HYDROLOGY, CLIMATE AND WATER-BORNE DISEASE TRANSMISSION: ROLE OF LARGE SCALE HYDROCLIMATOLOGY IN CHOLERA DYNAMICS OF BENGAL DELTA

A dissertation

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Dedicated to the countless victims of cholera in the developing world,

And to the hopes of reducing the future burden of this deadly disease …

ABSTRACT

With the ever-expanding geographic reach of the seventh cholera pandemic and alarming fatality rates in newly affected regions, it is apparent that global cholera prevention strategies warrant rethinking. The striking seasonality and annual recurrence of this infectious disease in endemic areas remain of considerable interest to scientists, epidemiologists, and public health workers. This interdisciplinary research study attempts to identify the hydroclimatic and environmental drivers of cholera dynamics, and the role of underlying large-scale processes in propagating the disease in different seasons and spatial locations that have sufficient temporal and spatial "memory" to allow the development of an early warning system. In this study, it is shown that cholera outbreaks in the Bengal Delta region, also known as the native homeland of cholera, are propagated from the coastal to the inland floodplain areas and from spring to fall by two distinctly different, pre- and post-monsoon, transmission cycles influenced by coastal and terrestrial hydroclimatic processes, respectively. Seasonal and interannual patterns of cholera transmission are strongly influenced by estuarine salinity and inland flood inundation patterns that may set the ecological and environmental 'stage' for epidemic outbreaks over large geographic regions. A coupled hydroclimatology-epidemiology model was developed to provide a framework for assessing the impact of hydroclimatic and environmental forcings on cholera dynamics; and has the potential to provide public health authorities a necessary spatially explicit early warning for preemptive intervention before epidemic cholera outbreaks and extreme climatic events such as droughts and floods, especially in light of changing climate patterns in the Bengal Delta region.

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Chapter 1

Introduction

1.1 The Geography of Cholera

Cholera, an acute water-borne diarrheal disease, continues to be a significant health threat across the globe. The world has witnessed an unprecedented rise in cholera infection and transmission since the 1990s, especially in areas of South Asia and Sub-Saharan Africa (*Griffith et al.,* 2006; *Sack et al.,* 2006). A billion people in the world still lack access to clean drinking water and thus remain vulnerable to cholera infection. In addition, global warming and natural disasters can give rise to new biotypes and contribute to outbreaks or occurrence of cholera in places where they normally do not pose a problem (*Colwell,* 2006; *Siddique et al.,* 2010).

The existence of an environmental reservoir of *Vibrio cholerae* (henceforth *V cholerae*), the causative agent of the disease, is well established (*Colwell,* 1996; *Worden et al.,* 2006). There is increased agreement on the role of global climate and the coastal nature of the cholera outbreaks (*Mourino-Perez,* 1998; *Colwell and Huq,* 2001); however, the striking seasonality of this infectious disease and annual recurrence in endemic areas has remained a mystery among epidemiologists and public health professionals across the world (*Collins,* 2003). An extensive research of the literature shows that there is no consensus regarding the role of the primary (environmental) and secondary (human-to-human) transmission mechanisms. Consequently, no 'climate informed' warning system currently exists in cholera endemic countries that may preemptively target and help prepare intervention strategies in regions with high chances of cholera outbreaks.

Cholera broke out as part of a global pandemic from the Bengal Delta region of the Indian subcontinent during the early 19th century (*Sack et al.*, 2004). The global pattern and magnitude of the ongoing pandemic suggests that cholera outbreaks are prominent in the coastal regions between the tropics (Figure 1.1). A closer look at the geography of cholera suggests that outbreaks primarily originate in coastal regions, suggesting a link with near shore waters; and then spread inland through secondary means (*Jutla et al.,* 2010). Recent studies focusing on the Bengal Delta region, also known as the native homeland of cholera, suggest the same. Although cholera cases have been reported in inland districts, the regions of endemicity are most frequently found near coastlines (*Lipp et al.,* 2002). Historic cholera mortality rates in the Bengal delta region were also shown to be associated with the coasts (*Bouma and Pascual,* 2001). A more recent study on cholera epidemiology in Bangladesh shows that cholera cases are more recurrent in locations close to the coastline (*Sack et al.,* 2003). The nature of the early outbreaks of cholera thus suggests a strong link with the near shore marine ecosystems.

1.2 The Ecology of Cholera

The cholera-coastal connection is usually explained by the fact that cholera is caused by two particular pathogenic strains of the bacterium *Vibrio cholerae*, the 01 and the 0139, which show strong association with different inland and marine plankton species (*Islam et al.,* 1994; *Colwell and Huq,* 2001). Phytoplankton and zooplankton, by serving as the primary sources of nutrients and also physical carriers of the bacteria, play an important role in facilitating the survival, growth, and transmission in the natural aquatic environment (*Lipp et al.,* 2002; *Huq et al.,* 1990; *Mouriño-Pérez,* 1998). Environmental factors such as sunlight, salinity, temperature, and nutrients (organic

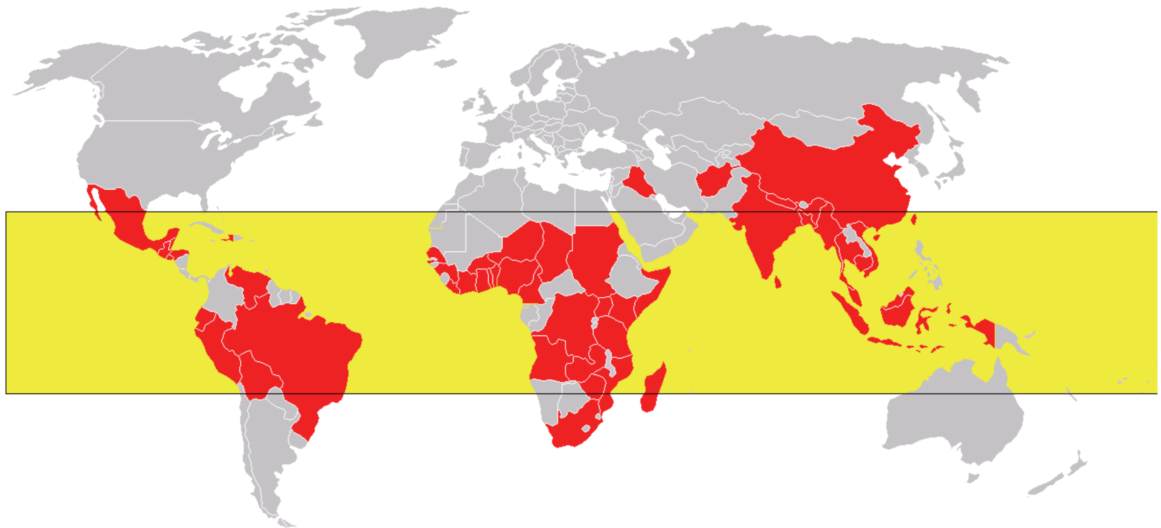

Figure 1.1: Countries Affected in the Seventh Global Cholera Pandemic

(Compiled from WHO, ProMED, and ICDDR,B Sources)

carbon, nitrogen, phosphorus) are suggested to be vital for the survival and growth of cholera bacteria in the aquatic environment (*Singleton et al.,* 1982; *Epstein*, 1993; *Huq et al.*, 2005). Cholera bacteria attach to zooplanktons, more specifically to crustacean copepods, and form a thin pathogenic biofilm that prolongs its survival (*Reidl and Klose*, 2002). Phytoplankton serves as the primary food source for copepods and other zooplanktons, also releasing nitrogenous nutrients into the water through disintegration. The bacteria then proliferate taking advantage of the nutrition conditions of the aquatic system (*Lipp et al.,* 2002). Consequently, one may expect an observed increase in the abundance of phytoplankton to correspond to an increase in the population of cholera bacteria. Such a role of coastal ecosystems working as environmental reservoirs of *V. cholerae* has also been suggested for Southern Africa (*Bertuzzo et al.*, 2008) and Latin America (*Gil et al.,* 2004; *Martinez-Urtaza et al.,* 2004).

Phytoplankton and zooplankton concentrations are found to be considerably higher in coastal Bay of Bengal (BoB), with high chlorophyll variability along the coast compared to relatively constant values further offshore (*Jutla et al.,* 2010). However, suggested roles of coastal plankton in causing cholera outbreaks in the Bengal Delta region (*Emch et al.,* 2008; *Constantin de Magny et al.,* 2008) remained unexplained due to the absence of plausible physical mechanisms. Questions remain on (1) How does the timing and location of coastal plankton blooms affect the timing of cholera outbreaks? (2) How are the bacteria in the coastal region transported inland and how are the water resources contaminated? (3) Which underlying environmental signatures can provide complementary evidence of these processes? And (4) How do hydroclimatic variability and extreme events impact cholera dynamics in affected regions?

1.3 The Hydrology of Cholera

The coastal nature of the cholera outbreaks (*Mourino-Perez,* 1998; *Collins,* 2003) and the established knowledge base on the association of *V. cholerae* with marine plankton species and environmental determinants (*Lipp et al.,* 2002; *Singleton et al.,* 1982; *Reidl and Klose*, 2002; Vital et al., 2007; *Worden et al.,* 2006) suggest a strong role of global climate on the cholera problem (*Colwell,* 1996). The striking seasonality and annual recurrence of this disease in endemic areas, and recent epidemic outbreaks across continents has raised questions about the role of local and regional climatic and hydrologic and ecological processes as well as environmental conditions. A closer investigation of cholera incidence and the relevant oceanic and terrestrial variables, however, shows a lack of understanding of the intraannual and interannual variability and the processes governing cholera transmission in various affected regions of the world.

Most existing literature related to cholera epidemiology, transmission, propagation, and intervention are based on long-term datasets generated by the International Center for Diarrhoeal Disease Research (ICDDR,B) in Bangladesh, where the disease is endemic (*Longini et al.,* 2002; *Glass et al.,* 1982). The coastal floodplains of Bengal Delta have a long history of endemic cholera with wide swings in prevalence being evident (*Longini et al.,* 2002; *Bouma and Pascual*, 2001). Spring outbreaks peak in coastal areas in contrast to larger fall outbreaks occurring in inland areas (Figure 1.2: *Akanda et al.,* 2011). Also, cholera outbreaks across other affected areas, such as Mozambique and DR Congo, show infection patterns with a single annual peak (*Hashizume et al.,* 2008). There is no consensus on the physical, environmental, or ecological factors that may be responsible for these seasonal and spatial fluctuations.

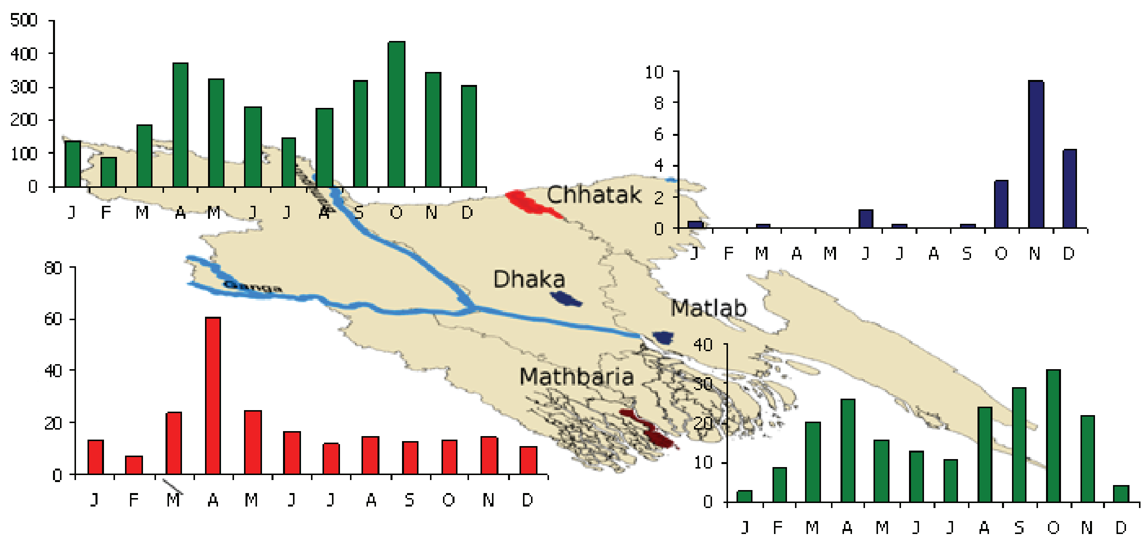

Figure 1.2: Monthly climatology of cholera incidence recorded at ICDDR,B Surveillance centers in Dhaka, Mathbaria, Chhatak and Matlab, Bangladesh

Previous studies have focused on prediction of cholera outbreaks based on environmental or climatic signatures, such as rainfall, coastal plankton abundance, sunlight, sea surface temperature and height, and oceanic processes (*Hashizume et al.,* 2008; *de Magny et al.,* 2008; *Koelle et al.,* 2005; *Islam et al.,* 2009; *Cash et al.,* 2009; *Pascual et al.,* 2008); but these studies did not adequately address plausible causal pathways of transmission. In addition, a mismatch often exists between the scale of observations of health impacts, sampling of causative agent, and related macro-scale drivers. For example, *Pascual et al.* (2008) failed to elaborate on how a large scale phenomenon such as the El nino–Southern Oscillation (ENSO) would translate to cholera incidence in local surveillance programs such as in Matlab, Bangladesh.

The above-mentioned studies, also, did not consider space explicitly. *Bertuzzo et al.* (2008; 2009) first developed a spatially explicit model that simulated the spreading of cholera along river channels during the KwaZulu-Natal 2001–2002 epidemic in South Africa. However, the authors failed to provide realistic explanations of the parameters used in their model, or to incorporate the effects of large scale climatic, ecological or hydrological processes. In summary, cholera outbreaks are the physical manifestations of a complex interplay of local and large-scale processes, extended over a vast range of spatial and temporal scales. Many of these transmission processes are highly complex, due to the nature of hydrologic response to climatic variability and regional specificity, as well as the ecological constraints over nutrient availability and biological growth. The common element involved in the cholera transmission cycle is, however, water. Thus, a model for cholera prediction will need to internalize the crucial functionalities played by hydrological and related climatic processes in both space and time.

1.4 Case for Presented Research

In summary, the life cycle of *V. cholerae* is intricately linked to both **micro**- and **macro**-environmental processes, with vastly different space and time scales of interacting variables (*Jutla et al.,* 2010). Here, we define **micro** as microbiological and genetic processes, while **macro** refers to hydrological, ecological, and climatic processes. We recognize the importance of micro-environmental understanding to develop vaccines and treatment protocols. However, as *V. cholerae* may survive and thrive in a wide range of natural conditions, and since evidence of new biotypes is emerging, it is unlikely that this disease will ever be eradicated. Consequently, we need a new approach to minimize the impact of this devastating disease by predicting where it may occur and proactively initiating effective intervention strategies. This study attempts to identify the macro-environmental processes and variables that have longer temporal and larger spatial "memory" to allow the development of an early warning system for cholera outbreaks.

The following empirical observations provide the motivation to explore the connection among cholera, climate, and hydrology: (a) cholera outbreaks primarily originate near coastal areas before infections move inland; (b) research studies suggest that *V. cholerae* is an autochthonous part of aquatic ecosystems, with a significant positive correlation observed between plankton abundance and pathogenic cholera bacteria; (c) cholera outbreaks across most affected regions show single annual peaks, but a spatio-temporal distribution of single to biannual peaks in the Indian subcontinent, the native homeland of cholera; and (d) climatic drivers such as sea surface temperature and precipitation as well as large scale phenomena such as the El Nino – Southern Oscillation (ENSO) have been suggested to have influence on cholera transmission. However, it is not clear how these climatic events manifest in the transmission and outbreaks of cholera, as our understanding of the cholera-hydrology-climate connection remains limited. Consequently, a physically consistent understanding of the impact of these large scale processes on the space-time characteristics of cholera transmission is needed.

The principal aim of this doctoral investigation is thus to identify the impacts of hydroclimatic variability on the initiation and modulation of cholera outbreaks and provide insights to plausible primary transmission pathways. We focus on the Bengal Delta region, the native homeland of cholera, where the longest and most comprehensive cholera datasets available in the world show an interesting variation in spatial and temporal patterns of cholera incidence (Figure 1.2). The role of the spatial distribution of temperature and rainfall in this region (Figure 1.3) and the seasonal variability of flow, coastal plankton, and regional sea surface temperature patterns (Figure 1.4) on the space-time distribution of cholera outbreaks (Figure 1.2) are not well understood.

We focus on the asymmetric regional hydroclimatology that may help set up the environmental and ecological 'stage' for cholera outbreaks in different seasons and extreme years and subsequent propagation into population centers. In addition, this study investigates the relationship of hydroclimatic processes and associated extreme events (e.g., droughts and floods) on their links to the outbreaks, occurrence, and transmission of cholera. The outcome of this research will help us identify how cholera transmission and outbreaks are most likely to respond to shifts in climatic, hydrologic, and ecological variability (Figure 1.4) and provide guidelines on setting up advanced warning mechanisms to predict cholera outbreaks and help prepare preemptive intervention strategies to lessen the disease burden.

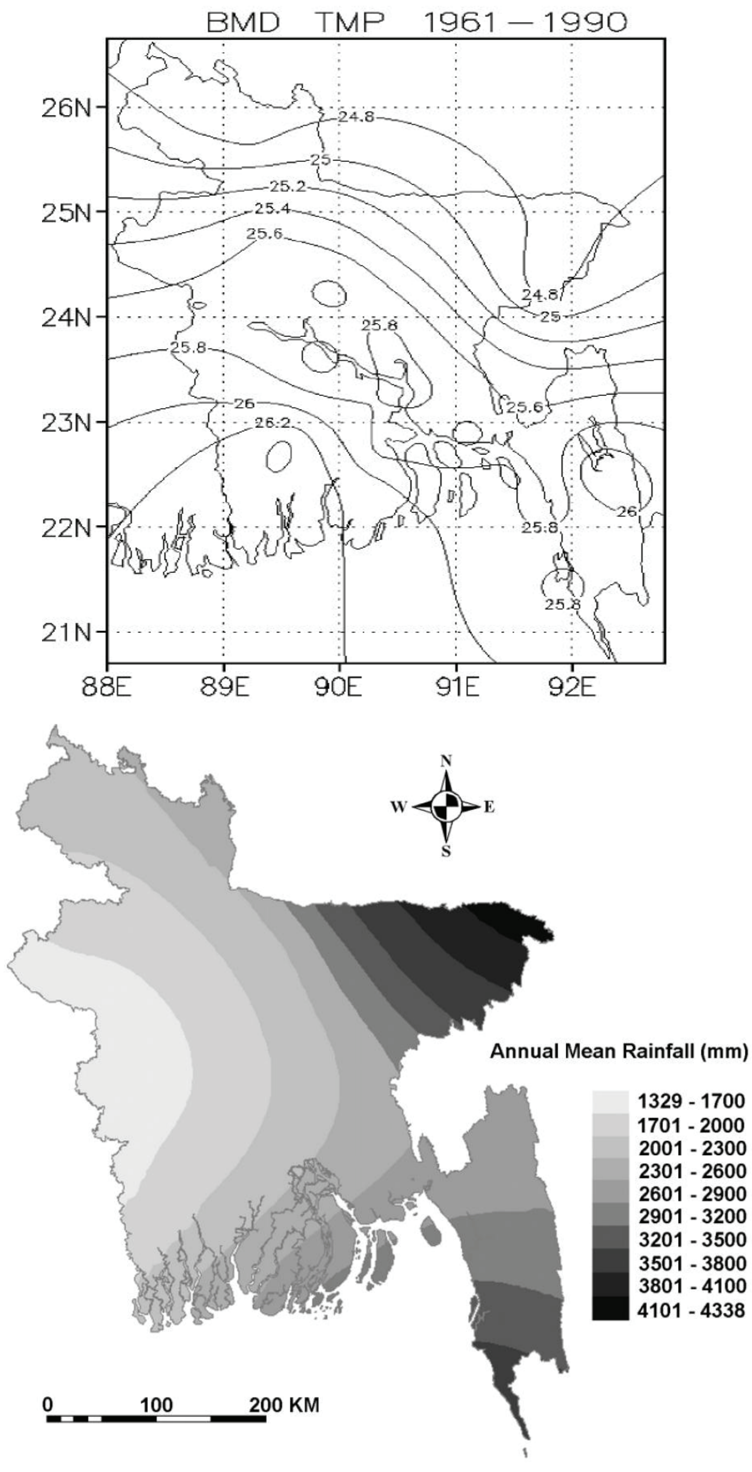

Figure 1.3: Spatial Distribution of Temperature and Rainfall in Bangladesh

(Islam et al., 2006; Shahid, 2008)

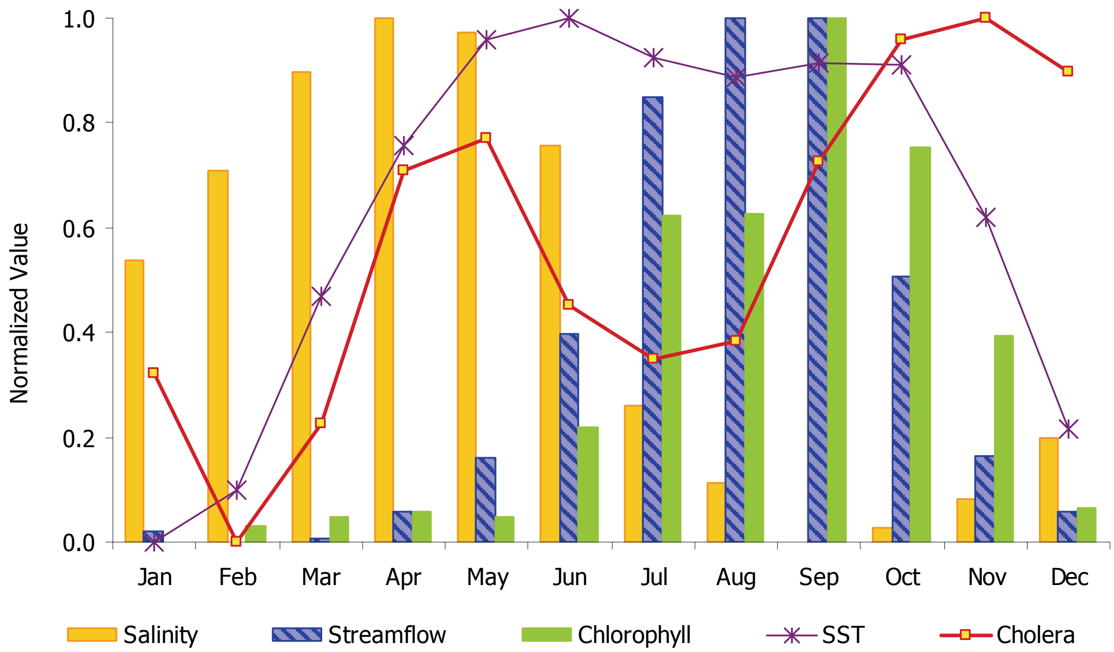

Figure 1.4: Monthly climatology of Streamflow, Salinity, Sea Surface temperature, Cholera Prevalence, and Coastal Plankton in Bangladesh and the Bay of Bengal

The following chapters of this dissertation provide detailed diagnostic analyses of a range of climate, hydrological, and ecosystem processes and variables relevant to *V. cholerae* growth and abundance, as well as proliferation and contamination of water resources with the bacteria. The chapters are organized as follows:

2. Dual Peak Cholera Transmission in the Bengal Delta: A Hydroclimatological Explanation [This chapter identifies separate drivers for the biannual outbreaks observed in Dhaka, Bangladesh and quantifies the asymmetric role of seasonal streamflow and coastal sea surface temperature patterns in the Bengal Delta region].
3. Hydroclimatic Influences on Seasonal and Spatial Cholera Transmission Cycles: Implications for Public Health Intervention in the Bengal Delta [This chapter quantifies the role of coastal and terrestrial processes on seasonal and interannual cholera dynamics, and explains how an asymmetric hydrology provides a coastal growth environment for bacteria and propagates the disease inland by flooding].
4. Understanding and Predicting Bengal Cholera Outbreaks through an Epidemiologic Application of Macro-scale Hydroclimatic Drivers [This chapter relates observed cholera incidence in six surveillance locations across the Bengal Delta region to underlying processes, such as estuarine salinity intrusion and inland flood inundation, and highlights large scale population vulnerability to seasonal cholera transmission].
5. A Spatially Explicit and Seasonally Varying Cholera Prevalence Model with Distributed Macro-scale Hydroclimatic and Environmental Forcings [This chapter combines the understanding of the previous chapters to develop a cholera prevalence model that is calibrated and validated to simulate cholera prevalence in four distinct locations in Bengal based on large scale hydroclimatic forcings].
6. Conclusions and Recommendations: Reducing the Global Cholera Burden [This chapter summarizes the major findings of the investigation and recommends research questions aimed to identify population vulnerability to epidemic cholera outbreaks in affected regions and reduce cholera burden through proactive intervention].

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Chapter 2

Dual Peak Cholera Transmission in Bengal Delta: A Hydroclimatological Explanation

Abstract

Cholera has reemerged as a global killer with the world witnessing an unprecedented rise in cholera infection and transmission since the 1990s. Cholera outbreaks across most affected areas show infection patterns with a single annual peak. However, cholera incidences in the Bengal Delta region, the native homeland of cholera, show bi-annual peaks. The mechanisms behind this unique seasonal dual peak phenomenon in cholera dynamics, especially the role of climatic and hydrologic variables, are not fully understood. Here, we show that low flow in the Brahmaputra and the Ganges during spring is associated with the first outbreaks of cholera in Bangladesh; elevated spring cholera outbreaks are seen in low discharge years. Peak streamflow of these rivers, on the other hand, create a different cholera transmission environment; peak flood volumes and extent of flood-affected areas during monsoon are responsible for autumn cholera outbreaks. Our results demonstrate how regional hydroclimatology may explain the seasonality and dual peaks of cholera incidence in the Bengal Delta region. A quantitative understanding of the relationships among the hydroclimatological drivers and seasonal cholera outbreaks will help early cholera detection and prevention efforts.

2.1 Introduction

Cholera, an acute water-borne diarrheal disease caused by the bacterium *Vibrio cholerae*, has reemerged as a global killer in recent decades. The world has seen an unprecedented rise in cholera infection and transmission since the 1990s, which have become a major public health concern for the World Health Organization (WHO) (Collins, 2003). Cholera records typically show single annual peaks in most affected areas, such as parts of Africa, South-east Asia and Latin America (Hashizume et al. 2008) (Figure 2.1a). However, cholera incidence records for the Ganges-Brahmaputra-Meghna (GBM) delta region of the Indian subcontinent show distinct bi-annual peaks (Lipp et al. 2002; Akanda et al. 2007). In this outbreak pattern, the first peak of the year occurs in the spring (March-May) season and a larger second peak occurs in autumn (September-December). No other region outside the Indian subcontinent shows a similar bi-annual cholera incidence pattern.

The seventh cholera pandemic, which started in 1961 in Indonesia, has been reported in over 50 countries. The global pattern and magnitude of the pandemic suggests that cholera outbreaks primarily originate in coastal environments and then spread inland through secondary means (Colwell, 1996; Mouriño-Pérez, 1998). The cholera-coastal connection is usually explained by the fact that cholera is caused by two particular pathogenic strains of the bacterium *Vibrio cholerae*, which are found mainly in marine plankton (Epstein, 1993; Colwell and Huq, 2001). Phytoplankton and zooplankton, by serving as the primary sources of nutrients and also physical carriers of the bacteria, play an important role in facilitating the survival, multiplication, and transmission of *Vibrio cholerae* in the natural aquatic environment (Lipp et al. 2002; Mouriño-Pérez, 1998).

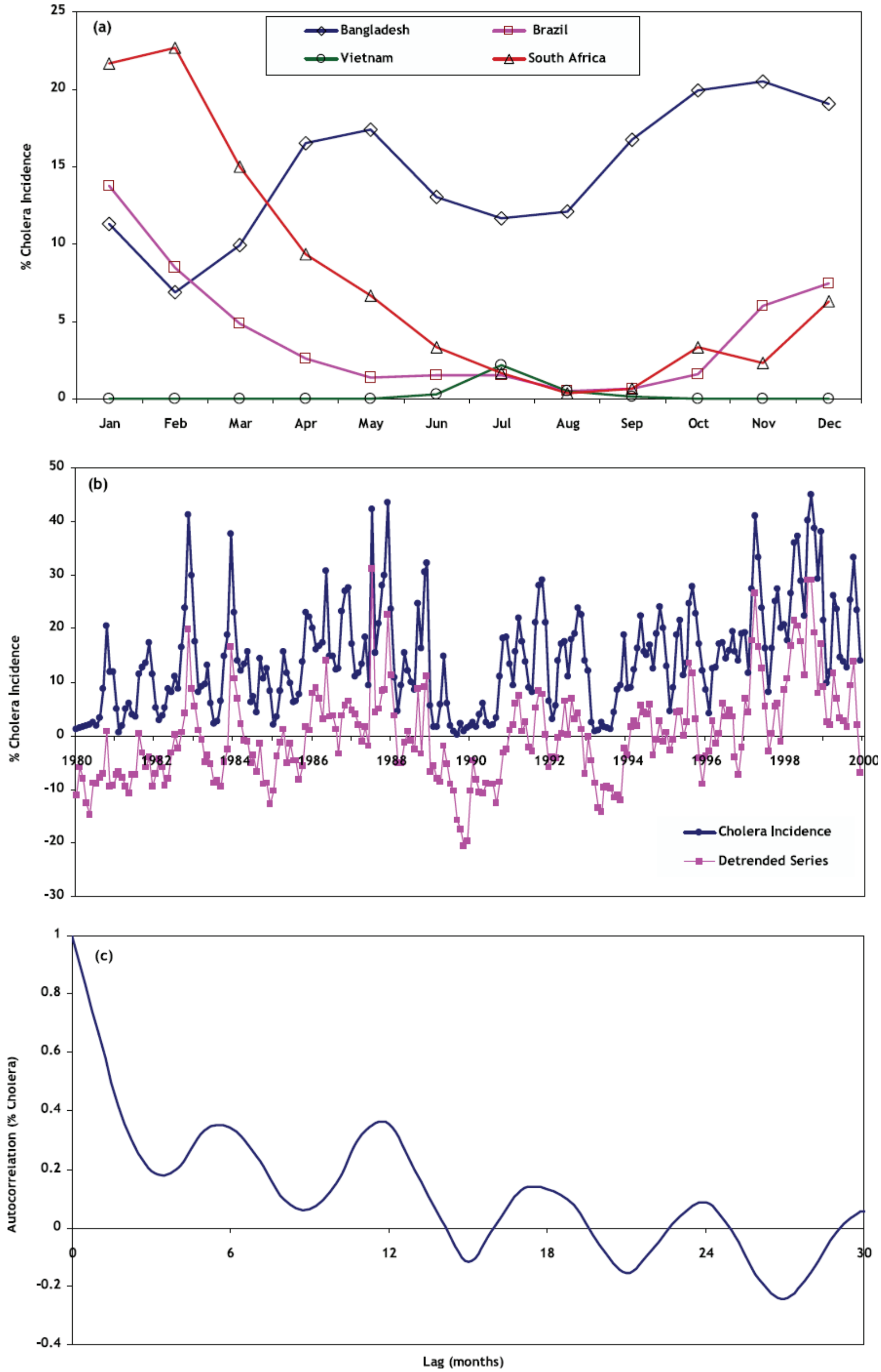

Figure 2.1 (a): Monthly climatology of recorded cholera incidences in four different regions of the world (b): Cholera incidence (% infected among all patients), recorded and detrended, during 1980-2000 (c): Autocorrelation function of monthly cholera incidence.

