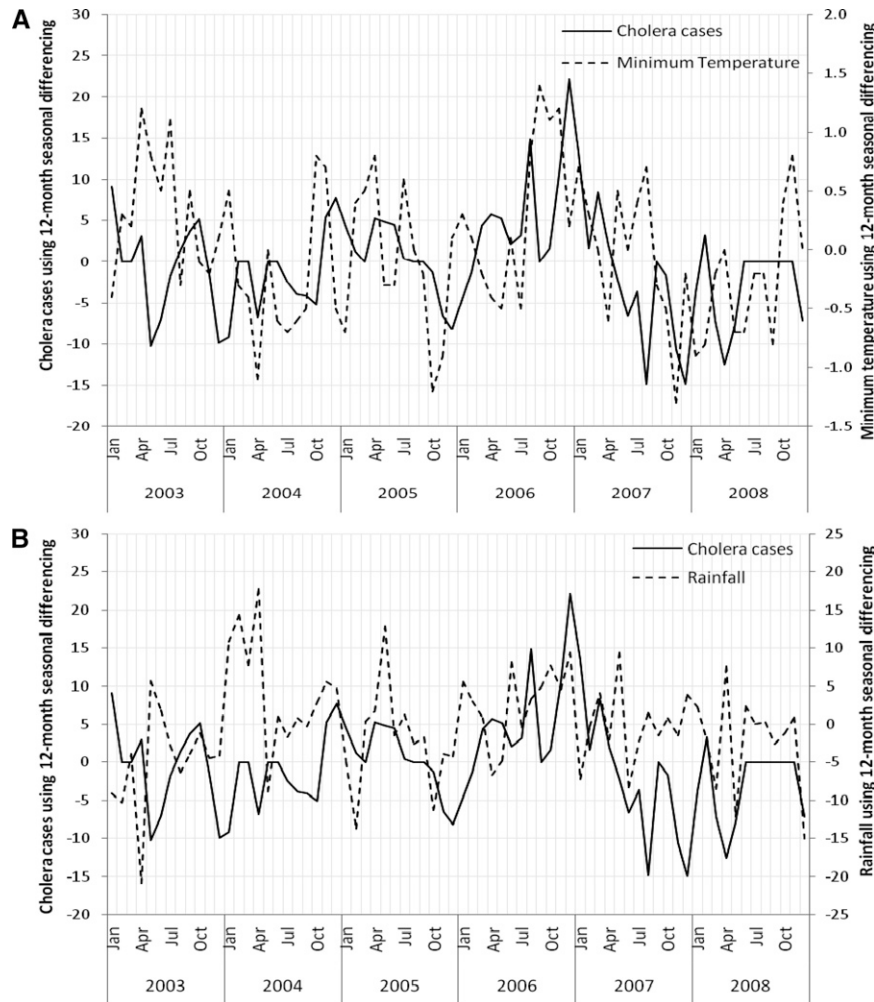

FIGURE 3.   Relationship between square root of monthly observed cholera cases and (**A**) minimum temperature and (**B**) rainfall using seasonal differencing in Unguja, Zanzibar during the period 2003–2008.

Regression coefficients of seasonal autoregressive integrated moving average (SARIMA) on monthly cholera cases in Unguja, Zanzibar, 2002–2008

Variables	Model without covariates			Model with covariates		
	Estimate	Standard error	P value	Estimate	Standard error	P value
Seasonal moving average	0.750	0.097	< 0.0001	0.749	0.120	< 0.0001
Autoregression at 1 month lag	0.526	0.105	< 0.0001	0.493	0.109	< 0.0001
Autoregression at 4 months lag				0.291	0.109	0.010
Minimum temperature at 4 months lag	–	–	–	2.208	1.021	0.034
Rainfall at 2 months lag				0.008	0.003	0.025
Minimum temperature × rainfall at 1 month lag				0.0003	0.0001	0.044
Akaike's information criterion (AIC)	423.35			390.62		

during times of low water pressure the surrounding ground water may be actively sucked into the pipes. Poor drainage is common in many cholera-affected areas, and during heavy rains, residential areas can be submerged in water for prolonged periods of time, promoting human *Vibrio* contact.

The relationship between temperature and amplification of cholera incidence is well documented.[5,8,12,14,27–30] Warmer temperatures increase SST facilitating *Vibrio* reproduction and hence the probability of ingesting an infectious dose.[5,14] Our concurring findings are important in light of the current global warming phenomenon, Climatologists predict a 1.4°C/35°F to 5.8°C/42°F rise in mean temperature over the next 100 years.[30] Increased sea temperatures and levels associated with global warming intuitively suggest the possibility of increased cholera incidence in many resource-poor regions of the world.

The main limitation of this study was the use of routine surveillance data. The majority of cases were clinically diagnosed with only a small proportion laboratory-confirmed. However, it is likely that these outbreaks were indeed caused by *V. cholerae* as indicated by laboratory confirmation of initial cases during each outbreak and by the case fatality rates. Consistent with international guidelines, not every suspected case was laboratory-confirmed, and this may have resulted in an overestimation of actual cholera cases. On the other hand, there is the possibility that the number of cases were under-reported as patients may not have sought care.

