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Quantification of rotavirus diarrheal risk due to hydroclimatic extremes over South Asia: Prospect of satellite based observations in detecting outbreaks

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Key Points:

- Rotavirus shows strong mortality and morbidity, as well as strong spatial and temporal variability in South Asia.
- Strong winter and weak monsoon transmission cycles dominate South Asia, modulated by regional climatic extremes.
- Satellite-derived information has potential in the forecast of rotavirus risk over Bengal delta.

Abstract

Rotavirus is the most common cause of diarrheal disease among children under five. Especially in South Asia, rotavirus remains the leading cause of mortality in children due to diarrhea. As climatic extremes and safe water availability significantly influence diarrheal disease impacts in human populations, hydroclimatic information can be a potential tool for disease preparedness. In this study, we conducted a multivariate temporal and spatial assessment of thirty-four (34) climate indices calculated from ground and satellite earth observations to examine the role of temperature and rainfall extremes on the seasonality of rotavirus transmission in Bangladesh. We extracted rainfall data from the Global Precipitation Measurement (GPM) and temperature data from the Moderate Resolution Imaging Spectroradiometer (MODIS) sensors to validate the analyses and explore the potential of a satellite-based seasonal forecasting model. Our analyses found that the number of rainy days and nighttime temperature range from 16°C to 21°C are particularly influential on the winter transmission cycle of rotavirus. The lower number of wet days with suitable cold temperatures for an extended time accelerates the onset and intensity of the outbreaks. Temporal analysis over Dhaka also suggested that water logging during monsoon precipitation influences rotavirus outbreaks during a summer transmission cycle. The proposed model shows lag components, which allowed us to forecast the disease outbreaks one to two-months in advance. The earth observations-driven forecasts also effectively captured the increased vulnerability of dry-cold regions of the country, compared to the wet-warm regions.

1 Introduction

Living in the age of satellites and nanotechnology, a significant fraction of the human population is still threatened by diarrheal diseases throughout the globe. Diarrheal diseases remain a major contributor to global mortality and morbidity, accounting for an estimated 3.1% of the total burden of disease in terms of Disability-Adjusted Life Year (DALY) and 1.3 million deaths annually, including a majority of children under five years (Troeger et al., 2017; WHO, 2014). Two of the most infectious and fatal diarrheal diseases, Rotavirus and Cholera, comprise more than one-third of the diarrheal burden in the developing countries of South Asia (Siddique et al., 2011). Yet, there is much room for improvement in understanding the underlying processes and the assessment of diarrheal disease risk over vulnerable regions (Akanda et al. 2014).

The transmissions of these diseases both at endemic and epidemic scales are primarily due to insufficient safe water access, inadequate sanitation and drainage infrastructures, and poor access to health care compounded by natural disasters or social upheavals. However, the development of water, sanitation and health infrastructures as a solution to intervene in the disease pathway requires a long timeframe and continuous financial commitment (Hutton and Bartram, 2008). Many developing countries failed to meet the 2015 Millennium Development Goals set by United Nations in 2000, predominantly in the sanitation sectors. As the global community transitions from the Millennium Development Goals (MDGs) to the Agenda 2030 Sustainable Development Goals (SDGs), the need to monitor and track the impact and progress of the global prevention efforts has become vital (H. Wang et al., 2016). Recent studies indicate that hydrologic processes and climatic variability strongly influence the outbreak of these diseases (Gurarie and Seto 2009; Remais, Liang, and Spear 2008; Bandyopadhyay, Kanji, and Wang 2012; Jutla, Huq, and Colwell 2015; Akanda and Jutla 2013). Moreover, the risk posed of the diarrheal diseases and uncertainty of the impacts are increasing under ongoing climate change (Maantay & Becker, 2012). Thus, innovative ways of advancing surveillance efforts to assess baseline conditions and strengthening health efforts through identifying disease *hotspots* in vulnerable regions is a critical need (Akanda, Jutla, and Colwell 2014). Here, we focus on rotavirus diarrhea as it has one of the highest number of diarrhea-related mortalities in children younger than five years of age, globally (WHO, 2011).

Most studies have explored the influence on rotavirus transmission for particular climatic extreme or related natural disasters, but the integration of multiple variables with disease cases has been limited. Martinez et al. (2016) explored the effect of flood and rainfall on rotavirus transmission of Dhaka, where the importance of multiple extremes was pointed out. Moors et al. (2013) integrated several climatic effects to explain the pattern of diarrheal disease outbreaks over India; however, a deterministic quantification of the diseases based on the climatic effects was absent. Jagai et al. (2012) as conducted a meta-analysis of rotavirus over south asia, but did not considered the climate extremes. Accurate identification of climatic events is also important for disease modeling. For example, water-logging causes diarrheal outbreaks in many parts of the world after consecutive rainfall for several days. Due to the combined effect of heavy intensive rainfall runoff and inefficient drainage systems, flood waters flow into low lying areas, thus causing water logging (Tawhid 2004). This areas help to connect the fecal-oral route of the disease transmission cycle through continued use of these interconnected and infected water bodies. As a result, diarrheal outbreaks spread from one locality to another (Bhavnani et al., 2014) Thus, evaluating the disease outbreak with extreme rainfall intensity but without considering the cumulative impact of consecutive rainy days left gaps in the understanding. Moreover, specific temperature conditions during daytime or nighttime could have potential to influence pathogen survivability (Lambrechts et al., 2011). Therefore, the relationships of specific climate phenomena with rotavirus diarrhea need to be explored in more detail.

