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Co-variation of Cholera with Climatic and Environmental Parameters in Coastal Regions of Tanzania

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Abstract — The bacterium causing cholera, *Vibrio cholerae*, is essentially a marine organism and its ecological dynamics have been linked to oceanographic conditions and climate. We used autoregressive models with external inputs to identify potential relationships between the number of cholera cases in the coastal regions of mainland Tanzania with climatic and environmental indices (maximum air temperature, sea surface temperature, wind speed and chlorophyll *a*). Results revealed that, between 2004 and 2010, coastal regions of mainland Tanzania inhabited by approximately 21% of the total population accounted for approximately 50% of the cholera cases and 40% of the total mortality. Significant co-variations were found between seasonally adjusted cholera cases and coastal ocean chlorophyll *a* and, to some degree, sea surface temperature, the outbreaks lagging behind by one to four months. Cholera cases in Dar es Salaam were also weakly related to the Indian Ocean Dipole Mode Index, lagging by five months, suggesting that it may be possible to predict cholera outbreaks for Dar es Salaam this period ahead. The results also suggest that the severity of cholera in coastal regions can be predicted by ocean conditions and that longer-term environmental and climate parameters may be used to predict cholera outbreaks along the coastal regions.

INTRODUCTION

Vibrio cholerae, which causes the acute enteric infection of cholera, is essentially a marine bacterium, with coastal waters acting as an important reservoir (Colwell *et al*., 1981). The bacterium has been found in coastal environments around the world, both in areas where cholera is endemic and in cholera disease-free areas (Karunasagar *et al*., 2003). It is now well known that cholera occurs in regions with natural aquatic reservoirs

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where the bacteria can persist in a free-living state, or in association with phytoplankton, zooplankton and detritus (Nelson *et al*., 2009). These environmental reservoirs may play a significant role in cholera epidemiology by favouring persistence of the pathogen in periods between epidemics (Vezulli *et al*., 2010). Indeed, the dynamics of cholera outbreaks have been linked to climate and environmental variables, such as air and water temperature, rainfall, wind direction (e.g. Paz and Broza, 2007; Jutla *et al*., 2011). The dynamics of environmental *V. cholerae* have been linked, for example, to water salinity, nutrients and plankton biomass (Vezulli *et al*., 2010). Water temperature, in particular, has been shown to be an important factor governing the seasonal and geographical variation in *V. cholerae* (Igbinosa & Okoh, 2008). Evidently the ecology of *V. cholerae* is important, as are the socio-economic factors for endemic and epidemic cholera. Studies have shown that the cumulative incidence of cholera is strongly correlated with low scores on several socio-economic development indices (Ackers *et al*., 1998), including lack of adequate water and sanitation infrastructure in densely populated areas and ineffective cholera management (Mhalu *et al*., 1984; Sedas, 2007; Sow *et al*., 2011). Inadequate and leaking sanitation provides opportunities for transmission of the virulent forms of the pathogen into environmental reservoirs (Vezulli *et al*., 2010) where it may survive and propagate depending on environmental and climatic conditions.

Studies on the relationship between cholera outbreaks and climatic or seasonal variables in Tanzania are few (Trærup *et al*., 2011) and mainly limited to the Lake Victoria Basin and the islands of Zanzibar (e.g. Nkoko *et al*., 2011; Reyburn *et al*., 2011). Furthermore, demonstrated relationships between cholera outbreaks and weather and climate in mainland Tanzania are scarce (Trærup *et al*., 2011). There has, for example, been no analysis of data for the mainland coastal regions connected to the marine environment. Given the potential importance of such relationships for the prediction of cholera outbreaks in a country like Tanzania, we sought to analyse the relationship between cholera cases and climate in the coastal regions of mainland Tanzania, focusing on the years 2004 to 2010. We also aimed to establish whether any identified co-variations of cholera with seasonal or climatic cues would be useful in predicting outbreaks in coastal Tanzania regions ahead of time.

METHODS

The study focused on the coastal regions of mainland Tanzania, East Africa using retrospective climatic and health data. The regions were Mtwara and Lindi in the south, Pwani and Dar es Salaam in the centre, and Tanga in the north (Fig. 1). We reviewed the national data on the number of cholera cases and deaths, and climatic cues (rainfall, air temperature and wind speed) recorded on a monthly basis from the years 2004 to 2010. In addition, we compared cholera cases and selected socio-economic health indicators (access to safe water and access to latrines) in the studied regions. The data for the number of cholera cases and deaths, as well as the socio-economic data, were obtained from the Ministry of Health and Social Welfare (MoHSW), United Republic of Tanzania. The cholera surveillance records were reported according to recommended WHO guidelines (Global Task Force On Cholera Outbreak, 2004). Case Fatality Rates (CFR) were calculated using the number of cases and mortality (i.e. deaths/cases x 100 = CFR). Demographic data were obtained from the National Bureau of Statistics (NBS) (Ministry of Planning, Economy and Empowerment, United Republic of Tanzania, 2008), while the monthly average data for rainfall and maximum air temperatures were obtained from the Tanzania Meteorology Agency (TMA). This study obtained ethical approval from the National Institute of Medical Research (NIMR/HQ/R.8a/Vol.IX/1155), Dar es Salaam, Tanzania.