Cholera epidemics in Bangladesh have been historically linked to a range of environmental and climate variables including precipitation (Hashizume et al. 2008), floods (Koelle et al. 2005), peak river level (Schwartz et al. 2006), sea surface temperature (SST) (Lobitz et al. 2000; de Magny et al. 2008), sea surface height (Lobitz et al. 2000), coastal salinity (Miller et al. 1982), and fecal contamination (Islam et al. 2006). None of these studies, however, successfully quantified the role of the seasonal hydroclimatological processes with bi-annual cholera incidences in Bangladesh.

The prevalence of *Vibrio cholerae* bacterium in brackish estuarine waters and the initial outbreaks of cholera near coastal areas link the initiation and transmission of this disease with coastal ecosystems (Colwell 1996; Collins 2003; Worden et al. 2006). If low and high flows were the two possible drivers for dual peak cholera incidences in Bangladesh, then, one would expect to see a spatial signature of such a process with the first cholera outbreaks occurring in coastal areas and the second peak in a wider geographical area. In the case of GBM basin region, Bouma & Pascual (2001) provide strong evidence of such a coastal link to cholera outbreaks in Bengal, showing endemic outbreaks in spring in coastal districts and epidemic outbreaks during autumn in regions situated further inland, suggesting roles of large physical events such as floods. Sack et al (2003), focusing on the evolution of cholera outbreaks in four locations in Bangladesh, found that spring outbreaks are more common in the two locations closer to the coast, while the other two remote locations are affected mostly by the autumn outbreak. Similar spatial progression of cholera outbreaks, diffusing through coastal rivers and water networks in South Africa, and causing cholera outbreaks in inland locations has been shown in Bertuzzo et al (2007).

We hypothesize that the pre and post monsoon cholera peaks are governed by two distinctly different hydroclimatological drivers. To make this point, we disaggregate cholera incidence data from Bangladesh into seasonal components and analyze those with corresponding seasonal GBM streamflow and Bay of Bengal (BoB) SST. More specifically, the paper attempts to answer the following two questions: What is the role of spring low flow volumes in the GBM Rivers on the first cholera outbreaks in the region? How high monsoon streamflow volumes and subsequent flooding impact the post-monsoon outbreaks?

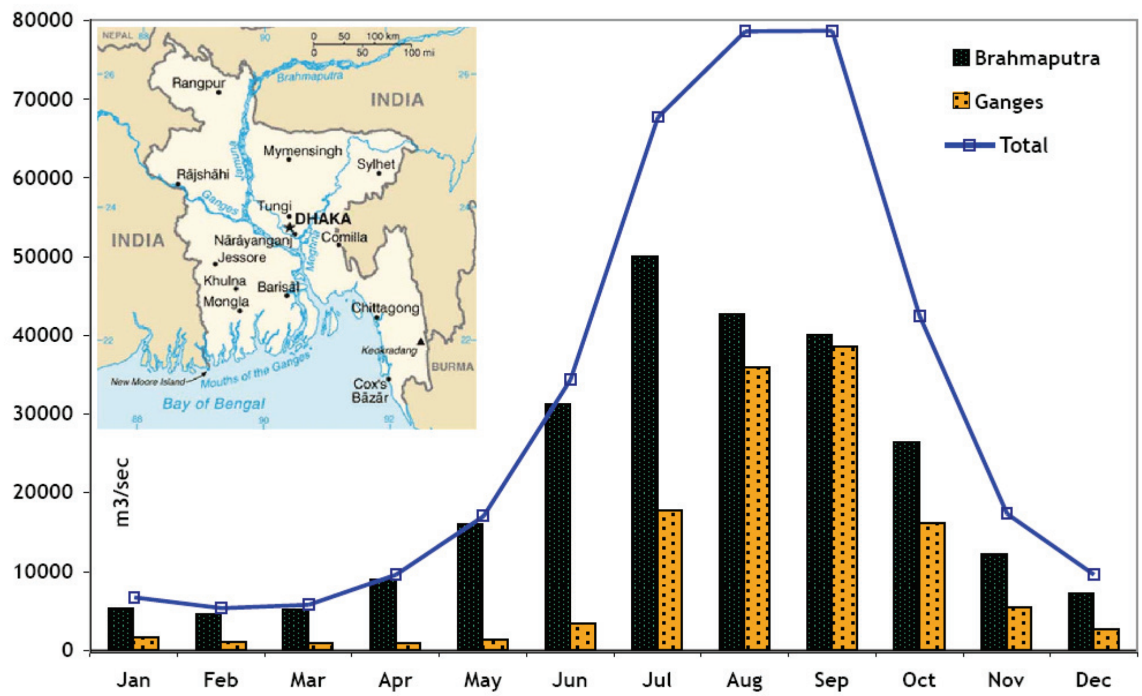

Figure 2.2 - Monthly climatology of streamflow (m^3/s) of the Ganges, the Brahmaputra, and the rivers combined for 1958-2007. (Inset map: CIA World Factbook)

2.2 Data and Background

Daily river discharge data for the GBM Rivers were obtained from the Bangladesh University of Engineering and Technology. The Reynolds $1^0 x 1^0$ SST database (Reynolds & Smith, 1994) was used to extract SST information for the coastal zone of the GBM Rivers in BoB (areas north of 21^0 N) based on available bathymetry and active production zone information (Chamarthi et al. 2008). The Flood Affected Area (FAA) time series, showing the annual extent of flooded land area, was obtained from Bangladesh Water Development Board.

2.2.1 Hydroclimatology of the Ganges-Brahmaputra-Meghna Basin

The GBM river system, one of the largest freshwater flow regimes in the world, shows a strong seasonal pattern (Figure 2). The GBM system is formed by two of the largest Himalayan Rivers, the Ganges and the Brahmaputra, which are joined by the Meghna in Bangladesh (Figure 2.2). Most of the annual precipitation in this basin occurs only during four monsoon months (Jun-Sep). The region thus has a contrastingly dry low flow season compared to its typically wet rainy reason. The lowest flows in the Brahmaputra and the Ganges are recorded during January-April and are typically one-tenth and one-twentieth of the average peak flows in respective rivers. Such drastic reductions cause a drop in the hydraulic head of the GBM system and its tributaries, which aid saltwater intrusion from the coast towards the inland freshwater resources (Rahman et al. 2000). Miller et al (1982) suggested strong links between coastal salinity and cholera outbreaks in Kolkata and London. Louise et al (2003) and Vital et al (2007) have found increased *Vibrio cholerae* population in water with brackish salinity conditions.

The rivers begin to rise rapidly due to monsoon rainfall starting from June and reach peak flow levels during the months of August and September. The entire country is situated on alluvial floodplains and thus prone to inundation by the overflowing of the GBM. On an average, about 20 percent land area of Bangladesh is inundated every year, with as much as 60 percent in high flood years, such as in 1988 and 1998 (Chowdhury & Ward, 2006). As open mixing of water between sewers, exposed drains, reservoirs, and rivers is very common during floods, the submerged areas quickly become contaminated with *Vibrio cholerae* through other infected water sources. Islam et al (2006) found an astounding 62.5% water samples carrying the cholera bacteria in the suburban reservoirs around Dhaka during the 2004 floods. Although river levels fall rapidly from September through November, water levels on adjoining flood plains fall more slowly because of low gradients, congested drainage, and substantial depression areas. Some areas stay submerged until December–January (Mirza et al. 2001), which can serve as ideal habitats for *Vibrio cholerae* even after the flood recedes and act as conduits of transmission within the surrounding population (Islam et al. 2006).

2.2.2 Seasonality of Cholera incidences in Bangladesh

The Bengal Delta with its extensive estuary formed by the Ganges and the Brahmaputra rivers has been considered the native homeland of cholera since the early 19^{th} century (Bouma & Pascual, 2001). The cholera surveillance program at the International Center for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) provides some of the longest and largest records available in the world. The program carries out a systematic sub-sampling of all patients visiting the hospital, which serves as the main treatment center for the most concentrated population center in Bangladesh. The cholera incidence climatology, constructed by averaging the monthly cholera records of the 1980-2000 time series, exhibits significant seasonal and inter-annual variability (Figures 2.1a, 2.1b). A closer look at the above reveals that the beginning of the spring cholera outbreaks coincides with the low flow season of the GBM Rivers. Monthly cholera numbers decrease in high monsoon and peak streamflow months (June through September). However, cholera infection starts increasing again in later monsoon, and a larger second peak is observed during the early winter months of November and December. Our analysis focuses on understanding the roles of the regional hydroclimatology behind these two seasonal peaks observed in cholera incidences, and the dominant processes behind each.

2.3 Methodology and Results

2.3.1 Seasonal Flow vs Cholera Analysis

We separated out the mean cholera incidences of the two seasons, spring (MAM: Mar-Apr-May) and autumn (OND: Oct-Nov-Dec) and created two new time series to examine interannual variability of cholera. These seasonal outbreaks are analyzed with the Ganges and Brahmaputra combined flow and Bay of Bengal SST. Mean streamflow values for the two lowest flow months, February and March, are combined to develop a low flow time series, and the two highest flow months (July and August) to develop the high flow time series. We have performed autocorrelation analysis for both the seasonal and the original monthly time series to validate the presence of two peaks in a year. Figure 1c on monthly autocorrelation function values shows the presence of two peaks in a year. The observed two peaks in the monthly climatology occur approximately in the months of May and November. The lag-1 autocorrelation value for the spring (MAM) and autumn (OND) time series are 0.55 and 0.22, respectively. In addition, the low flow values and pre-spring (DJF: Dec-Jan-Feb average) SST, show similar autocorrelation values (~0.50) as spring (MAM) cholera incidences, and high flow values and (JJA: Jun-Jul-Aug average) SST show similar autocorrelation values (~0.20) as autumn (OND) cholera incidences. Taken together, these values suggest the role of two separate hydroclimatological processes behind the two seasonal cholera peaks.

Seasonal cross-correlation values are calculated between low flow values and spring cholera incidences; and for high flow values and autumn cholera incidences for the period 1980-2000 (Table 2.1). We also use the seasonal mean (e.g., DJF, JFM, FMA) coastal BoB SST information for a similar seasonal cross-correlation analysis with spring and autumn cholera incidences, respectively. In addition to the calculated Pearson correlation coefficients, we perform non-parametric Kendall Tau significance tests on and report the corresponding Kendall Tau-a correlation and statistical significance information in the paper. The implications of these correlation values have been discussed in the following section.

Table 2.1: Correlation Matrix for Low and High Seasonal Streamflow, Flood Affected Area (FAA), Bay of Bengal (BoB) SST, and Seasonal (MAM/OND) Cholera Incidences

	Cholera MAM	Cholera OND	Low Flow	High Flow	FAA	DJF SST	JJA SST
Cholera MAM	-						
Cholera OND	0.68 (0.50)**	-					
Low Flow	-0.65 (-0.44)**	-0.34 (-0.23)	-				
High Flow	0.15 (0.08)	0.55 (0.34)*	-0.43 (-0.29)	-			
FAA	0.67 (0.40)*	0.67 (0.46)**	-0.53 (-0.36)*	0.66 (0.46)**	-		
DJF SST	-0.69 (-0.32)	-0.21 (-0.01)	0.48 (0.22)	-0.19 (-0.01)	-0.23 (-0.01)	-	
JJA SST	0.11 (0.01)	0.72 (0.37)	-0.20 (-0.09)	0.53 (0.27)	0.61 (0.40)*	-0.14 (-0.04)	-

DJF – Dec-Jan-Feb, MAM – Mar-Apr-May, JJA – Jun-Jul-Aug, OND – Oct-Nov-Dec,

Low (Feb-Mar) and High (Aug-Sep) Flow: Ganges & Brahmaputra combined.

(significant) for $0.01 < p < 0.05$ and ** (highly significant) for $p < 0.01$

We find strong negative cross-correlation (Table 2.1, $r = -0.65$ and -0.44, $p < 0.01$) between seasonal combined low flow volumes and average spring (MAM: March-May) cholera incidence. Recent studies on coastal ecosystems of GBM have pointed out significant salinity increases during spring (Islam and Gnauck, 2008; Wahid et al. 2007). An implication of these results is that more spring cholera outbreaks are likely in a drought year with higher salinity intrusion. Peak streamflow volumes cause substantial inundation along the major riverbanks of Bangladesh during monsoon, and usually lead to large-scale contamination of water systems such as rivers, canals, and ponds (Schwartz et al. 2006). Autumn cholera incidence (OND: Oct-Dec) values are found to be strongly correlated to high flow volumes ($r = 0.55$ and 0.34, $p < 0.05$), and also to flood inundation extent ($r = 0.97$ and 0.86, $p < 0.01$), as seen in Table 2.1. In summary, excess availability or the extreme lack of flow, both impact cholera dynamics in Bangladesh.

Our results show complementary evidence of two separate hydroclimatological processes within the context of coastal SST variability in the BoB and seasonal cholera incidences in Bangladesh (Table 2.1). Winter DJF (Dec-Feb) SST along the coast is negatively correlated to spring cholera incidences; the correlation coefficient between DJF SST and MAM cholera incidences is found to be -0.69 and -0.32 ($p = 0.11$). On the other hand, summer JJA SST in BoB shows high positive correlation with autumn cholera outbreaks. The correlation values of JJA SST with OND cholera incidences and flood-affected area (FAA) in Bangladesh are both found to be very strong (Table 2.1, $r = 0.70$ and 0.37 ($p = 0.08$) and $r = 0.61$ and 0.40 ($p < 0.05$), respectively). Results from Salahuddin et al (2006), with high positive correlation between monsoon rainfall and summer SST in BoB, further reinforce the high correlation between SST and FAA.

2.3.2 High Year vs Low Year Analysis

If the correlations presented in Table 2.1, linking low flow with spring cholera and high flow with autumn cholera, are to be physically consistent, one would expect to see the manifestations of these processes in the years with high and low cholera incidence values. In other words, the hypothesized relationships should hold true for the entire probability distribution of flow values, including the extreme years. To make this point, cholera incidence exceedance probability plots are constructed based on seasonal low and high flow values for the analysis period. The goal of this analysis is to understand the relationship of extreme hydroclimatic events such as droughts and floods with high and low cholera outbreaks.

Ten extreme drought years, five strongest and five weakest, are identified out of the twenty years based on streamflow volumes of the low flow months (average monthly cholera incidence during spring for these years are shown in Figure 2.3a). Figure 2.3b shows the probability of exceedance values for the entire period, the strongest drought years, and the weakest drought years. Cholera incidence information has been standardized by subtracting mean from seasonal incidence and dividing by standard deviation. The clear demarcation of the three categories shows the strong relationship between severity of low flow and spring cholera incidence. The probability of a spring cholera outbreak to exceed a certain threshold of incidence rates is always significantly higher in a water scarce year than in a water abundant year. Similarly, ten extreme flood years, five highest and five lowest, are identified within the same period, 1980-2000, based on combined monthly peak flow volumes. The autumn cholera incidence rates (Figure 2.3c) and associated probability of exceedance values (Figure 2.3d) are calculated

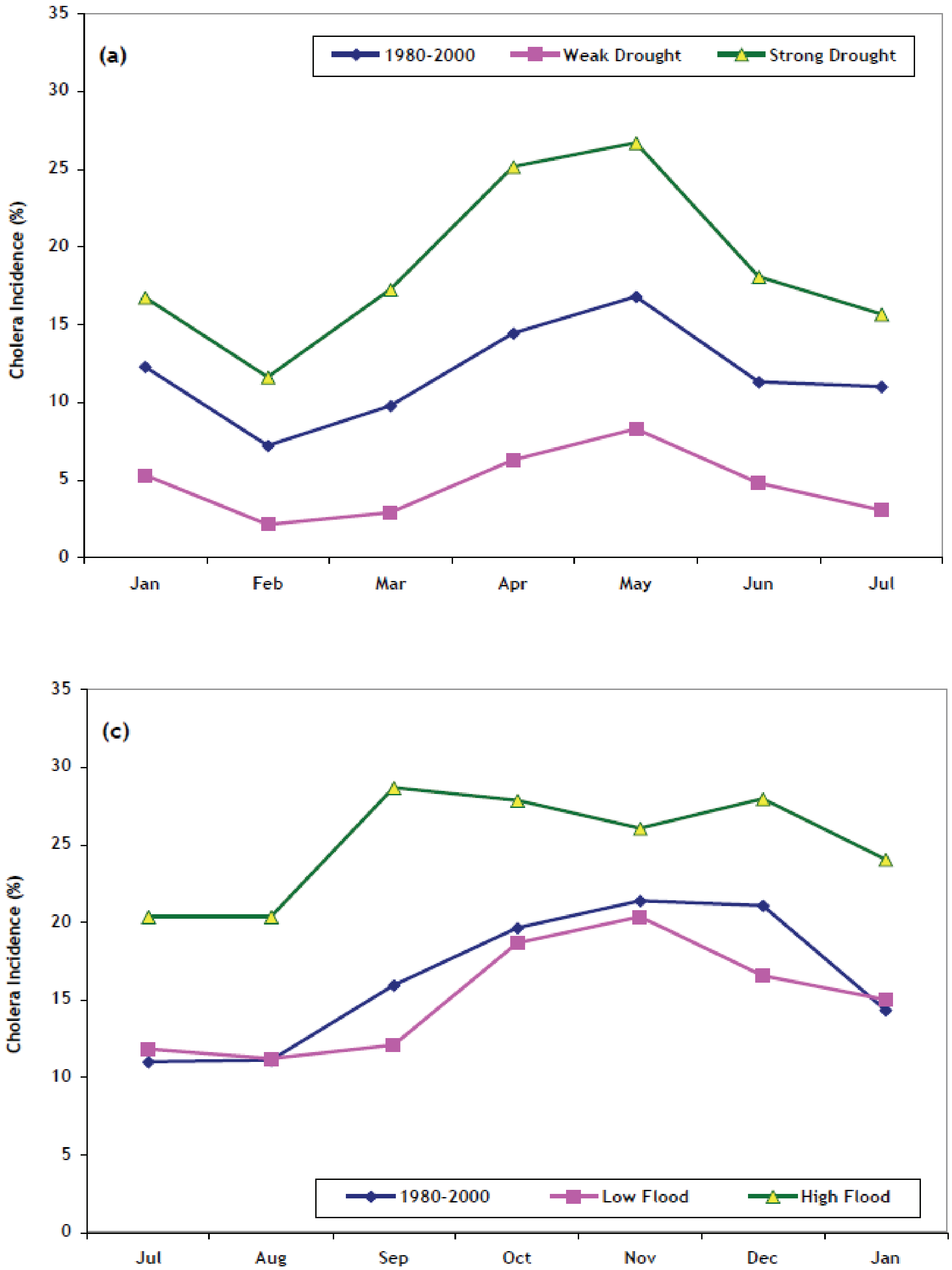

Figure 2.3 (a): Mean spring cholera incidence during weak and strong drought years

(c): Mean autumn cholera incidence during low and high flood years

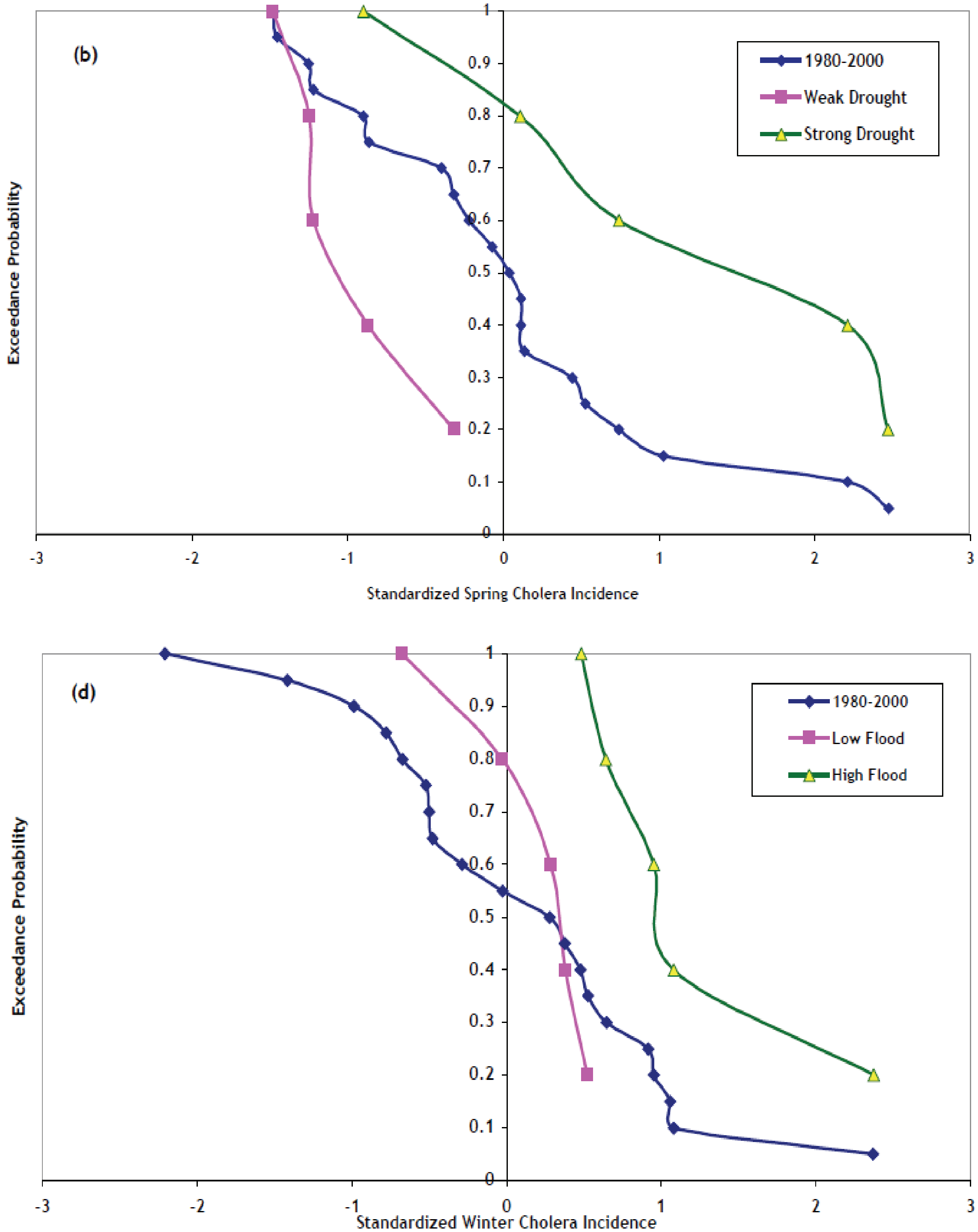

Figure 2.3 (b): Exceedance probability of spring cholera in low flow

(d): Exceedance probability of autumn cholera in high flow.

for the entire time series and the lowest and highest flood year sets. The probability of a large cholera outbreak during autumn is found distinctively higher for high flood years, however, the probability in a lower than average flood year was found to be indistinguishable from that of an average flood event in the Bengal Delta.

2.4 Discussion

The combination of seasonal hydroclimatology, high population density, floodplain geography and coastal ecology has made the Bengal Delta region especially vulnerable to periodic cholera outbreaks. In this study, we provide a working hypothesis on how the first outbreaks of cholera may be related to low flow discharge of the GBM Rivers and subsequent plankton intrusion during spring. Cholera incidence values in this season are inversely related to streamflow, i.e., bigger spring cholera peaks are seen in strong drought years. On the other hand, autumn cholera outbreaks are positively correlated to peak streamflow volumes, i.e., bigger autumn peaks are seen in high flood years. Evidence points to the role of fecal contamination of open water and inundation extent, which often impact a large population, gathered in few remaining dry areas.

This is perhaps the first study that attempts to link the seasonal dual cholera peaks in Bangladesh directly with river discharge and points at two separate, pre and post monsoon, hydroclimatological drivers. These results provide the rationale and motivation to identify complementary physical evidences, e.g. coastal phytoplankton measurements, salinity patterns in coastal Bangladesh, fecal contamination sampling during autumn, and flood inundation patterns. These measurable environmental signatures will provide a way to strengthen our hypothesis and estimate the risk of cholera outbreaks with a reasonable lead-time to develop targeted intervention strategies and preempt future outbreaks.

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Chapter 3

Hydroclimatic Influences on Seasonal and Spatial Cholera Transmission Cycles: Implications for Public Health Intervention in the Bengal Delta

Abstract

Cholera remains a major public health threat in many developing countries around the world. The striking seasonality and annual recurrence of this infectious disease in endemic areas remain of considerable interest to scientists and public health workers. Despite major advances in the ecological and microbiological understanding of *Vibrio cholerae*, the causative agent of the disease, the role of underlying large-scale hydroclimatic processes in propagating the disease for different seasons and spatial locations is not well understood. Here, we show that the cholera outbreaks in the Bengal Delta region, are propagated from the coastal to the inland areas and from spring to fall by two distinctly different, pre- and post-monsoon, transmission cycles influenced by coastal and terrestrial hydroclimatic processes, respectively. A coupled analysis of the regional hydroclimate and cholera incidence reveals a strong association of the space-time variability of incidence peaks with seasonal processes and extreme climatic events. We explain how the asymmetric seasonal hydroclimatology affects regional cholera dynamics by providing a coastal growth environment for bacteria in spring, while propagating the disease to fall by monsoon flooding. Our findings may serve as the basis for "climate-informed" early warnings, and prompting effective means for intervention and preempting epidemic cholera outbreaks in vulnerable regions.

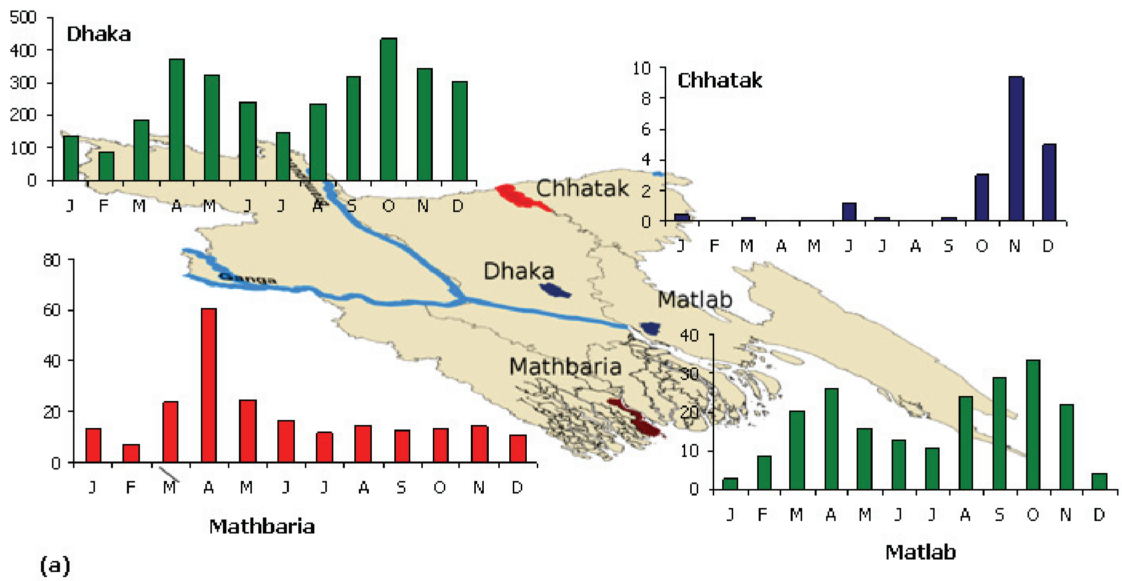
3.1 Introduction

Cholera broke out as part of a global pandemic in the Bengal Delta region of the Indian subcontinent during the early 19th century (*Sack et al.*, 2004). Two hundred years later, the disease still remains a major threat to public health in the developing world. Cholera is an acute water-borne diarrheal illness caused by two toxigenic strains of the bacterium *Vibrio cholerae*, O1 and O139, which are associated with marine plankton species (*Colwell and Huq*, 2001). There is agreement on the coastal nature of early outbreaks of this infectious disease (*Huq and Colwell*, 1996; *Worden et al*., 2007); however, the striking seasonality and strong inter-annual variability as well as its annual recurrence and spatial variability in endemic areas remain a mystery to scientists and public health professionals (*Bertuzzo et al.,* 2009; *Jutla et al.,* 2010).

The incidence of cholera in the Bengal Delta region shows distinct seasonal and spatial variations [Figure 1(a)]. In addition to the unique dual incidence pattern in some regions of the Bengal Delta (*Akanda et al.,* 2009), such as Dhaka and Matlab, we also see single annual peaks in coastal (spring peak in Mathbaria) and inland (fall peak in Chhatak) areas. In this outbreak pattern, the first cholera peak of the year occurs during the dry season in spring, and the second, and usually bigger, peak occurs in fall following the wet season. Other cholera affected regions in the world, such as South-East Asia (*Emch et al.,* 2008), Sub-Saharan Africa (*Hashizume et al*., 2008), Southern Africa (*Bertuzzo et al.,* 2008) and South America (*Gil et al.,* 2004) typically show single-incidence peaks in a year. A key objective of this study is to show that the biannual cholera peaks in the Bengal Delta region are governed by two spatially distinct seasonal transmission mechanisms, influenced by large-scale hydroclimatic processes.

For the past several decades, cholera research has primarily focused on clinical, microbiological, and ecological aspects of the bacterium, including vaccines, therapy, and improved treatment. The role of underlying hydrologic, climatic, and other large-scale environmental processes in transporting cholera bacteria through the ecosystem and propagating the disease in different seasons has received less attention (*Jutla et al*., 2010). Also, an overwhelming fraction of the investigations on cholera outbreaks (*Longini et al.,* 2002; *Cockburn and Casanos*, 1960; *Glass et al*., 1982) and the role of environmental factors (*Koelle et al.,* 2005; *Emch et al.,* 2008; *Constantin de Magny et al.,* 2008; *Islam et al.,* 2009) have relied on surveillance data from Matlab. Also, these studies did not attempt to explain how large-scale drivers (e.g., precipitation, flood, temperature) with single annual peaks create dual seasonal peaks in cholera incidence.

Akanda et al. (2009) provided a hydroclimatological explanation of the temporal nature of the dual peak cholera incidence in Dhaka. We build on these findings to investigate the spatial and temporal nature of cholera outbreaks throughout Bangladesh and the role of regional hydroclimatic processes and extreme events. We argue that the annual transmission process is governed by two separate transmission cycles propagating from spring to fall aided by the asymmetric nature of regional terrestrial and coastal processes. In this chapter, *we hypothesize the existence of two distinctly different physical drivers of cholera outbreaks influenced by two, pre- and post-monsoon, hydroclimatic controls.* More specifically, we attempt to answer the following questions: Does the hydroclimatology of the Bengal Delta region contribute to the propagation of cholera outbreaks from one season and one region to another? Are the record outbreaks in different years modulated by the significant hydroclimatic events in those years?