There is potential to develop an early warning system for cholera in Zanzibar using a predictive model, which would give public health authorities sufficient time to prepare medical equipment and mobilization of staff in the event of an
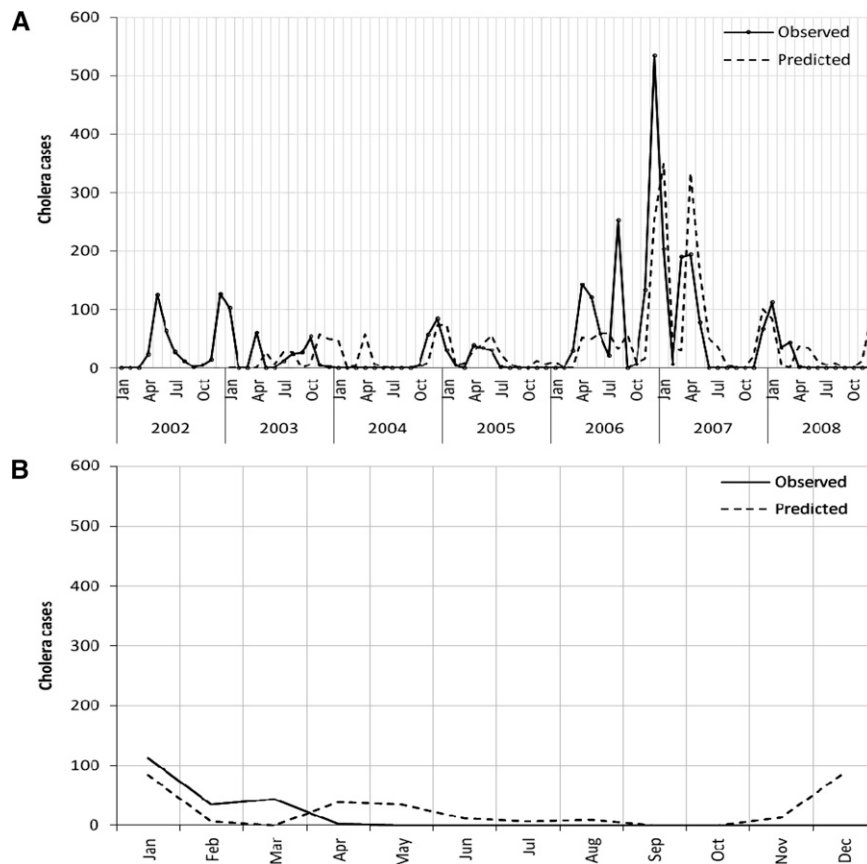

FIGURE 4. (**A**) Predicted vs. observed monthly cholera cases in Unguja, Zanzibar during 2003–2008. (**B**) Validation model for the period January to December 2008 with monthly cholera cases.
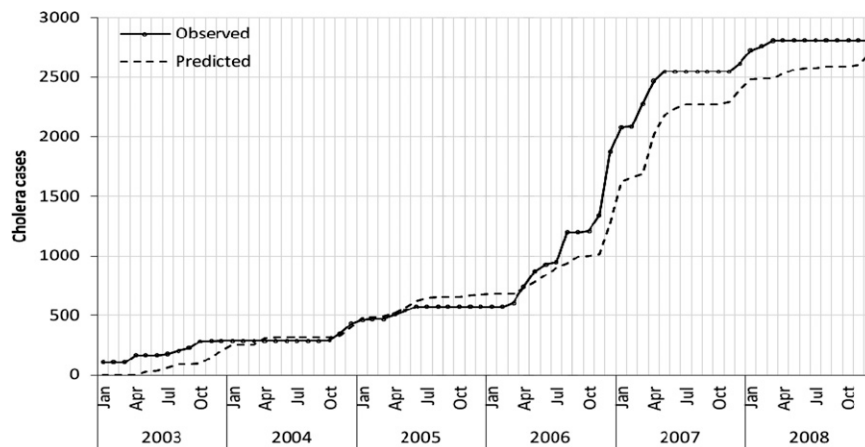
FIGURE 5.   Cumulative sums for observed and predicted cholera cases in Unguja, Zanzibar during 2003–2008.

outbreak. Prediction of outbreaks is imperative in order for cholera prevention strategies to be efficient and cost-effective such as targeted pre-emptive mass oral cholera vaccination. However, more work is needed on refining such a model before it is ready for routine use. In addition, this study provides useful clues on further elucidating the risk factors for cholera that can be used to direct public health strategies.

In conclusion, this study supports the findings of previous studies illustrating the link between cholera incidence and climatic factors. Rainfall and temperature observations could facilitate a warning signal for cholera outbreaks in Zanzibar. Our model contributes to the growing literature on the link between cholera and environmental factors, which can eventually be used to predict and prepare for cholera epidemics.

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