The development of satellite technologies and proliferation of earth observation datasets in recent years has enabled collection and analyses of hydro-climatic information from all over the globe in unprecedented time (Emamifar, Rahimikhoob, and Noroozi 2013; Hou et al. 2014; Brown et al., 2011). The satellites not only provide advanced knowledge of environmental variables, but also high-resolution spatial and temporal information. Most of these data products are available freely within the six hours to one-week intervals after their acquisition. For example, the Global Precipitation Measuring (GPM) mission can provide rainfall information in every 30 minutes with 0.1° spatial resolution, globally (Huffman et al., 2015). The Tropical Rainfall Measuring Mission (TRMM) data is another widely evaluated satellite data and the dataset has shown better performance in detecting rainfall in various applications (Kummerow et al., 1998). Similarly, in case of temperature, the Moderate Resolution Imaging Spectroradiometer (MODIS) land surface data product can provide temperature data up at 1km spatial resolution in daily temporal scale (Pagano & Durham, 1993). These data sets, not only improves data acquisition intervals compared to station data, but also provide more spatial information in a near-real-time basis.

With establishment of the links between diarrheal diseases and new generation earth data, including satellite observations, there is a great potential to develop models for disease prediction at higher spatial and temporal resolutions. Such a system is especially crucial in the developing countries, where the population faces a massive burden of rotavirus related mortality and morbidity each year. Bangladesh, a South Asian country, with an emerging economy still suffers a heavy toll due to rotavirus. In this study, we have explored the effect of climatic extremes on the rotavirus infection cycle in Bangladesh both spatially and temporally. We have evaluated rotavirus patterns over several cities inside Bangladesh and across South Asia to understand the larger context in relation to regional hydroclimatic processes. We also implemented a deterministic multivariate modeling for risk assessment and integrating near real-time satellite products in the proposed model (with GPM for rainfall and MODIS for temperature).

2 Methodology

2.1 Study Area:

A robust epidemiologic assessment of rotavirus diarrheal outbreak with climate requires a sufficiently long time series and good spatial coverage of disease data. Unfortunately, only few places in South Asia have such information. Located in the fast growing megacity of Dhaka, the International Centre for Diarrheal Disease Research, Bangladesh (ICDDR,B) has published surveillance data of rotavirus since 2003, thus providing a window to explore the relationship between the diseases and climate. As ICDDR,B conducts surveillance over the metropolitan city of Dhaka, we have selected the city as our primary study area. Dhaka is the capital city of Bangladesh has a population of nearly 14 million, and immensely vulnerable to rotavirus diarrhea. Situated in the tropical zone, the city has a warm climate dominated by monsoon dynamics. The average temperature of city is usually high (~28°C-30°C) during April through October and relatively low (~20°C-22°C) from November through February. We have also incorporated data from five other cities of Bangladesh namely; Rajshahi, Kishorganj, Sylhet, Barishal and Chittagong for this study. In addition, we have included data from four more cities of South Asia namely; Delhi, Kathmundu, Thimpu, Karachi for a wider spatial assessment. The cities are all located in the tropical monsoon region and rotavirus is endemic is all of the cities (Mullick et al., 2014; Sherchand et al., 2009; Shetty et al., 2016; Wangchuk et al., 2015).

Figure 1. The location of the rotavirus prevalent cities of South Asia. The cities with green dots were selected for the spatial analysis.

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2.2 Disease Data:

The cases of rotavirus incidences over Dhaka were obtained from the hospital-based surveillance system of ICDDR,B over a period from January 2003 to May 2015. The ICDDR,B Centre for Health and Population Research runs an urban hospital situated in Kamalapur, Dhaka, where, more than 100,000 patients are treated for diarrhea each year. At the hospital, cholera as well as rotavirus surveillance are conducted regularly; stool samples are collected to determine the presence of enteric pathogens in every 50th (2%) patient attending the hospital for treatment of diarrhea. From the hospital surveillance reports, information on monthly rotavirus isolates were summarized and a time series was formulated.

The rotavirus data from other cities within Bangladesh were collected from the national surveillance campaign of the Institute of Epidemiology, Disease Control and Research (IEDCR). The cities within Bangladesh resemble similar demographic and climatic patterns. Bangladesh, this is only available spatial data set with the same temporal length, to the best of our knowledge. Therefore, we have selected the surveillance data (January 2013 to December 2015) of these cities in the analysis. The rotavirus information for Delhi, Kathmandu and Thimpu were gathered from secondary literature, where the datasets range from 2005 to 2013 (Mullick et al., 2014; Sherchand et al., 2009; Shetty et al., 2016; Wangchuk et al., 2015). However, each city has only about two years of reliable data and distributed over different time periods. Thus, the disease outbreak information of these cities avoided in the main analysis and was only utilized to validate the larger spatio-temporal rotavirus pattern in South Asia.

2.3 Weather Data:

We obtained daily maximum (TMax) and minimum temperatures (TMin), and precipitation (PR) data for Dhaka from the Bangladesh Meteorological Department (BMD) from 2000 to 2014. We collected climatologic records for other cities from The Global Historical Climatology Network - Daily (GHCN-Daily), version 3 from January, 2013 to December, 2016 (Menne et al., 2012) . Homogeneity and quality control tests were conducted to ensure the removal of outliers. The tests were carried out using the RHtestsV4 software package which was developed by the joint CCl/CLIVAR/JCOMM Expert Team (ET) on Climate Change Detection and Indices (ETCCDI) (X. L. Wang & Feng, 2013).

For detecting spatial variability, we utilized two types of satellites data products in this study. The Global Precipitation Measurement (GPM) data were used as the source of the satellite precipitation, collected from March 2015 to December 2015. The GPM mission is an international network of satellites that provide the next-generation global observations of rain and snow (Hou et al., 2014). The satellite temperatures for both day and night were collected from Moderate Resolution Imaging Spectroradiometer (MODIS)-Aqua satellite. Satellite-derived temperatures for both day and night were collected from Moderate Resolution Imaging Spectroradiometer (MODIS)-Aqua satellite. The global Land Surface Temperature (LST) product were made available from the MYD11A1.005 version of MODIS data at a 1-km spatial resolution.

2.4 Method

Our study approach can be separated into three sections: temporal assessment, spatial analysis, and multi-variate modeling and validation with satellite data.