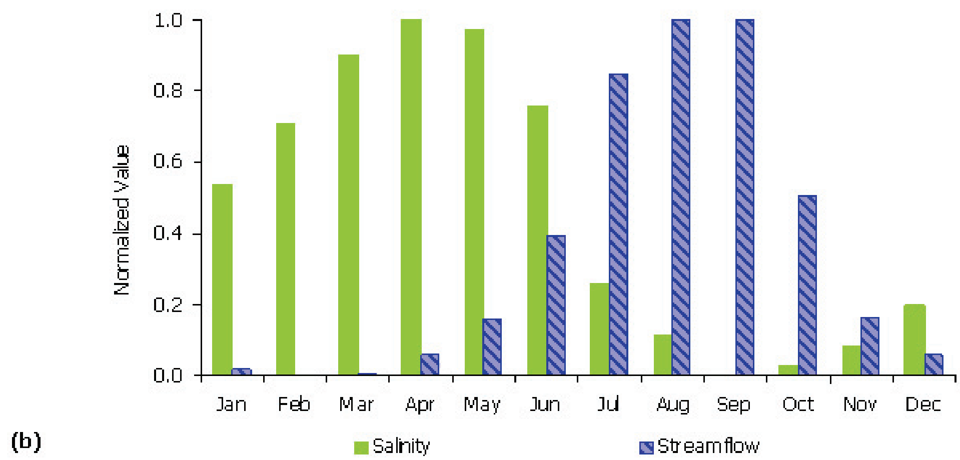


Figure 3.1: Monthly climatology of (a) cholera incidence recorded at ICDDR,B Surveillance centers in Dhaka, Mathbaria, Chhatak and Matlab, Bangladesh (b) Observed coastal salinity in Bangladesh (recorded at ten coastal river stations, Hoque et al., 2000) and combined Ganges and Brahmaputra streamflow (Paksey and Bahadurabad)

3.2 Background

Vibrio cholerae (henceforth *V. cholerae*), primarily known to be an estuarine aquatic bacterium, is indigenous to the macro-environment of aquatic ecosystems (*Colwell et al.*, 1981). Cholera is an ancient disease, occurring almost every year in many parts of the world, including Bangladesh; however, the source of the organisms remained unknown, as the causative agent could not be easily isolated between epidemics. *Huq et al.* (1990) first demonstrated the presence of the pathogen in aquatic environments of Bangladesh during all the months of the year using direct detection methods. The bacteria remain in a non-culturable state for most of the year in aquatic reservoirs, allowing the organisms to survive and multiply (*Huq et al.*, 2005; *Chun et al.*, 2009).

Different ecosystem variables such as water temperature, salinity, and other nutrients (organic carbon, nitrogen, phosphorus) have been associated with the abundance of plankton and the occurrence and persistence of *V. cholerae* in aquatic environments (*Singleton et al.*, 1982a; 1982b; *Huq et al*., 1984; *Vital et al*., 2007). Phytoplankton serves as the primary food source for zooplankton, also releasing nitrogenous nutrients into the water through disintegration, which aids proliferation of the bacteria (*Lipp et al.*, 2002). A brackish salinity of 5–20 ppt and water temperature above 20°C was found to be optimum for growth of *V. cholerae* in estuarine environments (*Louis et al*., 2003). In the Bengal Delta region, a 5°C increase in the water temperature was associated with a 3.3-fold increase (range 2.4–4.6; median 3.3) in the risk of cholera outbreaks, with a lag of 6 weeks (*Huq et al*., 2005). *Stine et al*. (2008) concluded that cholera outbreaks in different areas were of independent origin, suggesting that the bacteria may be triggered simultaneously by large scale processes, causing disease outbreaks in multiple locations.

The hydroclimatology of the Ganges–Brahmaputra–Meghna (GBM) basin region is highly seasonal in nature, with most of the annual precipitation occurring during the four monsoon months, June through September (*Chowdhury and Ward*, 2004). During the prolonged dry season (December through May), lower runoff availability and upstream diversions leave only a fraction of the combined average flow to reach the Bay of Bengal (BoB) [Figure 1(b)]. As a result, the salinity front in the estuarine region travels towards inland freshwater, as far as 100 kilometers in extreme dry years (*Rahman et al.,* 2000). Consequently, a large region in coastal Bangladesh exhibits brackish water conditions in spring (*Wahid et al.*, 2007; *Islam and Gnauck*, 2008), providing an optimum environment for *V. cholerae* growth (*Vital et al*., 2007; *Louis et al*., 2003).

The situation undergoes drastic changes as monsoon arrives in June; peak streamflow volumes cause substantial inundation along the major riverbanks of Bangladesh and lead to large-scale contamination of water systems such as rivers, canals, and ponds (*Schwartz et al*., 2006), with the bacteria present in the ecosystem (*Akanda et al*., 2009). Open mixing of water with sediment occurs within such systems during floods, and the submerged areas quickly become contaminated with *V. cholerae*. Some areas stay submerged and turbid until November (*Mirza et al*., 2001), providing an ideal condition for growth and proliferation of *V. cholerae* due to the availability of rain-flushed nutrients and plankton growth, acting as sources of transmission with the surrounding population (*Islam et al.*, 2006). This hypothesis is also supported by the significant 3 months-lagged correlation reported in *Akanda et al.* (2009) between monsoon floods and fall outbreaks, a plausible evidence of the delayed response of plankton and vibrio growth in inundated water bodies.

An ecological survey of *V. cholerae* in the coastal ecosystems of the Bay of Bengal provided firm evidence that *V. cholerae* O1 cells are present during epidemics in samples collected from water bodies serving as drinking water sources for two rural areas of Bangladesh. The molecular detection of toxigenic *V. cholerae* between 2004 and 2007 showed the presence of *V. cholerae* in Bakerganj between April and June and between August and December. During this study, *V. cholerae* was not detected in water samples during the winter months or during the peak monsoon months. For Mathbaria, *V. cholerae* was present in water samples mostly between March and June, and sporadically in the fall. These preliminary results thus strengthen the hypothesis of a contrasted seasonality of the presence of toxigenic *V. cholerae* in the environment and its potential link with the cholera incidence pattern in these areas (*Alam et al.,* 2006).

In summary, the life cycle of *V. cholerae* is intricately linked to both **micro**- and **macro**-environmental processes, with vastly different space and time scales of interacting variables (*Jutla et al.,* 2010). Here, we define **micro** as microbiological and genetic processes, while **macro** refers to hydrological, ecological, and climatic processes. We recognize the importance of micro-environmental understanding to develop vaccines and treatment protocols. However, as *V. cholerae* may survive and thrive in a wide range of natural conditions, and since evidence of new biotypes is emerging, it is unlikely that this disease will ever be eradicated. Consequently, we need a new approach to minimize the impact of this devastating disease by predicting where it may occur and initiating effective intervention strategies. Our approach in this study thus attempts to identify the macro-environmental processes and variables that have longer temporal and larger spatial "memory" to allow the development of an early warning system for cholera outbreaks.

3.3 Analysis and Results

3.3.1 Data and Methodology

Cholera incidence data for the period 1980–2007 were collected from the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B), located in Dhaka, Bangladesh. The *incidence* data is recorded as the people infected with *V. cholerae* among a statistical subset of the patients visiting the hospital each month. We use *prevalence rate*, a population corrected measure of incidence, for our analyses by normalizing the incidence data by the number of patients tested and reporting it as a percentage number. We separate out the mean cholera prevalence rate of the two outbreak seasons—spring (MAM: Mar-Apr-May) and fall (SON: Sep-Oct-Nov)—as well as summer (JJA: Jun-Jul-Aug) and winter (DJF: Dec-Jan-Feb) seasons to examine the intra-annual and inter-annual variability of outbreaks. Mean streamflow values for dry (JFMA: Jan to Apr) and wet (JASO: Jul to Oct) seasons were used to develop low and high streamflow time series, respectively. Flood-affected area (FAA) is an annual measure based on flood surveys conducted through the high-flow (JASO) season. For the SST, rainfall, and chlorophyll datasets, we developed similar seasonal time series (DJF, MAM, JJA, SON) for effective seasonal lead-lag comparisons with cholera outbreaks.

For this study, we use the Sea-viewing Wide Field-of-view Sensor (SeaWiFS) measured chlorophyll concentration (chl-a) as a surrogate of phytoplankton abundance for the coastal zone of the GBM rivers in the BoB (areas north of 21° N between 86°and 93° E). This zone was chosen on the basis of available bathymetric and active production zone information (*Chamarthi et al.*, 2008). The Reynolds 1°×1° sea surface temperature (SST) database (*Reynolds and Smith,* 1994) was used to extract SST information for the

BoB. Gridded rainfall time-series data ($2.5^{\circ} \times 2.5^{\circ}$ spatial resolution) for the GBM catchment areas were obtained from the NCEP/NCAR Reanalysis Project atmospheric datasets. Daily river discharge records for the Ganges and the Brahmaputra rivers, which were aggregated to monthly scales, and the Flood Affected Area (FAA) information, a measure of annual extent of flood inundation in Bangladesh, were obtained from the Bangladesh Water Development Board (BWDB).

3.3.*2 Fall to Spring, or Spring to Fall?*

Previous studies on the nature of cholera outbreaks in rural Bengal (*Cockburn and Casanos*, 1960; *Glass et al*., 1982) reported outbreaks in fall closely followed by those in spring. *Pascual et al*. (2000) and *Bouma and Pascual* (2001) reiterated a fall–spring transmission cycle, with the annual monsoon rainfall providing a “dilution” effect between the two major outbreak seasons (*Ruiz-Moreno et al*., 2010). This notion of a fall–spring transmission pattern, however, appears inconsistent with recent observations: A careful analysis of the spring (Mar-Apr-May), summer (Jun-Jul-Aug), and fall (Sep-Oct-Nov) cholera outbreaks for the last three decades of records from Dhaka, Bangladesh, in fact, suggests the opposite. Table 1 shows intra-annual and inter-annual cross-correlation values between mean seasonal cholera prevalence rates for 1980 through 2007. An intriguing observation from the table is that same-year seasonal cholera outbreaks are strongly correlated, but the correlation breaks down between successive years. These results imply that summer and fall prevalence are dependent on the preceding spring outbreaks. However, fall outbreaks do not have an impact on subsequent spring prevalence, suggesting a winter break in the annual transmission process.

Table 3.1 Intra- and Inter-annual Correlation between Seasonal Cholera Prevalence for the period 1980-2007

Beginning Season	**Ending Season**	**Correlation (n = 28)**
Spring	Summer (same year)	0.70**
Summer	Spring (next year)	0.23
Spring	Fall (same year)	0.73**
Fall	Spring (next year)	0.33
Summer	Fall (same year)	0.76**
Fall	Summer (next year)	0.37

Notes: Spring: Mar–Apr–May; Summer: Jun–Jul–Aug; Fall: Sep–Oct–Nov.

Statistical Significance Indicators: ** $p < 0.01$

Akanda et al. (2009) argue that lower discharge volumes during the dry season (from January through April) and associated saltwater and plankton intrusion may initiate early cholera outbreaks in the GBM basin. On the other hand, as streamflow direction is predominantly southward in regional rivers during and after the wet season (from June through November) (*Mirza et al.,* 2001), there is no realistic way for coastal plankton to reach estuarine rivers during these months. If coastal plankton abundance, salinity, and associated bacteria affect inland water resources only during spring, and if summer and fall prevalence are dependent on the preceding spring outbreaks [Table 1], one would expect to see a physically consistent pattern of prevalence between years of high and low coastal intrusion. Figure 2(a) shows a consistent progression pattern in cholera outbreaks from spring (MAM) to fall (SON) months during strong and weak drought years (i.e., years with higher and lower coastal intrusion in spring, respectively). We see a clear demarcation of higher and lower cholera prevalence in all months between these years, suggesting the influence of coastal and brackish plankton abundance. However, a similar progression pattern is not observed between the years with the highest and lowest flood events. Flood-induced contamination appears to have an impact on cholera prevalence during the immediate fall months, but not during the following winter or spring months [Figure 2(b)]. These results suggest an asymmetric role of regional hydroclimatology and provide secondary evidence of a break in the annual transmission process in winter.

3.3.3 Coastal to Inland Areas, or Inland to Coast?

Siddique et al. (1994) was perhaps the first study to suggest plausible pathways of the progression of cholera outbreaks from the coastal regions of Bangladesh to inland areas of the country during major epidemics. *Bouma and Pascual* (2001) provided historical evidence of a coastal link to cholera mortality. A more recent study, *Sack et al*. (2003), showed that spring peaks are more common in locations closer to the coast, while the inland locations are affected mostly by fall outbreaks. Taken together, these studies suggest a spatial heterogeneity of cholera outbreaks across the Bengal Delta region. However, these studies did not specifically investigate the spatial signatures with any climatic, ecological, or environmental processes.

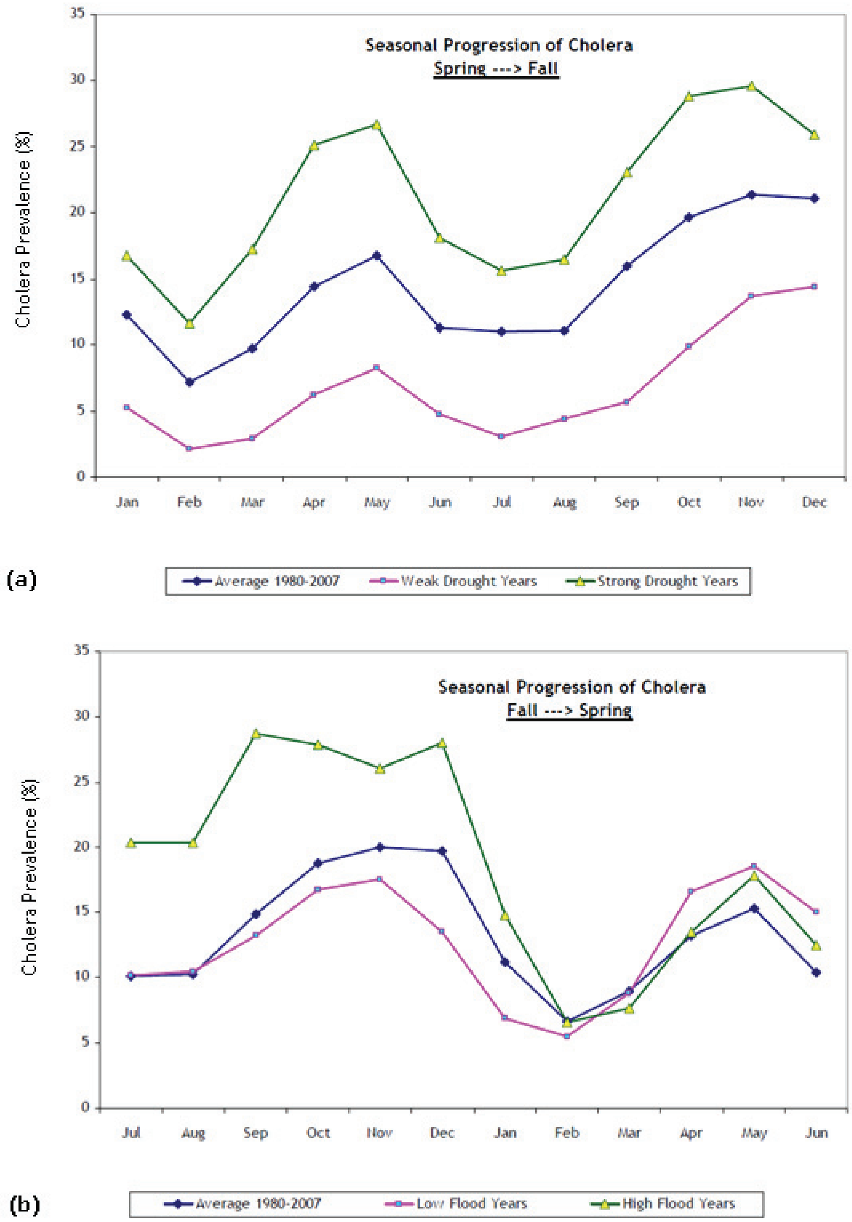


Figure 3.2: Comparison of seasonal progression of cholera prevalence from (a) Spring to Fall seasons between strong and weak drought years, and from (b) Fall to Spring seasons between high and low flood years, classified based on combined Ganges and Brahmaputra streamflow (BWDB) and cholera surveillance from Dhaka (ICDDR,B).

If the understanding of the seasonal and spatial processes and their asymmetric role are to be physically consistent, we should expect to see a spatial signature of these processes across a larger section of Bangladesh. To explore and validate this possibility, we investigate the seasonal nature of recently recorded cholera cases in four locations of Bangladesh. These four locations are distinctly different in their geographical and meteorological settings, as well as in their seasonal outbreak patterns. Dhaka is a freshwater ecosystem in central Bangladesh, surrounded by several distributaries of the GBM rivers. Mathbaria is a coastal area located in estuarine southwestern Bangladesh, close to the BoB coast. Mathbaria is not typically affected by floods, however, is prone to freshwater scarcity during the dry spring months due to the reduced amount of streamflow from upstream regions. Chhatak is located in northeastern Bangladesh and is the furthest away from the coast among the four locations; it is, however, prone to rainfall-driven flash floods in the Meghna basin region. Matlab is a well-reported cholera-endemic area frequented by floods, located near the confluence of the three major rivers of the region. However, Matlab is less than 150 kilometers from the BoB coast, and thus belongs to the coastal floodplains in our classification.

Figure 1(a) shows the monthly average number of cholera cases recorded at each of these four locations. We find that coastal hydroclimatic processes primarily modulate the first outbreak season in spring, whereas inland processes exhibit a strong influence on the second cycle of outbreaks. Mathbaria (data period: 2003–2007), a coastal location close to the BoB, shows cholera outbreaks only during the spring season. On the other hand, Chhatak (1997–2001), which is an inland location furthest away from the coast, shows outbreaks only during fall months. Dhaka (1980-2007) and Matlab (1998-2007), located in the floodplains of the GBM rivers, appear to be affected by both waves of outbreaks. Thus the two transmission cycles show distinctive seasonal and spatial signatures with respect to their coastal or terrestrial origins.

3.3.4 Intra-annual Variability: Asymmetric Influence of Seasonal Hydroclimatology

A contrasting influence of GBM streamflow and BoB SST on intra-annual or seasonal cholera outbreaks in Dhaka, Bangladesh was presented in *Akanda et al.* (2009). However, how these variables contribute to infection beyond individual seasons was not explored in that study. In addition, how related hydroclimatic variables such as rainfall and coastal plankton abundance affect the seasonal outbreaks were not quantified. The goal of this analysis is to identify if these macro-scale drivers contribute to cholera outbreaks in subsequent seasons. If the correlations between seasonal cholera prevalence in same and successive years [Table 1] were to be physically meaningful, one would expect to see the manifestations of these results in underlying physical processes. We hereby investigate seasonal lead-lag relationships between coastal and terrestrial hydroclimatic processes in the region and cholera outbreaks during spring, summer, winter, and fall seasons of one particular year, as well as the spring season of the subsequent year. Table 2 shows the cross-correlation coefficients between mean seasonal cholera prevalence in Dhaka and regional hydroclimatic variables. We calculate Pearson and non-parametric Kendall correlation values and perform statistical significance tests for all time-series pairs (the Pearson coefficients are reported in Table 2).

An important observation from the table is the consistent asymmetric influence of dry- and wet-season processes on same-year spring and fall cholera outbreaks, respectively: negative correlation in spring and positive values in fall. Winter (DJF) SST in coastal BoB, dry season (DJF and MAM) rainfall in Bangladesh, and low flow (JFMA) values in GBM rivers have all shown strong negative influences on spring cholera prevalence (r = –0.60, –0.60, both values significant at $p < 0.01$, and r = –0.49 and –0.47, both significant at $p < 0.05$, respectively). These variables also show consistent negative correlation values over subsequent summer and fall seasons [Table 2], suggesting that freshwater scarcity in upstream rivers and resulting saltwater and plankton intrusion, as well as the environmental changes during and following the first peak may have an influence on the cholera outbreaks in subsequent seasons of the year.

On the other hand, GBM streamflow in JASO months, FAA inside Bangladesh, and summer (JJA) SST in BoB, all suggest a strong positive influence on summer and fall cholera prevalence (r = 0.51, 0.66, and 0.54, and r = 0.45, 0.43, and 0.56, respectively, all values significant at $p < 0.05$, except r = 0.66 at p < 0.01). Unlike the dry season, none of the wet season variables show a significant relationship with cholera prevalence in subsequent winter or spring seasons. These results indicate that water abundance during summer and a warmer BoB may contribute to large-scale water contamination and atmospheric conditions conducive to cholera outbreaks in summer and fall. However, *V. cholerae* contamination in one particular monsoon season does not appear to persist over winter or impact cholera prevalence beyond fall. These observations thus provide plausible physical explanations of the correlations reported in Table 1, and strengthen the hypothesis of an annual transmission process beginning each spring and ending in winter.

Coastal phytoplankton, known to be a major source of bacterial abundance in estuarine areas, exhibits a positive relationship in fall (SON) and winter (DJF) seasons,

Table 3.2 Seasonal Cross-Correlation between Hydroclimatic Variables and Cholera Prevalence in Dhaka, Bangladesh for the period 1980-2007

Hydroclimatic Variable	**Seasonal Cholera Prevalence 1980-2007 (*n* = 28)**				
	Spring (Same year)	Summer (Same year)	Fall (Same year)	Winter (Year end)	Spring (Next year)
Flow					
JFMA	-0.47*	-0.41*	-0.30	-0.12	-0.08
JASO	-	0.51*	0.45*	0.16	0.01
FAA					
JASO	-	0.66**	0.43*	-0.09	0.05
Rainfall					
DJF	-0.60**	-0.40*	-0.39	-0.50*	-0.48*
MAM	-0.49*	-0.44*	-0.28	-0.32	-0.29
JJA	-	0.35	0.38	0.07	-0.07
SON	-	-	-0.19	-0.12	-0.17
SST					
DJF	-0.60**	-0.54*	-0.46*	-0.32	-0.40*
MAM	0.11	0.22	0.26	0.07	-0.16
JJA	-	0.41*	0.56**	0.13	-0.01
SON	-	-	0.34	-0.05	-0.10
Chl-a	**1998-2007 (*n* = 10)**				
DJF	0.14	0.30	0.07	0.20	0.67*
MAM	-0.01	0.12	0.21	0.45	0.41
JJA	-	0.11	-0.19	0.11	-0.09
SON	-	-	0.46	0.01	0.87**

[a]Source: International Center for Diarrhoeal Disease Research, Bangladesh.

Notes: **Spring**: Mar–Apr–May; **Summer**: Jun–Jul–Aug; **Fall**: Sep–Oct–Nov; Winter: Dec–Jan–Feb; **JFMA**: Jan–Apr Avg; **JASO**: Jul–Oct Avg.

Statistical significance indicators: ** $p < 0.01$; * $0.05 > p > 0.01$

with subsequent spring prevalence levels. Chl-a values for SON and DJF seasons show a strong relationship with following year spring cholera (SON: $r = 0.87$ and 0.67, values significant at $p < 0.01$ and $p < 0.05$, respectively). None of the other seasons show any meaningful relationship with cholera outbreaks. These results suggest the strong role of a coastal reservoir of the bacteria in southern Bangladesh, aided by fall and winter plankton abundance, responsible for cholera outbreaks in the following year.

Monsoon rainfall in the region also shows a consistently positive, albeit weaker, relationship with summer and fall cholera prevalence (r = 0.35, $p = 0.09$ and 0.38, $p = 0.06$, respectively). As streamflow is an aggregated measure of rainfall, we expect to see a positive influence of precipitation similar to that of streamflow (*Akanda et al*., 2009). However, as the arrival, duration, and intensity of monsoon rainfall, as well as the terrain and topography, are widely varied over the 1.5-million-square-kilometer GBM basin (*Ahmed and Karmakar*, 1993), and as the vast majority of water arrives from upstream regions (*Chowdhury and Ward*, 2004; *Mirza et al*., 2001), the role of monsoon rainfall in the contamination of water resources inside Bangladesh may be limited compared to that of associated flood inundation ($r = 0.66$, $p < 0.01$).

3.3.5 Inter-annual Variability: Role of Extreme Hydroclimatic Events

The goal of this analysis is to determine whether the year-to-year variability of seasonal cholera outbreaks is associated with the hydroclimatic signatures of those years. In other words, the physical mechanisms behind each seasonal outbreak should appear plausible and physically consistent under different hydroclimatic scenarios, including the extreme events. For example, if a particular year begins with anomalous low-flow conditions in the GBM rivers during the dry season, it is likely to observe elevated cholera outbreaks in spring. Cooler winter SST and higher plankton abundance in coastal BoB may also contribute to larger outbreaks in spring and subsequent seasons. On the other hand, if a particular year experiences strong monsoon rainfall, high river discharge, and associated floods in summer, the likelihood of strong fall outbreaks also rises considerably. In the event of these conditions occurring within the same year, the region is likely to observe epidemic outbreaks in both spring and fall. To understand these relationships better, we discuss the seasonal emergence of cholera outbreaks and the spatial nature of the mechanisms for record high or low years.

In this analysis, 15 years were selected and categorized on the basis of their total annual cholera **burden** (average prevalence for the entire year), presence of significant outbreaks, and also the lack of major outbreaks. Table 3 illustrates the seasonal progression of cholera outbreaks in Dhaka for the extreme (high, low, and at least one high outbreak) cholera burden years, and the relative state and contribution of coastal dry- (plankton, SST, low flow) and terrestrial wet- (high flow, SST, floods) season processes in those years. Seasonal mean values for hydroclimatic variables and cholera prevalence are converted to terciles (bottom 33rd percentile, the 33rd to 66th percentile, and above the 66th percentile) based on individual time series for the years analyzed (1980–2007) and then grouped within three categories (Low, Avg, High).

An important observation in Table 3 is that the years showing the highest cholera burden all began with low discharge and thus high saline conditions, reinforcing the role of coastal processes in spring. Except for 1987, all high cholera burden years had large outbreaks in the spring season. Among these years, we also see very large fall outbreaks

Table 3.3 Progression of Seasonal Cholera Outbreaks Associated with Significant Hydroclimatic Events during 1980–2007

Year	Dry Season Processes			Spring	Wet Season Processes			Fall
	SST	Chl-a[a]	Flow	**Cholera**	SST	Flood	Flow	**Cholera**
Five Highest Cholera Burden Years								
1987	Avg		Low	**Avg**	High	High	High	**High**
1997	Low		Low	**High**	High	High	Avg	**Avg**
1998	Low	High	Low	**High**	High	High	High	**High**
1999	Avg	High	Low	**High**	High	Avg	High	**High**
2005	Avg	High	Low	**High**	Avg	Avg	High	**Avg**
Five Lowest Cholera Burden Years								
1981	Avg		High	**Low**	Avg	Low	Low	**Low**
1989	High		High	**Low**	Low	Low	Low	**Low**
1990	High		High	**Low**	Avg	Low	Low	**Low**
1993	Avg		High	**Low**	Avg	Avg	Avg	**Low**
2007	Low	Low	High	**Low**	Avg	Low	Avg	**Low**
Years with One Significant Outbreak								
1982	High		Low	**Low**	Avg	High	High	**High**
1986	Avg		Low	**Avg**	Avg	Avg	Avg	**High**
1988	Avg		Avg	**Avg**	High	High	High	**High**
1991	High		Avg	**Avg**	Avg	Avg	High	**High**
2006	Avg		Avg	**Avg**	Avg	Avg	High	**High**

[a] Chl-a data are available only for 1998–2007.

Notes: The categories Low, Avg (average), and High are based on terciles (bottom 33rd percentile, 33rd to 66th percentile, and above the 66th percentile) of individual seasonal hydroclimatic or cholera time series.

in 1987 and 1998 in the wake of record flood events. Years such as 1982 or 1988 began with low to average spring outbreaks, but showed significant flood-induced fall outbreaks later in those years. In sharp contrast, no large outbreaks and unusually low cholera burden were observed in 1989, ’90, or ’93, due to no major hydroclimatic events.

3.3.6 Evidence of Large Scale Transmission Cycles

If the cholera transmission mechanisms proposed in the previous sections are to be plausible, a multivariate regression technique, using the seasonal hydroclimatic controls as predictors, is expected to explain a significant fraction of the variance of seasonal cholera prevalence values. We have thus used a linear multivariate regression analysis technique with a forward variable selection criterion, where we have incrementally added relevant hydroclimatic variables, based on the seasonal correlation values, and included them in the regression model, if they are statistically significant. Table 4 outlines the results of the multivariate regression analysis for seasonal cholera outbreaks in Dhaka during the study period (1980-2007) with the step-wise selection of variables from two separate sets of hydroclimatic controls during the spring and the fall season outbreaks, and corresponding statistical significance.

In Table 4, we find that the dry- and wet-season processes can explain 69% and 55% of the inter-annual variability of the spring and fall cholera outbreaks in Dhaka (62% and 44% predicted r^2), respectively. For spring, JFMA flow only explains 20% variance for MAM cholera prevalence. However, the inclusion of DJF SST significantly increases the explained variance to 57% (predicted r^2 50%), confirming the role of the coastal processes in spring cholera transmission. Addition of dry season rainfall (DJF) marginally increases the explained variance to 69% (predicted r^2 62%).

For the fall season, GBM monsoon flow (JASO) explains 39% (predicted r^2 34%) of the variability of SON cholera prevalence, while adding BoB SST (JJA) increases the performance of the regression model to 55%, with a predicted r^2 of 44%, However, using spring prevalence as a predictor variable strongly increases the predictability of the fall peak (adjusted r^2 jumps from 55% to 75%, and predicted r^2 increases from 44% to 68%). On the other hand, using previous fall prevalence to predict outbreaks in following spring shows no improvement (adjusted r^2 69% vs 68%, predicted r^2 62% vs 60%).

The above results, taken together, assert the role of an annual cholera transmission process consisting of two seasonal cycles — spring and fall — as shown by strong asymmetric correlations within the same year, and combined influences of hydroclimatic variables in extreme years. The PRESS (Prediction Sum of Squares) goodness-of-fit statistics also show consistent increased skill for combined models [Table 4], suggesting influence of multiple hydroclimatic controls behind each seasonal peak. The strong inverse relationship of dry-season processes with cholera in spring and subsequent seasons [Table 2], and the dependence of the fall peak on preceding spring peak [Table 1] signify the role of a spring-to-fall, coastal-to-inland transmission pattern.

Table 3.4 Multivariate Regression Analysis Results with Seasonal Mean of Hydroclimatic Variables and Seasonal Cholera Prevalence as Predictors

Predictor Variables	r^2	**Adj-**r^2	**Pred-** r^2	**PRESS**	**p**
Spring Cholera Prevalence (MAM)					
JFMA Flow	22.9	20.0	6.4	2216	0.01
JFMA Flow + DJF SST	60.1	56.9	50.5	1173	0.01
JFMA Flow + DJF SST + DJF Rainfall	72.3	68.8	62.3	893	0.03
JFMA Flow + DJF SST + DJF Rain + Prev Fall Cholera	73.1	68.4	60.4	938	0.01
Fall Cholera Prevalence (SON)					
JASO Flow	41.1	38.9	34.0	1485	0.01
JASO Flow + JJA SST	59.4	55.3	44.4	1276	0.006
JASO Flow + JJA SST + Prev Spring Cholera	78.0	75.3	68.0	720	0.001

Notes: **Spring**: Mar–Apr–May (MAM); **Summer**: Jun–Jul–Aug (JJA); **Fall**: Sep–Oct–Nov (SON). **JFMA**: Jan – Apr (dry season); **JJAS**: Jun – Sep (wet season).

r^2 : Coefficient of Determination; **Adj-**r^2 : Adjusted r^2; **Pred-** r^2 : Prediction r^2;

PRESS : Prediction Sum of Squares; **p** : p-value / statistical significance value.

3.4 Discussion and Conclusion

3.4.1 A Dual Space-Time Transmission Paradigm

The foregoing results and observations, taken together, strongly suggest the role of two spatially distributed and distinct seasonal physical processes together modulating annual cholera transmission in the Bengal Delta. *The first cholera outbreaks are initiated in spring near coastal areas as northward movement of the plankton-rich seawater and increased salinity of the estuarine environment favor increased growth and abundance of the cholera bacteria in river corridors.* The ubiquitous use of this river water for irrigation, sanitation, and consumption exposes the riverine societies to the infectious disease. *A second cholera transmission environment becomes dominant in summer and leads to fall cholera outbreaks through floods.* Open mixing of water bodies, channels, and sediments with dormant *V. cholerae* in heavy monsoon rainfall lead to breakdown in sanitation; submerged areas are enriched with bacteria already present in the ecosystem. Figure 3(a) is a proposed schematic diagram of the two seasonal transmission cycles progressing in a spring–fall sequence with five hypothesized components: (A) *Initiation:* Spring cholera outbreaks start when coastal plankton and bacteria move into brackish estuarine areas facilitated by low flow conditions. (B) *Transmission:* Aided by increased salinity, coastal water containing zooplankton and *V. cholerae* moves further inland, and cholera outbreaks are seen in many areas, including Dhaka and surroundings. (C) *Progression:* Floods inundate vast areas of Bangladesh and contaminate water resources across the country. (D) *Transmission:* Cholera bacteria proliferate in water-logged areas after floods recede and cause fall outbreaks. (E) *Termination:* Winter temperature, less nutrient, and settlement of sediment in inland water help end the fall outbreaks.