Remotely sensed data for sea surface temperature (SST), chlorophyll (Chl *a* in mg m^{-3}) and wind stress (Wind, N m^{-2})

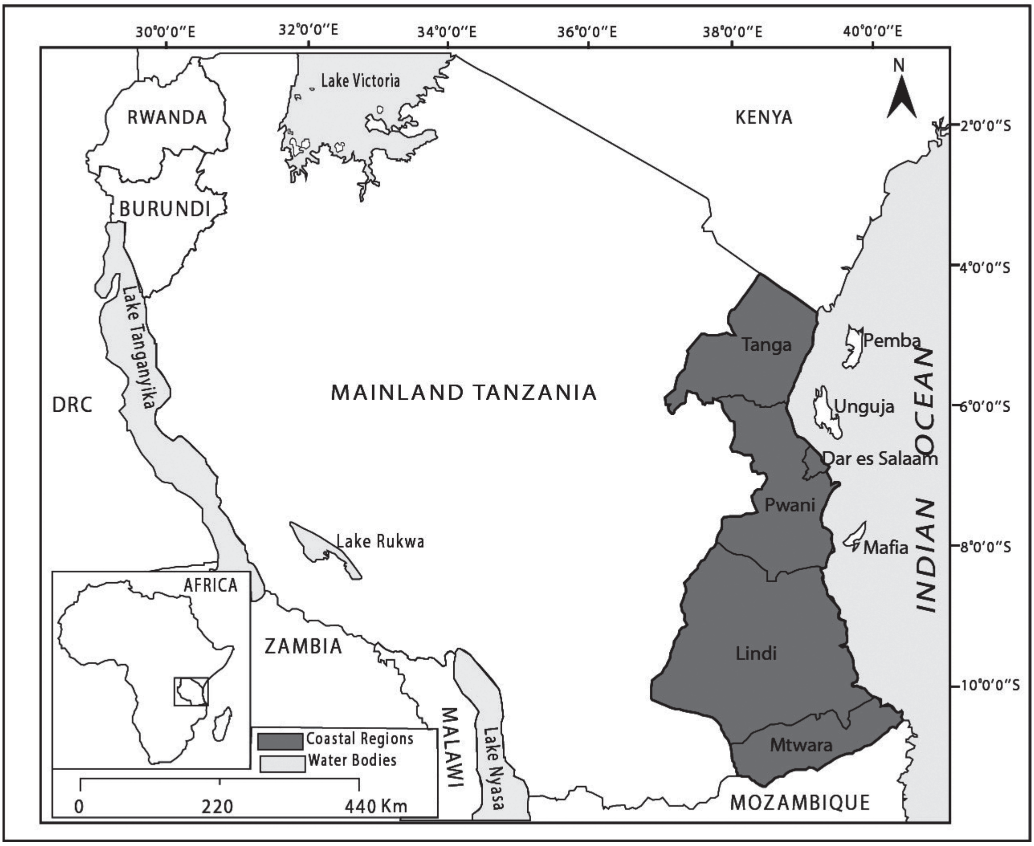

Figure 1. Map of Tanzania showing its five coastal regions: Tanga, Pwani, Dar es Salaam, Lindi and Mtwara.

were obtained from the United States of America National Oceanic and Atmospheric Administration Coastwatch website (http://coastwatch.pfeg.noaa.gov). The following datasets were used: SST (Aqua MODIS, NPP, Global, Daytime, Science Quality, 8-day Composite), Chl *a* (Aqua MODIS, NPP, Global, Science Quality and Monthly Composite) and wind (NOAA/NCDC Blended Monthly 0.25° Sea Surface Wind Stress). Data files covering 4.5-11°S to 38.5-42°E were extracted from the databases for 2004 to 2010. SST and Chl *a* data were extracted for the study regions from bands 0.208° wide (i.e. 5 pixel in width) along the coast. Wind data were similarly extracted from bands 0.5° longitude wide (2 pixels in width). Monthly averages were calculated from the 8-day SST data using simple averaging.

The number of cholera cases was compared between the different regions and seasons using non-parametric ANOVA (Kruskal Wallis) and the Mann Whitney U test, respectively. Time series analysis was performed using Matlab (2012a, The MathWorks, Natick, Ma., USA.). A Jarque-Bera test (jbtest) was used to test for normality of the data. An augmented Dickey-Fuller test (adftest) was used to assess the null hypothesis of a unit root in the data. All model estimation was carried out using the Matlab System Identification toolbox that is based on Ljung (1999). Autoregressive models with ARX (Box and Jenkins, 1970) external inputs were used to study the relationships between the incidence of cholera in the coastal regions and environmental parameters. Data from the two most populous regions, Dar es Salaam and Tanga, were subjected to time series analysis.