A robust analysis of the hydro-climatic influence on the transmission cycle of a disease requires specific climate realizations. For example, the mean or maximum state of a monthly temperature might not directly influence a disease outbreak, but a specific temperature range or consecutive rainfall events can trigger an epidemic. Therefore, for a comprehensive examination of environmental drivers on rotavirus diarrhoea, we selected 36 climate indices based on various properties of weather events (Table 1). We either applied or adopted the climate indices from the Expert Team on Climate Change Detection and Indices (ETCCDI)(WMO, 2007). These indices were used in various climate studies to analyze the extremity of the climatic phenomenon (Alexander, 2015; Hasan et al., 2013; Keggenhoff et al., 2015). The selections of the indices in those studies were conducted based on particular objectives of individual studies. In this case, we selected the indices that are most relevant to rotavirus transmission dynamics. In Table 1, we have defined the indices based on extremity, intensity, duration and magnitude of climate variables to capture the whole spectrum of short scale weather phenomenon. The average day or night temperatures and their variations in a month were defined by TMax, Tmin and DTR indices. For Tx*ij*GE and Tn*ij*GE, we categorized the mean monthly range of TMax and Tmin into 3°C intervals to understand the seasonal effects of various temperature range on rotavirus infections. During an annual cycle, the mean (monthly) TMax and TMin varies about 9°C over the region (Islam & Hasan, 2012). Therefore, we selected 3°C as threshold interval to classify 9°C temperature range for developing Tx*ij*GE and Tn*ij*GE indices. As the minimum monthly DTR of Bangladesh is 6°C, we selected half of that (which is 3°C) to capture the temperature effect in both day and night (Islam & Hasan, 2012). Any threshold interval lower than 3°C will result in redundant indices. On the other hand, any threshold interval higher than 3°C will plausibly miss the variation of temperature that can influence rotavirus. The duration of hot or cold days based on a particular threshold were described by the rest of temperature indices (i.e. Tn10, Tx90, etc.). In case of rainfall, intensity and amount were characterized with SDII and PRECIPTOT. The magnitude of rainfall was described with Rx1and Rx5 indices. The duration of various kind of storms were classified using the rest of the precipitation indices. However, among all the indices, many are season specific and have interdependency among them. On this ground, we categorized the indices into two seasons; October to April as the dry *winter* season and July to September as the wet *monsoon* season. The indices that have 60% or more zero values were dropped and eventually we concluded with 22 and 28 indices among 36 indices for winter and monsoon seasons, respectively. For example, we did not select Tn1618GE for the monsoon season. As days with minimum temperature range of 16 to 18 degree will be zero for monsoon months, any correlation value between rotavirus and Tn1618 will result in misleading information. Therefore, some indices were dropped from the pool of 36 indices, when we conducted the season specific analysis. All the indices for temporal and spatial analysis are generated from BMD observed data, where the validation analysis of the indices is generated with daily satellite data.

Evaluating spatial risk of a disease can be modeled with existing stochastic methods like the Bayesian approach (Cheng & Berry, 2013), Monte Carlo simulations (Prosser et al., 2016) or Susceptible-Infectious-Recovered (SIR) (Grassly & Fraser, 2008) models. While the stochastic methods are useful to capture probable spatial patterns of a diseases transmission, the complexity of the methods sometimes miss the deterministic influence of a particular driver on disease transmission. As the goal of our paper is to evaluate the influence of climate indices on rotavirus diarrhea, we utilized a deterministic model to formulate the risk of the disease and avoided the population effect. In the process to eliminate the influence of population, we standardized and scaled the disease cases for each of the selected cities and combined the disease cases into a single series of the same time frame (January 2013 to June 2015) to conduct spatial analysis. The standardization method were adopted from Jagai et al. (2012), where we considered our scaled values as z-scores of rotavirus. As a result of removing the effect of population, the analysis thus represents the severity of disease cycle rather than actual cases of diseases. Any values that exceed one (1) were considered as an outbreak.

From selected climate indices, we conducted a univariate correlation analysis considering three levels of relationships in each season. In the first level, we considered lag relationships of indices with rotavirus cases. In the next level, we considered one and two-months moving average of rotavirus infections, and in the final level, we considered a cross-correlation of moving average and lags. In all three levels, we examined the two seasonal periods both temporally and spatially. As rotavirus outbreaks are more prevalent during winter seasons (supportive analyses related to the phenomenon are provide in the results section), we have examined the winter cycle in detail. For the winter season, the evaluation of the transmission cycle was conducted into three phases; the rising, the peak and the falling phase. A descriptive definition of the phases is presented in the results section. From the spatial and temporal correlations, the most influential climate relationships were identified and utilized in multivariate regression modeling.

From the correlation assessment, we generated a deterministic model that can project the risk of rotavirus based on climate indices. The model was comprised of the selected three phase winter cycle, that can quantify the rotavirus outbreak from the influence of climatic factors. Finally, the model was utilized to forecast disease outbreak from the precipitation data from GPM and temperature data from MODIS sensors. As the data of GPM satellite are available from 2015, we performed validation of the model for October 2015 and November 2015, during the dominant winter transmission cycle. In the results section, we explored that the climate indices influences only winter cycle significantly in all selected cities of Bangladesh. Therefore, we selected winter cycle for validation purpose. On the other hand, the disease data for all cities are available up to December 2015 (during the time of this study). Therefore, we were only able to validate the rising phase of the winter transmission cycle using satellite data. As Rotavirus data from several spatial regions were available for 2 years only, we were unable to utilize new data before 2013 or beyond 2015 for spatial validation. However, to demonstrate the spatial capability of our model, we utilized TRMM data in conjunction with MODIS for formulating spatial risk maps of rotavirus for the 2014 winter season.

Table 1. Description of climate indices parameters.

3 Results

3.1 Seasonal characteristics of Rotavirus in South Asia:

In this section, we discuss the general spatio-temporal pattern of rotavirus outbreaks in seen in South Asian cities. Annual rotavirus cycles over South Asia are presented in Figure 2(a). December-January are the peak months of the outbreak for the Bangladeshi cities, with the exception of Sylhet. Thimpu of Bhutan experiences the peak in a post-winter month (March) where Delhi experiences the peak earlier than Bangladeshi cities. Among the cities of South Asia, a monsoon outbreak observed (smaller relative to winter outbreak) in Delhi (population ~19 million) and Dhaka (population ~ 14 million), where both cities have a massive population compared to other cities of South Asia (World Population Review, 2017).

