Local environmental drivers of cholera in Bangladesh and Vietnam

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Abbreviations and definitions:

ENSO	El Nino-Southern Oscillation
HDSS	Health and Demographic Surveillance System, Dhaka, Bangladesh
OCC	Ocean chlorophyll concentration
POET	Physical Oceanography DAAC Ocean ESIP Tool
SSH	Sea surface height
SST	Sea surface temperature
V. cholerae	Vibrio cholera
WHO	World Health Organization

Abstract

Background: Cholera is an acute infection caused by ingestion of *Vibrio cholerae* bacteria from contaminated food or water. Research on the indirect causes of cholera indicates that environmental factors such as sea surface temperature and ocean chlorophyll concentration play roles in the occurrence and severity of the disease. **Objectives**: This paper reports on temporal fluctuations of cholera incidence in Bangladesh and Vietnam and links these data with satellite-derived and *in situ* local environmental data to examine the relationships between cholera and the local environment. **Methods**: Ordered probit models examine associations between the environment and cholera severity in Bangladesh; probit models examine associations in two sites in Vietnam. **Results**: Increases in ocean chlorophyll concentration are related to an increased probability of severe cholera outbreaks in Bangladesh. Increases in sea surface temperature appear most influential in cholera outbreaks in Hue, Vietnam while increases in river height play a significant role in predicting cholera in Nha Trang, Vietnam. **Conclusions**: The local environment has unique effects on cholera depending on the study area. Potential predictive models must be site specific and dynamic to detect anomalous environmental conditions associated with cholera.

INTRODUCTION

While understanding of cholera etiology significantly increased during the past 20 years, cholera prevalence remains high in many areas of the world, and no predictive model exists to help government health departments prepare for or prevent outbreaks. This paper investigates whether local environmental information can be used to predict cholera outbreaks. The specific aims of this paper are: 1) to describe the temporal fluctuations of cholera during the past 20 years in three study areas with excellent surveillance systems; 2) to examine the role of local environmental drivers of cholera including sea surface temperature, sea surface height, ocean chlorophyll concentration, rainfall, ambient temperature, and river height/discharge; and 3) to compare associations between the local environment and cholera across three study sites in Bangladesh and Vietnam. The analysis measures the spatio-temporal associations between cholera incidence and environmental variables derived from satellite imagery (i.e., ocean chlorophyll concentration, sea surface temperature, sea surface height) and *in situ* data (i.e., rainfall, temperature, river discharge/height).

Previous research does not test the associations between environmental variables and cholera outbreaks over such a long time period nor examine both satellite-derived and *in situ* environmental data simultaneously (Lobitz, Beck et al. 2000). Current predictive and preventive efforts for cholera are limited, and the response is usually reactive (WHO 2004). Additionally, the efficacy of cholera vaccines is limited and wanes after short periods of time, especially in children (Emch 2006). Although responding to cholera after an outbreak is effective in preventing deaths and slowing the spread of infection, an early warning system could cue the vaccination of high risk groups, increasing the immunity of communities and reducing overall morbidity and mortality (Cavailler, Lucas et al. 2006; Emch 2006). The World Health Organization (WHO) recognizes these potential linkages and notes that cholera is an epidemic infectious disease with good potential for developing early warning systems based on climate/environmental drivers (WHO 2004). Therefore, this paper develops and tests probability models for cholera outbreaks and severity based on hypothesized linkages between environmental factors and cholera outbreaks.

BACKGROUND

In some endemic areas of the world, cholera outbreaks have predictable seasonal patterns. In Bangladesh epidemics occur twice a year in the spring and fall, before and after the monsoons (Merson, Black et al. 1980; Islam, Drasar et al. 1993; Emch and Ali 2001; Longini Jr, Yunus et al. 2002). During epidemics, the bacteria that cause cholera, *Vibrio cholerae* are isolated from patients as well as from surface water; however, during inter-epidemic seasons, the bacteria "disappear," i.e. cannot be cultured, from the environment(Khan 1981; Islam, Drasar et al. 1989; Islam, Drasar et al. 1990; Islam, Drasar et al. 1993; Colwell and Huq 1994; Islam, Drasar et al. 1994). Until recently, the reservoirs or sites of survival and multiplication of *V. cholerae* during interepidemic periods were unknown. Recent studies provide more satisfactory explanations of how seasonality and endemicity of cholera are maintained, providing clues about inter-annual variability as well.

