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Statistical Modeling of Health Effects on Climate-Sensitive Variables and Assessment of Environmental Burden of Diseases Attributable to Climate Change in Nepal

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Abstract An ecological time-series study is conducted to quantify health-effect coefficients associated with climate-sensitive variables namely temperature, rainfall, relative humidity, and wind speed and estimate environmental burden of diseases attributed to temperature as the main climatic variable together with climate change in Nepal. The study is based upon daily data of climate-sensitive variables and hospitalizations collected for 5 years between 2009 and 2014. Generalized linear model is used to estimate health-effect coefficients accounting distributed lag effects. Results show 3.08%, 10.14%, and 3.27% rise in water-borne, vector-borne, and renal disease hospitalizations, respectively, and 3.67% rise in water- and vector-borne disease deaths per 1 °C rise in average temperature. Similarly, 2.45% and 1.44% rise in heart disease hospitalization and all-cause mortality, respectively per 1 °C rise in absolute difference of average temperature with its overall average (20 °C). The computed attributable fractions are 0.3759, 0.6696, 0.2909, and 0.1024 for water-borne, vector-borne, renal, and heart disease hospitalizations, respectively, and 0.0607 and 0.4335 for all-cause mortality and disease-specific mortality of water- and vector-borne diseases, respectively. The percent change in attributable burdens due to climate change are found to be 4.32%, 4.64%, 7.20%, and −2.29% for water-borne, vector-borne, renal, and heart disease hospitalizations, respectively, and −1.39% and 6.55% for all-cause deaths and water-borne and vector-borne disease deaths, respectively. In conclusion, climate-sensitive variables have significant effects on many major health burdens in Nepal. In the context of changing climatic scenarios around the world including that of Nepal, such changes are bound to affect the health burden of Nepalese people.

Keywords Attributable fractions · Climatic conditions · Disease burden · Extended lag effects · Statistical modeling

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1 Introduction

Scientific evidences in the recent decades revealed global climate change assessed by increase in global average surface temperature and changes in nature, intensity and frequency of precipitation [18]. This has resulted in global warming, gradual melting of snow and icebergs, rise in sea levels, increased evidences of floods, landslides, drought and desertification, etc. The fifth report of the Intergovernmental Panel on Climate Change (IPCC) has reported that the atmosphere and ocean have warmed, the amounts of snow and ice have diminished, sea level has risen, and the greenhouse gas concentrations have increased [19]. Studies in Nepal have also found increase in temperature and shifts in rainfall pattern [8, 13, 28, 29, 35]. According to a report published by the Department of Hydrology Meteorology in 2007, an increase of around 2^0 C temperature is projected for the period 2039–2069 compared to 1961–1990 in a span of 80 years based upon Regional Climate Model RegCM3 which implies an average increase of 0.25 °C per decade [12]. Similarly, according to the World Bank Climate Change Knowledge Portal, an average increase of 0.55 °C temperature is estimated in the period 1990–2012 compared with 1960–1990. This implies an average increase of around 0.2 °C per decade in average temperature in the span of around 30 years [11]. However, the portal showed decrease in annual average rainfall from 1348 mm in baseline period (1960–1990) to 1213 mm in the period 1990–2012 which implies a decrease of 135 mm annual average precipitation. It means a decrease of around 11 mm monthly average rainfall. Other studies have indicated that from 1977 to 1994, mean annual maximum temperature in Nepal increased by 0.06 °C and average temperature rise is estimated at 0.5 °C per decade [13, 28, 35]. Precipitation is also becoming unpredictable and more erratic than ever, with more droughts and shorter periods of heavy rainfall [29]. Several regions in the country are already vulnerable to unevenly distributed and erratic weather [8]. These marked changes in climatic variables are bound to affect the people of Nepal specifically the public health concerns of Nepalese people. Many studies have been conducted concerning this issue of climate change and health burden in Nepal [2, 4, 8, 17, 21].

A study conducted in Nepal covering all the three ecological regions and based upon annual data of 26 years (1982–2007) showed mixed results in terms of occurrence of the number of incidences of malaria and diarrheal diseases with observed rainfall and temperature variability. The total numbers of incidences of malarial diseases in the country significantly declined during the period. However, incidences of the disease have increased during the last 6–7 years of the period, particularly in the hills and mountains of Nepal, indicating that malarial incidences are spreading to newer locations at higher altitudes of the country that traditionally were considered malaria free. The study tried to relate between climate changes and occurrences of climate-sensitive diseases but without obtaining health-effect coefficients [2]. The Capacity Strengthening in the Least Developing Countries (CLACC) working paper on climate change and health in Nepal has reported that global climate change has serious implications for Nepal. The temperature has risen in Nepal and expected to continue to rise in the coming years partly due to increases in the human population, vehicles, development activities, and changes in agricultural patterns. Vector- and water-borne diseases have been found to be increasing within the country, along with a strong identified relationship between these diseases and meteorological parameters like temperature and precipitation. The projected increase of climate disasters under climate change, particularly from floods related to glacier melt, would have a direct impact on the health of Nepalese people. It is already evident that malaria, kalaazar, Japanese encephalitis, and water-borne diseases such as typhoid and cholera are commonly seen in different parts of the country [17].