The rotavirus endemic cycle exhibits significant seasonal variability over South Asia (Figure 2(a)). The dominant cycle starts in October, reaches its peak in January and is followed by a recession phase in February and March. The autocorrelation analysis over Dhaka for the original monthly time series validates the presence of the dominant winter cycle. In Figure 2(c), the monthly autocorrelation function shows the presence of the strong annual winter peak. The auto-correlation figure also suggests a weaker outbreak during the monsoon season, typically during July, August and September. The z-score of the rotavirus over Dhaka also supports similar findings, where, as in 2004, the monsoon magnitude of rotavirus was higher than that of the winter (Figure 2(b)).

Characteristics of rotavirus incidences over Dhaka were analyzed following a 13-year time series data set (2003-2015) (Figure 2(b)). Rotavirus outbreak during the winter of 2008, 2011 and 2012 were the most intense outbreaks in recent history. Typically, rotavirus incidence becomes the highest during January, but some exceptions were observed during March 2009 and July 2004. In most years, the lowest incident rate of rotavirus diarrhea was observed during May. However, in 2012 and 2014, the lowest incidences were observed in August.

Figure 2. (a) Annual monthly rotavirus outbreaks over South Asian cities. (b) Z-score of rotavirus over Dhaka from 2003 to 2015 (c) Auto-correlation function of rotavirus in the city of Dhaka from 2003 to 2015.

In this analysis, we calculated temporal correlation only over Dhaka than other cities due to lack of data availability (the disease data of other cities starts from 2012). Among the precipitation indicators over the city, RR1 was found to be one of the influential indicators on rotavirus. The correlation analysis suggests (Figure 3 (a)) that a decrease in RR1 in September affects the winter rotavirus cycle especially for the month of November. The secondary outbreak during the July, August and September is affected by the number of days with rainfall events of 70mm or more (RR70) (Figure 3 (b)). However, both the rotavirus cases and RR70 were higher during the 2007 flood over the city.

Figure 3. (a) Rotavirus incidence for the month of November with RR1 of September (the y-axis is plotted in reverse order); (b) rotavirus of June-July-August with RR70 of June-July-August; (c) Rotavirus incidence for the month of December with Tmin (left) and (d) Tn1621GE (right) of same month (the y-axis of the indices are plotted in reverse order).

3.2 Univariate correlation between climate indices and rotavirus

To assess the effect of individual climate variables and indices on rotavirus transmission, we conducted univariate analysis considering moving average and lag of related variables. The correlations for the winter and monsoon seasons are presented in Figure 4.

Figure 4. (a) Temporal correlation of rotavirus in winter months over Dhaka from January 2003 to May 2015 and (b) Spatial correlation of rotavirus in winter months over six cites of Bangladesh from July 2012 to May 2015. (c) Temporal correlation of rotavirus in monsoon months over Dhaka from January 2003 to May 2015 and (d) Spatial correlation of rotavirus in monsoon months over six cites of Bangladesh from July 2012 to May 2015.

During the winter season, rotavirus outbreak in Dhaka shows a strong negative lag relation (1-month) with the selected rainfall-related indices (Figure 4(a)). In case of other cities (Figure 4(b)), the same indices show significant but lower correlation values. Unlike Dhaka, the correlations of indices in other cities do not exhibit any substantial lag effect. Thus, we can say that the low duration of rainfall events seems to an influential driver for the season, where the effects comes in delay (1-month) over Dhaka compared to other places. The temperature indices related to the colder spells strongly impact the winter epidemics in both spatial and temporal analysis. However, the spatial correlations are weaker than the temporal values in both type of indices, probable due to the varying rainfall pattern between six locations. The temperature indices that display the strongest correlation (0.5 or more) are Tmax, Tmin, Tn1621GE and Tn1921GE. All these indicators confirm the effect of colder temperature on the rotavirus cycle similar to Atchison et al. (2010).

During the monsoon season, the temporal investigation of rotavirus indicates significant correlation with all rainfall indices where such relationships are absent in the spatial assessment (Figure 4(c-d)). The outcome is expected, as the secondary monsoon outbreak and its impacts are most profound in Dhaka among the six selected cities of Bangladesh (Figure 4a). Tn2225GE significantly correlates with 2-month lag rotavirus outbreak, which is the strongest relationship among the indices during the seasons. The relationship suggests that a night temperature range of 22°C to 25°C has a potent role to in the monsoon cycle of rotavirus over Dhaka.

From Figure 2 and 4, it is evident that the winter cycle of rotavirus is more prominent than the monsoon cycle over the study region and is strongly influenced by climatic factors. Thus, we focused the investigation on the winter epidemic for the rest of the study. For a detailed understanding of the winter cycle, we characterized it into three phases; rising, peak and falling phases. The rotavirus outbreak starts to appear during the months of October and November, thus can be classified as the 'rising' phase. As the cycle, typically reaches its 'peak' during the months of December, January and February, we considered it as the 'peak' phase. From February to April, the cycle enters in its recession phase, therefore, this phase was defined as the 'falling' phase. Based on the three phases, we conducted two levels of correlation analysis as described previously between rotavirus cases and climate indices. As temperature and precipitation indices have dependency among them, many indices show similar correlation in particular phases. Therefore, to make a concise judgment, we presented only the most significant correlation for each phase of the epidemic cycle in Table 2.

Table 2. The spatial and temporal correlations between climatic indices and the three phases of the winter rotavirus epidemic.