Aquatic flora, including algae and phytoplankton, appear to serve as reservoirs of *V. cholerae* (Islam, Drasar et al. 1990; Islam, Drasar et al. 1993; Islam, Hasan et al. 1993). Other literature suggests that aquatic fauna, such as zooplankton and copepods, also play an important role as an environmental reservoir for cholera (Nalin 1976; Nalin, Daya et al. 1979). Lobitz et al hypothesized that the warming of the local sea surface temperature influences the growth of phytoplankton concentrations and that sea surface height increases human-vibrio contact by transporting the bacteria into inland waters through the tidal intrusion of plankton (Lobitz, Beck et al. 2000). The hypothesized associations and patterns between local or regional-level climate and cholera can be indirectly measured using satellite imagery. Using satellite sensors, Lobitz et al found that both sea surface temperature and sea surface height in the Bay of Bengal are correlated with temporal fluctuations of cholera in Dhaka, Bangladesh from 1992 to 1995 (2000).Other research echoes these findings, concurring that increases in sea surface temperature facilitate phytoplankton growth, encouraging the subsequent multiplication of commensal copepods (Kiorboe and Nielsen 1994; Huq and Colwell 1996).

Temporal fluctuations in cholera are likely related to variations in physical and nutritional aquatic parameters (Faruque, Naser et al. 2005) including conditions in both ocean reservoirs and the brackish ponds and canals of rural Bangladesh (Huq, Xu et al. 1996; Chakraborty, Mukhopadhyay et al. 2000). *V. cholerae* survival appears to be dependent on abiotic characteristics including alkalinity, salinity, and iron concentration (Miller, Drasar et al. 1982; Islam, Talukder et al. 2004) that influence the expression of virulent genes such as those that regulate the cholera toxin, the toxin responsible for watery diarrhea (Faruque, Albert et al. 1998; Lipp, Huq et al. 2002). Salinity may also partially explain the seasonal variation of cholera (Miller, Drasar et al. 1982). *V. cholerae* may be unable to persist in winter with colder water temperatures: aquatic reservoirs with salinities of 0.25-3.0% and temperatures consistently above 5°C may maintain cholera in endemic areas (Miller, Drasar et al. 1984).

Based on the disease ecology literature described above, it is hypothesized that increases in ocean chlorophyll concentration, sea surface temperature, and sea surface height will be positively associated with cholera severity and/or the appearance of outbreaks. It is also expected that increases in river height and river discharge will be negatively associated with cholera because of a dilution effect, a possible effect caused by the lower bacterial concentration due to more fresh water coming into the aquatic environment (Ruiz-Moreno, Pascual et al. 2007).

MATERIALS

Study areas. Cholera incidence time series and contemporaneous environmental variables are compiled for Matlab, Bangladesh (Figure 1), Nha Trang, Vietnam, and Hue, Vietnam from 1983 to 2003 (Figure 2). Matlab is the field research area for the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B), a research institute that implements a health and demographic surveillance system. Matlab is in south-central Bangladesh, a region of endemic cholera approximately 50 kilometers south-east of Dhaka, adjacent to the confluence of the Ganges and Meghna rivers. In Vietnam, cholera data are collected through a surveillance program implemented by the National Institute of Hygiene and Epidemiology (NIHE). NIHE conducts cholera surveillance through its provincial Centers of Preventive Medicine, including sites in both Vietnam study areas. Nha Trang and Hue are both in coastal regions of Vietnam. Nha Trang is adjacent to the ocean; Hue is separated from the ocean by several kilometers of estuary.

Environmental data. Table 1 summarizes source information for the environmental variables. For all three study sites, mean monthly sea surface temperature, sea surface height, and ocean chlorophyll concentration are derived from satellites. The satellite data for the sea surface temperature variable are available beginning in January 1985 and are collected by NASA's Jet Propulsion Laboratory. The sensor collects data for four kilometer areas. This analysis is based on eight by eight pixel areas; each record represents an average value for a 32 km × 32 km (1024 km^2) area. Sea surface height, which is a measure of sea level anomalies, is derived through satellite altimetry available from 1992 to 2002 from the Topex/Poseidon and Jason-1 sensors. Ocean chlorophyll concentration data are from SeaWiFS, a system that senses chlorophyll concentration at a spatial resolution of nine kilometers. Approximately the same area is used to compile these satellite-derived monthly environmental variables for all three sensors (Figures 1 and 2). Tables 2, 3 and 4 show summary statistics for each of the sites for the satellite-derived variables.

Environmental variables from *in situ* sources include monthly ambient temperature, rainfall, and river discharge/height (Tables 2-4). The source for the Bangladesh *in situ* data is the Water Resources Planning Organisation (WARPO), which monitors water resources using a network of observation stations throughout the country. The closest two river discharge stations to the Matlab study area, Demra and Bhairab, are included in the analysis. Discharge at Demra is recorded from June to October from 1983 to 1993 and in Bhairab from 1983 to1988. Ambient temperature and rainfall are available from 1985 to 2003 in Chandpur, which is just outside the study area. In Vietnam, the environmental data are from the Hydro-Meteorological Service of Vietnam (HMS), a government agency that manages a national network of meteorological and hydrological stations. In both Hue and Nha Trang, Vietnam, ambient temperature, rainfall, and river height/discharge data are available from late 1985 to 2003. River height is available on the main river flowing into Hue, the Perfume River, and on two rivers flowing into the Nha Trang study area (the Main River at Dong Trang station and the Dinh River at Ninh Hoa station). River discharge is also available for the Main River at Dong Trang.