Many studies have been conducted in various parts of the world in order to establish linkages between climate-sensitive variables with hospital morbidities and mortality. A study conducted in London investigated the relation between heat and mortality in London and determined the temperature threshold at which death rates increase and quantified the effect of extreme temperatures on mortality based upon 21 years of daily data. A plot of the basic mortality-temperature relation suggested that a rise in heat-related deaths began at about 19 °C. Average temperatures above the 97th percentile value of 21.5 °C excluding those days from a 15-day heat-wave period in 1976 resulted in an increase in deaths by 3.34% (95% CI, 2.47–4.23%) for every 1 °C increase in average temperature above this value [15]. Another study reviewed the impacts of climate change on human health in South China which highlighted that the daily mean surface air temperatures above or below 26.4 °C increases the death risk of the people in Guangzhou, China especially the elderly who are vulnerable to variations in temperature. Both malaria and dengue fever reach higher altitudes and mountainous areas due to atmospheric warming. Climate change is likely to bring stronger heat waves in the future, thereby increasing heat-wave-related illnesses and deaths, particularly in the metropolitan areas [42]. A study attempted to develop health risk-based metrics for defining a heat wave in Brisbane, Australia based upon Poisson-generalized additive model to assess the impact of heat waves on mortality and emergency hospital admissions (EHAs) in Brisbane. Results showed that the higher the intensity and the longer the duration of a heat wave, the greater were the health impacts [34].

A research article published in *Risk Analysis* mentioned about various diseases associated with climate such as heat-related deaths, cardio-pulmonary diseases, vector- and water-borne diseases, malnutrition by droughts, etc. and stressed the need of more researches in this area to reduce the potential impact of climate change on public health burden including more refined methods of quantitative risk assessment [23]. Similarly, in another research article published in *Environmental Health Perspectives*, several health impacts of climate change have been mentioned. These are mortality associated with temperature extremes, incidence of deaths and injuries with rainfall, dengue with temperature and rainfall, and diarrheal diseases with rainfall [6]. A study conducted in Sydney, Australia based upon data taken during 1991–2009 showed association between hot and cold days with several heat-related diseases like cardiovascular diseases, respiratory diseases, dehydration, etc. after controlling for humidity, ozone (O_3), and particulate matter with size of less than 10 μm (PM_{10}) with increased risk of the diseases associated with hotter days compared with colder days [36]. Other studies showed risks of hospitalization for fluid and electrolyte disorders, renal failure, urinary tract infection, septicemia, and heat stroke were statistically significantly higher on heat-wave days relative to matched non-heat-wave days. Relative risks for these disease groups were 1.18 (95% CI, 1.12–1.25) for fluid and electrolyte disorders, 1.14 (95% CI, 1.06–1.23) for renal failure, 1.10 (95% CI, 1.04–1.16) for urinary tract infections, 1.06 (95% CI, 1.00–1.11) for septicemia, and 2.54 (95% CI, 2.14–3.01) for heat stroke. Risks were generally highest on the heat-wave day but remained elevated for up to five subsequent days [5]. Checkley and colleagues used time-series regression techniques to analyze the health effects of the 1997–1998 EL Niño event on hospital admissions for diarrhea and revealed that for each 1 °C increase in temperature, hospital admission increased by 8% [9]. Singh et al. [32] used monthly data and showed that diarrhea notifications increased by approximately 3% per 1 °C increase in temperature [32]. Raju et al. linked higher occurrence of chronic kidney diseases (CKD) in warmer months (March–May) [27]. Hansen et al. showed that admissions for renal disease and acute renal failure increased during heat waves compared with non-heat-wave periods with an incidence rate ratio of 1.10 (95% CI, 1.003–1.206) and 1.255 (95% CI, 1.037–1.519), respectively [16].

In Nepal, studies based upon daily time-series data to establish linkages between climate-sensitive variables and health burden is still lacking. This emphasized the need to account, monitor, and document mortality and morbidities related to climate-sensitive diseases like water-borne, vector-borne, heart-related, and renal-related (urinary system) diseases along with changes in climatic variables to explore the extents of effects by climate-related variables on public health concerns. Consequently, the present study is being conducted with the objectives to quantify and assess environmental burden of diseases (EBD) which can be attributed to climate-sensitive variables as well as climate change in Nepal. The basic methodology is to link climate-sensitive disease burdens and weather-related variables through statistical modeling of daily changes in health burden data and corresponding changes in climate-sensitive parameters like temperature, rainfall, humidity, and wind speed. The estimated coefficients are used to quantify the number of people affected that can be attributed to climate-sensitive variables and climate change.

2 Methodology

The basic methodology for the development of health effect coefficients and then estimation of environmental burden of diseases is based upon ecological time-series modeling of health and weather-related data and application of the methodology developed by WHO for assessing the EBD that can be attributed to climate change [39, 40]. The study covers ten districts of Nepal from all the three ecological belts. These are Dolakha from mountain; Kathmandu, Lalitpur, Bhaktapur, Kavrepalanchowk, and Dhankuta from hill; and Chitwan, Sunsari, Morang, and Jhapa from terai.