Numbers of case in other regions were insufficient for this type of analysis. The case and environmental data were transformed to obtain stationary time series. Before exploring the model, collinearity between predictor variables was studied. Significant collinearity was observed, firstly between transformed temperature anomalies and transformed rain anomalies for Dar es Salaam, and secondly between transformed temperature anomalies and SST anomalies, also for Dar es Salaam, with respective r^2 values of 0.30 and 0.37. Collinearity for Tanga predictive variables was only found between transformed temperature anomalies and transformed SST anomalies, with an r^2 of 0.18. Belsley collinearity diagnostics were used to determine if these exceeded tolerance levels. This was not the case; condition indices were <2 in all cases.

The cholera case data were not normally distributed and varied seasonally, i.e. the data were non-stationary. Seasonality in the data was removed by normalizing data by monthly means. A square root transformation did not achieve normal distribution in the case data (jbtest: $p < 0.001$). This, however, was achieved using a log-transformation (jbtest: $p = 0.2$). Since values of zero are undefined when using a log-transformation, uniformly distributed pseudorandom values ranging from 0.2 to 4 were added to all cases data. This procedure was carried out 100 times and the resultant time series was subjected to statistical analysis. The augmented Dickey-Fuller test rejected the presence of a unit root in the transformed case data (adftest, model 'ar', 6 lags), suggesting that undifferentiated data could be used for the regression analysis. All data were further normalised by their mean and standard deviation (zscore). Box-Jenkins type autoregressions were fitted to the data with external inputs in an ARX model (na, nb, nk). Regressions of monthly data on the number of cholera cases for Dar es Salaam and Tanga against monthly values of the Indian Ocean Dipole Mode Index (DMI; Saji *et al*., 1999) were used to examine the influence of climate on cholera outbreaks.

RESULTS

On average, cholera cases in Tanzanian coastal regions occurred every month between 2004 to 2010 (Fig. 2a). The highest number of cholera cases was recorded in 2006, while the least number of cases occurred in 2008. The North East Monsoon (NEM) period (December – April) had significantly ($U = 382$; $p = 0.0069$) more cases of cholera compared to the South East Monsoon (SEM) period (June – October). The number of cases was also high during the inter-monsoon period (May and November). During the study period, a total of 43 560 cholera cases were reported on mainland Tanzania (Fig. 2b). Although the coastal regions are only inhabited by ~21% of the total population of mainland Tanzania (Table 1), approximately 50% of the cases (21 760) occurred in these regions. The most populated coastal regions, Dar es Salaam and Tanga, had higher rates of cholera cases on average (5.5 and 3.3 cases per one hundred thousand people respectively) compared to the less populated regions Lindi, Mtwara and Pwani (2.0, 1.5 and 1.0 cases per one hundred thousand people respectively).

Deaths attributable to cholera on mainland Tanzania totalled 902 during the study period (Table 1); of these 357 (40%) occurred in the coastal regions. The Case Fatality Rate (CFR) varied between years, the average being 2.1%. In the coastal regions, the highest mortality due to cholera was recorded in 2006 (120 deaths), while the lowest was recorded in 2008 (23 deaths). The total mortality differed between regions during 2004-2010, with Tanga and Dar es Salaam reporting the highest numbers of 148 (41.5%) and 128 (35.9%) respectively. Lindi, Pwani and Mtwara reported lower numbers of 49 (13.7%), 26 (7.3%) and 6 (1.7%) respectively.

In general, 60% of the coastal population had access to safe water, compared to 46% in the inland regions and 53% overall in mainland Tanzania in 2006 (Table 1). The population in Dar es Salaam had the best access to safe water, followed by Pwani Region, whilst the population in Mtwara Region had the lowest