The rising phase of rotavirus cycle has significant influence by the night temperature as Tn1621GE shows spatial and temporal correlation of 0.61 and 0.51 respectively. The lower number of 25 degree days (SU) were found to be influential on the spatial scale, where Tx2932GE also represented a similar message in the temporal scale. Number of rainy days (RR1) are strongly correlated (negatively) with rotavirus cases in both tests, more so for the onset of the epidemics in Dhaka. The rising phase of Dhaka is influenced by 2-month prior RR1 where the same index in other cities exhibits a no-lag relation. This analysis suggests that the dry and cold days in fall are potential drivers for the start of outbreak, where the timing of rainfall deviates the timing of outbreak from place to place. During the peak phase, both the number of hot days (SU) and Tmax shows negative correlation spatially. Therefore, the relationship suggests that the upper temperature threshold of cold days or nights affects the rotavirus magnitude in the peek phase. The values of the rainfall indices (except PRECIPTOT) during the peak are close to zero, thus any significant correlation of these indices will be misleading. Hence, we avoided such values in conferring our results. During the falling phase as well, RR1 plays an influential negative role in rotavirus cycle. Both temporal and spatial time series exhibits correlation of -0.61 and -0.69 respectively. However, the temporal correlations show no lag compared to the spatial correlations of the six cities during the phase. Tx10 and DTR demonstrated the strongest affinity with rotavirus in the temporal and spatial scales, respectively. Similar to the rising phase, the falling phase shows convincing connections towards dryness and demonstrate variability in the timing of the infections depending on the location.

The synthesis of the analysis revealed that the Tn1621GE and RR1 are commonly correlated during the rising and falling phase both temporally and spatially (Table 2). The temporal time series or Dhaka cases also disclose the significant relationship of Tn1621GE at the winter peak. On that account, we can say that a specified night temperature range with dry weather is a prominent force to the spread of the disease during the winter.

The assessment between three selected phases of the rotavirus winter cycle confers the effect of climate more strongly in the rising and falling phases rather than peak phase. Therefore, to achieve more clarity, we have conducted the moving average analysis of one, two and three months between indices and rotavirus. The month-wise temporal analysis indicates a strong correlation of -0.81 between Tn1621GE and rotavirus cases during the peak month (December). Tmin also showed a robust correlation (-0.84) with same month's epidemic cycle (Figure 3). The matching pattern of the two indices with rotavirus cycle from 2003-2014 confirms the relationship in Figure 3. It should be noted here that, the values of Tmin during the period varied between 14.5°C and 16.5°C (only 2°C). Such small changes in temperature variation can be misleading regarding the effect of a minimum temperature.

The month-wise correlation analysis for the individual cities would be statistically insignificant, as a common data period between the six cities are only available for approximately 3 years (in a monthly scale, it will generate 3 points in three years). In this case, we considered two of the most influential variables of winter cycle; Tn1621GE and RR1, and compared them with rotavirus proportions of these cities in Figure 5. Both of the indices reflect an ensuing pattern with rotavirus cases in six selected cities of South Asia. Between the observed dual cycles of Tn1621GE, the first cycle tends to trigger the rotavirus peak in same month in the Sylhet area. Similarly, the same cycle of Tn1621GE of Mymensingh have influence in the rotavirus cases of one-month delayed. In case of Rajshahi, the same cycle shows a two-month lag relation instead of one. On the other hand, the rotavirus peak also follows distinct pattern with RR1 or rainy days. In case of Barisal and Sylhet, the peak of rotavirus occurs during the driest month (or lowest RR1) without showing any lag. Over Rajshahi, this relationship extends for two-months lag. This variation in lag for both indices explains why there is no significant relationship found during the peak phase (Table 2) in the spatial analysis. In each city, only three or fewer rotavirus cycle were observed; thus, it is difficult to draw a generality from the data. Upon availability of more surveillance data in future, such analysis can be explored in more detail.

Figure 5. The rotavirus cycle in the six selected cities with compared to RR1 and Tn1621GE from June 2012 to May 2015.

3.3 Multivariate assessment

From the univariate analysis, we identified the RR1 and Tn1621GE as the most influencing variables on the winter rotavirus cycle. Using these climatic indices, we developed a multivariate regression model for evaluating the winter cycle. As the indices poses different correlation values in explaining the transmission process in different phases, we conducted three separate multivariate models for three phases of the cycle and combined them into a single model. As we explored the spearman rank correlation values, we also incorporated non-linear relationship between the indices and rotavirus cases. For checking the distribution of the response (response here is z-score of rotavirus) variable of the model, we conducted Shapiro-Wilk (Shapiro & Wilk, 1972) and Kolmogrorov-Sminov (Massey, 1951) tests. The tests confirms that the response variable follow a gamma distribution and rejects the null hypothesis of normality. Considering the gamma distribution, we generated optimized models with the most dominant climate indices by utilizing both linear and non-linear regression. We selected the best model for each phase of the cycle by evaluating the Akaike information criterion (AIC). The combined model from three individual phase models are presented in Eq. 1.

$$X_t = -0.1 * RR1_{m-1} + 0.04 * Tn1621GE_m - 0.07 * RR1_{n-1} + 0.07 * Tn1621GE_{n-1} - 0.03 * RR1_{o-1} + 0.02 * (Tn1621GE_{o-1} + Tn1621GE_o) + 7.47 \quad (1)$$

The subscript of RR1 and Tn1621GE refers their respective month's value in the equation. 'm', 'n' and 'o' represent the values for month of October-November, December and January-February-March, respectively. X is the scaled z-score of rotavirus for any selected month of the winter cycle. The R value of the equation is 0.67, referring to one-third of the explained variance for the whole transmission cycle. The result is higher than the previously reported climatic influence on rotavirus over South Asia (Jagai et al., 2012).

Using the formulated model, we can forecast rotavirus prevalence all over Bangladesh with localized climatic indices. In this context, based on the reported results of this study, reliable real time information of RR1 and Tn1621GE can give advance information one-to-two months prior to the occurrence of an impending outbreak. To calculate near real-time RR1 and Tn1621GE, we utilized the GPM daily precipitation data and MODIS temperature data. Magnitude of GPM rainfall products poses a magnitude bias with observed daily rainfall. However, for 1mm rainy days in a month (RR1), the GPM data provide same value as in-site observed (BMD) data from June 2015 to December 2015. In case of MODIS land surface temperature data; there are some missing values in the night temperature of the selected period. We replaced the missing values with GHCN data to formulate a complete Tn1621GE time series over the selected cities.