2.1 Basic Steps

In order to fulfill the objective of linking health burdens assessed by hospital morbidity and mortality with climate-sensitive variables, the following four major steps were adopted as mentioned in WHO methodology [40].

I. Data collection on weather and health effects
II. Exposure-response modeling
III. Estimation of EBD attributable to climate-sensitive variables
IV. Estimation of attributable burdens due to climate change

2.2 Data Collection

Data are collected for health burden and climate-sensitive variables as detailed below.

2.2.1 Weather Data

Climate-sensitive variables considered for modeling are meteorological parameters namely temperature, rainfall, humidity, and wind speed. Observed daily data of these parameters were collected for 2009–2014 from 16 stations located within the districts covered for the study which included 2 from mountain, 8 from hill, and the remaining 6 from terai. Data from 16 meteorological stations with 6 meteorological variables (maximum and minimum temperatures, relative humidity at two different times in a day, rainfall, and wind) for 6 years comprised around 200,000 data points. The source of these data is the Department of Hydrology and Meteorology (DHM), Kathmandu.

2.2.2 Health Burden Data

In order to build exposure-response models, data on health effects assumed to be linked with climate change were collected from the leading hospitals of the study area including government hospitals, teaching hospitals, and some private hospitals of the study area. Altogether, 22 hospitals were referred from the selected districts which included 2 hospitals from mountain region, 13 hospitals from hill, and 7 hospitals from terai. Daily data of hospital admission and death records were collected for the reference period of 5 years from April 2009 (2066 BS) to May 2014 (2070 BS). Morbidity and mortality data were collected for water-borne, vector-borne, heart, and renal (urinary system) diseases and also all-cause mortality. Water-borne (WB) diseases considered are enteric fever (typhoid and paratyphoid) and diarrheal diseases (with/without dehydration) including gastroenteritis/diarrhea, cholera, dysentery, and hepatitis (A and E). Vector-borne (VB) diseases include malaria, dengue, encephalitis, leishmaniasis, and filariasis. Heart diseases (HD) include mainly ischemic heart disease (including angina pectoris), cardiovascular arrest (CVA), hypertension (HTN), cardiac failures, and other cardiovascular diseases. Similarly, renal diseases (RD) include chronic kidney diseases (CKD), urinary tract infections (UTI), and renal failure. Mortality includes all-cause mortality and disease-specific mortality of the above diseases. Total disease burden for Nepal were collected from the annual reports of the Department of Health Services. Inpatient records from 22 referred hospitals showed around 50,000 hospitalizations of the concerned diseases for the study period and around 10,000 all-cause deaths and 435 water- and vector-borne disease deaths.

2.2.3 Confounding Variables

The confounding variables included are seasonal dummy variables, day of week (Saturday) to account holiday effect since Saturday is a public holiday in Nepal, and secular trend.

2.3 Exposure-Response Modeling

For exposure-response modeling, generalized linear model (GLM) with log link function (Poisson model) is used since in all the developed models the dependent variable is a count variable. Time-series models have distinct advantage over cross-sectional models since individual cofactors like socio-economic conditions, nutrition, behavior, and other potential confounding factors used in cross-sectional studies are unlikely to be confounders in these models since they are not generally associated with day-to-day basis along with daily changes in weather-related variables. The potential confounders are usually the variables that vary with time such as seasonal and trend variables.

2.3.1 Statistical Model

The generalized linear model with log link function can be expressed as follows. The model has count as the dependent variable with one or more predictor variables.

$$y_i = e^{\beta_0+\beta_1 x_{1i}+\beta_2 x_{2i}+\ldots.+\beta_p x_{pi}} + \varepsilon_i \qquad (1)$$

where y_i is the dependent variable and measures the daily hospitalizations or deaths; β_i is the ith parameter to be estimated; x_{ki} is the kth-independent variable like temperature or humidity or rainfall, etc.; and ε_i is the stochastic error term of the model. The model can also be expressed as:

$$\mathrm{Ln}(\mu_i) = \beta_0 + \beta_1 x_{1i} + \beta_2 x_{2i} + \ldots. + \beta_p x_{pi} \qquad (2)$$

where $E(y_i) = \mu_i$ and has the natural logarithm as the link function. The model is suitable to link hospital admissions (or mortality count) with weather-related variables as mentioned above.

2.3.2 Lag Effects

Health effects on a particular day can depend not only on the weather condition of the same day but may also have resulted due to weather conditions of previous days as well. Moreover, consideration of lag effects is necessary while modeling health effects are based upon daily time-series data as shown by other daily time-series studies [30, 31]. For this purpose, several lag structures are considered namely moving average (MA), geometrical decay, and arithmetic decay. Another aspect while considering lag effects is the choice of suitable lag length. For this purpose, several extended lag effects are considered and the length which suites the best regarding extent of effects and statistical significance is finally chosen. Additionally, incubation periods of bacteria/viruses that causes WB and VB diseases are noted as shown in Table 1 in order to choose the lag lengths for statistical modeling. It is noted that incubation period range between 0.5 and 14 days (excluding hepatitis) for WB diseases whereas the period range between few days to months/years for VB diseases [1, 7, 37, 38, 41].