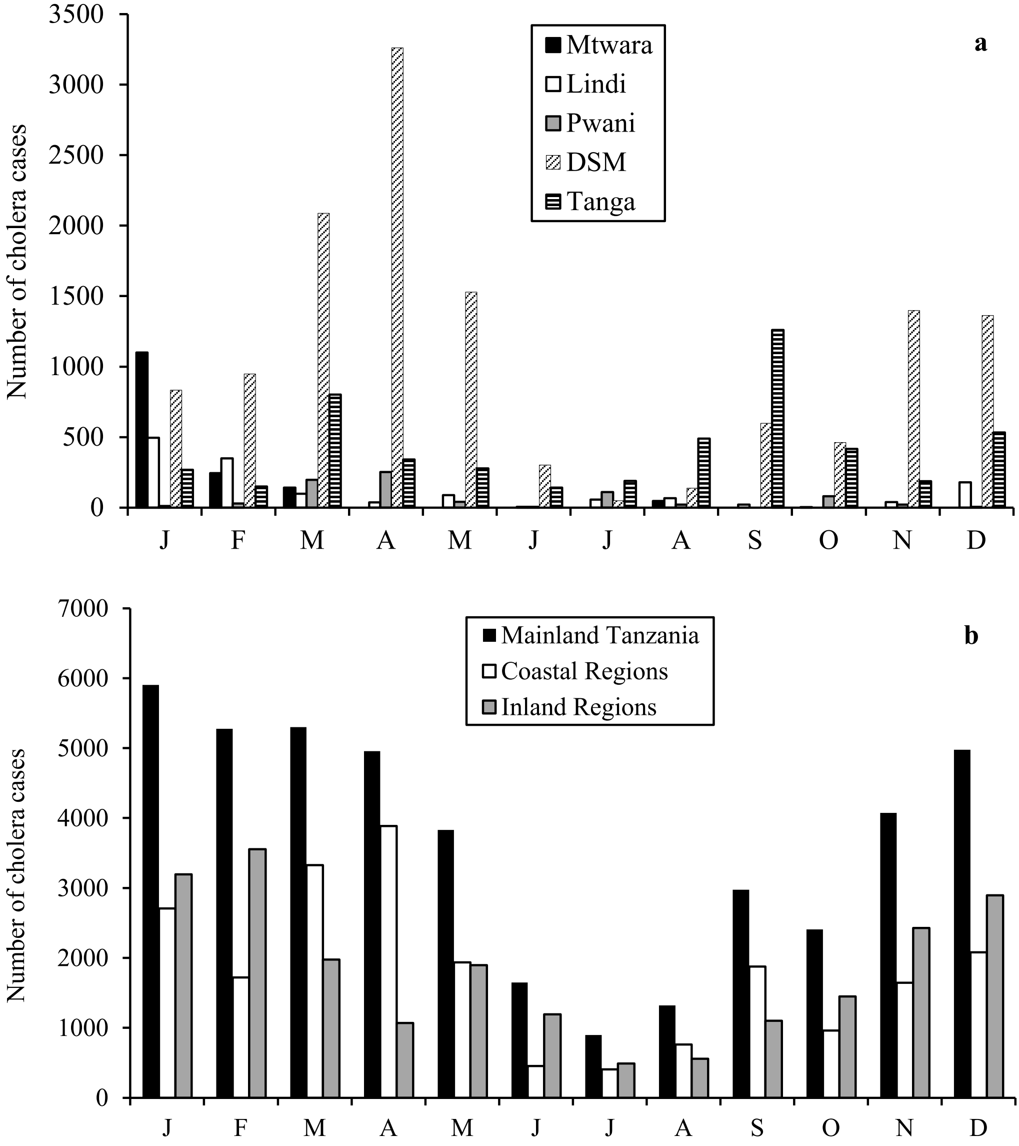

Figure 2. The total number of cholera cases during 2004-2010 in a) the coastal regions of mainland Tanzania and b) a comparison between the coastal regions and interior.

access. Similarly, coastal populations had better access to latrines (70%) compared to inland populations (60%). Dar es Salaam had a higher provision of latrines, indicating better sanitation, followed by Tanga Region, while Pwani Region had the lowest. Country wide, the provision of latrines was 65% in 2006 and, according to the Ministry of Health and Social Welfare (Tanzania), this increases annually by ~1%.

Air temperature and SST values in all coastal regions were highest from December to March (Fig. 3a, b) and significantly higher during the NEM period compared to the SEM (t = 7.528, p = 0.0001; U' = 625, p = 0.0001 respectively), with June to August being the coldest. Although there was weak evidence for differences between the regions, these were not significant for air temperature or

Table 1. Cholera mortality (number of deaths), human population, access to infrastructure (safe water and sanitation expressed as a percentage of total population) in the coastal regions of Tanzania (CFR = Case Fatality Rates).

Region	Mortality (number of deaths) and CFR (%)							Population (n)		Access to infrastructure (2006)	
	2004	2005	2006	2007	2008	2009	2010	2004 ($x10^6$)	2010 ($x10^6$)	Safe water	Sanitation
Dar es Salaam	4	0	101	1	1	3	18	2.64	3.118	90	81
Mtwara	2	0	1	0	0	0	3	1.17	1.324	36	66
Lindi	15	0	0	13	14	0	7	0.82	0.924	54	63
Tanga	35	48	6	11	6	35	7	1.71	1.967	59	77
Pwani	7	0	12	1	2	4	0	0.92	1.063	61	62
Coastal Regions	63	48	120	26	23	42	35	7.26	8.396	60	70
Inland Regions	179	60	134	44	27	39	60	27.6	33.52	46	60
Tanzania mainland	242	108	254	70	50	81	95	34.9	41.91	53	65
CFR	2.4	3.3	1.3	2.1	2.5	1.0	2.0	-	-	-	-