Cholera data. Monthly mean cholera case data for the Bangladesh research site originate from the Matlab field location of the ICDDR,B and are available between 1983 and 2003. Two outcome variables, cholera severity at the 70th percentile and cholera severity at the 85th percentile, are created by categorizing the average monthly cholera cases. First, all 21 years of data are sorted by month. For each month-only grouping, the data are ordered based on their monthly cholera cases, and a severity category is assigned. This cholera ranking system assigns the value “1” to the months with lowest 30% of cholera cases; the number “2” for the months within the middle 40% of cholera cases; and, a “3” value for the months with the highest 30% of all cholera cases. For example, all 21 years of February observations are grouped and ordered based on cholera cases. The years with the lowest 30% of February cholera cases receive the severity ranking of 1 (low); the years with the middle 40% of February cholera cases receive the severity ranking of 2 (medium); and the years with the highest 30% of all February cholera cases receive the severity ranking of 3 (high). After assigning the relative, within-month rank, the data are resorted by month and year, treating each month as an observation with a ranking coded 1, 2, or 3. The same procedures are followed to create the outcome variable of cholera at the 85th percentile, coding “1” for the lowest 15% of cases; “2” for the middle 70%; and “3” for the highest 15% of cholera cases. The relative rank makes sense since the goal is to understand why some monthly cholera outbreaks are extraordinarily higher or lower than the same month in other years. Figure 3 shows monthly cholera incidence fluctuation in Bangladesh over the entire study period.

Data on monthly cholera cases are available in Hue from 1985 to 2003 and in Nha Trang, from 1985 to 1995. There are no reported cholera cases in Nha Trang since 1995; the reason for the disappearance is unknown. The dependent variable for cholera in both Hue and Nha Trang, Vietnam is created by dichotomizing the monthly cholera cases. Presence of any cholera case is coded “1,” while no recorded cholera months are coded “0.” This is appropriate in both Vietnam sites as epidemics are infrequent, and there is no measurable cholera between outbreaks. Figures 4 and 5 illustrate the sporadic cholera epidemics in the two Vietnam study areas.

METHODS

To investigate the relationships between cholera and the environment, an exploration of patterns over time is necessary. In Bangladesh, higher cholera incidence is expected just before and after the monsoon, but some seasonal epidemics are worse than others. Since there is always a measurable level of cholera in the Bangladesh study area, examination of the severity of monthly average epidemic level in comparison to the same monthly average epidemic level in other years is warranted. In Vietnam, seasonal patterns are apparent, but seasonal outbreaks do not occur every year; therefore, examination of the environmental factors that enable cholera outbreaks are necessary. In all three study sites, there are anomalies in both environmental factors and cholera cases. It was hypothesized that these extraordinary seasonal and monthly effects are key to understanding the relationships between the environment and cholera.

It is possible that environmental factors have a delayed effect on cholera outbreaks; therefore, two-month lag effects of each independent variable are created. Also, since the ultimate goal of this project is to determine whether and how environmental variables can be used in an early warning system, it makes sense to examine these relationships before cholera epidemics occur. A correlation matrix between variables and their lag effects reveal low correlations. Therefore, lags of each variable are tested for independent significance. Correlation matrices and variance inflation factors (VIF) are utilized to test the degree to which collinearity among the predictor variables degrades the precision of the estimates; a VIF value greater than 10 is considered high. High correlations between significant variables limited multivariate model development. In Bangladesh, river discharge variables are positively correlated (0.71), but the variance inflation factor (VIF) is acceptably low at 2.06. In Hue, Vietnam, river height, sea surface height, and rain show tolerable VIF values of 7.06, but high correlations above 0.80 are worrisome. In Nha Trang, Vietnam, the Main River height and discharge are correlated at over 0.95 with a VIF approaching 10, suggesting collinearity. The correlation matrix for Nha Trang variables also reveals high correlation between Main River height and discharge with rainfall at approximately 0.70 and with Dinh River height at 0.55.

Bivariate and multivariate statistical models are built and tested using STATA 9.0. For Bangladesh, an ordered probit model is built since the cholera severity outcome variable is ordinal. For Vietnam, probit models are built due to the dichotomous outcome. All models are adjusted for robust standard errors to correct for the heteroskedasticity of the non-linear models. To test for significance in bivariate models, Wald chi-square and z statistics are utilized with significance reported at the $p<.05$, .01, and .001 levels. In multivariate models, z statistics are utilized to assess significance of individual variables; Wald chi-square and log likelihoods are utilized to assess significance of the full model. Due to the difference in number of observations of independent variables, specification tests of goodness of fit in multivariate models are not conducted.