2.4 Estimation of EBD Attributable to Climate Change

Computation of attributable fraction (AF) is done by standard methodology as mentioned in WHO literatures

Table 1 Incubation periods in water- and vector-borne diseases

Water-borne/viral diseases		Vector-borne diseases	
Disease	Period	Disease	Period
Cholera	0.5–4.5 days	Filariasis	Few days–1 year
Typhoid	8–14 days	Malaria, *Plasmodium falciparum*	9–14 days
Paratyphoid	1–10 days	Malaria, *Plasmodium vivax*	12–18 days
Gastroenteritis	1–4 days	Malaria, *Plasmodium malariae*	18–40 days
Bacillary dysentery	1–5 days	Lieshmeniasis	3 weeks–2 years
Hepatitis A	15–45 days	Encephalitis	4–10 days
Influenza	1–3 days		

and computed for total mortality and morbidities as follows.

$$\mathrm{AF} = \frac{\sum P_i \mathrm{RR}_i - 1}{\sum P_i \mathrm{RR}_i} \tag{3}$$

In eq. 3, AF represents attributable fraction, P_i is the proportion of days with categorized groups of climatic conditions out of the total number of days, and RR_i is the relative risk of exposure category i compared with the reference level or threshold value. Attributable burden (AB) is computed as

$$\mathrm{AB} = \mathrm{AF} \times \mathrm{TB} \tag{4}$$

where TB is the total burden. Attributable burdens are computed separately for different groups of similar diseases. Finally, the estimation of attributable burden due to climate change in Nepal is computed as follows.

$$\mathrm{AB}_{\text{Climate Change Scenario}} - \mathrm{AB}_{\text{Baseline Scenario}} \tag{5}$$

Total disease burden for EBD assessment is based upon available data collected from the Department of Health Services (DoHS) Annual Reports. Temperature data of Nepal for baseline period is obtained as the gridded atmospheric reanalysis data provided by National Centers of Environmental Protection (NCEP) and National Center for Atmospheric Research (NCAR). Future scenario temperature data is approximated using Regional Climate Model (RegCM3) for Nepal.

Table 2 Occurrences of disasters by types

Disaster	Frequency	Percent
Cold wave	458	4.8
Flood	3520	36.6
Hail storm	725	7.5
Heat wave	46	0.5
Landslide	2908	30.3
Snow storm	195	2.0
Storm	123	1.3
Strong wind	456	4.7
Thunderstorm	1175	12.2
Total	9606	100.0

Source: OpenNepal [25]

2.4.1 Threshold Values for Computing Relative Risks

The threshold values of temperature for computation of attributable fractions are based upon the finding of studies and also upon the observed frequency curve of hospitalizations at different temperatures. Studies have been conducted to examine about weather variables and survival and development of bacteria/parasites/viruses and their carriers and showed that a pathogen needs a certain temperature range to survive and develop. For instance, a minimum temperature of 25–26 °C is required for the transmission of Japanese Encephalitis Virus (JEV) [24, 33]. The development of malaria parasite (*Plasmodium falciparum* and *Plasmodium vivax*) ceases when temperature exceeds 33–39 °C [26]. Reproduction of *Salmonella* increases as temperature rises in the range between 7 and 37 °C [20]. Similarly, since the *P. falciparum* malaria mostly exists when temperature is above 16 °C [3], a temperature dropping below this threshold will benefit

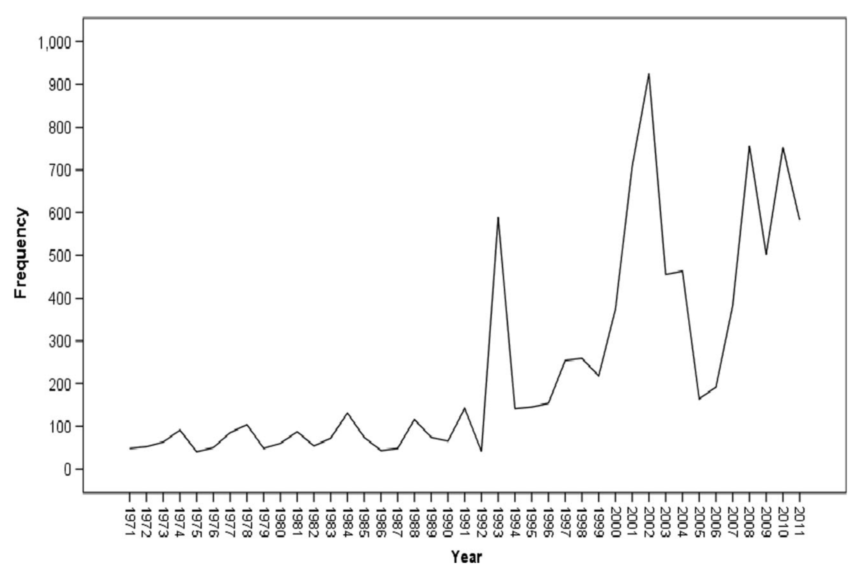

Fig. 1 Annual frequency of disasters in Nepal during 1971–2011

Table 3 Parameter estimates, relative risks, and percent changes of water-borne disease model