SST, (f = 2.262, p = 0.074; f = 0.083, p = 0.983 respectively). Rainfall was on average lowest from June to September and highest from March to May (Fig. 3c), with no significant differences between the five regions (f = 0.098 p = 0.983). Significantly higher rainfall was recorded during the NEM compared to the SEM (U' = 574, p = 0.0001). Wind speed was high in Mtwara and Lindi compared to Pwani, Dar es Salaam and Tanga (Figure 3d; KW = 51.78, p <0.0001). However, average monthly wind speeds in all the coastal regions of Tanzania (pooled data) did not differ significantly between the NEM and SEM (U' = 339, p = 0.614). Coastal chlorophyll *a* (Chl *a*) concentrations differed significantly between the coastal regions (KW = 37.45, p < 0.0001; Fig. 3e); the Pwani Region had significantly higher levels compared to the others. Chl *a* concentrations were on average higher during the months of January to May but were not significantly different between the NEM and SEM (U = 314, p = 0.985).

Partial autocorrelation of the cholera case time series with environmental parameters for Dar es Salaam and Tanga, the regions with the highest numbers of cholera cases, suggested that the time series could be modeled using an

Table 2. Regression coefficients (±SE) derived from autoregression models of monthly cholera case numbers for Dar es Salaam and Tanga and corresponding data for sea surface temperature (SST), wind speed (wind) and concentration of chlorophyll *a* (Chl *a*), for lags of 1-4 months. Significance levels are 5%* or 10%$^+$.

Location	Variable	Lag 1	Lag 2	Lag 3	Lag 4
Dar es Salaam	SST	0.093 ± 0.062	-	-	-
Dar es Salaam	Wind	0.089 ± 0.067	-0.066 ± 0.068	-0.120 ± 0.064$^+$	-
Dar es Salaam	Chl. *a*	0.132 ± 0.063*	0.162 ± 0.066*	-	-
Tanga	SST	-	-	0.192 ± 0.098 +	-0.177 ± 0.099
Tanga	Wind	-	-0.084 ± 0.094	-	-
Tanga	Chl. *a*	-0.162 ± 0.090 +	-	-	-