The calculated indices from GPM and MODIS are inserted in Eq. 1 to validate the model results for October and November, 2015. Figure 6 shows the spatial prevalence of observed and model estimated rotavirus over Bangladesh. For October, the eastern parts of the country largely agree with the observed disease incidences, where magnitude slightly deviates. In case of

November, the observed patterns are well captured by the model; however, magnitude deviates over the Barisal and Rajshahi regions. We also presented the potential of using TRMM satellite with MODIS datasets (Figure 7) to predict the disease over the region. Figure 7 shows the October and November outbreaks from model and observed data during 2014. The TRMM derived disease map is able to capture better than GPM derived product. However, it should be noted that 2014 winter data are also utilized in model formulation, thus it cannot be considered as a validation result.

Figure 6. Spatial distribution of the observed (left) and model-estimated (right, GPM + MODIS) z-score of rotavirus incidence for (a-b) October and (c-d) November, 2015.

Figure 7. Spatial distribution of the observed (left) and model-estimated (right, TRMM + MODIS) z-score of rotavirus incidence for (a-b) October and (c-d) November, 2014.

4 Discussion

Our initial assessment infers that the rotavirus cycle is strongly influenced by the dry and cold seasonal climate in the city of Dhaka. In Great Britain, Atchison et al. (2010) explored the temperature dependence of rotavirus and conferred that above the 5°C threshold, an increase of the average temperature decreased the infection rate of the disease. A similar understanding was also found in Australia (D'Souza et al., 2008), where rotavirus diarrhoea admissions are associated with lower temperatures and lower humidity. Although these two studies were conducted in different climatic zones altogether, we believe that the dearth of overall number of studies linking rotavirus with climatic indices, their findings are still important evidences towards the influence of temperature on rotavirus incidence. In South Asia, Jagai et al. (2012) also showed that the reduction in annual temperature and precipitation increases the level of infections of rotavirus, supporting our findings.

As our assessment separated the timeframe into two seasonal cycles, the correlation from winter cycle over all six selected cities strengthens the findings of previous studies. However, we also found significant positive association of rotavirus infections during monsoon over Dhaka. Dhaka is a densely populated city with a high number of informal settlements, or *slums*, with poor water and sanitation conditions (Akanda and Hossain, 2012). As rotavirus pathogens can be transmitted through the fecal oral route, high precipitation events can create waterlogging and eventually connects to the pathogen transmission pathways (Dennehy, 2000). Thus, Dhaka experienced an extra monsoon outbreak compared to other cities and the outbreak may be influenced by the heavy rainfall events. Such phenomenon also clarify why the monsoon indicators showed insignificant relationship with rotavirus in cities other than Dhaka. The city typically observes the annual highest rotavirus incidence during January, but some exceptions were observed during March 2009 and July 2004 (Figure 2b). The 2004 flood event was one of the most devastating floods of the last decade in Bangladesh (Schwartz et al., 2006). Two-thirds of the country was under water including a large portion of Dhaka during the month of July (flooding started on 8 July and reached its peak on 23 July). Floods connect the fecal oral transmission route of the disease thus results unusual outbreak (Levy et al., 2009). In many years, the lowest incident rate of rotavirus diarrhea was observed during May. However, in 2012 and 2014, the cycle reached its lowest crest during August. In 2012 and 2014, medium flooding happened in outskirts of Dhaka, which might act as the hindering phenomenon of rotavirus outbreaks (FFWC, 2012, 2014). Dhaka experienced one of the highest rotavirus outbreaks during the flood of 2007 (Figure 2(b)). Our analysis showed that the outbreak was correlated to extreme rainfall events (RR70), a potential indicator of floods. During the floods of 2007, there was a massive outbreak of diarrheal diseases in Dhaka including cholera, rotavirus, and dysentery (Harris et al. 2008,Cash et al. 2014)).

Our detailed assessment of the winter cycle provides some insight about the winter rotavirus cycle. We found that the rising phase of rotavirus is negatively correlated with SU or Tx2532GE, which represents the amount of warm days in month. Because rotavirus favored low temperatures, the lower number of warm days eventually helps to initiate the spread of the disease. Previous studies indicated that the rotavirus can be active for up to 4 weeks or one month without a host body (Levy, Hubbard, and Eisenberg, 2009). Therefore, reduction of warm days may increase the rotavirus sensitivity and the effect can be delayed up to one month. Our findings also suggest that the beginning of winter cycle (October-November) is highly correlated with RR1 and Tn1621GE both spatially and temporally. Average night temperature during September-October are 25°C. As Tn1621GE represents the night temperature of 16°C to 21°C, some nights in September starts to experience temperatures below 21°C. Therefore, the index can be reflected as colder nights of that month. In a laboratory test, the rotavirus found to be active for several days in 4°C and 20°C temperatures without human contact (Moe & SHIRLEY, 1987). In aerosol, the virus is also infectious in low temperatures (Moe & Harper, 1983). Therefore, higher values of Tn1621GE, which act as cold nights during September-October, may promote the infectivity of the rotavirus up to a 4-week delay. On the other hand, the RR1 index represents the number of wet days in a month rather than magnitude or intensity of rainfall events. As rotavirus transmission can be driven with air, reduction of rainfall may raise the propensity of aerial transport (Ansari et al., 1991) of contaminated fecal matter. Therefore, RR1 can be considered a barrier to air-borne transport of rotavirus. Consequentially, the joined effect of RR1 and Tn1621GE trigger the one month delayed outbreak during the rising phase of the winter cycle. During the peak month of rotavirus in December, RR1 becomes nearly zero over Dhaka thus allows aerial transport of the virus to its highest potential. In this phase, the correlation of Tn1621GE shifts from positive to negative. During the month of December, the average nighttime temperature also drops below 21°C. Such a drop of night temperature, transforms the Tn1621GE index to a representative of warm night, as temperature can be higher than 21°C during this month. As Atchison et al. (2010) and Cunliffe et al. (1998) both referred, the lower temperature can increase of infection rate of rotavirus, higher number of Tn1621GE inversely affects the rotavirus incidence during December. Similarly, understanding also supported by Tmin over Dhaka. Therefore, as the number of warm nights increase, the magnitude of rotavirus cases decrease in the peak month. During the falling phase, when it starts to rain again from February, the air transport of the virus starts to be limited again and alongside the temperature remain under 21°C, until March. Thus, Tn1621GE serves as an indicator of warm nights during winter and lower rotavirus infection.