RESULTS

Table 5 shows the results of the ordered probit models to estimate the severity of cholera outbreaks at both the 70th and 85th percentiles in Bangladesh. Ocean chlorophyll concentration is found to have a positive and significant association with cholera severity at both the 70th and 85th percentile, and the 2-month lag effects are also significant and positively related to the probability of a severe cholera outbreak. Mean cleaned tidal discharge at Bhairab is significant and negatively associated with the probability of a severe cholera outbreak at the .05 level in models at the 70th and 85th percentile. Mean cleaned tidal discharge at Demra is negatively associated with the probability of a severe cholera outbreak, but it is only significant in the model of severity at the 85th percentile at the .05 level. Sea surface temperature, rainfall, sea surface height, and temperature are not significantly associated with cholera severity.

The marginal effects of ocean chlorophyll concentration, ocean chlorophyll concentration 2-month lag, cleaned tidal discharge at Bhairab, and cleaned tidal discharge at Demra are calculated separately for severity at the 70th percentile. The change in average of the probabilities method is utilized to measure the effects of an increase in one standard deviation (values listed in Table 2). The results indicate that for every 0.41mg/m^3 increase in ocean chlorophyll concentration, the average probability of a month being placed in the lowest 30% severity category of all same months decreases by 19.5%; placement in the top 30% of severity increases by 13.2 % (Table 6). The lag effects are also strong: a 0.41mg/m^3 increase in the ocean chlorophyll concentration 2-month lag decreases the average probability of a month being placed in the lowest 30% of severity by 31.2% and increases the probability of placement in the top 30% of severity by 24.5%. In contrast, an increase in 4870 m^3/s of river discharge at Bhairab increases the probability of low severity month by 7.3% and decreases the likelihood of being in the most severe category by 9.3%. The effects of an increase at Demra are similar to those at Bhairab; an increase of 360 m^3/s discharge increases the probability of being in the lowest 30% category by 7.5% and decreases the likelihood of a severe outbreak by 7.6%.

The marginal effects of an increase in one standard deviation are also calculated for the model at the 85th percentile of cholera severity. The effects of ocean chlorophyll concentration and its lag are positive, but smaller. An increase in 0.41mg/m^3 of ocean chlorophyll concentration decreases the probability of a month's placement in lowest 15% severity by 8.3% and raises the probability of placement in the top 15% of severe months by 3.6%. A similar rise in its lag decreases the probability of placement in the lowest category by 6.2% and raises the likelihood of cholera severity by 2.6%. In Bhairab, an increase of 4870 m^3/s of river discharge increases the probability of being within the lowest 15% of monthly cholera severity by 5.5% and decreases the likelihood of a severe outbreak by the same amount. Lastly, in Demra, an increase in 360 m^3/s increases the average probability of a month being placed in the lowest 15% of all same months by 7.8%; with this same increase, placement in the top 15% of severity deceases by 5.9%.

Table 7 shows the probit model results estimating the probability of cholera outbreak in Hue. River height, sea surface height, sea surface height 2-month lag, and rainfall 2-month lag have negative and significant associations with cholera outbreaks in the bivariate analysis.

Sea surface temperature has a positive and significant effect on the probability of cholera outbreak. ocean chlorophyll concentration and temperature are not significantly associated with the probability of cholera outbreak. In multivariate analysis, the effect of sea surface temperature has a significant, positive effect on the probability of cholera outbreak while controlling for sea surface height.

The marginal effects of an increase in one standard deviation of cholera outbreaks in Hue are calculated for all significant variables from bivariate models: river height above sea level, river height above sea level 2-month lag, sea surface temperature, sea surface height, sea surface height 2-month lag, and rainfall 2-month lag. The change in average of the probabilities method is utilized to measure the effects of an increase in one standard deviation (values noted in Table 3). For every 31cm increase in river height, the probability of cholera decreases by 2.9%; the same increase in its lag effect decreases the probability of outbreak by 6.3% (Table 8). Most striking, for every 3.6 degrees Celsius increase in sea surface temperature, the probability of cholera increases by 15%. In the multivariate model, for every 3.6 degrees Celsius increase in sea surface temperature, the probability of cholera increases by 12.2%, controlling for the effects of sea surface height.

Table 9 shows the results of the probit models to estimate the probability of cholera outbreak in Nha Trang. Monthly rainfall, Main River height, Dinh River height, Dinh River height 2-month lag, and Main River discharge have a positive and significant effect on the probability of cholera outbreak. Sea surface temperature, sea surface height, and ambient temperature are not significantly associated with the probability of cholera outbreak. In multivariate analysis, the effect of Dinh River height has a significant, positive effect on the probability of cholera outbreak while controlling for the height of the Main River.