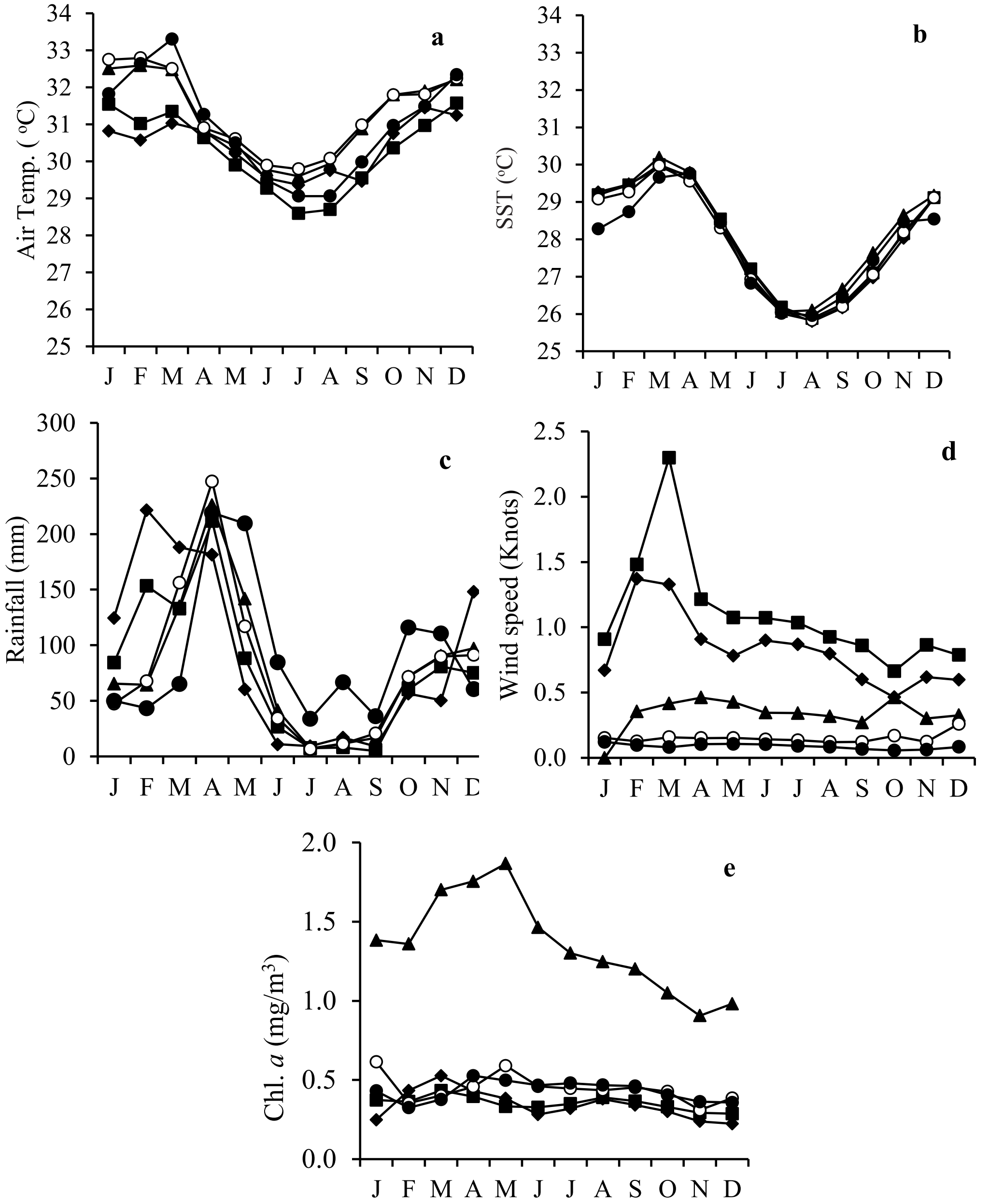

Figure 3. Average a) maximum air temperature, b) sea surface temperature, c) rainfall, d) wind speed and e) chlorophyll *a* in Mtwara (♦), Lindi (■), Pwani (▲), Dar es Salaam (○) and Tanga (●) during 2004 – 2010.

autoregressive process with a lag of one month, i.e. AR(1). This result was confirmed during the system identification step when fitting the data to an ARX model, resulting in an autoregression coefficient of 0.79 ± 0.06 (95% confidence interval) for the Dar es Salaam time series. The environmental parameter with the highest predictive value for cholera was Chl *a* in the Dar es Salaam Region (Table 2). The relationship between cholera cases and this parameter in the Dar es Salaam dataset was positive and significant at the 5% level for lags of one and two months. The other parameters which were potentially correlated with the incidence of cholera were SST and wind speed. Weak predictions of cholera cases one or two months ahead of time became possible when combined with results of the other variables. The relationships between cholera cases and these parameters were similar in the Tanga