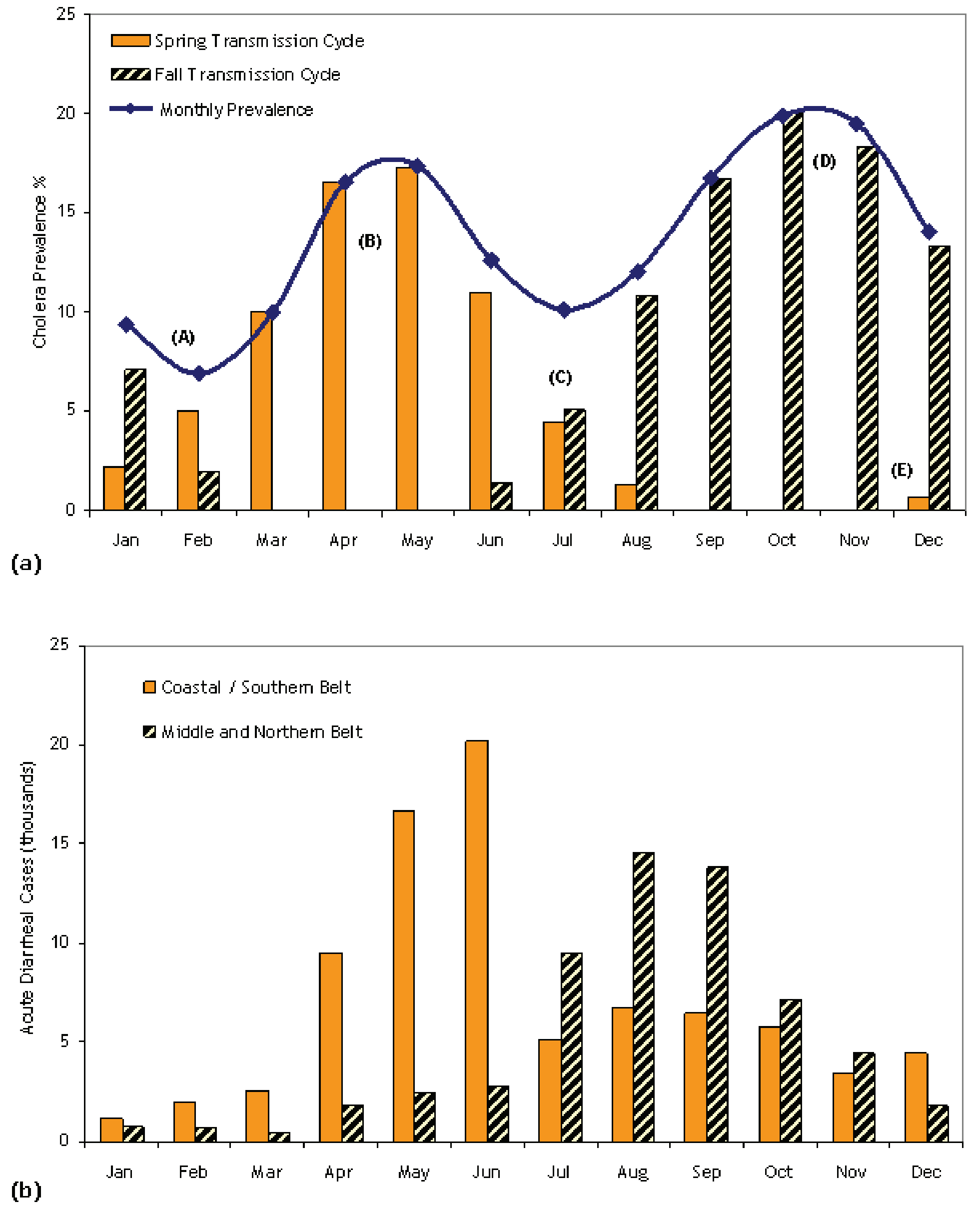


Figure 3.3: (a) A hypothesized schematic of two seasonal cholera transmission cycles observed in Bangladesh during the spring and fall seasons: Monthly prevalence rates for two separate transmission cycles (b) Average monthly acute diarrheal infection observed in southern (coastal) and northern (middle/inland) areas of Bangladesh, 1995–2000.

3.4.2 Implications for Public Health Intervention

An important finding of this study is that GBM cholera outbreaks are propagated from spring to fall and from coastal to inland regions through macro-scale drivers. This finding has significant policy implications as the intrusion of plankton-laden water and the brackish estuarine environment early in the year has a significant impact on subsequent outbreaks throughout the year. Limited intrusion of coastal plankton and lower salinity in estuarine rivers thus may lead to lower cholera burden for the entire year. Future research needs to focus on a detailed characterization of estuarine salinity in the region, which will be helpful for early intervention and targeted mitigation of spring outbreaks. Also, maintaining higher dry-season discharge in specific rivers (for example, through the Gorai, the main distributary of the Ganges into southwestern Bangladesh) may have significant beneficial impacts on public health in later seasons of the year. Schwartz et al (2006) reported that *V. cholerae* strains isolated during peak monsoon months are identical to the strains detected in subsequent fall outbreaks, strengthening our hypothesis of a second transmission cycle beginning in summer and continuing into fall. An early prediction of flood extent using spatial hydrodynamic modeling will thus provide much needed lead-time to predict the magnitude and location of fall outbreaks.

Our findings are further corroborated by the available evidence of water-borne disease infection data from the Director General of Health Survey (DGHS) records (1992–2000) in Bangladesh. Figure 3(b) clearly shows a pattern of two distinctly different outbreak seasons of diarrheal infections in Bangladesh, affecting the coastal belt during the pre-monsoon months and affecting the northern/middle floodplain belt during and after the monsoon months. It is worthwhile to note that the transmission mechanisms hypothesized in Figure 3(a) and the observed outbreaks in Figure 3(b) show affirming similarities in their progression. Further investigation of the regional hydroclimatology and associated transmission cycles may thus provide important insight into the seasonal patterns of other diarrheal diseases in the coastal and inland areas of the Bengal Delta.

In this study, we have reported consistent relationships between macro-scale environmental processes and cholera outbreaks in spring and fall, respectively. Our results show how major cholera outbreaks were linked to significant hydroclimatic events during the last three decades. An understanding of the hydroclimatic influences on cholera dynamics is also crucial in light of changing climate patterns in this region. Projected runoff decrease in the Ganges basin and increasing monsoon runoff in the Brahmaputra basin may cause extreme events such as prolonged droughts and record floods in South Asia (*Goswami et al.,* 2006*; Milly et al.,* 2005), causing water-borne epidemics and introducing new biotypes of the bacteria (*Siddique et al.,* 2010).

This study provides a basis for using available hydrologic, meteorological, and satellite remote sensing data sources to monitor the coastal and terrestrial processes influencing the two distinct seasonal and spatial cholera transmission cycles. It also provides a guideline for initiating preemptive efforts at intervention based on the environmental signatures associated with the macro-scale processes before cholera breaks out in potentially vulnerable areas. In addition, the study outlines a new scope for using dry-season water management as a tool for preventing cholera and other diarrheal diseases in specific areas, which may yield significant and widespread public health benefits throughout the year, thus creating useful actionable knowledge for water management and public health officials in Bangladesh.

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Chapter 4

Understanding Population Vulnerability due to Bengal Cholera Outbreaks Through Epidemiologic Application of Macro-Scale Hydroclimatic Drivers

Abstract

The coastal floodplains of the Bengal Delta have a long history of cholera outbreaks, with temporal peaks occurring during the spring in coastal areas and during the fall in inland locations. The highly populated proximal areas to the corridors of the major rivers of the region, the Ganges-Brahmaputra-Meghna (GBM) system, bear the brunt of both waves of outbreaks, experiencing a biannual incidence pattern. Previous studies focusing on environmental and hydroclimatic drivers of cholera dynamics have not highlighted the spatio-temporal nature of population vulnerability in floodplain areas due to the influence of these large-scale drivers. Here we show that the seasonal and interannual patterns of cholera transmission mechanisms are strongly influenced by estuarine salinity and inland flood inundation patterns that may set the ecological and environmental 'stage' for epidemic outbreaks over large geographic regions. We argue that a major segment of the population in floodplain areas remain vulnerable to the dual peak cholera transmission mechanisms associated with these large-scale drivers. An epidemic outbreak of cholera compounded with the concurrent appearance of droughts or floods may thus seriously overburden the public health response system in Bangladesh.

4.1 Introduction

Cholera, an acute diarrheal illness caused by the bacterium *Vibrio cholerae*, remains a major public health threat in the developing world. The seasonal recurrence of this infectious disease in endemic areas, hypothesized role of climate in its proliferation, and recent epidemic outbreaks across continents have greatly intrigued scientists, epidemiologists, and public health professionals. The life cycle of *V. cholerae*, the causative agent of the disease, is intricately linked to two different types of processes with vastly different spatial and temporal scales. Despite major advances in the understanding of the **micro-scale** (microbiological and human genetic) processes surrounding the bacterium, the role of the **macro-scale** (hydrological, ecological, and climatic) processes in propagating the disease in space and time is not well understood. For example, the existence of an aquatic environmental reservoir of *V. cholerae* and its association with marine plankton species has been firmly established (*Colwell,* 1996); however, the role of river discharge or ocean temperature in aiding bacterial growth or propagation of the disease are not well understood (*Jutla et al.,* 2011).

The coastal floodplains of Bengal Delta have a long history of endemic cholera with wide swings in prevalence being evident (*Longini et al.,* 2002; *Bouma and Pascual*, 2001). Bengal Delta cholera outbreaks are subject to strong seasonal influences and display a great variation in location and magnitude. Spring outbreaks peak in coastal areas in contrast to larger fall outbreaks occurring in inland areas (*Akanda et al.,* 2011). The low elevation downstream floodplains, in between the coastal and inland areas of the Ganges-Brahmaputra-Meghna (GBM) delta region, however, are affected by outbreaks in both spring and fall, and show a biannual incidence pattern unique to this region.

However, a majority of the Bangladeshi population lives in these fertile floodplains and remains vulnerable to outbreaks in both seasons (*CIESIN,* 2009). It is generally accepted that the extent of cholera outbreaks across the region is under reported and the disease burden remains severely under estimated (*Zuckerman,* 2007; *Sack,* 2006). In addition, an overwhelming fraction of the investigations on cholera outbreaks and the role of environmental factors (*Longini et al.,* 2002; *Koelle et al.,* 2005; *de Magny et al.,* 2008; *Islam et al.,* 2009; *Cash et al.* 2008; *Emch et al.,* 2008) have relied on surveillance data from Matlab, a small rural coastal town in Bangladesh. Matlab is the location for a longstanding (since 1966) prospective cholera surveillance effort conducted under the auspices of the International Centre for Cholera and Diarrheal Disease research (ICCDR,B) (*Glass et al.,*1982). The geographical and hydrological dissimilarities between Matlab and other cholera prone areas were reported as early as 1978 (*Briscoe, 1978*). Despite the existence of a sophisticated disease surveillance system, Matlab may not be representative of the cholera disease dynamic in the broader Bengal Delta. Studies utilizing Matlab as a data source may have thus failed to address the spatial and temporal variability of the outbreaks and underlying processes present throughout the region.

With the availability of long-term cholera surveillance data from the inland mega-city of Dhaka (1980 onwards), as well as the recent production of cholera surveillance data from other affected areas in Bangladesh and India, we can now investigate the seasonal nature of cholera outbreaks in multiple locations, and explore the likelihood that major outbreaks are associated with the underlying macro-scale climatic drivers evident throughout the region. Recently, *Akanda et al* (2009) provided a hydroclimatological explanation of the dual peak seasonality of cholera incidence in Dhaka, associating

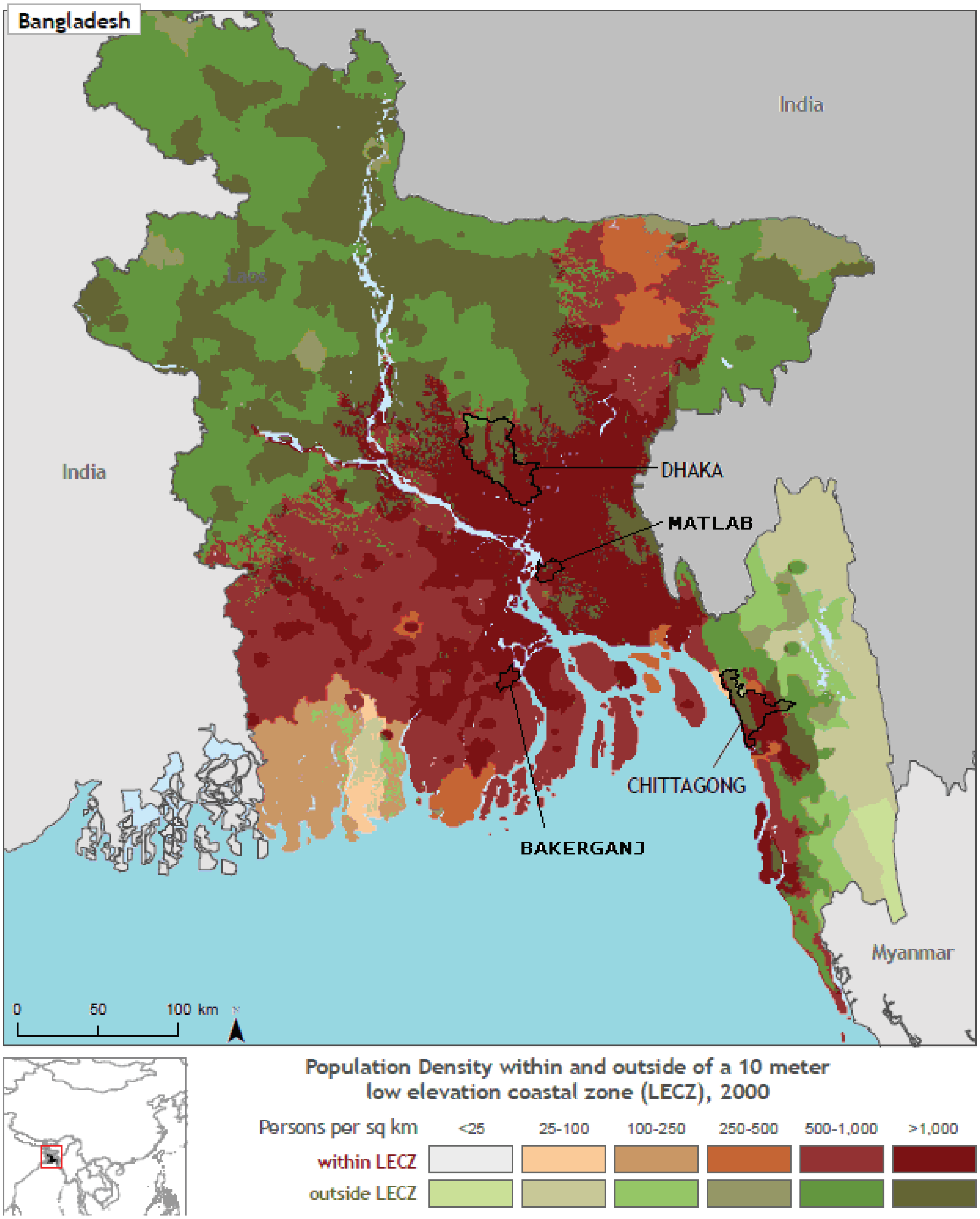

Figure 4.1: Population Density and Elevation Map of Bangladesh, showing surveillance locations and major regional rivers (Source: CIESIN, Columbia University, 2009)

droughts and floods with epidemic outbreaks in spring and fall, respectively. The increased salinity of the estuarine environment during spring provides the optimum environment for growth and increased abundance of the bacterium (*Louis et al.,* 2003; *Vital et al.,* 2007). Inundated lowland areas following monsoon floods, on the other hand, provide vast inland areas with standing water and rain flushed nutrients, enhancing *V. cholerae* abundance (*Schwartz et al.,* 2006; *Islam et al.,* 2006). However, as these transmission mechanisms are manifested at a scale likely to exert impacts to be felt on a regional basis, the implication is that other regional population centers in the floodplains region are also vulnerable during the same time period. Thus an improved understanding of the macro-scale hydroclimatic drivers and coupled with the ability to provide an early estimate of salinity intrusion and flood inundation extent would greatly aid the identification of population centers at increased risk of epidemic outbreaks.

In this study, we investigate the seasonal and interannual variability of cholera outbreaks and their relationship to macro-scale hydroclimatic processes in the Bengal Delta region. Our goal is to understand how the drivers such as estuarine salinity and flooding modulate cholera dynamics in major cholera-prone areas. More specifically, we seek to answer the following: Do the cholera outbreaks in different locations of the floodplains region show similar intraannual and interannual variation? Do seasonal streamflow patterns show an asymmetric relationship with spring and fall disease outbreaks in different surveillance locations? Do we see estuarine salinity and flood extent signatures in the propagation of cholera outbreaks? And, can the understanding of these macro-scale transmission mechanisms help us estimate population vulnerability to seasonal epidemic cholera outbreaks throughout the affected region?

4.2 Materials and Methods

4.2.1 Study Area and Surveillance Locations

Bangladesh is situated on alluvial floodplains in the downstream parts of the GBM basin (Figure 1). The hydroclimatology of this region is highly asymmetric in both time and space, with over 80% of the annual precipitation occurring during the four monsoon months of June through September, and with annual average rainfall ranging from 1500 mm in the Ganges basin catchments in the west to over 4000 mm in the Meghna basin catchments in the east (*Mirza,* 2003). As a result, the region experiences an asymmetric pattern of water availability with severe scarcity of water predominating during the winter and spring months, followed by an abundance of water beginning in summer.

Dhaka (Latitude: 23°41′ N, Longitude: 90°24′ E), a mega-city with a population of 18 million, is a freshwater ecosystem in central Bangladesh, surrounded by several tributaries of the GBM rivers. Matlab (Lat: 23°21′ N, Lon: 90°42′ E) is a cholera-endemic area in southeastern Bangladesh, located near the confluence of the GBM rivers. However, it is less than 100 kilometers from the coast of the Bay of Bengal (BoB) and is subject to tidal fluctuations. Matlab (population: 250,000) is sustained predominantly by the agriculture sector and enjoys a more complete coverage of the population with regards to healthcare than other rural locations in Bangladesh. The ICDDR,B has maintained a large surveillance operation tracking cholera and other water-borne diseases since 1966. However, only ten years of data (1998-2007) were available for this study. Other surveillance locations across the Bengal Delta region were chosen based on concurrent availability of data with Dhaka and Matlab, and geographic characteristics representing coastal and inland communities.

Bakerganj (Lat: 23°06′ N, Lon: 90°15′ E) is a district town in southern Bangladesh; however, it is also adjacent to the main GBM outlet, known as the Meghna Channel, and thus prone to major flood events, typically during the later months of the monsoon season (*Mirza et al.,* 2003). The area has a high rural population density and a lower per capita income than much of the country. The region has a large fishing industry and numerous estuarine channels leading to the BoB, and thus the likelihood of population based exposure to brackish water is high.

Mathbaria (Lat: 22°46′ N, Lon: 89°36′ E), a coastal locality close to the BoB, is known for freshwater scarcity as the region is served by only one major river from the north, the Gorai. Chhatak (Lat: 24°09′ N, Lon: 90°45′ E), an inland location farthest away from coast, experiences the heaviest rainfall in monsoon months among the surveillance locations and prone to flash floods in the Meghna basin. Mathbaria shows cholera outbreaks predominantly in spring, whereas Chhatak shows outbreaks only during fall. The other surveillance locations in Bangladesh, Dhaka, Matlab, and Bakerganj are located along the central floodplains of the GBM river system and are affected by both waves of the previously mentioned cholera outbreaks, in spring and fall (Figure 1).

We also use additional cholera surveillance data (1998-2007) obtained from Kolkata (Lat: 22°33′ N, Lon: 88°20′ E), which experiences biannual cholera incidence peaks in spring and fall seasons similar to the other locations. Kolkata is a major city in eastern India, home to over 20 million people, and is situated on the Bhagirathi-Hooghly river system flowing through eastern India. This river system is directly supplied by upstream diversions from the Ganges river (*Rahman et al.,* 2000) and experiences similar drought-flood cycles as the rest of the Bengal Delta.

4.2.2 Surveillance and Hydroclimatic Data

The ICDDR,B has maintained a sophisticated disease surveillance program in Dhaka since 1980, where cholera incidence is assessed via testing for *V. cholerae* infection among a sequential sample of the patients visiting the hospital each week. The weekly hospital visits are aggregated to monthly and seasonal levels for this study. We also obtain cholera incidence records from Matlab and Bakerganj (1998-2007), where the ICDDR,B maintains satellite surveillance operations. Kolkata cholera incidence is obtained from the National Institute of Cholera and Enteric Diseases (NICED) in India. Daily river discharge records for GBM rivers (1958-2007) were obtained from the Bangladesh Water Development Board (BWDB). Combined flow volumes for the Ganges and the Brahmaputra are used for locations in Bangladesh. On the other hand, the Hooghly is supplied by upstream diversions from the Ganges; thus only Ganges streamflow was used for the analysis on Kolkata cholera incidence.

The lack of a continuous salinity time series in estuarine Bangladesh as well as detailed inundation information during flood events has prevented previous research studies from investigating the role of these important variables in the transmission of cholera. A MIKE11 water resources modeling setup developed by the Danish Hydraulic Institute is used to simulate the dominant hydrological processes in the region, including rainfall-runoff, streamflow and river levels. These outputs are further used in a Salinity Model and a Flood Inundation Model to estimate estuarine river salinity in southwestern Bangladesh and flood extent in inland Bangladesh at a district level for spring and fall seasons, respectively (Figure 2). More details of the salinity and flood inundation model setup can be found in *Wahid et al.* (2007) and *Nishat and Rahman* (2009), respectively.

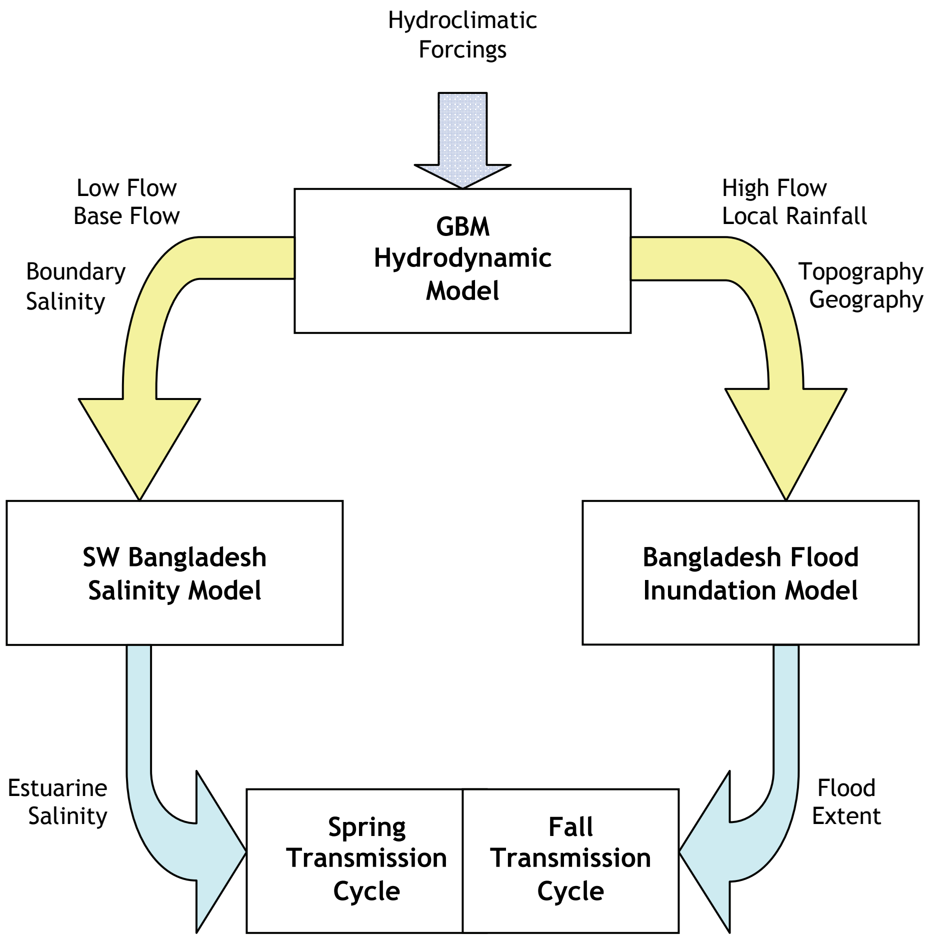

Figure 4.2: Schematic of Hydroclimatic-Hydrodynamic Conceptual Model Setup for the Lower Bengal Delta Region Used in Analysis

4.3 Analyses and Results

4.3.1 Intraannual and Interannual Variability of Cholera

We start our analyses with a comparison of the mean monthly cholera incidence in Dhaka, Matlab, Bakerganj, and Kolkata for the period 1998-2007. In Figure 3(a), we see a similar dual peak nature of cholera incidences in all four locations, with the first outbreaks occurring in the spring and a second major outbreak later in the year during fall months; both peaks surpass the annual mean with significant margins. In addition, the winter months (January-February) and the peak monsoon months (July-August) exhibit the lowest level of outbreaks for all locations in the region. From a climatological perspective, we see higher cholera outbreaks in the spring and fall in all four areas and less severe outbreaks during winter and summer. However, Mathbaria exhibits a predominant spring peak, whereas Chhatak experiences outbreaks in late fall.

To understand the interannual variation of individual seasonal outbreaks, we disaggregate the cholera time series into two seasonal components, spring and fall, for each location. Mathabaria and Chhatak were excluded from this analysis due to the shorter temporal length of available data. Seasonal cholera incidence anomalies are calculated as deviations from the mean for 1998-2007 and normalized with the respective standard deviations. This is a common practice in hydrologic and climate science (*Jutla et al.,* 2006), which allows us to effectively compare the incidence from all locations with their respective interannual variations from the seasonal mean. Figures 3b and 3c show the comparison of spring and fall cholera incidence in seasonal anomalies between Dhaka, Matlab, Kolkata, and Bakerganj. Here we find that cholera incidence in all locations show similar deviations for most years in both seasons. Such similarities of variation across these different geographic locations over ten years suggest the influence of the same large scale hydroclimatic processes on cholera transmission.

4.3.2 Cholera and Streamflow

The GBM river system exhibits a distinct dual pattern of influence over regional cholera dynamics (*Akanda et al.,* 2009; 2011). Cholera incidence in Dhaka for spring (MAM: Mar-Apr-May) is inversely associated with low flow volumes during the dry season, while a strong positive correlation is seen between peak flow volumes and fall (SON: Sep-Oct-Nov) cholera. If our hypothesis of large-scale hydroclimatic controls of cholera dynamics is to be valid, we should expect to see a dual role of river discharge as in *Akanda et al.* (2009) for all the surveillance locations along these major rivers. In other words, a region-wide inverse relationship between low flow and spring cholera, and a positive relationship between fall cholera with high flow are likely to be observed.

To make this point, seasonal low and high flow volumes for the Ganges and the Brahmaputra rivers are compared with mean spring and fall cholera incidence anomalies, respectively. Figure 4 shows seasonal low flow (Feb-Mar mean) and high flow (Aug-Sep mean) anomalies for the Ganges and Brahmaputra rivers plotted against average spring (MAM) and autumn (SON) cholera incidence anomalies for each location. A key observation from Figures 4a and 4b is the reversal of linear relationships between streamflow and cholera incidence between the two seasons. Seasonal low flow volumes are negatively correlated with spring cholera incidence in all locations; on the other hand, high flow volumes show a strong positive relationship with fall cholera. In other words, scarcity of water heightens the risk of cholera outbreaks throughout the region in spring, while an abundance of water in monsoon season leads to further epidemics in the fall.