Parameter	Estimate	Lower 95% CI	Upper 95% CI	*p* value	Relative risk (RR)	% change	Lag structure	Lag length (days)
Intercept	3.512	3.257	3.766	<0.0001	–	–	–	–
Temperature	0.030	0.027	0.034	<0.0001	1.0308	3.08	Geometric	7
Rainfall	0.022	0.018	0.026	<0.0001	1.0223	2.23	MA	15
Humidity	−0.015	−0.018	−0.013	<0.0001	0.9847	−1.53	MA	15
Wind	0.021	0.003	0.038	0.0200	1.0209	2.09	MA	15
Summer	−0.129	−0.161	−0.096	<0.0000	0.8793	−12.07	–	–
Saturday	−0.207	−0.24	−0.174	<0.0001	0.8131	−18.69	–	–
Trend	−0.026	−0.036	−0.015	<0.0001	0.9745	−2.55	–	–

malaria control. Additionally, the hospitalization frequency-temperature curves showed around 100 cases of water-borne hospitalization (<1%) between 5 and 10 °C, only around 10 cases of vector-borne (<1%) and renal disease hospitalizations (<1%) below 10 °C. Based upon the review and findings, the threshold values of minimum average temperature considered for WB, VB, and renal disease (urinary system) are chosen as 5, 10, and 10 °C, respectively.

2.5 Analysis of Extreme Atmospheric Conditions and Disease Burden

Nepal is a disaster-prone country with an annual number of disasters related to climate change having significantly increased in the last two decades (Fig. 1) in which floods, landslides, and thunderstorm comprise the majority of disasters that occurred during a period of 40 years (Table 2) from 1971 to 2011 excluding earthquakes [25]. The upward trend of the number of disaster occurrences is indicative of an increasing number of extreme weather conditions in Nepal since disasters are strongly related to extreme weather conditions such as heavy rainfall, unusually high or low ambient temperatures, humidity, and wind. As a result, analysis of extreme atmospheric conditions is necessary to the study of effects of climate-sensitive variables on burden of diseases. In order to examine and assess the effects of extreme weather conditions on hospital morbidity and mortality, observed daily values of meteorological parameters are categorized according to their threshold values that separates extreme conditions from normal situations. The cutoff values are taken as values above 95% percentile, below 5% percentile and in case of low rainfall, a dry condition with no rain is taken for the purpose of categorization. Generalized linear model is used to account the effects of the extreme conditions on disease burdens based upon weekly data of the number of days of occurrence of such extreme events.

3 Results

Results are presented in three main sections: statistical modeling, estimation of environmental burden of diseases, and analysis of extreme weather conditions as follows.

3.1 Statistical Models

Several statistical models are developed in order to link and assess health effects including hospital inpatient morbidity and mortality with climate-sensitive variables and confounding variables. Altogether, six models are developed accounting WB, VB, heart disease, and renal

Table 4 Parameter estimates, relative risks, and percent changes of vector-borne disease model

Parameter	Estimate	Lower	Upper	*p* value	Relative risk (RR)	% change	Lag structure	Lag length
Intercept	−4.062	−4.991	−3.132	<0.0001	–	–	–	–
Temperature	0.097	0.082	0.111	<0.0001	1.1014	10.14	MA	45
Rainfall	−0.041	−0.055	−0.027	<0.0001	0.9597	−4.03	MA	45
Humidity	0.040	0.030	0.050	<0.0001	1.0407	4.07	MA	45
Wind	0.050	0.007	0.094	0.0230	1.0515	5.15	MA	1
Saturday	−0.562	−0.687	−0.436	<0.0001	0.5703	−42.97	–	–
Trend	−0.151	−0.181	−0.121	<0.0001	0.8602	−13.98	–	–

Table 5 Parameter estimates, relative risks, and percent changes of renal (urinary system) disease model

Parameter	Estimate	Lower	Upper	*p* value	Relative risk (RR)	% change	Lag structure	Lag length
Intercept	−0.063	−0.685	0.559	0.843	–	–	–	–
Temperature	0.032	0.020	0.044	<0.0001	1.0327	3.27	Geometric	7
Rainfall	−0.007	−0.014	0.000	0.042	0.9927	−0.73	Geometric	7
Humidity	0.005	−0.001	0.012	0.093	1.0055	0.55	Geometric	7
Wind	−0.042	−0.081	−0.003	0.035	0.9590	−4.10	Geometric	7
Summer	−0.090	−0.217	0.038	0.170	0.9144	−8.56	–	–
Autumn	−0.109	−0.232	0.014	0.081	0.8966	−10.34	–	–
Saturday	−0.443	−0.537	−0.348	<0.0001	0.6424	−35.76	–	–
Trend	0.060	0.036	0.085	<0.0001	1.0623	6.23	–	–

disease (urinary system) hospitalizations and all-cause and disease-specific deaths. Models are discussed separately as follows.