In other cities of Bangladesh, the timing of the cycles did not match in the same way, thus correlation values decreased. In spatial cases, the rising and falling phase still showed a significant correlation with RR1 and Tn1621GE but values of the correlation coefficient are lower than the values of the temporal analysis. During September, Tn1621GE acts as an indication of cold night. In Sylhet and Barishal, as the increase of cold and dry nights coincide together, rotavirus infection experiences a sharp rise, thus no lag relationship is observed. However, in places like Dhaka and Mymensingh, where dryness comes early but temperature suitability comes in a delayed manner, the places experience a one-month delay in an outbreak. If these two phenomena have a much wider gap, it can result in up to a two month delay, which was observed in Rajshahi. Therefore, our findings suggest that the timing of coldness and dryness can locally affect the spread of a rotavirus epidemic. This finding increases the potential of using a high-resolution satellite data product in forecasting the local onset of the outbreaks.

From the multivariate analysis, we are also able to confirm our hypothesis through the models selection process. All the components of equation 1 significantly influence corresponding prevalence values of the rotavirus cycle and confirm the role of environmental factors on the total rotavirus transmission cycle. The forecasted prevalence matched some spatial areas of observed value during November but not in October. As we conducted a detail analysis of the climate extremes that are able to explain about 44% variance, such discrepancy was expected in spatial mapping. Due to the lack of spatial diseases data and climate data, the spatial signature was not captured properly, thus accuracy of the model suffers. Moreover, there are other factors like population dynamics, social behavior or environmental factors like flood and soil moisture can be important in the modeling accuracy. In addition to that, the accuracy of satellite datasets can also be a possible reason for the less than satisfactory performance of the spatial mapping. However, the satellite products such as GPM, TRMM and MODIS not only give real time information but also great spatial coverage, and have great potential to improve the resolution of the risk maps for such infectious diseases.

Understanding the role of climatic extremes can contribute to several pre- outbreak and post-outbreak solutions. As the developed disease model suggests, with the knowledge of an imminent outbreak one month ahead, the health management organizations can implement extra vaccination efforts as well as awareness in the most vulnerable communities. In the developing world, where preventive resources are limited, prioritizing vaccination efforts and locations by public heath authorities could save significant morbidity and mortality. During the epidemic, further outbreaks can be prevented by implementing disinfectant byproducts in water sources, solving drainage issue in the most vulnerable areas, and ensuring potable water in the infected communities. The post-outbreak measures can be improvement of the sanitation situations by developing sewage structures, or educating the high-risk communities about the transmission pathways of rotavirus. Structural solutions such as dikes, canals or sewage networks can also be constructed to reduce water logging and improve sanitary and drainage conditions.

Immunization efforts targeting vulnerable communities would be another preventive measure to reduce the spread of rotavirus diarrhea. The efficacy of the vaccination is found to be 51% effective in reducing morbidity and mortality in recent trials in developing countries (Jiang et al., 2010). Two primary rotavirus vaccines have been certified (RotaTeq, Merck & Co and Rotarix, GSK Biologicals) in major countries of the world and are slated to be incorporated across the developing world (Ruiz-Palacios et al., 2006; Vesikari et al., 2006). The vaccination is usually administered to childrenunder one year of age and typically costs from $1 to $7 per dose (Atherly et al., 2009).

5 Conclusions

In this study, we have analyzed the relationship of various climate variables and indices with rotavirus outbreaks in South Asia, formulated epidemic models and proposed a forecast mechanism. In the validation process, we have utilized satellite driven climate products, which have the capacity to provide climatic information within a 24-hour latency period after the acquisition of data. To quantify the disease outbreaks, we used a spatial risk indicator to show the spatial pattern of rotavirus outbreaks throughout Bangladesh and South Asia, and validated forecasted values with observed number of cases for October 2015 to November 2015.

The study strongly distinguished the effect of night and day time temperatures on the epidemiology of rotavirus. Previously, Hashizume et al. (2008) pointed out that the cold and dry climate is favorable for rotavirus spread, whereas the role of day and night temperature was unexplored. Our analyses found that the number of colder nights one month before an epidemic dictates the magnitude of the rotavirus outbreak in subsequent months. This effect also matches with the number of 1 mm rainy days, as fewer numbers of rainy days or drier winters facilitate the transmission of the disease. Higher number of cold nights with less amount of rainfall during September and October may trigger the outbreak and the relationship was significant in all six cities of Bangladesh. Metropolitan areas of Dhaka and Chittagong experience similar, but smaller outbreaks during the monsoon season due to the number of heavy rainfall events. As the cities have poor water supply, sanitation and drainage systems, the heavy rainfall events eventually connect the fecal-oral route of rotavirus transmission pathway. Our analysis also showed that the rainfall and temperature product from GPM and MODIS, respectively, could be utilized to predict the occurrence and magnitude of rotavirus outbreak. The forecasted spatial patterns from satellite products matched with observed progression of rotavirus over Bangladesh.

The proposed disease forecasting mechanism provides great potential to improve the existing disease preparedness and vaccination strategies. The detection of risky hotspots can facilitate the vaccination programs in a similar climate. As our model deterministically explained the environmental variability of the disease, future investigations can incorporate population-based disease models to improve the performance of the forecasts. As shown in our study, satellite-based forecasting has great potential to improve the health and well-being and contribute towards sustainable development of the growing population of the planet.