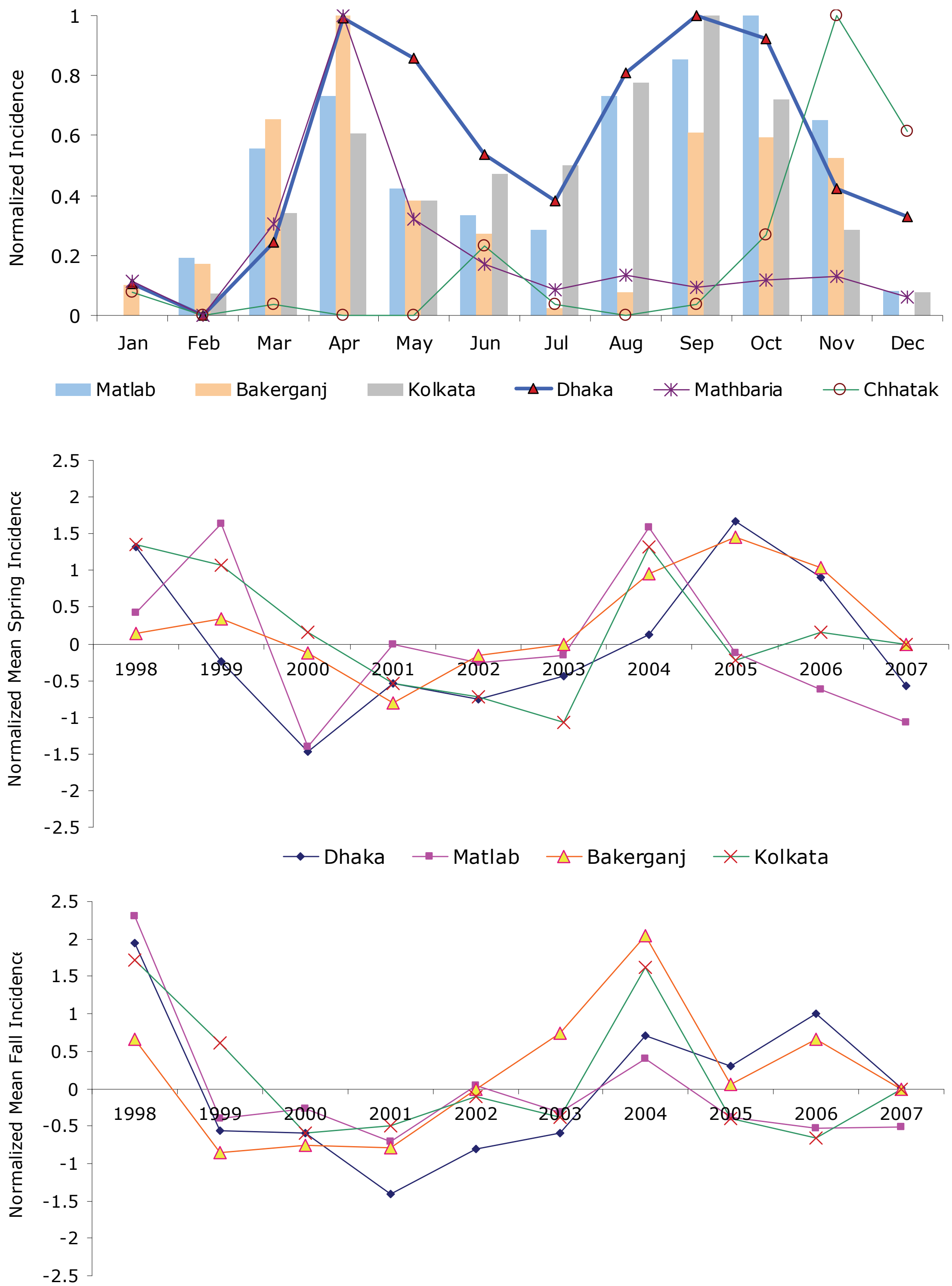

Figure 4.3: Comparison of Normalized (a) Mean Monthly Cholera Incidence for All Locations (b) Mean Spring Incidence Anomaly and (c) Mean Fall Incidence Anomaly for Selected Surveillance Locations

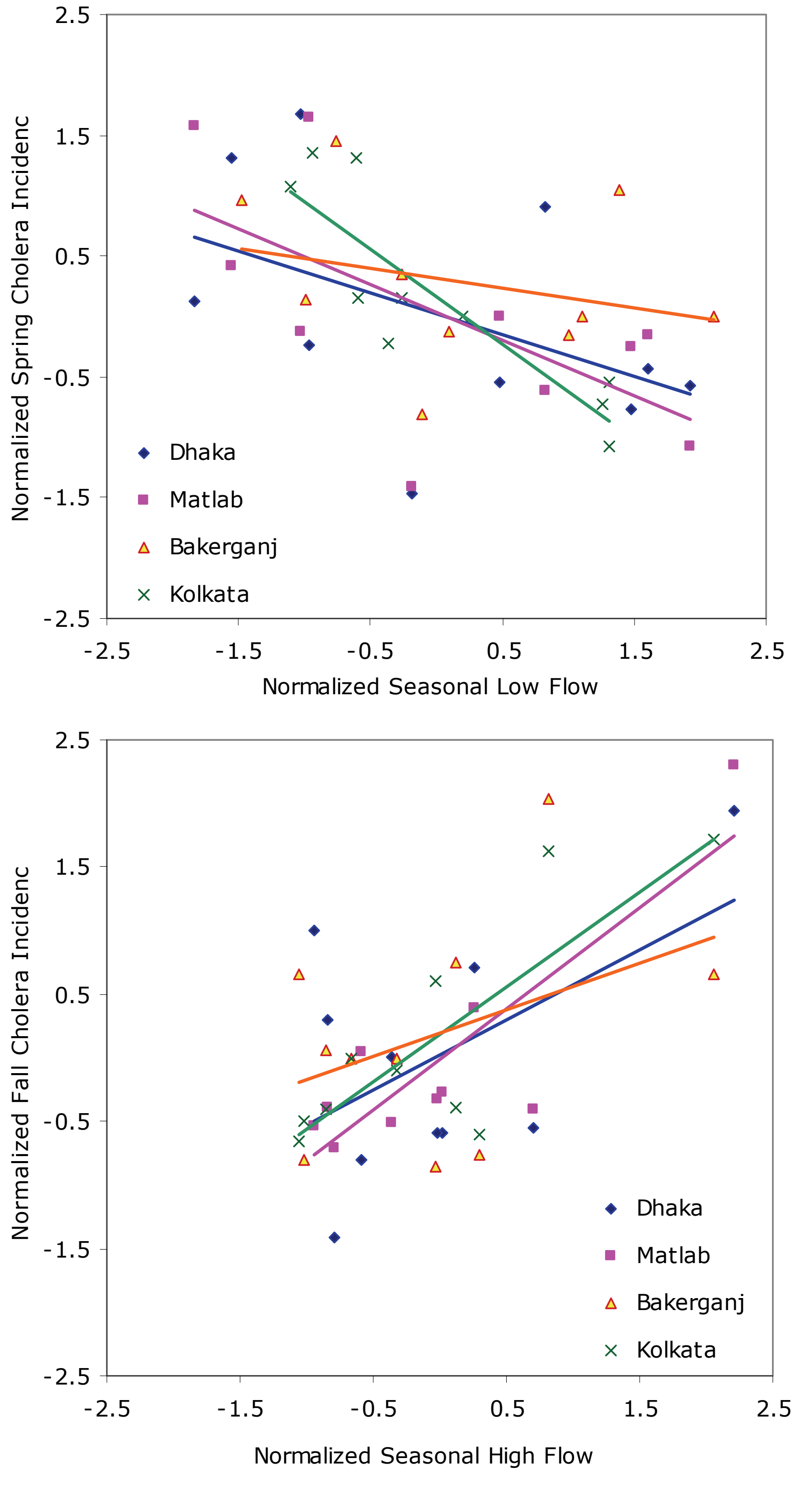

Figure 4.4: Mean Seasonal Cholera Incidence and Streamflow Anomaly in Bengal Delta for (a) Dry and (b) Wet Seasons for the period 1998-2007

4.3.3 Role of Estuarine Salinity and Flood Extent

The goal of this analysis is to identify plausible physically consistent relationships between salinity-aided bacterial-reservoirs and cholera outbreaks in the estuarine and inland areas of Bangladesh in subsequent months. If the hypothesis of such a coastal reservoir were valid, one would also expect to see elevated cholera incidence following increased salinity, and lower cholera incidence following decreased salinity levels in coastal areas. Figure 5a shows a strong positive relationship between mean spring cholera anomalies in Dhaka for the 1988-2007 analyses period with respect to mean estuarine salinity in spring for southwestern (SW) Bangladesh. Similarly, Figure 5b shows a co-varying relationship between mean cholera incidence anomaly in fall and corresponding flood area extent in north-central (NC) Bangladesh.

We expand this analysis further by examining the pattern of monthly cholera incidence in all four (Dhaka, Matlab, Kolkata and Bakerganj) surveillance locations following high and low salinity levels in estuarine areas. We divide the 10 year analysis period (1998-2007) into two high and low bins, based on the variability of salinity levels in outbreak seasons; and compare the average monthly cholera incidence between the selected sets of five high and five low years across all four surveillance locations.

We see larger cholera outbreaks in the years beginning with higher salinity levels and spatial coverage in coastal Bengal Delta, and smaller outbreaks following lower salinity (Figure 6). The consistent picture of variability and the clear separation between high and low salinity signatures suggest that estuarine salinity and associated bacterial growth in spring may contribute to cholera outbreaks across the floodplains across all four locations in all subsequent months of the year.

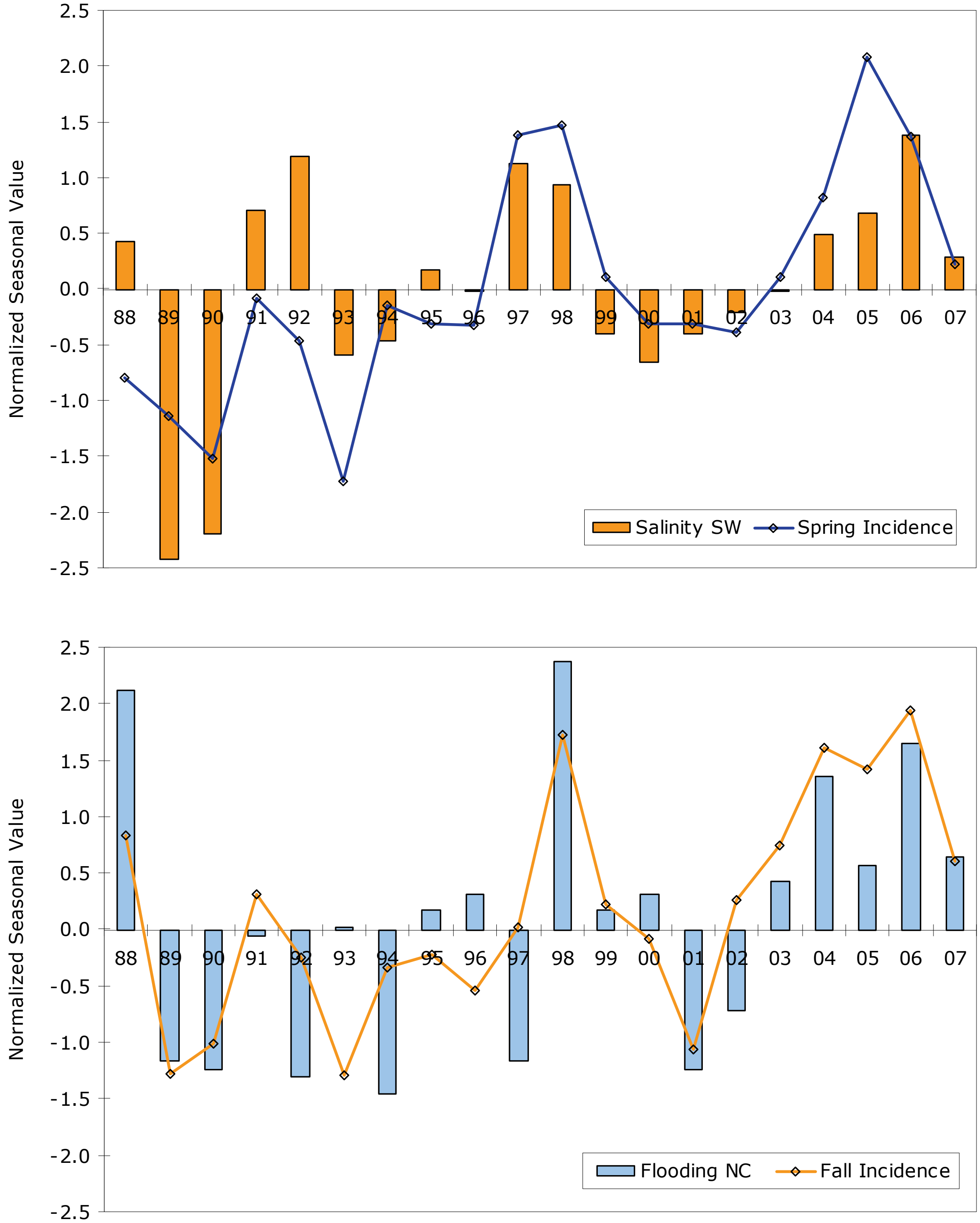

Figure 4.5: Seasonal Cholera Incidence in Dhaka with (a) Estuarine Salinity (SW: southwest) and (b) Flood Extent (NC: North Central) for the period 1988-2007

Similarly, to establish the physical role of flood inundation in perpetuating the progression of cholera outbreaks from spring to fall, we divide the 10 year (1998-2007) period of analysis into two high and low bins based on the variability of flood extent in the wet season (JASO: Jul-Aug-Sep-Oct months); and average the monthly cholera incidence in Dhaka, Matlab, Kolkata and Bakerganj for the selected five high and five low years. As seen in Figure 7, cholera incidence values in the fall season of years with high and low flood extent levels are distinctly separate for each location. This consistent variability of cholera incidence with respect to high and low flood signatures supports the importance of the role of monsoon driven processes contributing to large scale water contamination and bacterial proliferation of the GBM floodplains.

Table 1 quantifies these seasonal associations through Pearson correlation coefficients calculated between MAM (Mar-Apr-May mean) salinity and corresponding spring cholera incidence. Similarly, correlation values between JASO (Jul-Aug-Sep-Oct mean) flood extent values and fall cholera incidence are shown for Dhaka, Bakerganj, Kolkata, and Matlab in Table 1. We observe a consistent pattern of strong positive association between estuarine salinity levels and spring cholera incidence in all locations except Matlab. We also see a strong positive relationship between flood extent values and fall incidence in those locations. Statistical significance tests were performed for the time series pairs and reported in Table 1. We also see a contrasting dual influence of flow volumes (negative correlation values in spring and positive in fall). Due to the lack of a sufficiently long cholera incidence time-series from Mathbaria and Chhatak, we present monthly local salinity and flood extent data in Figure 8, which shows the seasonal associations of these processes with cholera incidence in spring and fall, respectively.

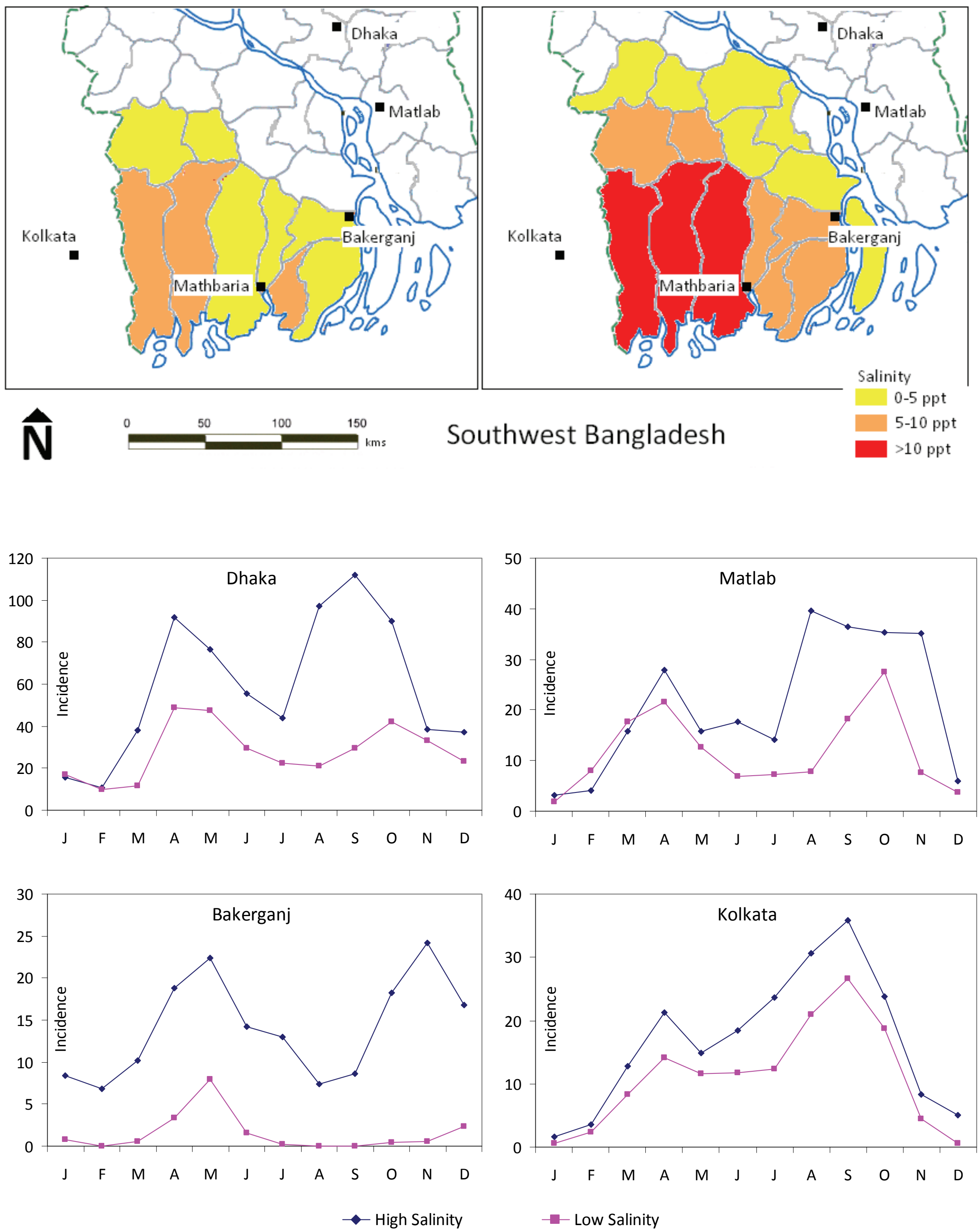

Figure 4.6: Monthly Cholera Incidence in Dhaka, Matlab, Bakerganj and Kolkata, and High and Low Estuarine Salinity in Southwest Bangladesh for the period 1988-2007

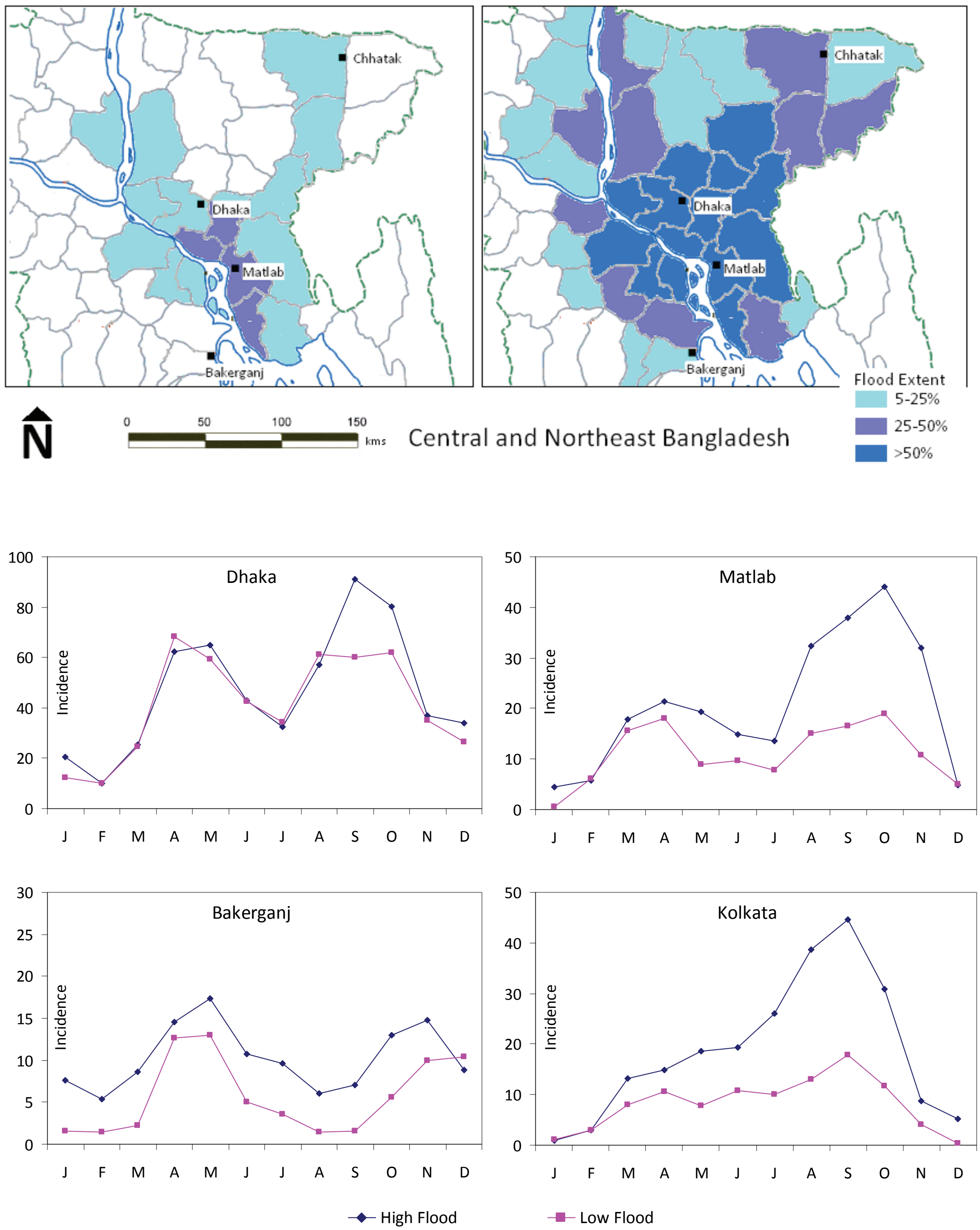

Figure 4.7: Monthly Cholera Incidence in Dhaka, Matlab, Bakerganj and Kolkata, and High and Low Flood Inundation in Central and Northeast Bangladesh during 1988-2007

Table 4.1: Relationship between Seasonal Mean Cholera Incidence Values and Large Scale Hydroclimatic Controls in the GBM Basin Region

Location	Cholera Season	Low Flow	Estuarine Salinity	High Flow	Flood Extent
Dhaka (n=20)	Spring	-0.48*	0.68**	-	-
	Fall	-0.48*	0.86**	0.69**	0.77**
Matlab (n=10)	Spring	-0.64*	0.41	-	-
	Fall	-0.52	0.36	0.86**	0.81*
Bakerganj (n=10)	Spring	-0.44	0.67*	-	-
	Fall	-0.23	0.63*	0.40	0.37
Kolkata (n=10)	Spring	-0.79*	0.63*	-	-
	Fall	-0.67*	0.25	0.81*	0.79*

Statistical significance indicators: ** $P < 0.01$; * $0.05 > P > 0.01$

n = number of years of data used in the analysis

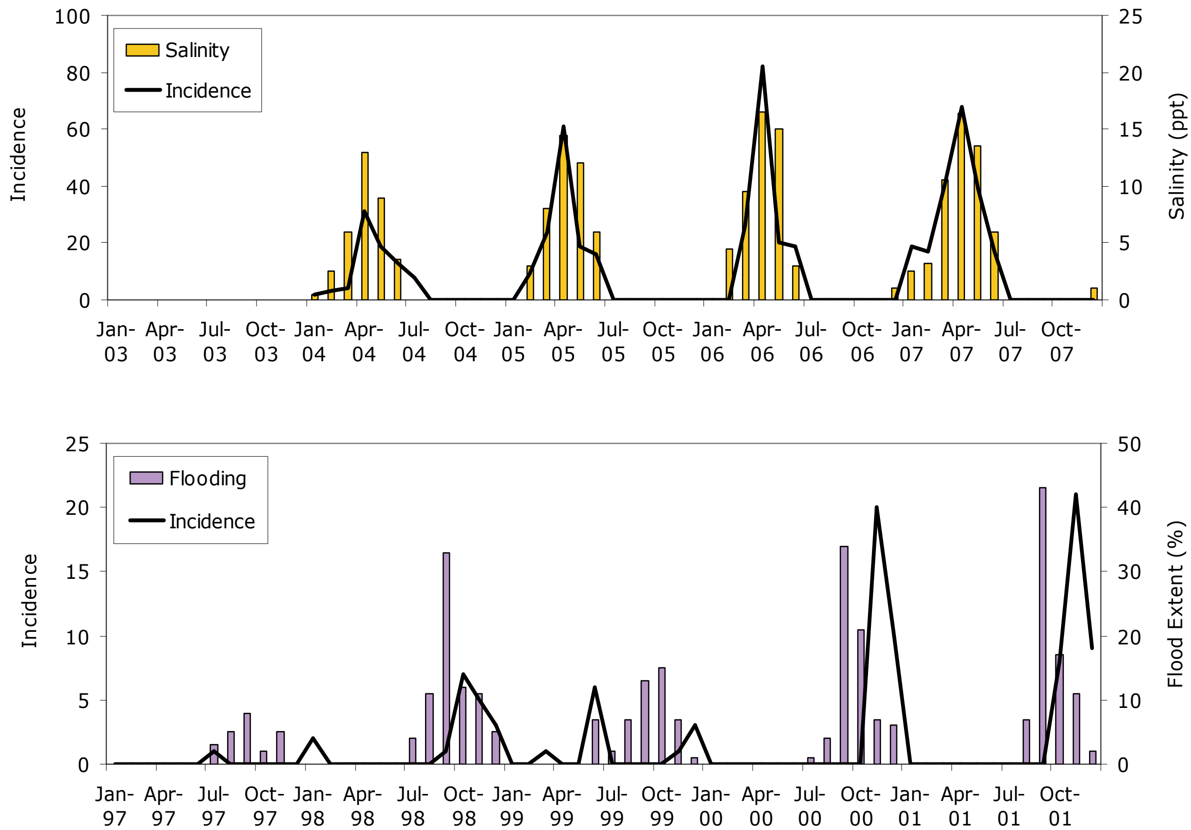

Figure 4.8: Monthly Cholera Incidence and Hydroclimatic / Environmental Signatures for (a) Spring Cholera Incidence and Estuarine Salinity (ppt) for Mathbaria (2003-2007); and (b) Fall Cholera and Regional Flooding information for Chhatak region (1997-2001)

4.4 Discussion

The presented analyses indicate that estuarine salinity and inland flood inundation can significantly affect cholera transmission in the Bengal Delta region. Our results and the hypothesized role of the two processes are validated across available surveillance locations throughout the region. In addition, our analyses show that large areas of the highly populated floodplains in this region remain at high risk of epidemic outbreaks in spring and fall due to the large spatial coverage of salinity intrusion and flood inundation, respectively (Figure 6-7). Population centers along the floodplain corridors of the GBM river system remain vulnerable to such seasonal and interannual variability of cholera transmission mechanisms in relation with underlying macro-scale hydroclimatic drivers during the spring and fall seasons, respectively,

Akanda et al. (2011) postulated the presence of two spatially distinct and seasonal cholera transmission cycles in this region, a pre-monsoon phase in estuarine areas and a post-monsoon inland phase following the wet season. The physical basis of this argument is that the highly asymmetric hydrology of the GBM region leads to a drastic reduction of streamflows in the dry season and a significant drop in the hydraulic head, accelerating the saline front movement from BoB towards inland freshwater (*Rahman et al. 2000*). This inward movement of seawater may help transport *V. cholerae* from coastal areas and the increased salinity of the estuarine rivers then provides a larger optimal growth environment for the bacterium. *Miller et al.* (1982) proposed the importance of salinity in cholera transmission in Kolkata and London using historical data, however, these analyses were not supported by sufficient grounding in environmental science on the possible role of the regional hydroclimate in influencing such a transmission pathway.

Similarly, an investigation of diarrheal diseases during recent major floods in Bangladesh (*Schwartz et al. 2006*) reported that *V. cholerae* strains isolated during peak monsoon months (Jun-Aug) were identical to those detected during the subsequent fall outbreaks, which suggests that contamination may occur as early as the months of June and July, before cholera outbreaks peak in the fall. *Akanda et al.* (2009) reported a strong correlation between an annual Flood Affected Area (FAA) measure and fall cholera incidence. However, as that FAA measure is available only after the flood season officially ends in September, it cannot be employed as a useful predictor. If the extent of flood inundation in specific geographic locations such as Matlab can be estimated as early as July or August, it could provide a valuable 2-to-3 month lead-time before the fall outbreak peaks in October, within which to predict and prepare for cholera outbreaks.

Lack of reliable and continuous cholera incidence data as well as poor coverage in both time and space has traditionally hindered research on understanding the climate-cholera connection. Most published literature on Bengal cholera and climate have only used data from Matlab (e.g., *Pascual et al.,* 2008; *Koelle et al.,* 2005; *Cash et al.,* 2008; *Islam et al.,* 2009), a small coastal town in Bangladesh, and consequently, provided a potentially skewed and incomplete understanding of transmission and propagation of cholera in the Bengal Delta region. Thus in this study, we have used a 30-year dataset from Dhaka along with shorter time series from other locations in the GBM floodplain region to assess the role of macro-scale drivers in perpetuating and propagating the seasonal cholera transmission cycles. Our findings strengthen the plausibility for the role of a coastal bacterial reservoir aided by estuarine salinity earlier in the year and subsequent contamination of water resources by post monsoon flood inundation.

Recent data indicate that *V. cholerae* outbreaks can be highly local, occurring simultaneously in various locations possessing favorable environmental conditions (*Stine et al.,* 2008; *Alam et al.,* 2011). As the underlying transmission mechanisms are better understood at the macro-scale, the likelihood of an epidemic cholera outbreak in Dhaka due to an extreme hydroclimatic event, such as a drought or a flood, also implies that Matlab and Bakerganj as well as other major population centers along the floodplains are also concurrently vulnerable. Taken together, Figures 4 through 8 imply that these seasonal processes extend over a large portion of the Bengal Delta and may modulate cholera incidence across all surveillance locations analyzed here. The results also suggest that with such an understanding of the underlying large scale drivers, there is potential to predict the timing and magnitude of cholera outbreaks.

4.5 Conclusions and Public Health Implications

In Summary, we show that macro-scale hydroclimatic processes such as estuarine salinity intrusion and inland flood inundation can significantly affect cholera dynamics in the Bengal Delta region. A region-wide analysis of the spatial and temporal patterns of cholera incidence reveals strong influences of estuarine salinity and inland flooding patterns that may set the ecological and environmental 'stage' for epidemic cholera outbreaks over large geographic regions. The hypothesized role of two distinct seasonal cholera transmission processes are validated across six surveillance locations in the region. We present evidence that population centers along the floodplain corridors of the GBM river system remain vulnerable due to the spatial nature of these transmission mechanisms, depending on salinity or flooding signatures in coastal and inland regions that can be measured two to three months in advance

The World Health Organization has long supported the development of an early warning system for epidemic cholera outbreaks using climatic and environmental data. Although researchers have attempted to predict epidemic cholera outbreaks, an accurate climate-based early warning system is yet to be developed and implemented at an operational level. More importantly, their studies did not sufficiently identify and incorporate the asymmetric and large scale nature of climatic and environmental influences. The findings of the present study do not directly represent a causal connection; however, it identifies two plausibly important physical variables in the transmission process, estuarine salinity and inland flood inundation, and suggests that seasonal asymmetry and spatial heterogeneity of underlying hydroclimatic processes should be taken into account for developing meaningful predictive models.

Our findings can be incorporated into a predictive surveillance capability that would help identify vulnerable population groups in the region at risk of imminent cholera outbreaks. Such a capability would help save lives not just in Dhaka, but also in other population centers along the floodplains that are affected by these seasonal and spatial macro-scale drivers (Figure 9). A predictive system based on the geographic specificity of salinity and flood signatures holds the promise of predicting future intensity of disease transmission and plausibly providing the public health authorities spatially specific warnings necessary for alerting medical personnel and implementing preventive measures ahead of epidemic outbreaks. Coupled with the advances at the micro-scale of cholera management as demonstrated via markedly improved survival rates, increased efficacy of palliative care and diagnostics, the future of the public health response to this age old nemesis may continue to improve.