3.1.1 Model 1: Water-Borne Diseases Hospitalization

Generalized linear model with WB hospitalizations as the response variable shows statistically significant associations with all the considered climate-sensitive variables namely average temperature, rainfall, relative humidity, and wind speed. Confounding variables associated are trend, seasonal dummies, and day of week effect (Saturday or holiday effect). Associations are found to be positively associated with temperature, rainfall, and wind whereas negative with humidity and trend. Estimates show 3.08% rise in WB hospitalization per 1 °C rise in temperature (7 day geometrical decay lag effect), 2.23% rise in the hospitalization per 1 mm rise in rainfall (15 day moving average (MA) effect), 1.53% decrease in the hospitalization per 1% rise in relative humidity (15 day MA effect), and 2.09% rise in the hospitalization per 1 m/s rise in wind speed (15 day MA effect). Also, Saturday is associated with 18.69% decrease in the hospitalization and 2.55% decrease in the hospitalization per year. Effects of seasonality in summer months are associated with 12.07% less hospitalizations compared with remaining months as the reference (Table 3).

3.1.2 Model 2: Vector-Borne Diseases Hospitalization

GLM with VB hospitalizations as the response variable shows statistically significant positive associations with temperature, relative humidity, and wind speed whereas statistically significant negative associations with rainfall and trend. Estimates show 10.14% rise in VB hospitalization per 1 °C rise in temperature (45 day MA effect), 4.03% decrease in the hospitalization per 1 mm rise in rainfall (45 day MA effect), 4.07% increase in the hospitalization per 1% rise in relative humidity (45 day MA effect), and 5.15% rise in the hospitalization per 1 m/s rise in wind speed (1 Day MA effect). Moreover, Saturday is associated with 42.97% decrease in the hospitalization and 13.98% decrease in the hospitalization per year (Table 4).

3.1.3 Model 3: Renal (Urinary System) Diseases Hospitalization

GLM with renal disease hospitalizations as the response variable shows statistically significant positive associations with temperature, humidity, and trend whereas statistically negative associations with rainfall and wind speed. Estimates show 3.27% rise in renal disease hospitalization per 1 °C rise in temperature, 0.73% decrease in the hospitalization per 1 mm rise in rainfall, 0.55% increase in the hospitalization per 1% rise

Table 6 Parameter estimates, relative risks, and percent changes of heart disease model

Parameter	Estimate	Lower	Upper	*p* value	Relative risk (RR)	% change	Lag structure	Lag length
Intercept	1.183	1.070	1.295	<0.0001	–	–	–	–
Temperature	0.024	0.011	0.038	<0.0001	1.0245	2.45	Geometric	15
Wind	0.034	0.009	0.060	0.008	1.0350	3.50	Geometric	15
Spring	0.091	0.020	0.163	0.012	1.0957	9.57	–	–
Saturday	−0.322	−0.403	−0.241	<0.0001	0.7246	−27.54	–	–
Trend	−0.047	−0.067	−0.026	<0.0001	0.9544	−4.56	–	–

Table 7 Parameter estimates, relative risks, and percent changes of all-cause mortality model

Parameter	Estimate	Lower	Upper	p value	Relative risk (RR)	% change	Lag structure	Lag length
Intercept	1.288	0.818	1.759	<0.0001	–	–	–	–
Temperature	0.014	0.002	0.026	0.020	1.0144	1.44	PMA	3
Humidity	0.005	0.000	0.010	0.075	1.0048	0.48	PMA	30
Wind	0.035	0.007	0.064	0.016	1.0359	3.59	PMA	30
Spring	0.125	0.055	0.194	<0.0001	1.1326	13.26	–	–
Autumn	0.102	0.036	0.168	0.002	1.1074	10.74	–	–
Saturday	−0.129	−0.188	−0.070	<0.0001	0.8788	−12.12	–	–
Trend	−0.043	−0.061	−0.025	<0.0001	0.9578	−4.22	–	–

in relative humidity, and 4.1% decrease in the hospitalization per 1 m/s rise in wind speed with all the above effects due to 7-day geometrical decay. Additionally, Saturday is associated with 35.76% decrease in the hospitalization and 6.23% increase in the hospitalization per year. Seasonally, summer and autumn months are associated with 8.56% and 10.34% less hospitalizations with remaining months as the reference (Table 5).

3.1.4 Model 4: Heart Diseases Hospitalization

GLM with heart diseases hospitalizations as the response variable shows statistically significant positive associations with absolute temperature difference between a day average and its overall average (20 °C) and wind speed, statistically insignificant associations with rainfall and relative humidity and negative association with trend. Estimates show 2.45% rise in HD hospitalization per 1 °C rise in absolute temperature difference and 3.5% rise in the hospitalization per 1 m/s rise in wind speed (both the effects are 15 day lag geometrical decay). Moreover, Saturday is associated with 27.54% decrease in hospitalization and 4.56% decrease in hospitalization per year. Seasonally, spring months are associated with 9.57% more hospitalizations with remaining months as the reference (Table 6).