The marginal effects of an increase in one standard deviation on cholera outbreak in Nha Trang are calculated for all significant variables from bivariate models: monthly rainfall, Main River height, Dinh River height, Dinh River height 2-month lag, and discharge at Dong Trang (Table 10). The change in average of the probabilities method is utilized to measure the effects of an increase in one standard deviation (values noted in Table 4). For every 121mm increase in rainfall, the probability of cholera increases by 9.8%, and for every 61 cm increase in Main river height, the probability of cholera increases by 8.8%. Moreover, an increase in 39 cm in the Dinh River increases the probability of cholera by 14% while the same increase in its 2-month lag increases the probability of cholera by 10%. Lastly, an increase of 85 m^3/s Main River discharge increases the probability of cholera by 11.6%. In the multivariate model, for every 39 cm in the Dinh River height, the probability of cholera increases by 14.3%, controlling for Main River height.

DISCUSSION

In Bangladesh, increases in ocean chlorophyll concentration appear associated with increased cholera severity, and this effect is also evident in the 2-month lag. These effects are stronger in the model of cholera severity at the 70^{th} percentile than in the model at the 85^{th} percentile. Since lag effects might prove beneficial in the creation and implementation of an early warning system, this finding is particularly useful. Moreover, the marginal effects of a change in one standard deviation in ocean chlorophyll concentration are two to three times greater than the effects of an increase in one standard deviation in tidal discharge, further demonstrating the potential strength of this relationship. Furthermore, increases in river discharge at both Bhairab and Demra appear associated with a decrease in cholera severity. Although the effects are smaller than ocean chlorophyll concentration, river discharge maintains similar strength at both the 70^{th} and 85^{th} percentile. These discharge stations are located upstream from the study site, and the relationship is consistent with what some have called a dilution effect. Neither sea surface temperature nor sea surface height had a significant effect on the severity of cholera in Bangladesh. This finding differs from previous research on the importance of these factors. Temperature and rainfall are also not associated with the severity of cholera in Bangladesh.

In Hue, unlike in Bangladesh, sea surface temperature has a highly significant effect on the probability of a cholera outbreak. It is the only environmental factor that is positively associated with an increased probability of cholera outbreak in that study area. River height, sea surface height 2-month lag, and rainfall 2-month lag all have significant negative relationships with the probability of a cholera outbreak. The marginal effects are also revealing. An increase in 3.6 degrees Celsius raises the probability of an outbreak by 15%, the strongest effect of any environmental factor. Also in contrast to Bangladesh, sea surface height is significant, although it has a small and negative impact, reducing the probability of an outbreak by 3.7%. Interestingly, lag effects appear more significant in Hue than in Bangladesh: 2-month lag effects of river height, sea surface height, and rainfall all decrease the probability of cholera outbreaks by between 4 to 7%. Overall, in Hue, the effects of sea surface temperature increase the probability of a cholera outbreak. In contrast, increases in river and sea height as well as the lag effects of these factors and rain, all have a negative influence on cholera outbreaks. Ocean chlorophyll concentration and ambient temperature have no significant relationship with the probability of a cholera outbreak.

Nha Trang shows significant variation in the effect of environmental factors on the probability of cholera outbreaks. Unlike Matlab or Hue, the effects of rain, river height, and river discharge appear to have a positive effect on cholera, increasing the likelihood of an outbreak. These factors also appear more influential in Nha Trang. The marginal effect of an increase in one standard deviation in each of these local environmental variables is larger than the effect of similar increases in either Hue or Bangladesh. Increases in rain, Main River height, and Main River discharge impact the probability of cholera by approximately 10%. Dinh River height has the most significant impact: an increase in one standard deviation (39 cm) increases the likelihood of an outbreak by more than 14%, and its 2-month lag is almost as influential, raising the probability by more than 10%. These results and the strength of these effects are unexpected and suggest an inundation effect, perhaps related to Nha Trang location on the coast. An inundation effect is when the aquatic environment is inundated with bacteria possibly because of flooding but this is speculative. The divergence of Nha Trang results from those of the other research sites supports the strength of local-level factors in cholera outbreak.

There are several limitations to this study. The data set is relatively small, limiting the ability to achieve statistical significance. The reason it is small is because the satellite record is short. However, despite the small sample size, the results of the initial analysis suggest that a larger sample would increase both the magnitude and significance of the results. Due to these data availability constraints, aggregation by month is necessary, potentially reducing variation in the data. With additional years of data, or the addition of weekly or daily satellite data, it is expected that significant variables such as ocean chlorophyll, sea surface temperature, and river height could reveal stronger effects on cholera outbreak and severity. Additionally, it is possible that these environmental factors have additional relationships, and the role of interaction and mediation are not explored in this analysis because of limitations in a long enough record for all variables collected for the same time period.

CONCLUSION

Despite previous studies that concentrate primarily on ocean chlorophyll concentration, sea surface temperature, and sea surface height, this study illustrates that additional local-level environmental factors are important in predicting cholera outbreaks and severity of cholera. This finding is especially applicable in the endemic cholera area of Bangladesh where outbreaks are both frequent and severe. The severity of a cholera epidemic in an endemic situation is clearly related to the environment; but translation of this information into the development of a cholera early warning system poses complex challenges. In Vietnam, where cholera is sporadic and occurs with low incidence levels, it may be possible only to identify the necessary, but not sufficient, causes of outbreaks. In these types of situations, a cholera early warning system may not prove accurate or cost effective.