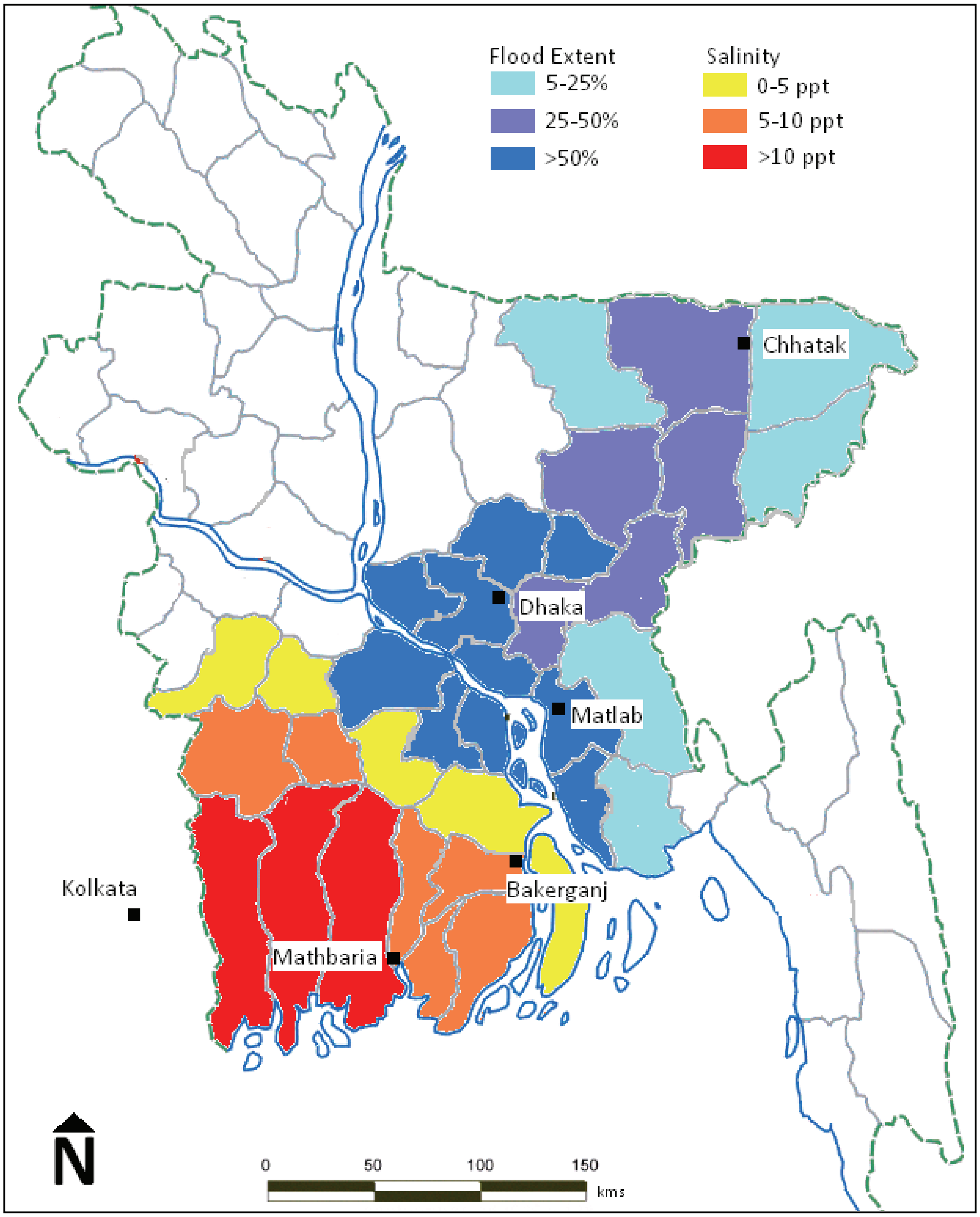

Figure 4.9: Areas at Risk of Recurrent Cholera Outbreaks in Spring and Fall Seasons due to Salinity Intrusion and Flood Inundation (Average for the period 1998-2007)

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Chapter 5

A Spatially Explicit and Seasonally Varying Cholera Prevalence Model With Distributed Macro-Scale Environmental and Hydroclimatic Forcings

Abstract

Despite major advances in the ecological and microbiological understanding of *Vibrio cholerae*, the causative agent of cholera, the role of underlying large-scale hydroclimatic processes in the progression of the disease in space and time is not well understood. We postulate that environmental cholera transmission is modulated by two spatially and seasonally distinct transmission mechanisms - influenced by distinctive dry and wet season hydroclimatic determinants. To test the hypothesis, a spatially explicit coupled hydroclimatology-epidemiology model has been developed for understanding regional scale cholera prevalence in response to large scale forcings. The semi-distributed model is applied to the Ganges-Brahmaputra-Meghna Basin areas in Bangladesh to simulate spatially explicit cholera prevalence rates in $1^{o}x1^{o}$ grids spanning the region. A long time series of cholera data from Dhaka and shorter-interval regional surveillance data from selected locations are used to validate model results. The model reproduces the variability of cholera prevalence at monthly, seasonal, and interannual timescales and identifies the importance of the asymmetric large scale hydroclimatic processes as the dominant drivers of cholera transmission. Our findings have important policy implications, for formulating effective intervention through water management, providing advance warning to public health authorities and for advancing our understanding of the impacts of changing climate patterns on the seasonal transmission of cholera.

5.1 Introduction

5.1.1 Background

Cholera remains a major public health threat in many developing countries around the world, especially in parts of South Asia, Sub-Saharan Africa, and Latin America. The striking seasonality and annual recurrence of this infectious disease in endemic areas, and recent outbreaks across three continents in Haiti, Pakistan, and Nigeria, remain of considerable interest to scientists and public health workers. Despite major advances in the **micro-scale** (e.g., microbiological and genetic processes) understanding of the causative agent, *Vibrio cholerae*, the role of the **macro-scale** (hydroclimatic, ecological and coastal processes) drivers in propagating the disease in multiple seasons and years is not well understood (*Jutla et al.,* 2010). More specifically, how the spatial and temporal variability of cholera outbreaks and associated transmission mechanisms expose populations at risk to infection in different areas of a vulnerable region is not known.

Previous studies have focused on the prediction of cholera outbreaks based on environmental or climatic signatures, such as rainfall, coastal plankton abundance, sunlight, sea surface temperature and height, and oceanic processes (*Hashizume et al.,* 2008; *de Magny et al.,* 2008; *Koelle et al.,* 2005; *Islam et al.,* 2009; *Cash et al.,* 2009; *Pascual et al.,* 2008); but these studies did not adequately address plausible causal pathways of transmission. In addition, a mismatch often exists between the scale of health impacts, the sampling of causative agent, and the visualization of the related macro-scale drivers. For example, *Pascual et al.* (2008) failed to elaborate on how a large scale phenomenon such as the El nino–Southern Oscillation (ENSO) would affect cholera incidence in local surveillance programs such as in Matlab, Bangladesh.

The above-mentioned studies, also, did not consider space explicitly. *Bertuzzo et al.* (2008; 2009) first developed a spatially explicit model that simulated the spreading of cholera along river channels during the KwaZulu-Natal 2001–2002 epidemic in South Africa. However, the authors failed to provide realistic explanations of the parameters used in their model, or to incorporate the effects of large scale climatic, ecological or hydrological processes. In summary, cholera outbreaks are the physical results of a complex interplay of micro and macro-scale processes, extended over a vast range of spatial and temporal scales. Many of these transmission processes are highly complex, due to the nature of hydrologic response to climatic variability and geographic specificity, as well as the ecological constraints that govern nutrient availability and biological growth. The common element involved in the cholera transmission cycle is water. Thus a model for cholera prediction needs to internalize the crucial functionalities played by hydrological and related climatic processes in both space and time.

Here, we propose an integrated framework where macro-scale hydroclimatic forcings can be translated into region specific cholera prevalence estimates to identify how associated changes in hydrologic and ecological conditions may impact cholera transmission dynamics. More specifically, this framework will give a detailed spatial orientation at how seemingly anomalous hydroclimatic events may expose population centers to the risk of epidemic cholera outbreaks. In addition, the following questions will be addressed: Which combination of hydroclimatic and ecological conditions lead to an increased level of cholera prevalence in coastal regions? How does water abundance in monsoon affect cholera outbreaks in inland floodplains? How is population vulnerability affected during extreme hydroclimatic events such as droughts or floods?

5.1.2 Study Area: Hydroclimatology and Cholera in Bengal Delta

Most existing literature related to the epidemiology, transmission, propagation, and control of cholera are based on long-term datasets generated by the International Center for Diarrhoeal Disease Research (ICDDR,B) in Bangladesh, where the disease is endemic. A curious feature of cholera dynamics in this region is the existence of biannual peaks in the populated floodplain regions; yet, existing studies appear to have primarily focused on environmental and ecological variables that only have a single annual peak. For example, *de Magny et al.* (2008) and *Emch et al.* (2008) used plankton abundance and sea surface temperature to simulate cholera outbreaks in the region, but they failed to provide any physical evidence for the transmission mechanism. Similarly, *Koelle et al* (2005) reported a 14-month lag correlation between upstream rainfall and Matlab cholera, without any plausible physical or hydroclimatological explanation. Consequently, these investigators were unable to identify the underlying seasonal processes, and thus were unable to provide meaningful predictors for the biannual cholera peaks.

Preliminary analyses and results suggest that in the Bengal Delta region, coastal hydroclimatic processes primarily modulate the first transmission cycle of the year in the spring. Terrestrial processes such as monsoon peak flow in inland rivers and resulting flood processes distinctly exhibit a strong influence on the second transmission cycle in fall (*Akanda et al.,* 2011a). Mathbaria, a coastal location close to the Bay of Bengal (BoB), shows cholera outbreaks only during spring; while Chhatak, an inland location farthest away from the coast, shows outbreaks only during fall. Matlab and Dhaka, on the other hand are located along the floodplain corridor of the GBM rivers and are affected by both waves of cholera outbreaks (*Akanda et al.,* 2011b).

Recently, *Akanda et al.* (2009) provided a hydroclimatological explanation of the dual peak seasonality of cholera prevalence in Bangladesh associating dry season water scarcity in the GBM basin with early cholera outbreaks in spring. This implies that the scarcity of freshwater in upstream regions during the dry season and resulting intrusion of plankton and bacteria-laden seawater encompasses the estuarine region, and may trigger cholera outbreaks in coastal areas. Physical and chemical conditions of the water and abundance of phytoplankton in coastal BoB in previous seasons may thus provide an optimum growth environment for cholera bacteria in early spring. Later in the year, intense monsoon precipitation and upstream flow generation, and resulting overland flow in floodplains mixes open and closed water networks, and contaminates unprotected water resources with the bacteria already in the ecosystem, triggering cholera outbreaks in fall. Inundated lowland areas following monsoon floods can saturate vast inland areas with standing water and rain-flushed nutrients, enhancing *V. cholerae* abundance and transmission in surrounding communities during fall months.

In summary, the seasonal cholera transmission mechanisms in the Bengal Delta region are strongly modulated by two distinct sets of macro-scale environmental and climatic drivers (*Akanda et al.,* 2011a). However, no previous study has combined this asymmetric role of the drivers with a cholera model that allows the simulation of transmission scenarios influenced by seasonal and spatial processes. Here, we present a spatially explicit and seasonally varying cholera prevalence model with distributed macro-scale environmental and hydroclimatic forcings to show how the asymmetric seasonal hydrology and anomalous climatic events may influence the risk of epidemic cholera outbreaks in different locations within the GBM region.

5.2 Material and Methods

5.2.1 Model Structure and Description

The presented model was developed to evaluate the influence of large scale hydroclimatology on the ecological and environmental conditions necessary for *V. cholerae* growth and causal pathways of transmission. Figure 5.1 shows the conceptual schematic of the model framework and interlinks between the various model components. Cholera Prevalence, a population corrected measure of cholera incidence, will be estimated based on spatio-temporal signatures of the seasonal hydroclimatic processes and relevant hydrological and ecological conditions at 1ºx1º grid scale. The role of a coastal reservoir of bacteria has been previously established (*Worden et al.,* 2006). Cholera Prevalence can be defined as a function of vibrio growth, a measure of *V. cholerae* abundance in the aquatic reservoir, and spread, a measure of human exposure and consumption of bacteria contaminated water sufficient to transmit disease.

Vibrio growth can be defined as a function of ecological variables; salinity (S), water temperature (T) and nutrients (N), which are vital for *V cholerae* growth and proliferation (*Vital et al.,* 2007; *Singleton et al.,* 1982a; 1982b), Also, vibrio spread can be expressed as the function of physical variables such as precipitation (P), streamflow (Q), and a measure of flood inundation, flood affected area (FAA) (*Bertuzzo et al.,* 2008; *Koelle et al.,* 2005; *Akanda et al.,* 2011). Nutrient accumulation can also be approximated as a function of precipitation (P) (*Ruiz-Moreno et al.,* 2010). Thus, a more complete characterization of cholera prevalence for the hypothesized seasonal transmission cycles in space and time can be represented at a particular location *x,y* and at a time step *t* as:

$$\text{Prevalence}_{x,y,t} = f(\text{P}, \text{Q}, \text{S}, \text{SST}, \text{FAA}, \text{T})_{x,y,t}$$

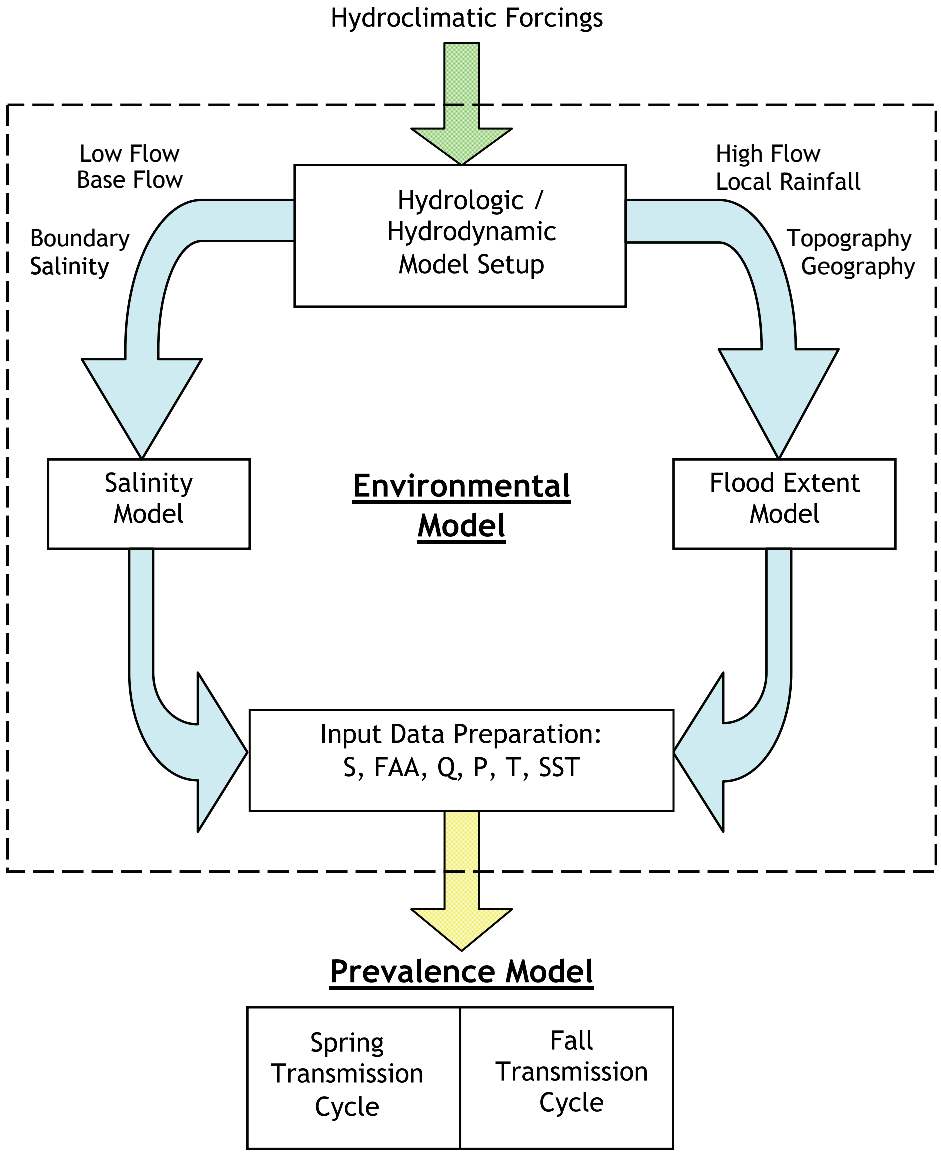


Figure 5.1: Proposed Spatially Explicit Seasonally Varying Environmental (Hydroclimatology) – Prevalence (Epidemiology) Model Schematic

The exact functional form of this transmission pathway is not well understood (as described in Section 1.1). However, recent research studies and available evidence show a strong influence of seasonal (spring and fall) and spatial (coastal and inland) processes on cholera outbreaks in the Bengal Delta region (*Akanda et al.,* 2009, 2011; *Jutla et al.,* 2010; 2011), we separate the transmission pathway into two seasonally varying components, the environmental (hydroclimatology) model component and the prevalence (epidemiology) model component. The environmental model operates according to the schematic shown in Figure 5.1. It computes the water balance components such as rainfall-runoff, regional streamflow, evapotranspiration and groundwater flow. These outputs, in turn, are used to potentiate an adversion-dispersion model to derive estuarine salinity patterns and in a physical flood inundation and mapping model to simulate regional flood extent patterns (more details in Section 5.2.3).

Macro-scale environmental inputs, in the form of observed hydroclimatic forcings as well as the hydroclimatology model simulation outputs are used in the epidemiology (prevalence) model. The model does not assume any particular type or form of the underlying processes, as we do not have *a priori* knowledge of the nature of these processes. However, we start with a linear multivariate regression approach as a tentative first step into developing the model, as previous studies (*de Magny et al.*, 2008; *Emch et al.*, 2008; *Akanda et al.,* 2009) have shown high linear correlation between environmental variables and cholera incidence. The adaptive nature of this model also gives us the option to assess the amount of variance explained with a linear structure and to update it to include non-linear processes in order to improve our results and also that increases our understanding of the processes (more details in Section 5.3.2).

5.2.2 Cholera Surveillance and Hydroclimatic Data

Our model domain is found in the lower parts of the Ganges-Brahmaputra-Meghna basin region of the Indian Subcontinent (Figure 5.2) and incorporates inputs from a variety of sources, such as surveillance records of hospital admissions and hydroclimatic forcings that are both observed and model derived (Table 5.1). The ICDDR,B has a sophisticated surveillance program in place since 1980, where cholera incidence is recorded as the number of new people infected with *V. cholerae* among a statistical subset of the patients visiting the hospital each week. We also obtain cholera incidence records (monthly number of new cases) from Matlab (1998-2009), Mathbaria (2003-2007) and Chhatak (1997-2001), where the ICDDR,B maintains surveillance operations. (We compute *period prevalence rate* (termed as just 'prevalence' in later sections), a population corrected measure of incidence, by normalizing the incidence data with the number of patients tested and reporting it as a percentage number. This metric thus provides a way to understand the impact of hydrologic and climatic variability, with the assumption that the people visiting the hospital is a representative sample of the populace affected by diarrheal diseases, while also correcting for growth in the catchment area.

Mean streamflow values for dry (JFMA: Jan to Apr) and wet (JASO: Jul to Oct) seasons were used to develop low and high streamflow time series, respectively. For the SST, FAA, rainfall, and salinity datasets, we developed similar seasonal time series (DJF, MAM, JJA, SON) for effective seasonal lead-lag comparisons with cholera outbreaks. For this study, we use sea surface temperature as a surrogate of plankton and vibrio abundance for the coastal zone of the BoB (areas north of 21° N between 86° and 93° E). This zone was chosen on the basis of available bathymetric and active production zone

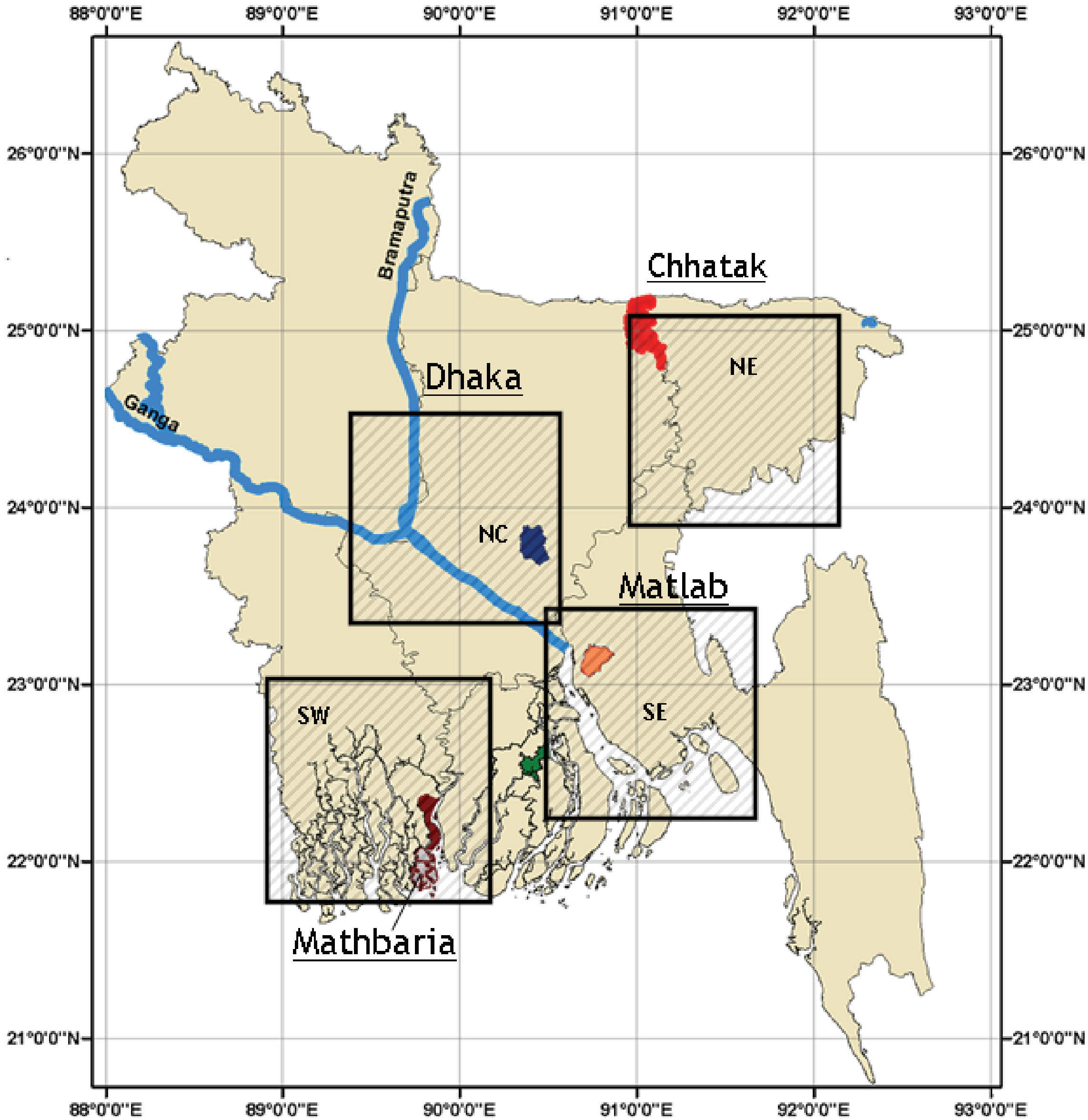


Figure 5.2: Map of Bangladesh, Major Regional Rivers, Surveillance Locations, and Spatial Extent of Proposed Hydroclimatology Model Domain

information (*Chamarthi et al*., 2008). The Reynolds $1^{\circ}\times1^{\circ}$ sea surface temperature (SST) database (*Reynolds and Smith,* 1994) was used to extract SST information for the BoB. Gridded rainfall time-series data ($2.5^{\circ}\times2.5^{\circ}$ spatial resolution) for the GBM catchment areas were obtained from the NCEP/NCAR Reanalysis Project atmospheric datasets. Daily river discharge records for the Ganges and Brahmaputra rivers and rain gauge data for the region were obtained from Bangladesh Water Development Board (BWDB), which were then aggregated to monthly scales for this study. All monthly datasets were detrended by removing the respective monthly mean from the length of the time-series.

Table 5.1: Model Variables and Inputs

A list of the datasets used in developing the model to estimate Cholera Prevalence

Data	**Spatial Scale**	**Source**
Cholera	Surveillance	ICDDR,B
Rainfall	Gauge, 2.5x2.5 Deg	BWDB, NCEP/NCAR
Stream flow	Gauge	BWDB, BUET
Temperature	Gauge, 2.5x2.5 Deg	BWDB, NCEP/NCAR
Estuarine Salinity	Average of 1x1 Deg	Tufts, IWM
Flood Affected Area	Average of 1x1 Deg	Tufts, IWM
Sea Surface Temperature	1x1 Deg	Reynolds & Smith, 1994

5.2.3 Environmental Model

Lack of representative salinity samples from estuarine ecosystems, as well as lack of detailed flood inundation information from post-monsoon scenarios, has prevented previous research studies from investigating the role of these variables on cholera transmission. We have thus used a physically based mathematical model to circumvent the need for intensive data collection and to generate flow and salinity data at ungauged locations of complex river systems such as the GBM (Figure 5.1). A MIKE11 modeling package developed by the Danish Hydraulic Institute (*DHI*, 2000) is used to simulate the dominant hydrological processes in this large river basin, rainfall-runoff, river stage and flow level, salinity, and flooding conditions in the coastal ecosystems of the region. The rainfall-runoff module generates overland flow from hydroclimatic data (upstream flow, rainfall, evaporation and groundwater fluctuation) and uses it as lateral inflow into the hydrodynamic (HD) module. The HD module is based on an implicit finite difference scheme solution of the Saint Venant equations (*DHI*, 2000) and known boundary conditions at upstream inflow points and downstream tidal water level boundaries.

For validation of the environmental component of the model, runoff values are compared with water level (WL) and flow (Q) observations from existing gauging stations. The model is calibrated against the measured values at locations across the river system using calibration parameters such as Manning's Number, channel geometry, soil type, etc. The HD module outputs (flow and water level, channel cross-sectional area and hydraulic radius) are then used as inputs to the Advection–Dispersion (AD) module to simulate salinity of river waters (*Wahid et al.,* 2007), and to the Flood Inundation Module (FIM) for computing flooded land area (*Nishat and Rahman*, 2009).

The AD module applies advective transport with the mean flow volume and dispersive transport for concentration gradient to solve for one-dimensional conservation of mass. Observed salinity concentrations are used at all model boundary locations as initial conditions. The salinity model is calibrated separately for the dry (JFMA: January–April) season and wet (JASO: July–October) season to reflect the seasonal variation of the salinity in the rivers. Two important parameters used for salinity calibration are the mixing and dispersion coefficients (*Wahid et al.,* 2007). The Flood Inundation Module (FIM) uses detailed digital elevation models (DEM) of the spatial domain and HD outputs of river water levels (WL) at locations across the basin to compute water inundation depth and generate flood extent maps. The computed flood area values are then aggregated to the desired spatial and temporal scales, and validated with national and local flood assessments. We use monthly salinity and flood area statistics over four 1°x1° degree grids spanning Bangladesh for analysis with cholera incidence data in the relevant surveillance locations. More details of this model setup and calibration can be found in previous publications (*Wahid et al.,* 2007; *Nishat and Rahman,* 2009).

5.3 Analysis and Results

5.3.1 Simulation of Regional Cholera Prevalence

In the proposed model, variable selection originates from physically based processes, based on the understanding in preliminary findings of the influences of seasonally distributed coastal and terrestrial processes on cholera prevalence (*Akanda et al.,* 2009; 2011; *Jutla et al.,* 2010; 2011). We begin with a set of multiple regression models for the four locations (details in Section 4.2.1) in Bangladesh using six independent predictor variables in order to simulate cholera prevalence in both spring and fall seasons. A key objective is to provide a statistical explanation of cholera outbreaks based on seasonal and spatial processes. Table 5.2 summarizes the characteristics of estimated model parameters related to spring and fall cholera prevalence for all four locations. However, Temperature (T) was not retained in final models (Tables 5.2 and 5.3) as it consistently showed poor significance values. This finding implies that in a warm tropical region such as in Bengal Delta, physical processes may be bigger and more dominant factors compared to temperature, which acts as a catalyst for growth.

As we hypothesized earlier, environmental cholera transmission is modulated primarily by two spatially and seasonally distinct transmission mechanisms - influenced by dry and wet season hydroclimatic determinants - more specifically through estuarine salinity and flood inundation during spring and fall, respectively (Chapter 3). If our understanding of the asymmetric role of the regional hydroclimatology is correct – then for the spring season, we should expect to see the model explain an increased amount of variance with the inclusion of physical variables such as salinity (S), with respect to the contribution of just dry season discharge (Q) during the coastal transmission phase.

Table 5.2: Linear Regression Model Results / Coefficients

A generic form of the model equation to estimate Cholera Prevalence would be:

Prev (x,y,t) = $\alpha + \beta$ (Salinity) + γ (Flow) + δ (SST) + η (Rainfall) + μ (FAA)

<u>All variables are functions of (x,y,t): average over 1x1 degree / monthly</u>

Variable/ Location	Season	Constant α	Salinity Β	SST γ	Flow δ	Rainfall η	FAA μ	Adj-r^2 / Pred-r^2
NC (Dhaka)	Spring	0.09 (0.024)	0.44 (0.001)	-0.26 (0.027)	-0.02 (0.731)	-0.13 (0.048)	-	71.9% 70.0%
	Fall	-0.03 (0.05)	0.22 (0.001)	0.09 (0.050)	0.27 (0.007)	0.07 (0.076)	0.32 (0.010)	73.9% 71.1%
SW (Mathbaria)	Spring	0.19 (0.005)	0.54 (0.034)	-0.26 (0.002)	0.005 (0.977)	0.23 (0.033)	0.03 (0.672)	79.1% 71.8%
	Fall	-	-	-	-	-	-	
SE (Matlab)	Spring	0.08 (0.001)	0.21 (0.001)	-0.17 (0.047)	-0.1 (0.490)	-0.02 (0.847)	0.03 (0.753)	68.0 % 67.2 %
	Fall	0.19 (0.010)	0.06 (0.647)	0.20 (0.042)	0.33 (0.010)	0.09 (0.618)	0.38 (0.017)	64.2 % 61.1 %
NE (Chhatak)	Spring	-	-	-	-	-	-	
	Fall	0.10 (0.010)	0.02 (0.446)	0.12 (0.001)	0.02 (0.644)	0.39 (0.049)	0.42 (0.037)	63.3 % 57.4 %

Highlighted in Yellow: Significant - Spring
Highlighted in Cyan: Significant - Fall

Similarly, we should expect an increased influence of macro-environmental variables such as flood affected areas (FAA) and precipitation (P) to help predict autumn cholera prevalence compared to simply using peak monsoon flow (Q). We found that for the coastal location of Mathbaria, a Q+SST+P combination explained 71% (Pred-r^2 58%) variance for spring prevalence, while a S+SST+P combination explained 79% (Pred-r^2 72%) variance. Similarly, for Chhatak, including FAA substantially improves the variance explained by the model – a FAA+P combination explains 63% (Pred-r^2 57%) variance compared to 55% (Pred-r^2 51%) instead of Q+P (Table 5.2). The results were thus improved as the representative formulation of the underlying processes improved.

5.3.2 Assumption of Underlying Dominant Processes

As explained in Section 5.2.1, we do not have *a priori* knowledge of the nature of the underlying processes. We start with a linear multivariate regression approach as a first step as previous studies have shown high linear correlation (*Emch et al.,* 2008; *de Magny et al.,* 2008; *Akanda et al.,* 2009) with similar physical variables. However, it also gives us reasonable baseline results (Table 5.2) and the option to improve our results and increase our understanding through incorporating non-linear processes. The physical basis of our hypothesis is that estuarine salinity provides an ideal environment for vibrio growth in southwestern Bangladesh in spring. Similarly, widespread contamination caused by flooding and nutrient driven vibrio growth in flood-inundated areas contributes to the second peak in fall. Laboratory experiments (*Singleton et al.,* 1982a; 1982b) suggested that salinity, temperature, and nutrients strongly impact *V. cholerae* growth. Recently, *Vital et al.* (2007) have shown that a log-linear relationship exists between *V. cholerae* abundance and water salinity, ambient temperature and nutrient concentration.

Taken together, if these relationships are valid and if salinity intrusion and flood inundation are indeed physical variables responsible for cholera transmission, we should expect to see improved explanatory power with a log-transformed regression model. We find that both explained variance and predictive accuracy of the model improved substantially for all locations with the choice of a log model in both seasons. Table 5.3 shows that Dhaka spring prevalence Adj-R^2 values increased from 72% to 84% (Pred-R^2 increased from 70% to 81%) with the model choice. Also, explained fall variance increased from 74% to 83% (Pred-R^2 from 71% to 81%) for Dhaka. Figures 5.3 and 5.4 together show that the models adequately capture the monthly, seasonal and interannual variability of spring and fall cholera outbreaks in all four locations: NC (Dhaka), SW (Mathbaria), SE (Matlab), and NE (Chhatak).

A key observation from Tables 5.2 and 5.3 is the asymmetric and seasonally dependent role of the variables in the model. The presented model coefficients show that there is a consistent negative relationship of streamflow and rainfall, and sea surface temperature with spring cholera prevalence – for all locations except Chhatak. This consistent behavior across all locations suggests that scarcity of freshwater flow from upstream regions and resulting increased salinity in estuarine channels in strong drought situations have a profound impact on an environmental reservoir of *V. cholerae* growth and proliferation from the southwest region of Bengal delta to inland regions and reaffirms our earlier hypothesis (*Akanda et al.,* 2011a). On the contrary, a strong positive role of S, P, Q, SST, and FAA shows that water abundance and cross-contamination of water resources through flood inundation may increase cholera prevalence in inland regions, primarily the eastern part of the Bengal Delta.