3.1.5 Model 5: All-Cause Mortality

GLM with all-cause mortality as the response variable shows statistically significant positive associations with absolute temperature difference between a day average and its overall average (20 °C), relative humidity, and wind speed whereas statistically significant negative associations with trend. Estimates show 1.44% rise in deaths per 1 °C rise in the absolute difference in temperature (3-day prior moving average (PMA) effect), 0.48% increase in deaths per 1% rise in relative humidity (30-day PMA effect), and 3.59% rise in deaths per 1 m/s rise in wind speed (30-day PMA effect). Moreover, Saturday is associated with 12.12% decrease in deaths and 4.22% decrease in deaths per year. Seasonally, autumn and spring months are associated with 10.74% and 13.26% more deaths, respectively, with remaining months as the reference (Table 7).

3.1.6 Model 6: Disease-Specific Mortality (WB and VB)

GLM with WB and VB disease mortality as the response variable shows statistically significant positive associations with temperature and negative associations with wind speed and trend with 3.67% increase in the deaths per 1 °C rise in temperature (7-day geometrical decay effect) and 12.83% decrease in the deaths per 1 m/s rise in wind speed (7-day geometrical decay effect). Moreover, 25.2% decrease in the deaths per year is also estimated (Table 8).

3.1.7 Model Adequacy Tests

Model tests are done related to goodness of fit, residual analysis, and multicollinearity. Goodness of fit is checked through Omnibus test and found to be good with p values nearly zero

Table 8 Parameter estimates, relative risks, and percent changes of water- and vector-borne mortality models

Parameter	Estimate	Lower 95% CI	Upper 95% CI	p value	Relative risk (RR)	% change	Lag structure	Lag length (days)
Intercept	−1.124	−1.613	−0.636	<0.0001	–	–	–	–
Temperature	0.036	0.015	0.057	0.001	1.0367	3.67	Geometric	7
Wind	−0.137	−0.228	−0.047	0.003	0.8717	−12.83	Geometric	7
Trend	−0.290	−0.367	−0.213	<0.0001	0.7482	−25.18	–	–

for all the fitted models. Residual analysis showed deviance residuals distributed normally for four models though two models had p values less than 0.1. In all of the fitted models, standardized deviance residuals are scattered randomly and with reasonably constant variances when plotted against predicted values. Screening of residual autocorrelations at different lags showed almost all low values less than 0.15 even though some were statistically significant at 5% level because of very large sample size (1826 days) and were ignored. Moreover, the plot of standardized residual in time sequence showed no visible pattern with fairly constant spread which is also an indication of absence of autocorrelations. There were no high multicollinearity among predictors in the models with variance inflation factors (VIFs) smaller than 5 for all the predictors of the built models. In two of the models (with VB and all-cause death as response variables), two potential outliers were detected and deleted.

3.2 EBD Attributable to Climate-Sensitive Variable (Temperature) and Climate Change in Nepal

Computation and assessment of EBD are done in the following sub-sections as follows.

3.2.1 Computation of EBD Attributable to Temperature as the Main Climate-Sensitive Variable

Estimated EBD due to temperature for different health burdens are given in Table 9. In the table, attributable fractions along with total and attributable burdens due to temperature rise are given. Burden per year is the average value obtained from available 17 years (1997/98-2014/15) of morbidity and mortality data reported in annual reports of the Department of Health Services (DoHS), Kathmandu. The computations of attributable fractions (AFs) and then attributable burden (AB) are based upon several assumptions. Minimum threshold values of average temperature for computation of attributable fractions of WB diseases, VB diseases, renal diseases, and disease-specific mortality of WB and VB diseases are chosen as 5, 10, 10, and 5 °C, respectively. In case of temperature taken as absolute difference, the threshold is taken as 0 °C. Threshold values were chosen based upon literature review as well as observed values of temperature averages for the considered stations of Nepal in the study period and assumed that considered health effects below these threshold values are negligible.

Results show AFs in between 0.1 and 0.67 for hospitalizations with highest AF computed for VB disease hospitalization and lowest for HD hospitalization. AFs for WB and renal-related disease hospitalizations are computed as 0.38 and 0.29, respectively. Considering hospital mortalities, AFs for all-cause mortality and disease-specific mortality (WB and VB) are found to be 0.06 and 0.43, respectively. The attributable burdens due to temperature rise are given in the last column of Table 9.