Future studies should examine possible interactive and mediating effects of environmental factors as the high correlations between variables are suggestive of unexplored relationships. This will require a longer record of environmental data, a limiting factor in this study due to the limited history of satellite sensor information. Investigation into within-site variation is also needed, and exploration of the differences in local- or neighborhood-level characteristics could prove informative and valuable. Inclusion of local-level population variables and utilization of multi-level models of neighborhood and climate effects would complement and enhance studies of these relationships.

Overall, the results of this paper serve as a foundation for future studies of the local-level environmental and climactic influences on cholera. The possibility of a cholera early warning system exists since in all study areas there is a clear relationship with environmental parameters. However, the predictive model might be quite complex. This paper demonstrates that the local environmental parameters, including ocean chlorophyll concentration, sea surface temperature, and sea surface height, have significant effects on cholera existence and severity of outbreaks in Vietnam and Bangladesh. Local environmental factors have differential effects on cholera severity and outbreaks, and variations exist within Vietnam and between study sites in Vietnam and Bangladesh. For application in the development of prediction models, it appears that warning systems may need to be adapted for the local environmental context in epidemic situations. Site-specific prediction models might prove useful in forecasting cholera, especially in areas of frequent outbreaks, thus enabling appropriate preparation and vaccination to reduce morbidity and mortality.

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Table 1: Environmental variables and data sources

Variable	Data Source and Availability
Satellite-derived Environmental Variables	
Ocean chlorophyll concentration	SeaWiFS (1997-) Source: http://oceancolor.gsfc.nasa.gov/
Sea surface temperature	AVHRR (1982-) Source: http://poet.jpl.nasa.gov/
Sea surface height	TOPEX/ Poseidon (1992-), Jason-1 (2002-) Source: http://www.aviso.oceanobs.com/
In-Situ Environmental Variables	
Rainfall	Weather stations in Chandpur, Bangladesh; Hue & Nha Trang, Vietnam
Temperature	Weather stations in Chandpur, Bangladesh; Hue & Nha Trang, Vietnam
River discharge/ height	Gauges in Hue & Nha Trang, Vietnam

Table 2: Monthly average of cholera and environment variables in Matlab, 1983-2003

Variable	N Months	Mean	Std. Dev.	Min	Max
Number of cholera cases	252	34.69	44.58	1	327
Ocean chlorophyll concentration (mg/m^3)	75	0.42	0.41	0.18	2.49
Sea surface temperature (°C)	228	25.66	5.33	0.06	31.37
Sea surface height (cm)	135	0.75	8.95	-20.81	18.21
Ambient temperature (°C)	228	30.61	2.68	22.42	35.13
Rainfall (mm)	243	5.82	5.65	0.00	29.98
Bhairab River discharge (m^3/s)	104	7114.89	4869.89	75.29	17245.16
Demra River discharge (m^3/s)	61	1307.15	360.63	244.39	2257.00

Table 3: Monthly average of cholera and environment variables in Hue, 1983-2003

Variable	N Months	Mean	Std. Dev	Min	Max
Cholera incidence/1,000,000	253	34.08	242.23	0	2707
Ocean chlorophyll concentration (mg/m$^{3)}$	100	.544	.342	.149	2.37
Sea surface temperature (°C)	228	26.50	3.57	8.12	31.29
Sea surface height (cm)	148	2.31	13.76	-24.12	34.51
Ambient temperature (°C)	228	25.1	3.40	17.9	30.2
Rainfall (mm)	228	254.33	330.30	3.00	2451.70
Perfume River height (cm)	240	12.60	31.11	-26.53	122.00

Table 4: Monthly average of cholera and environment variables in Nha Trang, 1983-1995

Variable	N Months	Mean	Std. Dev.	Min	Max
Cholera incidence/1,000,000	131	26.26	121.59	0	1302
Ocean chlorophyll concentration (mg/m$^{3)}$	101	0.42	0.30	0.09	2.06
Sea surface temperature (°C)	228	27.00	2.73	10.02	30.52
Sea surface height (cm)	148	0.70	7.81	-23.37	16.43
Ambient temperature (°C)	131	26.59	1.76	22.90	29.60
Rainfall (mm)	131	96.74	121.58	0.10	549.20
Dinh River height (cm)	215	272.95	39.16	110.26	386.53
Main River height (cm)	228	462.42	61.06	381.45	717.45
Main River discharge (m^3/s)	228	73.33	85.24	9.08	520.16

Table 5: Relationship between cholera severity and the environment, Matlab, Bangladesh