TABLE 5.3: Log-Linear Regression Model Results / Coefficients

A generic form of the model equation to estimate Cholera Prevalence would be:

$$\log Prev = \alpha + \log(Salinity)^{\beta} + \log(Flow)^{\gamma} + \log(SST)^{\delta} + \log(Rainfall)^{\eta} + \log(FAA)^{\mu}$$

All variables are functions of (x,y,t): average over 1x1 degree / monthly

Variable/ Location	Season	Constant α	Salinity B	SST γ	Flow δ	Rainfall η	FAA μ	Adj-r^2 / Pred-r^2
NC (Dhaka)	Spring	0.29 (0.024)	0.95 (0.001)	-0.36 (0.023)	-0.11 (0.379)	-0.23 (0.001)	-	84.0 % 80.7 %
	Fall	-0.30 (0.05)	0.51 (0.001)	0.09 (0.050)	0.27 (0.001)	0.25 (0.082)	0.39 (0.010)	82.9 % 81.6 %
SW (Mathbaria)	Spring	0.24 (0.005)	1.10 (0.001)	-0.32 (0.041)	0.005 (0.977)	0.27 (0.013)	0.03 (0.672)	84.2 % 80.4 %
	Fall	-	-	-	-	-	-	
SE (Matlab)	Spring	0.28 (0.001)	0.47 (0.001)	-0.21 (0.047)	-0.1 (0.590)	-0.02 (0.645)	0.03 (0.753)	79.2 % 77.1 %
	Fall	-0.29 (0.010)	0.09 (0.473)	0.20 (0.032)	0.23 (0.010)	0.04 (0.312)	0.68 (0.017)	78.0 % 72.4 %
NE (Chhatak)	Spring	-	-	-	-	-	-	
	Fall	0.40 (0.010)	0.12 (0.556)	0.12 (0.001)	0.02 (0.344)	0.49 (0.049)	0.62 (0.027)	79.1 % 74.5 %

Highlighted in Yellow: Significant - Spring
Highlighted in Cyan: Significant - Fall

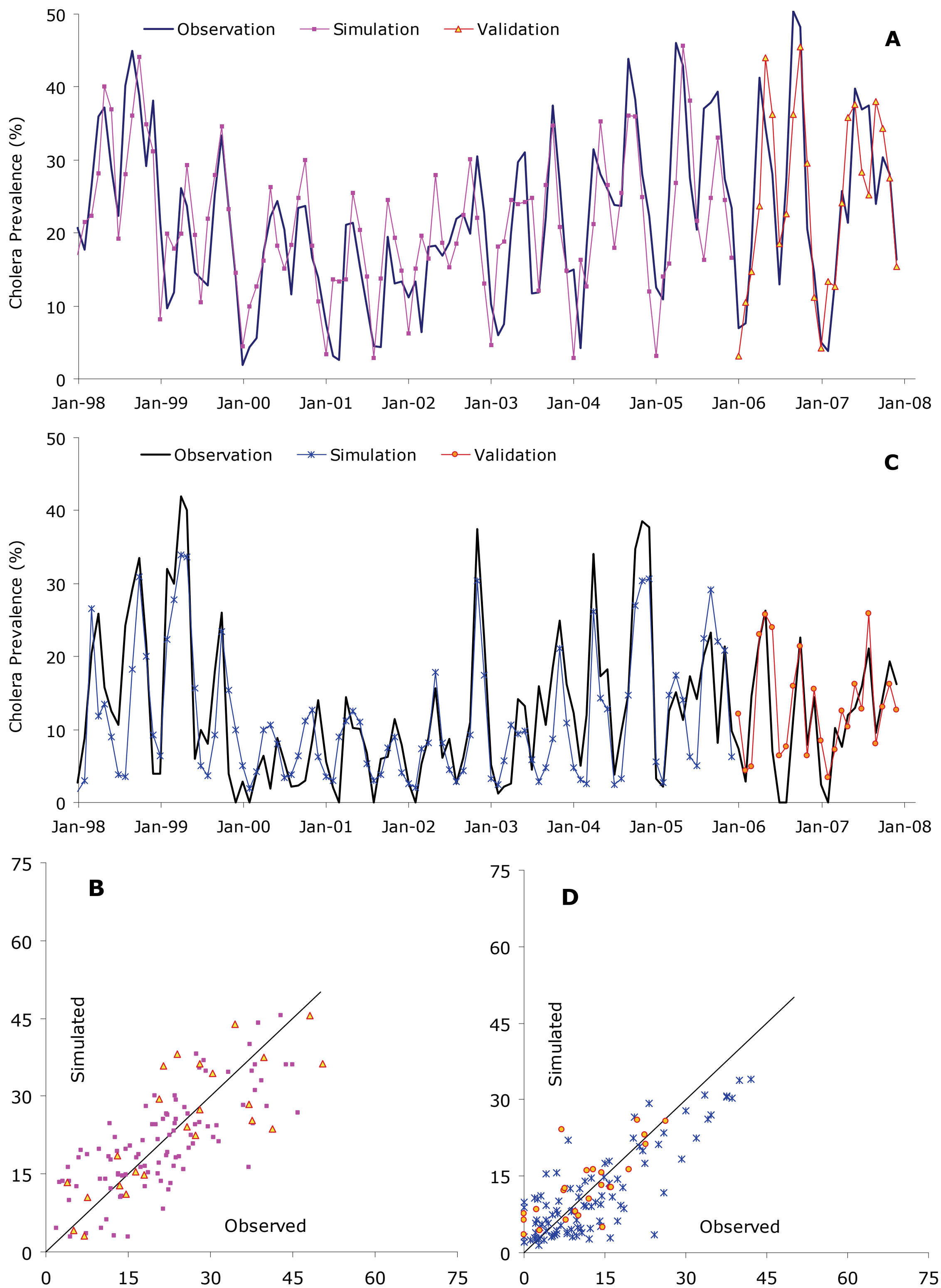
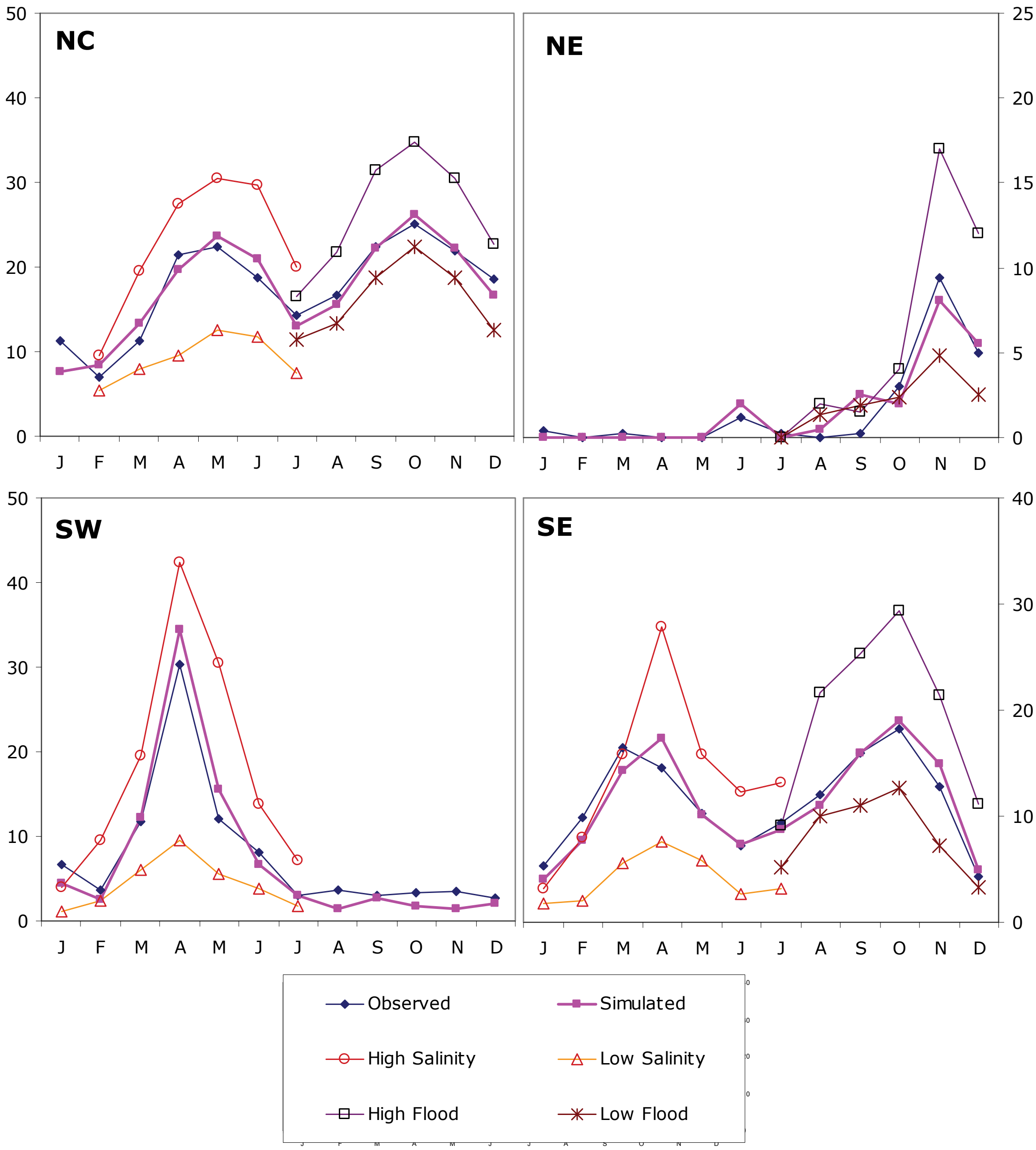


Figure 5.3: Observation, Simulation, Validation of Cholera Prevalence for 1998-2007
A: Monthly Prevalence for Dhaka, B: Observed-vs-Simulated Scatter Plot of Dhaka
C: Monthly Prevalence for Matlab, D: Observed-vs-Simulated Scatter Plot of Matlab



NC: Dhaka   NE: Chhatak   SW: Mathbaria   SE: Matlab

All Y-axis values are Cholera Prevalence (%)

Figure 5.4: Monthly Climatology of Model Results - Observed and Simulated Cholera Prevalence in All Locations: NC: Dhaka NE: Chhatak SW: Mathbaria SE: Matlab. with Simulated Average Monthly Prevalence for High and Low Salinity and Flood Scenarios

5.3.3 Prediction of Extreme Hydroclimatic Events

In a drought year, if freshwater flow from upstream regions is anomalously lower during the dry season, the resulting increased coastal salinity extent is expected to expose a bigger segment of the population living in the coastal belt to an environment conducive to vibrio growth and subsequently increased risk of cholera transmission in spring. An opposite scenario of the above hypothesis would be a weak drought year, with anomalously high flow in the GBM rivers during the dry season, when we should expect to see lower salinity and limited vibrio growth in estuarine areas and subsequently, lower manifestations of spring cholera incidence. To make this point, we ran Monte-Carlo simulations with 20% higher and lower salinity and computed resulting prevalence using the spring model. Figure 5.4 shows that higher salinity levels can cause elevated spring prevalence in Mathbaria and Dhaka, and to a lesser extent in Matlab.

For the later parts of the year, the situation is dominated by water abundance in the region. Anomalously higher flow during monsoon leads to flood events and inundation (FAA) across lower Bengal delta, and to an elevated risk of cholera infection. Increased levels of local precipitation (P) and lack of flood drainage (discussed in Section 5.3.4) can further endanger urban population centers located in floodplains across Bangladesh and elevate the risk of fall outbreaks. In the absence of flood events, or in the future with improved floodwater management, there would be less spread of contaminated water in central and northern floodplains and subsequent breakdown of sanitation. Such situations are thus expected to lead to lower fall cholera outbreaks and low prevalence levels in the region. Fall simulation results with 20% higher flood affected area yields substantial increases in cholera prevalence for Matlab, Chhatak, and Dhaka (Figure 5.4).

5.4 An Environmental Transmission Model

Our results demonstrate that a regional scale modeling effort can capture the seasonal and interannual variability of cholera prevalence through hydroclimatology and epidemiology model components with a satisfactory level of accuracy. In an asymmetric hydrologic setting such as the Bengal Delta, the pre-monsoon and post-monsoon seasonal processes and associated coastal and terrestrial drivers are major drivers of cholera transmission. *Akanda et al.* (2011) postulated the presence of two spatially distinct and seasonal cholera transmission cycles in this region, a pre-monsoon phase in estuarine areas and a post-monsoon inland phase following the wet season. Here, we show that the model, forced with macro-scale environmental and hydroclimatic information, captures this asymmetric nature of cholera dynamics across the region.

A key distinction between the presented framework and existing cholera prediction models is the use of physically based variables in this study as opposed to other cholera prediction models. For example, with various combinations of monthly and seasonal autoregressive variables, such as incidence in previous months with one or two months lag, and average incidence of the previous seasons, these models explained over 72% variability of cholera incidence in Bangladesh, Vietnam and Tanzania (*de Magny et al.,* 2008; *Emch et al.,* 2008; *Matsuda et al.,* 2008; *Reyburn et al.,* 2011). However, persistence effects of the cholera time series itself largely overshadowed the contributions of environmental or physical variables in these models. Conversely, the simulation results presented in this study are based macro-scale physical variables and no auto-regressive features. These findings illustrate the feasibility of using environmental and climatic predictors to estimate and predict cholera prevalence over large geographic regions.

However, underlying cholera transmission mechanisms such as vibrio growth or exposure are not explained with actual physical and mechanistic data. Major steps in the cholera transmission process are represented statistically in this study - the role of salinity intrusion in estuarine channels on vibrio growth, as well as the role of flood inundation in the cross-contamination of inland water resources and further vibrio growth in inundated areas. A mechanistic formulation of these processes is needed to develop a robust representation of an environmental transmission pathway. More specifically, the role of the brackish environment in aiding vibrio growth and the quantification of human population potentially exposed to the bacteria in the environment need to be represented in the modeling framework to have a set of physical data which could potentially confirm our overarching hypotheses. Similarly, the role of flood inundation in contaminating vibrio-free water resources and a spatially explicit representation of vibrio growth and human exposure to flood inundated areas are needed to complement the causal pathway during the fall transmission cycle.

Figure 5.5 shows a revised version of our presented environmental-prevalence model with two new components, vibrio growth and exposure. The functionalities of these two models will be influenced by the existing physical models in the framework (shown by arrows); for example, while salinity intrusion in estuarine channels will affect vibrio growth, the spatial extent of salinity and the intensity of drought will influence human exposure to the pathogen. Similarly, while flood inundation and peak flow in GBM rivers will impact the level of contamination and exposure, the spatial extent and coverage of the inundated areas and local rainfall patterns may influence vibrio growth and subsequent transmission in this season.

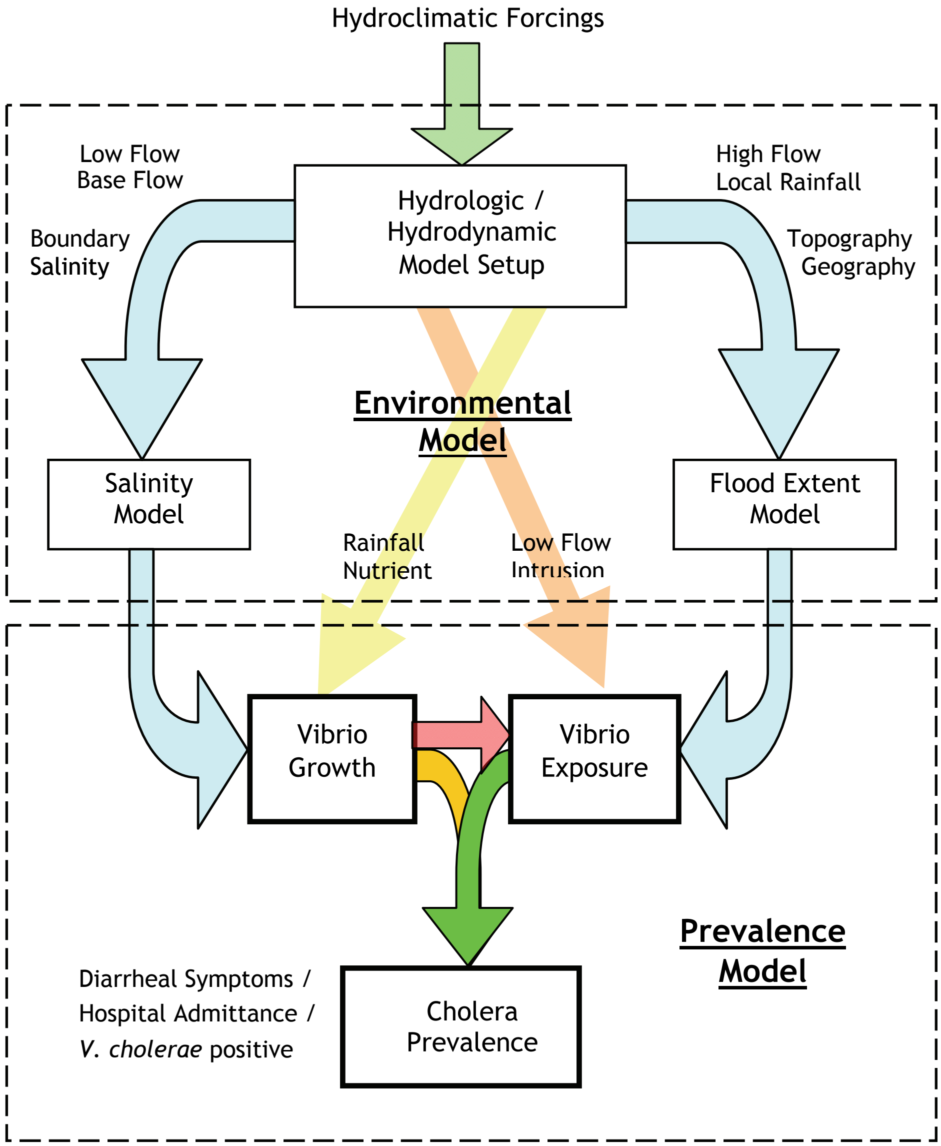


Figure 5.5: Revised Environmental (Hydroclimatology) – Prevalence (Epidemiology) Model Framework Schematic showing areas in need of further improvement in terms of mechanistic representation of underlying processes such as vibrio growth and exposure

5.5 Discussion

Cholera prevalence in coastal and central Bangladesh during spring months (Mar-Apr-May) are strongly influenced by salinity intrusion into estuarine channels of the Bengal Delta region and overall water scarcity in the region. Cholera prevalence in the post-monsoon months and in central, north-eastern and south-eastern Bangladesh, are influenced by peak flow volumes and post-monsoon flood inundation during fall months (Sep-Oct-Nov). It is important to note that the low elevation floodplains, in between coastal and inland areas of the Ganges-Brahmaputra-Meghna (GBM) delta region, such as Dhaka and Matlab (see Figure 5.1), are affected by the regional-scale cholera transmission processes in both spring and fall, and show a "characteristic" biannual incidence pattern (*Akanda et al.,* 2009). Our findings illustrate the feasibility of using environmental and climatic predictors of the large-scale transmission mechanisms to estimate population vulnerability to epidemic cholera outbreaks across the region.

A significant focus in this research effort has been on salinity and flood area simulations, in order to produce reliable mechanistic simulations of the physical variables responsible for cholera transmission (*Akanda et al.,* 2011b). These model outputs can be compared to the extensive hydrological information that is available for the GBM basin for internal validation. However, the impacts of climatic variables 'external' to this physical model, such as SSH changes due to large scale climatic events like the ENSO or the IOD (Indian Ocean Dipole) (*Han and Webster,* 2001; *Saji et al.,* 1999), which may affect both flooding and salinity intrusion, are not directly captured in this framework. Future studies should also try to incorporate ocean-atmospheric processes that may impact regional climatic conditions and subsequently affect cholera dynamics.

In addition, the models help explain significant and anomalous cholera outbreaks that appear to conflict with stated processes. For example, the region experienced a strong flood event during the monsoon months of 2007. However, the floods dissipated quickly, with the lack of consistently high rainfall in upstream and local catchments (*Alam et al.,* 2011). Modeled prevalence in Dhaka showed a sharp increase in August; however, the outbreaks were short-lived and showed lower prevalence in fall. As salinity conditions were not conducive for a strong spring outbreak, the lack of a strong monsoon also did not lead to a strong fall cholera outbreak.

On the other hand, Matlab observed high fall cholera outbreaks in 1998, 2002 and 2004, but these events were not captured well by the presented model (Figure 3 B-D). One plausible explanation is that Matlab, being closer to the coast, is subjected to tidal and sea level fluctuations. *Han and Webster* (2001) and *Hashizume et al* (2011) reported unusually higher the Bay of Bengal sea surface height during the fall months of these years, which may have prohibited flood drainage in southern Bangladesh – and caused the flood events to persist in southern parts of the country, such as in Matlab. As SSH changes are not included in our physical model, these flood events were not captured in our model – and plausibly contributed to the loss of predictive accuracy.

Our model can be used to evaluate the impacts of a variety of hydroclimatic conditions and explore a range of climate variability and change scenarios for the GBM region. An understanding of the hydroclimatic influences on cholera dynamics is also crucial in light of changing climate patterns in this region. Increasing hydroclimatic extremes and coastal salinity intrusion due to sea level changes associated with global warming suggest the possibility of increased cholera prevalence in South Asia, impacting both the coastal and the inland transmission mechanisms (*Akanda et al.,* 2011a; 2011b). With this model, the impacts of climatic variability and changes on Bengal Delta cholera dynamics can be explicitly evaluated by incorporating seasonal and interannual climate variability, and future changes in climate conditions in the mechanistic simulations of salinity and flooding patterns.

Similarly, water management scenarios to manage or mitigate environmental and ecological conditions conducive to cholera transmission can be evaluated through this model. For example, augmenting dry season flow in the Gorai and Kobadak rivers in southwestern Bangladesh with increased diversions from the Ganges may help minimize the extent of estuarine salinity intrusion in coastal Bangladesh, and subsequently reduce risk of cholera infection in central floodplains during the spring season, as evidenced by model simulation results for Mathbaria and Dhaka in low salinity conditions (Figure 5.4 SW-NC). Similarly, if inland flood drainage from inundated areas can be improved in the eastern parts of the country so that low elevation areas in Sylhet and Comilla divisions do not stay inundated with floodwater beyond the monsoon season, and if the main river channels can be dredged in advance in anticipation of high flood events in the delta region, the potential public health benefit in terms of reduced post-monsoon cholera prevalence in population centers in these areas could be significant (as seen in simulations for Chhatak and Matlab; Figure 5.4 SE-NE). These simulation results thus open the way for testing and validating a variety of plausible water management guidelines and resulting scenarios that may subsequently help formulate a sound public health engineering policy with regards to improving low flow conditions in spring and minimizing the extent of monsoon flood inundation to limit epidemic cholera outbreaks.

The ability of the presented model setup to use easily available macro-scale hydroclimatic datasets such as gridded rainfall and sea surface temperature, or observed streamflow time series increases the ability to use it in other geographic settings. A mechanistic simulation for salinity or flood inundation data may require additional time; however, gridded interpolations of salinity observations or dry season river discharge can also be used as surrogates. Similarly, satellite detected vegetation information or water bodies can be useful surrogates of flood inundation. We should note that transmission characteristics elsewhere in affected regions may be due to processes that are a variation or a combination of the drivers we observe for the Bengal Delta region. For example, cholera transmission on the Mozambique coast maybe dominated by the coastal mechanism like Mathbaria, whereas cholera in the Democratic Republic of Congo Lakes region exhibits similarities to the inland transmission mechanism as seen in Chhatak.

However, choices of different precipitation and SST datasets, size of streamflow catchment regions, and lead-lag times between dependent and independent variables have a clear influence of the predictive power of the model setup presented in this study. For example, Mathbaria has a 0(zero)-month lag between peak local salinity and peak cholera incidence – compared to a one-month lag between peak salinity and cholera in Dhaka. This difference in lag can be explained by the proximity to the coast for Mathbaria, which is located less than 40 km from the BoB – compared to about 150 km for Dhaka. Also, rainfall time series over the Meghna basin region helped achieve better results for Chhatak than using data from the local rain gauge stations. In summary, the model produces the best results when the selection of variables, data sources, and lead-lag times are adjusted based on the physical understanding of the underlying processes.

5.6 Conclusion

In this study, we show that macro-scale hydroclimatic and resulting environmental conditions can significantly influence the seasonal and spatial variability of cholera prevalence. The presented hydroclimatology-epidemiology model was applied to the Bengal Delta region to show how estuarine processes dominate cholera transmission in coastal areas in the southwest and up to central floodplain areas in Bangladesh; it also shows how a monsoon-dominated transmission processes can further influence cholera prevalence in inland regions. Our results indicate that in a drier spring season in the Bengal Delta, when salinity in estuarine rivers is anomalously higher, the risk of cholera transmission occurring in coastal areas and in the peri-urban regions of Dhaka remains very high. Similarly, a wetter monsoon season and subsequently anomalously higher flood inundation can lead to large increases in fall cholera outbreaks and higher prevalence rates in Dhaka, Matlab, and Chhatak in the northeastern region.

Estuarine Salinity and Flood Affected Area, and associated surrogate variables such as streamflow in major regional rivers and macro-scale precipitation and sea surface temperature signatures can thus serve as important predictor variables to develop a cholera warning system with about two to three-months of lead time. In summary, prediction of cholera outbreaks with sufficient lead-times based on the understanding of the underlying spatio-temporal transmission mechanisms is imperative for cholera prevention strategies to be effective and feasible. The presented model provides a framework based on the variability of macro-scale hydroclimatic forcings and has the potential to provide public health authorities a much-needed spatially explicit warning capability sufficient to support planning, preparation, and early intervention.

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Chapter 6

Conclusions and Recommendations:

Reducing the Global Cholera Burden through Prediction and Prevention

Abstract

This is perhaps the first study to identify separate drivers for the biannual cholera outbreak cycles in affected regions and to quantitatively explain how large scale hydroclimatic processes and resulting environmental conditions can influence the nature of cholera transmission mechanisms. With the ever-expanding geographic reach of the seventh cholera pandemic and alarming fatality rates in newly affected regions, it is apparent that global cholera prevention strategies are failing. However, the disease burden could be significantly reduced if the traditional preventive measures could be implemented ahead of time with improvements to the prediction of impending outbreaks in a particular geographic region. A spatially explicit cholera prediction model based on environmental and climatic signatures can potentially provide critical lead-time to deploy medical and human resources and mount preventive interventions in vulnerable areas to save lives and reduce the disease burden during and following epidemic outbreaks.

6.1 Research Summary

The primary goal of the proposed research was to identify, characterize, and quantify the role of the large scale hydrological and climatic processes, which affect the seasonal and spatial variation of cholera incidence. A secondary goal was to understand how these large scale processes and related hydroclimatic and environmental variables can influence primary transmission pathways of cholera. To achieve these goals, three closely related research objectives were selected based on available datasets from the Bengal Delta region. These objectives were: (i) identifying the seasonally distinct drivers for the biannual outbreaks observed in the Bengal Delta region and quantifying the asymmetric role of coastal and terrestrial processes on seasonal and interannual cholera dynamics; (ii) understanding the spatio-temporal nature of observed cholera incidence in surveillance locations across the Bengal Delta region and relating them to physical variables such as estuarine salinity intrusion and inland flood inundation that may have impacts on population vulnerability over large geographic areas in the region (iii) developing a coupled hydroclimatology-epidemiology model framework where large scale hydroclimatic forcings can be translated to cholera prevalence, in four spatially distinct surveillance locations in Bangladesh.

This is perhaps the first study to identify separate drivers for the biannual cholera outbreak cycles in a region and to quantitatively explain how large scale hydroclimatic processes and resulting environmental conditions can influence the mechanisms of cholera transmission. This study also shows how these large scale physical drivers can be used to simulate and explain the spatial and temporal variability of outbreaks in coastal, inland, and floodplain locations throughout the region.

Chapter 1 summarizes the state of research on the ecology, microbiology, and epidemiology of cholera and identifies the key knowledge gaps regarding the role of hydrology and climate on the underlying processes contributing to cholera transmission. In Chapter 2, we presented results showing low flow in the Brahmaputra and the Ganges rivers during spring is associated with the first outbreaks of cholera in Bangladesh; whereas monsoon driven streamflow and peak discharge volumes show a strong positive relationship with fall outbreaks. Chapter 3 demonstrated that the cholera outbreaks in the Bengal Delta region are propagated from estuarine to inland areas and from spring to fall by two distinct, pre- and post-monsoon, transmission cycles influenced by coastal and terrestrial hydroclimatic processes, respectively. A coupled analysis of the regional hydroclimate and cholera incidence revealed a strong association of the space-time variability of incidence peaks with seasonal processes and extreme events.

In Chapter 4, we focused into the spatial nature of cholera transmission in this region and identify plausible physical variables such as estuarine salinity and inland flood inundation patterns that may set the ecological and environmental 'stage' for epidemic outbreaks over large geographic regions. Finally, in Chapter 5, we postulated that environmental cholera transmission is modulated by two spatially and seasonally distinct transmission mechanisms - influenced by dry and wet season hydroclimatic determinants. To summarize our findings in a quantitative manner, we have presented a spatially explicit coupled hydroclimatology-epidemiology model and applied it to the Ganges-Brahmaputra-Meghna Basin areas in Bangladesh to simulate and predict cholera prevalence rates in a spatially explicit manner. Cholera data from Dhaka and regional surveillance locations are used to validate the model results.

6.2 Recommendations for Further Research

Cholera outbreaks are physical manifestations of a complex interplay of micro and macro scale processes, extended over a vast range of spatial and temporal scales. Major steps in the cholera transmission process are statistically represented in this study: the plausible impacts of salinity intrusion on vibrio growth in brackish areas and spreading into estuarine river channels, as well as the roles of flood inundation in propagation of the contamination in inland water resources and further vibrio growth in inundated areas inland. However, these processes contributing to these environmental transmission pathways are not represented mechanistically. More specifically, the presented modeling framework does not provide a physical representation of vibrio growth in environmentally conducive areas, or a spatially explicit representation of the extent of human exposure to the environmental reservoirs of *V. cholerae*.

Chapter 5 thus shows an updated schematic of the modeling framework with the projected incorporation of physical model components of such transmission processes. As seen in Figure 5.5, the two unexplored components in the model framework are the vibrio growth and the human exposure model components. Future research should thus focus on the creation of a robust and mechanistic representation of these links in the coastal transmission pathway, which would represent vibrio growth in brackish areas along the southwestern coast of Bangladesh, and the extent and expectation of human exposure to the pathogen as a result of increased vibrio growth in such areas. Similarly, a mathematical formulation of the physical processes involving inland water contamination due to monsoon floods and vibrio growth and transmission from inundated areas in Bangladesh would form a welcome complement to the inland transmission pathway.

It should be noted there that the above mentioned findings only represent the primary transmission paradigm, the role of the natural environment in initiating and propagating cholera outbreaks. Secondary transmission due to anthropogenic factors such as population density, movement, lack of access to safe water and sanitation services, and population immunity levels has not been addressed in this study. Although the present research captures a significant fraction of the intraannual and interannual variability of cholera incidence in this region (in excess of 80%) future research should try to merge the findings of the current study with disease propagation and epidemiologic models that incorporate population health parameters such as possibly fluctuating human immunity to *V. cholerae*, health coverage, safe water and sanitation access coverage in community, factors that may actually help shape prevalence in affected communities.

In addition, the increasing frequency of hydroclimatic extremes and coastal salinity intrusion due to sea level changes associated with global warming suggest the possibility of continued increases in cholera prevalence in South Asia due to both, coastal and inland transmission mechanisms. With the presented understanding of seasonal and spatial cholera transmission cycles and the hydroclimatology-epidemiology model, the impacts of climatic variability and changes in the distribution of cholera within the Bengal Delta can be explicitly evaluated by incorporating future changes in climate conditions in the macro-scale forcings and simulations of salinity and flooding patterns. The model has the potential to serve as the basis of a cholera early warning system where macro-scale hydroclimatic forcings and climate outlooks can be translated into cholera outbreak warnings, giving valuable planning and preparation time for medical and public health professionals to proactively target an area for intervention to limit disease burden.