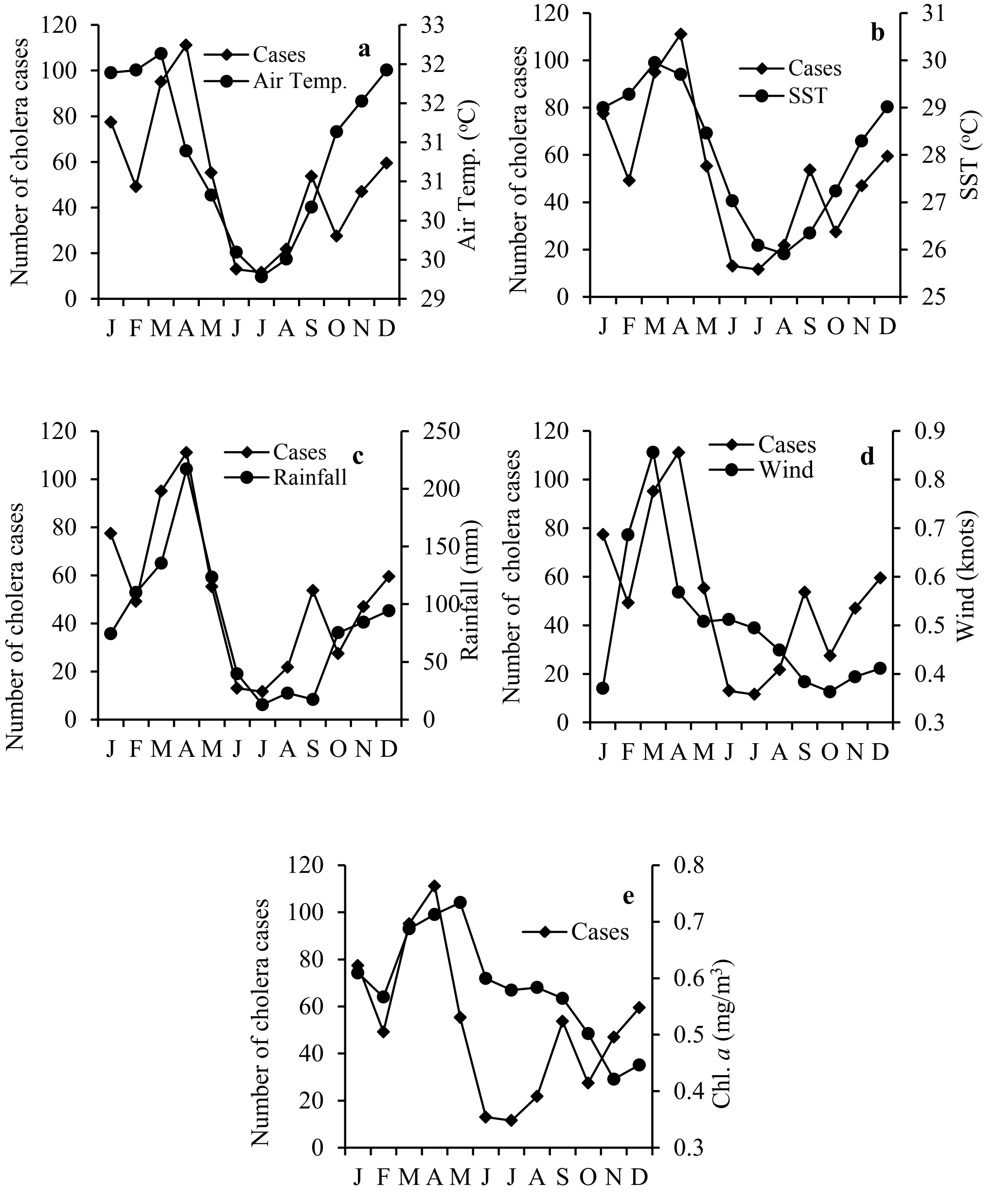

Figure 4. Co-variation between monthly (2004 – 2010) average number of cholera cases in the five Tanzanian coastal regions relative to a) air temperature, b) sea surface temperature, c) rainfall, d) wind speed and e) chlorophyll a concentration.

Table 3. Regression coefficients (±SE) derived from autoregression models of the number of cholera cases in Dar es Salaam and Tanga and Indian Ocean Dipole Mode Index data, for lags of 3-6 months.

Location	Lag 3	Lag 4	Lag 5	Lag 6
Dar es Salaam	-	-0.061 ± 0.096	-0.179 ± 0.121	-0.025 ± 0.1
Tanga	-0.146 ±0.135	0.203 ± 0.179	-0.042 ± 0.140	-

Region, however, whereas Chl *a* at a lag of one month was positively correlated with the incidence of cholera in the Dar es Salaam Region, the results were negative in the Tanga Region. Wind had a weak negative effect at a lag of two months in the Tanga Region and SST had a significant effect at the 10% confidence level at lags of three and four months, which contrasts with the Dar es Salaam Region where it had a weak effect at a lag of one month.

When monthly numbers of cholera cases for Dar es Salaam and Tanga were regressed against monthly values of the Indian Ocean Dipole Mode Index (DMI) using an ARX model, weak relationships were found between the number of cholera cases at Dar es Salaam and the DMI data at a lag of five months (Table 3). The relationship between the numbers of cases in Tanga and the DMI was even weaker (Table 3).

DISCUSSION

A higher number of cholera cases were recorded along the Tanzanian coast compared to its inland regions during this study. This is probably due to the close proximity of the coastal regions to the natural reservoir of *Vibrio cholerae*, the marine environment (Dalusi *et al*., 2015). Previous studies elsewhere have shown that cholera usually strikes villages in coastal regions before it occurs inland (Colwell *et al*., 1981; Karunasagar *et al*., 2003; Julta *et al*., 2010). The Tanzanian coast also has rivers and estuaries that provide an environmental niche for *V. cholerae*, as it associates with organic material such as detritus or biofilms and plankton (Colwell *et al*., 1981; Dalusi *et al*., 2015; Vezzulli *et al*., 2010). These riverine corridors and networks, which undergo tidal flux, may allow the passage of the free-living or attached bacterium inland through a combination of different hydroclimatic macro-scale drivers and less well described active and passive transport mechanisms (Paz & Broza, 2007; Akanda *et al*., 2011). Once humans have ingested the pathogen, asymptomatic infections and a pre-epidemic build-up may occur before the index case of cholera emerges (Faruque *et al*., 2004). In densely populated areas, as is the case in Dar es Salaam and Tanga, cholera may then rapidly spread among the population (Mhalu *et al*., 1984) via contaminated water or human interactions.

We found that cases of cholera and climatic variables co-vary on a seasonal basis in coastal regions of Tanzania (Fig. 4), hot months typically having high numbers of cholera cases. Nevertheless, our analyses did not reveal significant relationships between cholera cases and maximum air temperatures or rainfall but rather between cholera and ocean and ocean-related climate conditions, i.e. sea surface temperature, wind and phytoplankton biomass. The incidence of cholera lagged behind peaks in these variables by a month or months in relationships that ranged in strength. Some results were contradictory and this may reflect the complex aetiology of cholera. Seasonally changing air temperature and rainfall may nevertheless provide the necessary, but insufficient, conditions for the outbreak and severity of cholera. During strong rains and monsoon flooding, the salinity in coastal environments is reduced, potentially affecting the physiological state of *V. cholera* and its association with zooplankton, which are important for its survival (Thomas *et al*., 2006). On the other hand, if salinities drop too far, this can have a negative effect on *V.*

cholera abundance and survival (e.g. see Hashizume *et al*., 2011), particularly the free-living cells.