Variable	N	Severity at the 70th Percentile	Severity at the 85th Percentile
Ocean chlorophyll concentration	75	1.47*** (.443)	.955** (.367)
Ocean chlorophyll concentration 2-month lag	75	2.75*** (.695)	.654* (.275)
Mean cleaned tidal discharge at Bhairab	104	-.0000546 * (.0000217)	-.0000473* (.0000213)
Mean cleaned tidal discharge at Demra	61	-.000677 (.000379)	-.000905* (.000390)
Sea surface temperature	228	.0138 (.014)	-.004 (.012)
Rainfall	243	-.003 (.012)	.002 (.013)
Sea surface height	135	-.005 (.0105)	-.011 (.013)
Temperature	228	.011 (.026)	.003 (.027)

Results of Wald Chi Square from ordered probit model, bivariate analysis. Robust standard errors in parenthesis. *p< .05, **p< .01, ***p< .001

Table 6: Marginal effects on Probability of Cholera Severity Ranking, Matlab, Bangladesh

Marginal effects*	70th percentile			85th percentile		
	Severity Ranking			Severity Ranking		
Variable	Low	Middle	High	Low	Middle	High
Ocean chlorophyll concentration	-.195	.063	.132	-.083	.047	.036
Ocean chlorophyll concentration 2-month lag	-.312	.067	.245	-.062	.036	.026
Mean cleaned tidal discharge at Bhairab	.073	.019	-.093	.055	.00039	-.055
Mean cleaned tidal discharge at Demra	.075	.00143	-.076	.0784	-.0189	-.059

*average expected percentage point change

Table 7: Relationship between cholera severity and the environment, Hue, Vietnam

Variable	N	Bivariate	Multivariate†
River height 2-month lag	228	-.044*** (.012)	
Sea surface semperature	148	.233*** (.063)	.194* (.0934)
Sea surface height	148	-.029* (.012)	-.010 (.015)
Sea surface height 2-month lag	228	-.041** (.014)	
Rainfall 2-month lag	228	-.004*** (.001)	
Temperature	100	.183 (.044)	
Ocean chlorophyll concentration	240	-1.18 (1.16)	
Overall Wald Chi-Square	148		13.94***.

Results of Wald Chi Square from probit model. *p< .05, **p< .01, ***p< .001. Robust standard errors in parenthesis. †Log Likelihood =-30.19

Table 8: Marginal effects of environmental variables cholera, Hue

Variable	Bivariate	Multivariate
River height above sea level	-.029	
River height above sea level 2-month lag	-.063	
Sea surface temperature	.150	.122
Sea surface height	-.037	(in model)
Sea surface height 2-month lag	-.045	
Rainfall 2-month lag	-.067	

*average expected percentage point change

Table 9: Relationship between cholera severity and the environment, Nha Trang, Vietnam

Variable	N	Bivariate	Multivariate
Monthly rainfall	131	.002* (.001)	
Main river height	228	.004** (.002)	.0000186 (.002)
Dinh River height	215	.0123*** (.003)	.0123*** (.003)
Dinh River height 2-month lag	215	.008** (.002)	
Discharge at Dong Trang	228	.004* (.002)	
Sea surface temperature	228	-.007 (.032)	
Sea surface height	148	-.012 (.017)	
Temperature	131	.093 (.065)	
Overall Wald Chi-Square	215		20.45***

Results of Wald Chi Square from probit model. Significance at *p< .05, **p< .01, ***p< .001. Robust standard errors in parenthesis. †Log Likelihood= -126.412.

Table 10: Marginal effects of increases in environmental variables on probability of cholera in Nha Trang, Vietnam

Variable	Bivariate*	Multivariate*
Monthly rainfall	.0978933	
Main river height	.0879012	(in model)
Dinh River height	.1429594	.143
Dinh River height 2-month lag	.1016215	
Mean discharge at Dong Trang	.1162993	