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Table 1. Description of climate indices parameters.

Name (Number of indices that represented)	**Description**	**Types of indices**
Tmin (1)	Average daily minimum temperature of a month.	Temperature
Tmax (1)	Average daily maximum temperature of a month.	Temperature
Tx10 / Tx90 (2)	Number of days in a month when TMax < 10^{th} percentile* / when Tmax > 90^{th} percentile*.	Temperature
Tn10 / Tn90 (2)	Number of days in a month when TMin < 10^{th} percentile* / when TMin > 90^{th} percentile*.	Temperature
SU (1)	Number of days in a month when TMax > 25°C.	Temperature
TR (1)	Number of days in a month when TMin > 20°C.	Temperature
DTR (1)	Monthly mean difference between TX and TN.	Temperature
Tx*ij*GE (4)	Number of days in a month when TMax is in between i °C and j °C., where, i = {26,29,33,26} and j = {28,32,35,32}[i]	Temperature
Tn*ij*GE (4)	Number of days in a month when TMin is in between i and j °C., where, i = {16,19,22,16} and j = {18,21,25,21}[ii]	Temperature
SDII (1)	Intensity of rainfall in a month (in mm/day)	Precipitation
CR*m* (4)	Highest number of consecutive *m* mm rainfall events in a month, where, *m* = 1, 5, 10, 20 [iii]	Precipitation
CR*n*S3 (2)	Number of 3-days or more storm with rainfall > *n* mm where, *n*=1,5 [iv]	Precipitation
CR*n*D*f* (4)	Number of rainfall events in a month with rainfall > *n* mm for *f* days where, *n*=1,5 and *f*=4,5 [v]	Precipitation
PRECIPTOT (1)	Total amount of rainfall in a month. (in mm)	Precipitation
RR*j* (5)	Number of rainy days with *j* mm or more rainfall, where, *j* = 1, 5, 10, 20,70. [vi]	Precipitation
Rx1 / Rx5 (2)	Maximum amount of 1-day / 5- day rainfall in a month	Precipitation

* Percentile are calculated based on 10-year baseline period of 2003 to 2013.
[i] For example, when i=26 and j=28, name of index would be Tx2628GE: The Number of days in a month when Tmax is between 26 °C to 28 °C.
[ii] For example, when i=16 and j=18, name of index would be Tn1618GE: The Number of days in a month when Tmin is between 16 °C to 18 °C.
[iii] For example, when m=1 and j=28, name of index would be CR1: Highest number of 1 mm rainfall events in a month.
[iv] For example, when n=1, name of index would be CR1S3: Number of 3-days or more storm with rainfall greater than 1 mm.
[v] For example, when n=1 and f=4, name of index would be CR1D4: Number of rainfall in a month that greater than 1 mm for 4 days.

[vi] For example, when j=1, name of index would be RR1: Number of rainy days with 1 mm or more rainfall.

Table 2. The spatial and temporal correlations between climatic indices and the three phases of the winter rotavirus epidemic.

	Rising phase (Oct- Nov)				**Peak phase (Dec-Jan-Feb)**				**Falling phase (Jan-Feb-Mar-Apr)**			
	Index Name	Correlation	Lag from Outbreak	Monthly assumption of moving average	Index Name	Correlation	Lag from Outbreak	Monthly assumption of moving average	Index Name	Correlation	Lag from Outbreak	Monthly assumption of moving average
Spatial	SU	-0.58	2	1	SU	-0.64	0	2	**Tn1621GE**	-0.45	1	2
	RR1	-0.48	1	2	Tmax	-0.57	0	2	Tx10	0.62	0	1
	Tn1621GE	0.61	1	1	Tx10	-0.52	2	2	**RR1**	-0.61	1	2
	Tn1921GE	0.68	1	1	Rx1	-0.47	0	2	Tmin	-0.62	0	1
Temporal	**Tn1621GE**	0.51	1	1	**Tn1621GE**	-0.44	0	2	RR5	-0.7	0	2
	RR1	-0.69	2	2	**Tn1621GE**	-0.43	0	1	**RR1**	-0.69	0	2
	RR5	-0.69	2	2					PRECIPTOT	-0.66	0	2
	Tx2932GE	-0.61	2	1					DTR	0.73	0	2

*The bold indices are common in all three phases.

The captions of the figures:

Figure 1. The location of the rotavirus prevalent cities of South Asia. The cities with green dots were selected for the spatial analysis.

Figure 2. (a) Annual monthly rotavirus outbreaks over South Asian cities. (b) Z-score of rotavirus over Dhaka from 2003 to 2015 (c) Auto-correlation function of rotavirus in the city of Dhaka from 2003 to 2015.

Figure 3. (a) Rotavirus incidence for the month of November with RR1 of September (the y-axis is plotted in reverse order); (b) rotavirus of June-July-August with RR70 of June-July-August; (c) Rotavirus incidence for the month of December with Tmin (left) and (d) Tn1621GE (right) of same month (the y-axis of the indices are plotted in reverse order).

Figure 4. (a) Temporal correlation of rotavirus in winter months over Dhaka from January 2003 to May 2015 and (b) Spatial correlation of rotavirus in winter months over six cites of Bangladesh from July 2012 to May 2015. (c) Temporal correlation of rotavirus in monsoon months over Dhaka from January 2003 to May 2015 and (d) Spatial correlation of rotavirus in monsoon months over six cites of Bangladesh from July 2012 to May 2015.

Figure 5. The rotavirus cycle in the six selected cities with compared to RR1 and Tn1621GE from June 2012 to May 2015.

Figure 6. Spatial distribution of the observed (left) and model-estimated (right, GPM + MODIS) z-score of rotavirus incidence for (a-b) October and (c-d) November, 2015.

Figure 7. Spatial distribution of the observed (left) and model-estimated (right, TRMM + MODIS) z-score of rotavirus incidence for (a-b) October and (c-d) November, 2014.