6.3 Conclusions

The major contribution of this research study is the identification of the distinctly separate and seasonally and spatially sensitive large-scale drivers that influence cholera transmission over large geographic regions. The results from this research based on available datasets from the Bengal Delta region (Chapters 2-5) strongly suggests that the observed asymmetric relationship, role of water scarcity and coastal growth environment for *V. cholerae* in spring, and role of water abundance and inland contamination in fall, are important physical variables in the causal transmission pathway.

Another significant contribution of this research is the innovative integration of **macro-scale** processes (hydrological, climatic, ecological, and coastal) with **micro-scale** (microbiological, epidemiological, and human biological) processes achieved by using an integrated framework that can be used to translate macro-scale hydroclimatic forcings into region specific cholera prevalence estimates to identify how associated changes in hydrologic and ecological conditions may impact the patterns of local cholera transmission. This framework can be used to generate scenarios to discern the impacts of hydroclimatic extreme events on cholera dynamics, understanding the implications of climate change with respect ot the cholera transmission cycles, as well as evaluating and validating water management guidelines that can be used to mitigate environmental and hydroclimatic conditions conducive to cholera transmission. This integration has enormous impact on science and society, as this hydroclimatology-epidemiology (termed as, **Hydro-Epidemiology,** a new sub-discipline within the geophysical domain) modeling architecture may serve as the basis for a cholera early warning system with an actionable lead-time of two to three months that can aid existing cholera prevention efforts.

6.4 The Case for Preemptive Intervention

After two centuries and six global pandemics, cholera remains a major killer in the developing world. With the ever-expanding geographic reach and disease burden of the seventh pandemic, as well as the alarming case fatality rates seen in newly affected regions, it is apparent that global cholera prevention strategies are failing (*Ryan et al.,* 2011). The three known methods to treat or prevent mortality from cholera, oral rehydration, water and sanitation, and vaccination, have performed well in a favorable scale such as at the local to regional level, but are yet to be implemented at the global scale due to economic, logistic, or other practical constraints. However, the disease burden could be significantly reduced if these preventive measures were implemented ahead of time through the benefit of an advance warning of the impending outbreak.

With the devastating recent return of cholera to the Caribbean, there has been a tremendous interest in the Haitian outbreak (*Harris et al.,* 2010; *Waldor et al.,* 2010). The existence of an environmental reservoir of *Vibrio cholerae*, the causative agent of the disease, is well established (*Colwell et al.,* 1996). The striking seasonality and recurrence in endemic areas, as well as recent epidemic outbreaks across three continents, in Haiti, Pakistan and Nigeria, have greatly intrigued scientists, epidemiologists, and public health workers. A predominant focus appears to be on vaccination, prompting health authorities to incorporate it into existing intervention methods to reduce infection rates and minimize future epidemics (*Reyburn et al.,* 2011; *Ivers et al.,* 2010; *Ryan et al.,* 2011). With increasing prevalence in endemic regions, high fatality in newly affected regions, and emerging evidence of new biotypes, the efficacy of existing intervention strategies and application of proactive intervention benefiting from prediction need to be explored.

Most existing literature related to cholera epidemiology, transmission, propagation, and intervention are based on long-term datasets generated by the International Center for Diarrhoeal Disease Research (ICDDR,B) in Bangladesh, where the disease is endemic. A closer look at the last 30 years (1980-2010) of surveillance data reveals some important trends of cholera infection in Dhaka, Bangladesh. While the case-fatality rate (CFR, %) has decreased markedly in the last three decades, a strong increasing trend of cholera prevalence (%) is also seen during this period (Figure 6.1). In recent years, the ICDDR,B Hospital in Dhaka has had to arrange for makeshift accommodation and treatment centers to care for the surge in patients during the outbreak seasons (*Sack,* 2011). A large outbreak compounded with natural calamities may thus seriously overburden the public health response system in Bangladesh.

The above analyses pose a paradox – decreasing trends of fatality but increasing rates of infection – and raise questions about the efficacy of preventive measures in reducing the disease burden. What type(s) of prevention measures have been effective in reducing cholera burden? Figure 6.1 shows that CFR has dropped substantially in the last three decades and death from cholera is now a rare occurrence in Bangladesh, where resources are limited but cholera infection rates are among the highest in the world. The Oral Rehydration Solution (ORS) therapy, an inexpensive and highly effective treatment, has been successful there due to aggressive education and outreach regarding its use and effectiveness (*Sack et al.,* 2006). Yet, such treatment could not be translated to actionable intervention in Haiti because of our inability to predict cholera outbreaks.

What about primary prevention? ORS therapy, while extremely effective, is considered tertiary prevention. It works only after people get sick; it cannot prevent people from getting sick. Efforts at using vaccines to reduce infection and spread of cholera remain at an early stage of development (*WHO,* 2010; *Sack et al.,* 2006). Shanchol, an affordable alternative of the well known cholera vaccine Dukoral, is on its way to be approved by the WHO after trial studies (*Ryan et al.,* 2011). The two-dose vaccine appears to be promising in reducing transmission rates and courses of hospitalization in Haiti (*Ivers et al.,* 2010; *Harris et al.,* 2010). However, the use of vaccination as a global prevention strategy needs to be reassessed within the context of available resources, as well as implementation and technological constraints.

More than a billion people in the world still lack access to clean water and remain vulnerable to cholera outbreaks (*Harris et al.,* 2010). Manufacturers of the two vaccines, Dukoral and Shanchol, together produce about 2 million doses a year. Even if production was ramped up to 5 million doses a year as proposed (*Cyranoski et al.,* 2011), it would take decades to vaccinate the approximately 100 million vulnerable people in Bangladesh alone. Meanwhile, the immunity provided by the vaccines would start to taper off in 2-3 years (*Ryan et al.,* 2011). Mass use of vaccines with anti-biotics can also cause the spread of resistant strains, compromising long-term public health (*Sack et al.,* 2006). Also, few countries in the developing world are in a position to provide and sustain adequate funding for countrywide cholera vaccination programs. Even if necessary funding could be obtained from donor organizations, it would be very difficult to implement effective mass vaccination for a majority of the population in developing countries. However, selective use of vaccination for vulnerable demographic groups - children and elders - ahead of impending outbreaks instead of vaccinating entire populations can be very effective in minimizing the impact (*WHO,* 2010).

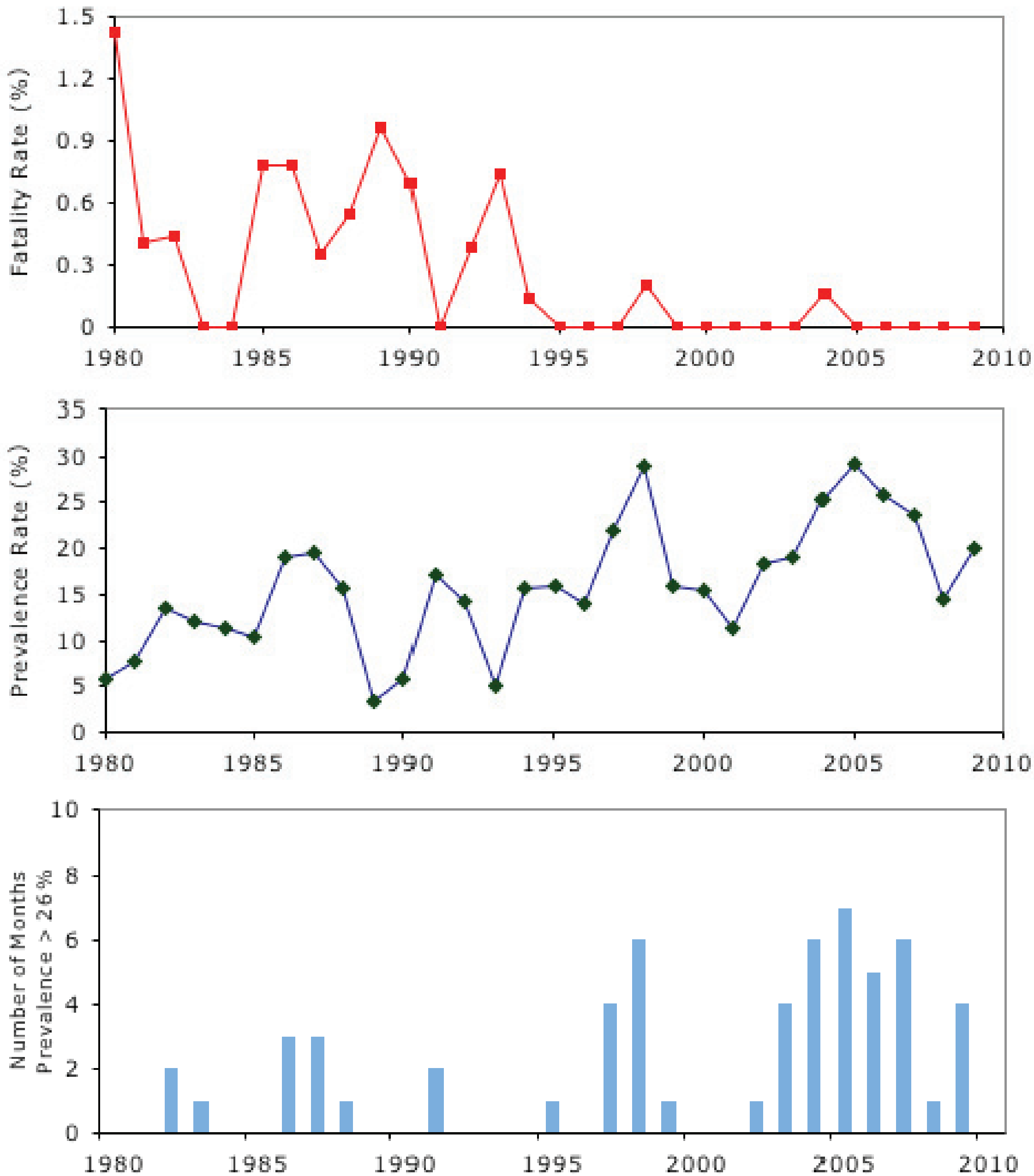

Figure 6.1: Selected Cholera Statistics at ICDDR,B, Dhaka(1980-2010)

(a) Mean Annual Case-Fatality Rate (%) (b) Mean Annual Prevalence (%)

(c) Number of months with average cholera prevalence higher than 26%, the long-term monthly mean observed in Dhaka, Bangladesh (based on 1980-2010)

Water purification, improved sanitation (*Bartram et al.,* 2010), and filtration techniques (*Colwell et al.,* 2006) have shown promise in reducing cholera infection at the point-of-use level, but scaling up such programs to national levels has yet to be worked out. Evidence suggests that a planned implementation of Water, Sanitation, and Hygiene (WASH) infrastructures in vulnerable localities can significantly reduce diarrheal disease prevalence; it has been effective in Haiti recently in bringing the overall CFR down to less than 2% from as high as 12% in the initial weeks of the outbreak (*USAID,* 2011). However, over 3000 people had already died before WASH was effectively implemented; arguably, many of these lives could have been saved if the infrastructure were installed preemptively.

Thus efficacious intervention strategies would greatly benefit from a predictive surveillance capability that would be able to identify vulnerable population groups at risk of imminent cholera outbreaks at regional scales. Controlling cholera burden will require an integrated proactive intervention strategy – a combination of prediction and prevention – based on recent advances in predictive capabilities and demonstrated successes in primary and tertiary prevention in endemic regions. A reliable and robust cholera prediction model coupled with a spatially explicit vulnerability map of cholera outbreaks will allow the mobilization of expert resources (physicians and health workers) and material (vaccines, water purification and sanitation equipment, and ORS) to vulnerable areas. WASH regulations and practices can be put in place and vulnerable demographic groups (such as children and elders) may be vaccinated in advance.

For example, as explained in Chapter 5 of this dissertation, if Mathbaria on the Bangladesh coast is expected to have an elevated spring outbreak of cholera due to anomalous low flows in the dry season and higher estuarine salinity above normal, this forecast can be issued as early as February based on streamflow and SST signatures thus providing a lead time of 2 months. ICDDR,B medical teams and material resources can thus be promptly relocated there to advocate and implement cholera warnings and WASH practices, and treat the already affected. Similarly, if the strong likelihood of a new cholera epidemic in Port-Au-Prince could have been known two months in advance, health authorities in Haiti could prepare for and minimize the impact of the elevated incidence of cholera in potentially vulnerable localities by implementing carefully planned prevention approaches. The fatality and transmission rates in such a scenario are expected to be far lower than what was experienced in the recent outbreak.

Cholera outbreak warnings can be issued in mass media and propagated through cellular-phone based networks for community awareness, especially in remote areas of the developing world where new generation technologies such as the mobile telephone is infiltrating rapidly in all spheres of life. Such networks have proved to be extremely successful in the coastal areas of Bangladesh in reducing cyclone fatality in recent years and have great potential to be used for epidemic warnings. For cholera intervention, time is a critical element for reducing transmission, providing effective oral or intravenous rehydration therapy, and saving lives. The disease burden can be significantly reduced if efficacious prevention measures are implemented, proactively, ahead of impending outbreaks. A spatially explicit prediction model can potentially provide the critical lead-time to deploy medical and human resources and mount preventive interventions in vulnerable areas to reduce the disease burden both during and after epidemic outbreaks. Using prediction and prevention together, we can bring cholera burden down.

6.5 References

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APPENDIX

A. List of Publications

B. Accompanied Abstracts

A. LIST OF PUBLICATIONS

This research thesis has resulted in or significantly contributed to following publications:

<u>*Articles Accepted / Published*</u>

1. **Akanda, A.S.,** Jutla, A.S. and Islam, S. 2009. Dual peak cholera transmission in Bengal Delta: A hydroclimatological explanation, *Geophysical Research Letters*, 36, L19401. (<u>Also as Chapter 2 of this Thesis</u>)
2. Jutla, A.S., **Akanda, A.S.** and Islam, S. 2010. Tracking Cholera in Coastal Regions using Satellite Observations. *Journal of American Water Resources Association*, 46(4): 651-662.
3. **Akanda, A.S.,** Jutla, A.S., de Magny, G.C., Alam, M., Siddique, A.K., Sack, R.B., Huq, A., Colwell, R.R. and Islam, S. 2011. Hydroclimatic Influences on Seasonal and Spatial Cholera Transmission Cycles: Implications for Public Health Intervention in the Bengal Delta, *Water Resources Research,* 47, W00H07. (<u>Chapter 3</u>)
4. Jutla, A.S., **Akanda, A.S,** Griffiths, J., Islam, S. and Colwell, R.R. 2011. Warming oceans, phytoplankton, and river discharge: Implications for cholera outbreaks. *American Journal of Tropical Medicine and Hygiene,* Vol. 85, No. 2.
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6. Jutla, A.S., **Akanda, A.S.** and Islam, S. 2011. Satellite Remote Sensing of Space-Time Plankton Variability in the Bay of Bengal: Connections to Cholera Outbreaks. *Remote Sensing of Environment* (Accepted).

<u>*Articles Submitted*</u>

7. **Akanda, A.S.,** Jutla, A.S., Gute, D.M., Evans, T. and Islam, S. 2011. Reducing Cholera Burden through Proactive Intervention. *Bulletin of the World Health Organization* (Submitted). (<u>Chapter 6</u>)
8. **Akanda, A.S.,** Jutla, A.S., Gute, D.M., and Islam, S. 2011. Understanding and Predicting Bengal Cholera Outbreaks Through an Epidemiologic Application of Macro-Scale Hydroclimatic Drivers, *Am. J. Epidemiology.* (Submitted). (<u>Chapter 4</u>)
9. Jutla, A.S., **Akanda, A.S** and Islam, S. 2011. Predicting cholera outbreaks in South Asia using satellite derived macro-scale environmental determinants. *Environmental Modeling and Software.* (Submitted).

<u>*Articles In Preparation*</u>

10. **Akanda, A.S.,** Jutla, A.S., Eltahir, E. and Islam, S. 2011. A Spatially Explicit and Seasonally Varying Cholera Prevalence Model using Macro-Scale Hydroclimatic Forcings (*In Preparation*). (<u>Chapter 5</u>)
11. Jutla, A.S., **Akanda, A.S.** and Islam, S. 2011. Predicting Cholera Outbreaks in South Asia and Sub-Saharan Africa using Satellite Water Impurity Marker (*In Preparation*).
12. Jutla, A.S., **Akanda, A.S.,** Mazumdar, M., Colwell, R.R., and Islam, S. 2011, Predicting Cholera Outbreaks: Where is the next Haiti? (*In Preparation*).

B. ACCOMPANIED ABSTRACTS

1. Dual Peak Cholera Transmission in Bengal Delta: A Hydroclimatological Explanation

Cholera has reemerged as a global killer with the world witnessing an unprecedented rise in cholera infection and transmission since the 1990s. Cholera outbreaks across most affected areas show infection patterns with a single annual peak. However, cholera incidences in the Bengal Delta region, the native homeland of cholera, show bi-annual peaks. The mechanisms behind this unique seasonal dual peak phenomenon in cholera dynamics, especially the role of climatic and hydrologic variables, are not fully understood. Here, we show that low flow in the Brahmaputra and the Ganges during spring is associated with the first outbreaks of cholera in Bangladesh; elevated spring cholera outbreaks are seen in low discharge years. Peak streamflow of these rivers, on the other hand, create a different cholera transmission environment; peak flood volumes and extent of flood-affected areas during monsoon are responsible for autumn cholera outbreaks. Our results demonstrate how regional hydroclimatology may explain the seasonality and dual peaks of cholera incidence in the Bengal Delta region. A quantitative understanding of the relationships among the hydroclimatological drivers and seasonal cholera outbreaks will help early cholera detection and prevention efforts.

2. Tracking Cholera in Coastal Regions using Satellite Observations

Cholera, an acute water-borne diarrheal disease, continues to be a significant health threat across the globe. The pattern and magnitude of the seven global pandemics suggest that cholera outbreaks primarily originate in coastal regions and spread inland through secondary means. Cholera bacteria show strong association with zooplankton and phytoplankton abundance in coastal ecosystems. This review study investigates relationship(s) between cholera incidences and coastal processes and explores the utility of using remote sensing data to track coastal plankton blooms and subsequent cholera outbreaks in vulnerable regions. Most of the studies over the last several decades have primarily focused on the microbiological and epidemiological understanding of cholera outbreaks, however, successful identification and mechanistic understanding of large scale climatic, geophysical and oceanic processes governing chlorophyll-cholera relationships is important for developing any predictive model for disease outbreak. Development of a holistic understanding of these processes requires long and reliable chlorophyll dataset, which is now available through satellites. We have presented a plausible pathway relating cholera, sea surface temperature, chlorophyll, and terrestrial hydrology through river discharge and satellite estimated coastal plankton abundance. Remote sensing, with its unprecedented spatial and temporal coverage, has capabilities to monitor coastal processes and track potential cholera outbreaks in endemic regions.

3. Hydroclimatic Influences on Seasonal and Spatial Cholera Transmission Cycles: Implications for Public Health Intervention in the Bengal Delta

Cholera remains a major public health threat in many developing countries around the world. The striking seasonality and annual recurrence of this infectious disease in endemic areas remain of considerable interest to scientists and public health workers. Despite major advances in the ecological and microbiological understanding of *Vibrio cholerae*, the causative agent of the disease, the role of underlying large-scale hydroclimatic processes in propagating the disease for different seasons and spatial locations is not well understood. Here, we show that the cholera outbreaks in the Bengal Delta region, are propagated from the coastal to the inland areas and from spring to fall by two distinctly different, pre- and post-monsoon, transmission cycles influenced by coastal and terrestrial hydroclimatic processes, respectively. A coupled analysis of the regional hydroclimate and cholera incidence reveals a strong association of the space-time variability of incidence peaks with seasonal processes and extreme climatic events. We explain how the asymmetric seasonal hydroclimatology affects regional cholera dynamics by providing a coastal growth environment for bacteria in spring, while propagating the disease to fall by monsoon flooding. Our findings may serve as the basis for “climate-informed” early warnings, and prompting effective means for intervention and preempting epidemic cholera outbreaks in vulnerable regions.

4. Warming oceans, phytoplankton, and river discharge: Implications for cholera outbreaks

Phytoplankton abundance is inversely related to sea surface temperature (SST). However, a positive relationship is observed between SST and phytoplankton abundance in coastal waters of Bay of Bengal. This positive relationship has been proposed as an important element in understanding cholera dynamics. It has led to an assertion that in a warming climate scenario, rise in SST may increase phytoplankton blooms and, therefore, cholera outbreaks. This study has two objectives: (i) explain why a positive SST-phytoplankton relationship exists in the Bay of Bengal and (ii) understand the implications of such a relationship on cholera dynamics. We used regression and wavelet analysis on satellite derived chlorophyll, a surrogate for phytoplankton abundance, and SST in Bay of Bengal as well as in three other major coastal regions (Amazon, Orinoco, and Congo rivers basin) with the high-discharge. We found clear evidence of two independent physical drivers for phytoplankton abundance. The first, primarily based on literature, is the phytoplankton blooming produced by the upwelling of cold, nutrient-rich deep ocean waters. The second, which explains positive relationship between SST and phytoplankton abundance in the Bay of Bengal, is the blooming of coastal phytoplankton from terrestrial nutrients discharge during high river discharges. The reported positive association between SST and phytoplankton for the Bay of Bengal may not be causal. Therefore, caution should be used when associating SST with phytoplankton and subsequent cholera outbreaks in regions where freshwater discharge rivers are a predominant mechanism for phytoplankton production.

5. Clonal Transmission, Dual Peak, and Off-Season Cholera in Bangladesh

Vibrio cholerae is an estuarine bacterium associated with a single peak of cholera (March – May) in coastal villages of Bangladesh. However, for unknown reason cholera occurs in a unique dual peak (March - May and September - November) pattern in Dhaka city that is bordered by a heavily polluted freshwater river systems and flood embankment. In August 2007, extreme flooding was accompanied by an unusually severe diarrhea outbreak in Dhaka that resulted in a record high severity of illness. This study was aimed to understand the unusual outbreak and if it was related to circulation of a new *V. cholerae* clone. Nineteen *V. cholerae* isolated during the peak of the 2007 outbreak were subjected to extensive phenotypic and molecular analyses, including multi-locus genetic screening by PCR, sequence-typing of the *ctxB* gene, and pulsed-field gel electrophoresis (PFGE). Factors associated with the unusual incidence of cholera were determined and analysis of the disease severity was done. Overall microbiological and molecular data confirmed that the hyper-virulent *V. cholerae* was O1 biotype El Tor that possessed cholera toxin of the classical biotype. PFGE (*Not*I) and dendrogram clustering confirmed that the strains were clonal and related to the pre-2007 variant El Tor from Dhaka and Matlab and resembled one of two distinct clones of the variant El Tor confirmed to be present in the estuarine ecosystem of Bangladesh. Results of analyses of both diarrheal case data for three consecutive years (2006 - 2008) and regional hydroclimatology over three decades (1980 - 2009) clearly indicate that the pattern of cholera occurring in Dhaka and not seen at other endemic sites, was associated with flood waters transmitting the infectious clone circulating via the fecal-oral route during and between the dual seasonal cholera peaks in Dhaka. Circular river systems and flood embankment likely facilitate transmission of infectious *V. cholerae* throughout the year that leads to both sudden and off-season outbreaks in the densely populated urban ecosystem of Dhaka. Clonal recycling of hybrid El Tor with increasing virulence in a changing climate and with a growing population represents a serious public health concern for Bangladesh.

6. Satellite Remote Sensing of Space-Time Plankton Variability in Bay of Bengal: Connections to Cholera Outbreaks

Cholera bacteria exhibit strong association with coastal plankton. Characterization of space-time variability of chlorophyll, a surrogate for plankton abundance, in Northern Bay of Bengal is an essential first step to develop any methodology for tracking cholera outbreaks in the Bengal Delta region using remote sensing. This study quantifies the space-time distribution of chlorophyll in Bay of Bengal region using ten years of satellite data. Variability of chlorophyll at daily scale, irrespective of spatial averaging, resembles white noise. At a monthly scale, chlorophyll shows distinct seasonality and chlorophyll values are significantly higher close to the coast than in the offshore regions. At pixel level (9 km) on monthly scale, on the other hand, chlorophyll does not exhibit much persistence in time. With increased spatial averaging, temporal persistence of chlorophyll increases and lag one autocorrelation stabilizes around 0.60 for 1296 km^2 or larger areal averages. Spatial analyses of chlorophyll suggest that coastal Bay of Bengal has a stable sill at 100 km. Offshore regions, on the other hand, do not show a stable sill. This study puts a lower limit on space-time averaging of satellite measured plankton at 1296 km^2-monthly scale to track cholera outbreaks from space in Northern Bay of Bengal.

7. Reducing Cholera Burden through Proactive Intervention

With the ever-expanding geographic reach of the seventh pandemic and alarming fatality rates in newly affected regions, it is apparent that global cholera prevention strategies are failing. However, the disease burden could be significantly reduced if the established preventive measures could be implemented ahead of time with the advanced knowledge of impending outbreaks in a particular region. A spatially explicit cholera prediction model based on environmental and climatic signatures can potentially provide the critical lead-time to deploy medical and human resources and mount preventive interventions in vulnerable areas to save lives and reduce the cholera disease burden during and following epidemic outbreaks.

8. Understanding and Predicting Bengal Cholera Outbreaks Through An Epidemiologic Application of Macro-Scale Hydroclimatic Drivers

The coastal floodplains of the Bengal Delta have a long history of cholera outbreaks, with temporal peaks occurring during the spring in coastal areas and during the fall in inland locations. The highly populated proximal areas to the corridors of the major rivers of the region, the Ganges-Brahmaputra-Meghna (GBM) system, bear the brunt of both waves of outbreaks, experiencing a biannual incidence pattern. Previous studies focusing on environmental and hydroclimatic drivers of cholera dynamics have not highlighted the spatio-temporal nature of population vulnerability in floodplain areas due to the influence of these large-scale drivers. Here we show that the seasonal and interannual patterns of cholera transmission mechanisms are strongly influenced by estuarine salinity and inland flood inundation patterns that may set the ecological and environmental 'stage' for epidemic outbreaks over large geographic regions. We argue that a major segment of the population in floodplain areas remain vulnerable to the dual peak cholera transmission mechanisms associated with these large-scale drivers. An epidemic outbreak of cholera compounded with the concurrent appearance of droughts or floods may thus seriously overburden the public health response system in Bangladesh.

9. Predicting cholera outbreaks using satellite derived macro-scale environmental determinants

There is growing evidence that outbreaks of several water-related diseases are potentially predictable by using satellite derived macro-scale environmental variables. Cholera remains one of the most prevalent water-related infections in many tropical regions of the world. Macro-environmental processes provide a natural ecological niche for *Vibrio cholerae* and because powerful evidence of new biotypes is emerging, it is highly unlikely that cholera will be fully eradicated. Consequently, to develop effective intervention and mitigation strategies, it is necessary to develop cholera prediction models with several months' lead time. Three observations motivate us to explore the use of satellite data derived macro-scale environmental variables to develop a cholera prediction model: (a) almost all cholera outbreaks originate near the coastal areas; (b) cholera bacteria exhibit a strong relationship with coastal plankton; and (c) cholera bacteria cannot be measured easily and regularly over large areas. Using chlorophyll as a surrogate for plankton bloom in coastal areas, recent studies have postulated a relationship between chlorophyll and cholera incidence. Here, we show that seasonal cholera outbreaks in the Bengal Delta can be predicted two to three months in advance with an overall prediction accuracy of over 75% by using satellite-derived chlorophyll and air temperature data. Such high prediction accuracy is achievable because the two seasonal peaks of cholera are predicted using two separate models representing distinctive macro-scale environmental processes. We have shown that interannual variability of pre-monsoon cholera outbreaks can be satisfactorily explained with coastal plankton blooms and a cascade of hydro-coastal processes. Post-monsoon cholera outbreaks, on the other hand, are related to macro-scale monsoon processes and subsequent breakdown of sanitary conditions. Our results demonstrate that satellite data over a range of space and time scales are effective in developing a cholera prediction model for the Bengal Delta with several months' lead time. We anticipate our modeling framework and findings will provide the impetus to explore the utility of satellite derived macro-scale variables for cholera prediction in other cholera prone regions.

10. A Spatially Explicit and Seasonally Varying Cholera Prevalence Model With Distributed Macro-Scale Environmental and Hydroclimatic Forcings

Despite major advances in the ecological and microbiological understanding of *Vibrio cholerae*, the causative agent of the deadly diarrheal disease cholera, the role of underlying large-scale processes in the progression of the disease in space and time is not well understood. Here, we present a semi-mechanistic spatially explicit coupled hydroclimatology-epidemiology model for understanding regional scale cholera prevalence in response to large scale hydroclimatic and environmental forcings. The model simulations show that environmental cholera transmission is modulated by two spatially and seasonally distinct transmission mechanisms - influenced by dry and wet season hydroclimatic determinants. The semi-distributed model is applied to the Ganges-Brahmaputra-Meghna Basin areas in Bangladesh to simulate spatially explicit cholera prevalence rates, validated with long-term cholera data from Dhaka and shorter-term records from regional surveillance locations. The model reproduces the variability of cholera prevalence at monthly, seasonal, and interannual timescales and highlights the role of asymmetric large scale hydroclimatic processes as dominant controls. Our findings have important implications for formulating effective cholera intervention, and for understanding the impacts of changing climate patterns on seasonal transmission.

11. Predicting seasonal cholera outbreaks using a global index: Satellite Water Impurity Marker (SWIM)

Cholera remains a significant health threat across the globe. Since coastal brackish water provides a natural ecological niche for *Vibrio cholerae* and because powerful evidence of new biotypes is emerging, it is highly unlikely that cholera will be fully eradicated. Therefore, it is necessary to develop cholera prediction model with several months' of actionable lead time. Satellite based estimates of plankton have been associated with proliferation of cholera bacteria. However, survival of cholera bacteria in variety of coastal ecological environment puts physical constraints on predictive abilities of plankton abundance for cholera outbreaks. Here, we propose a new remote sensing reflectance based statistical index: Satellite Water Impurity Marker, or SWIM, which has shown potential to predict cholera outbreaks in two endemic regions (South Asia and Sub-Saharan Africa). This statistical marker is based on the variability observed in the difference between the blue (412nm) and green (555nm) wavelengths in coastal waters and cholera incidence. The developed marker has the ability to predict cholera outbreaks in the Bengal Delta with a predicted r^2 of 78% with two months lead time. The marker was validated in the coastal Mozambique region, where we obtained a predicted r^2 of 57% with two months' lead time. We anticipate that a predictive system based on SWIM will provide essential lead time allowing effective intervention and mitigation strategies to be developed for other cholera-endemic regions of the world.

12. On Predicting Cholera Outbreaks: Where is the next Haiti?

Despite significant advances in knowledge on *Vibrio cholerae*, recent cholera outbreak in aiti indicated that the disease remains a global threat. Here, we present a forward thinking ramework for developing cholera prediction models in the endemic (ER) and non-endemic regions (NER). The sharp contrast in mortality rates between ER and NER exists not because we do not know how to treat cholera patients, but because of a persistent "knowledge barrier" between ER and NER. We proposed a pragmatic and adaptive framework which hypothesizes that convergence of three enabling situations- Inception, Conditions, and Transmission- are necessary for cholera outbreak to become an epidemic. Based on observations, it can be reasonably hypothesized that the next cholera epidemic will occur in tropical NER following disaster that devastates water and sanitation infrastructure during season with climatic and environmental conditions conducive to cholera proliferation.