*average expected percentage point change

Figure 1: Bangladesh Study Area

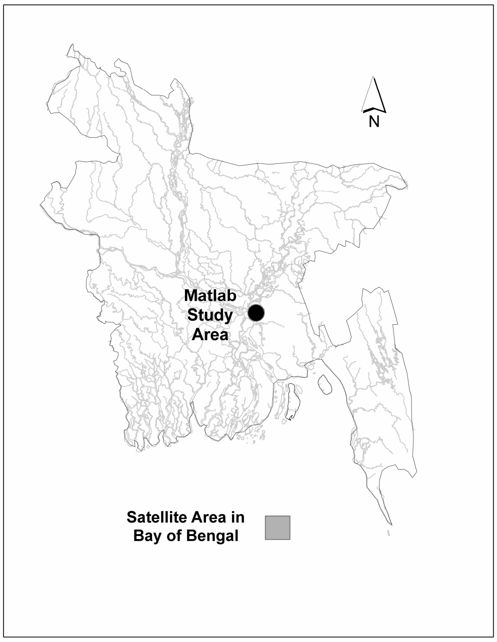

Figure 2: Vietnam Study Areas

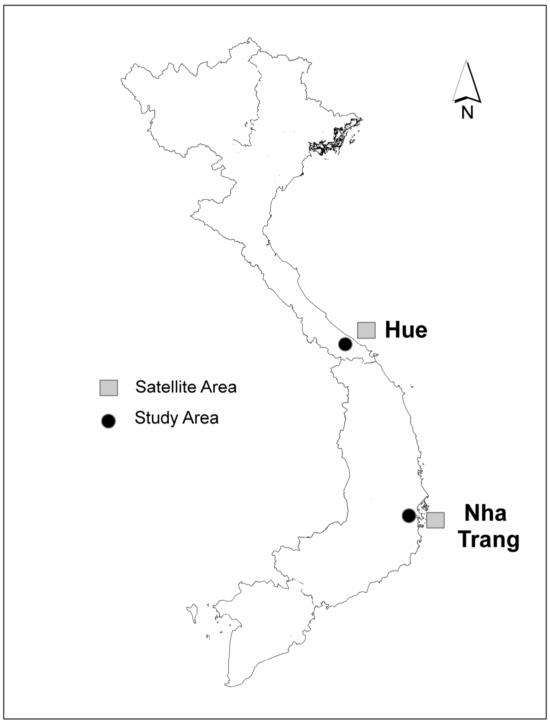

Figure 3: Cholera cases per 10,000 in Matlab, Bangladesh by month, 1983-2004

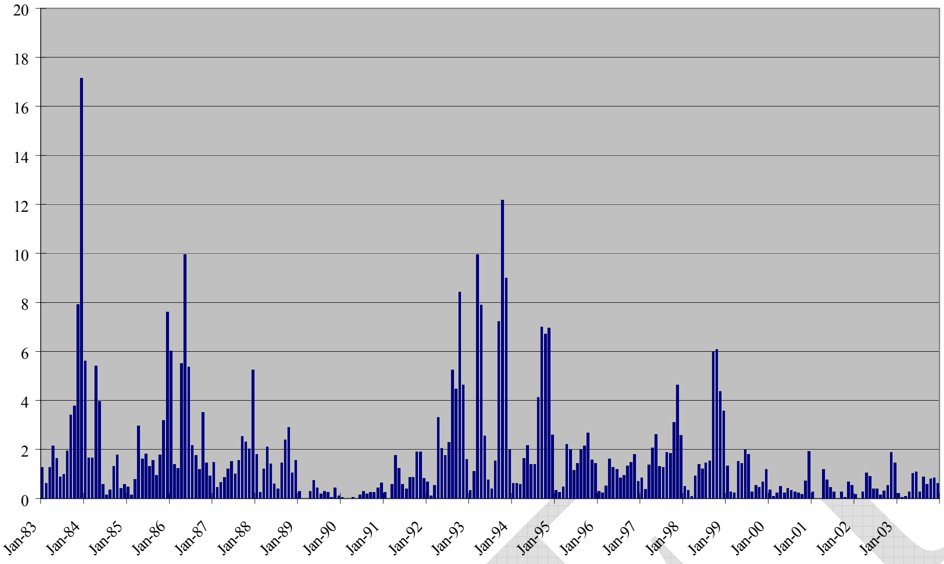

Figure 4: Cholera cases per million in Hue, Vietnam: 1986-2004

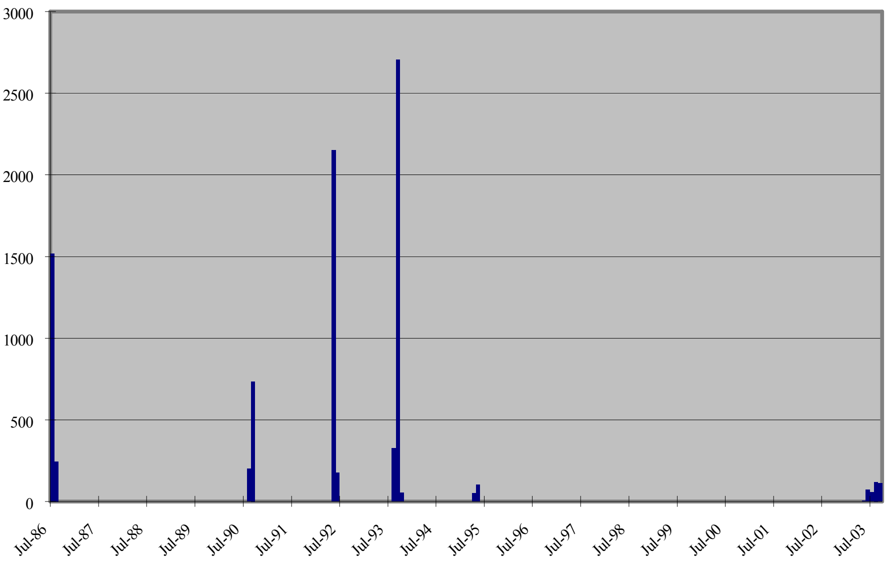

Figure 5: Cholera cases per million in Nha Trang, Vietnam: 1984-2004