The lag effects we encountered could, for example, be attributable to strong rainfall increasing the riverine discharge of inorganic nutrients and organic material into estuaries, resulting in turn in phytoplankton and zooplankton blooms, indicated by an increase in Chl *a* (Jutla *et al*., 2011). As environmental conditions become optimal for zooplankton, this may be benefit the physiological state of *V. cholera* as it is associated with plankton (Colwell *et al*., 1981). Such a change in physiological state might not be sufficient for a cholera outbreak if the bacteria are low in number, insufficient become virulent, or the mechanisms for their transport into human populations are absent. It is also possible that, during the wet season, storm-water overflow may enter sewage systems, introducing faecal-contaminated water into rivers. Indeed, heavy rainfall and flooding is known to facilitate outbreaks of diarrhoeal disease in low-income countries (McMichael and Hales, 2006).

Conditions which promote the growth and virulence of the pathogen, or those, that facilitate its transfer from the marine environment to human populations, might thus constitute sufficient conditions for a cholera outbreak. Significantly higher number of cholera cases occur in Tanzanian coastal regions during the NEM with its high temperatures, low wind speeds and calm seas, and this could be due to several factors, including increased plankton biomass along the Western Indian Ocean during this period (Lugomela *et al*., 2002). Plankton and other organic particles provide a surface area for the attachment of *V. cholera* (Colwell *et al*., 1981). In addition, inorganic particles and the chitin of zooplankton provide nutritional substrates for the pathogen, and induce natural competence (Meibom *et al*., 2005), important for environmental adaptation and survival.

Our regression analyses suggested that sufficient conditions for cholera outbreaks are indicated by elevated sea surface temperatures, phytoplankton biomass and wind but this does not suggest that there are direct causal relationships between these parameters: they should be viewed as proxies. For example, Chl *a* co-varies with sea surface temperature, zooplankton biomass, total particulate matter etc., and thus serves as a proxy for all these. Other studies have similarly linked cholera to environmental and oceanographic conditions (plankton biomass, sea surface temperature, winds and season; De Magny *et al*., 2008; Igbinosa & Okoh, 2008; Koelle *et al*., 2005; Vezzulli *et al*., 2010, Jutla *et al*., 2011). The exact nature of these interactions is unknown. However, the advantage of using such proxies is that they can be remotely sensed, and thus could be used to predict cholera caseloads months ahead of time.

The observed seasonal patterns in cholera outbreaks relative to rainfall and temperature, in conjunction with the regression analyses on the seasonally adjusted data, suggest that the severity of cholera outbreaks may not depend on how much it rains or how hot it is. Rather, wet or hot conditions must occur before other factors can trigger an outbreak. The ephemeral nature of cholera outbreaks in Tanzania – it is always hot and wet during the NEM but cholera epidemics do not always occur – supports this hypothesis. The functional relationship between cholera cases, air temperature and rain is thus not a simple monotonic relationship (e.g. linear or quadratic) but might be a step-function. This implies that, once the wet and or hot season has advanced sufficiently, the conditions necessary for a cholera outbreak occur, but not necessarily at the required intensity. Our results thus suggest a complex relationship between cholera outbreaks and climatic conditions.

We also found a relationship between the number of cholera cases and a five-month lag in the Indian Ocean Dipole. The DMI is based on the temperature difference between the eastern and western tropical Indian Ocean and reflects the Indian Ocean Dipole Mode Index, which has been shown to be a predictor of East African rainfall (Saji *et al*., 1999). This suggests that it may be possible to predict cholera outbreaks for Dar es Salaam five months ahead of time. These results corroborate similar findings on the subject in Bangladesh (Hashizume *et al*., 2011). Luo *et al*. (2007) also suggested that it may be possible to predict the severity of cholera outbreaks months in advance using climate indices. Inter-relationships between climate indices and cholera outbreaks have been used to assess the effects of global climate change on the incidence of cholera in Tanzania (Trærup *et al*., 2011).

Insufficient sanitary conditions and health care are factors that exacerbate outbreaks; however, these do not vary strongly on a seasonal basis or from year to year. The lower mortality from cholera in Tanzanian coastal regions compared to the interior may be due to improved socio-economic conditions. Here, improved awareness, the availability of and access to better health care facilities, and cholera management in coastal regions may also reduce outbreaks. However, the Dar es Salaam and Tanga Regions have the highest levels of sanitation, yet had a higher incidence of cholera, suggesting the importance of the environmental reservoir. Generally, the access to clean and safe water in Tanzania was only 53% in 2006 and the access to latrines was 65%. Despite this, the Case Fatality Rate (CFR) in Tanzania has decreased from 11.7% in the 1970s to 2% in 2010, a reduction similar to the global trend (WHO, 2010). Nonetheless, endemic outbreaks remain a major health problem in Tanzania. Their successful prevention in cholera-endemic countries must include developing an awareness of the relationship between the outbreaks, the environmental reservoir and climate.

In summary, our results have shown that the coastal regions of Tanzania are more prone to cholera outbreaks than the interior, probably due to their proximity to the marine environment, the natural reservoir of *V. cholerae*. It is evident that climate indices show promise in predicting these outbreaks and studies of this nature will become increasingly important in managing the disease and developing early warning systems of outbreaks in this era of climate change.

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