Table 10 Monthly temperatures in climate scenarios

Season	Month	Baseline period (1985–2014)	Seasonal increase	Future period (2016–2046)
Winter	January	12.08	0.81	12.89
	February	13.62	0.81	14.43
Pre-monsoon	March	17.61	0.66	18.27
	April	20.86	0.66	21.52
	May	23.58	0.66	24.24
Monsoon	June	23.74	0.75	24.49
	July	22.39	0.75	23.14
	August	22.00	0.75	22.75
	September	20.97	0.75	21.72
Post-monsoon	October	17.88	0.79	18.67
	November	15.22	0.79	16.01
Winter	December	13.19	0.81	14.00
Nepal	Total	18.60	0.75	19.34

3.2.2 Effects of Climate Change in Attributable Burdens

For estimating the effect of climate change, two scenarios are considered, the baseline scenario (1985–2014) and the future scenario (2015–2045). Monthly average temperature for the

Table 9 Attributable factors and attributable burdens

Model no.	Type	Response variable	AF	Burden/year (outpatients)	Burden/year (inpatients)	Total burden/ year	Attributable burden/year
1	Hospitalization	WB	0.3759	1,572,625	22,746	1,595,371	599,700
2	Hospitalization	VB	0.6696	76,230	1891	78,121	52,310
3	Hospitalization	Renal	0.2909	174,616	4250	178,866	52,032
4	Hospitalization	HD	0.1024	115,855	4631	120,486	12,338
5	Death	All cause	0.0607			2620	159
6	Death	WB and VB	0.4335			148	64

Table 11 Attributable burdens due to climate change in Nepal

	Model 1 Hospitalization (type)	Model 2	Model 3	Model 4	Model 5 Deaths (type)	Model 6
	Response variable					
	WB	VB	Renal	HD	All cause	WB and VB
AF in baseline period	0.3402	0.5972	0.2473	0.0853	0.0503	0.3848
AF in future period	0.3549	0.6249	0.2651	0.0834	0.0496	0.4100
Total burden/year	1,595,371	78,121	178,866	120,486	2620	148
Burden/year (inpatients)	24,797	1481	8211	5678	2620	73
AB in baseline period	542,745	46,654	44,234	10,277	132	57
AB in future period	566,197	48,818	47,417	10,049	130	61
AB due to climate change	23,452	2164	3184	−229	−2	4
% change in AB	4.32	4.64	7.20	−2.23	−1.39	6.55
Change in AF	0.0147	0.0277	0.0178	−0.0019	−0.0007	0.0252

baseline period is obtained as the gridded atmospheric reanalysis data with a resolution of 2.5° × 2.5° provided by the National Centers of Environmental Protection (NCEP) and National Center for Atmospheric Research (NCAR). The monthly average is the average obtained from 5 grid points with which best represents Nepal and for EBD assessment. One grid point around the east-north border of Nepal is left out since population around the grid point is almost nonexistent at this region of Nepal. The monthly averages in future scenario (2015–2045) are approximated by adding an average temperature rise of 0.25 °C per decade for 30 years using regional climate model (RegCM3) for Nepal which shows an average rise of 2 °C temperature in 80 years from baseline period (1960–1990) to future period (2039–2069) [12]. This closely resembles with World Bank Climate Change Knowledge Portal historical temperature data with around 0.20 °C rise per decade. The seasonal increases in temperature according to the RegCM3 model are approximately 2.15, 1.75, 2.00, and 2.1 °C for winter, pre-monsoon, monsoon, and post-monsoon seasons, respectively, taking average of eastern and western regions of Nepal (Table 10).

Table 12 Threshold values for computation of RRs

Parameter	Threshold	Percentile
High temperature	31.44	95
Low temperature	4.55	5
High rainfall	21.81	95
Low rainfall	0.00	–
High humidity	90.13	95
Low humidity	62.16	5
High wind	4.66	95
Low wind	0.44	5
High temperature difference	8.23	95

Attributable burdens are computed for both scenarios, taking account of only climate change while assuming that total burdens remain the same in the two scenarios. The computed AFs and corresponding ABs in both scenarios are shown with higher AFs and hence ABs for all the health effects including morbidities and mortalities in the future scenario due to climate change (temperature rise). The percent rises in ABs are found to be highest for renal disease hospitalization (7.2%) and least for WB disease hospitalization (4.32%). Similarly, attributable burdens for VB hospitalization and WB and VB disease deaths are found to be 4.64% and 6.55%, respectively. In contrast, attributable burdens decrease for HD hospitalization and all-cause mortality with 2.23% and 1.39% decrease in ABs in climate change scenario, respectively. Changes in AFs are also shown in Table 11.

3.3 Analysis of Extreme Atmospheric Conditions and Disease Burdens

Analysis of extreme weather conditions are measured by weekly data of days with extremely high values and low values of temperature, rainfall, relative humidity, and wind speed and their effects are assessed by relative risks through GLMs. The threshold values of extreme events for the computation of relative risks are given in Table 12.

Results of analysis are shown in Tables 13 and 14. Analysis shows that extremely hot days (above 95 percentile of maximum temperature) are associated with higher risks of WB (RR = 1.053) and renal disease (1.024) hospitalizations whereas lower risks in case of VB disease hospitalization (0.973) and WB & VB deaths (0.926). Similarly, extremely high differences between average temperature of a day and its overall average increase the risks of heart disease hospitalization (1.019) and all-cause mortality (1.012). Similarly, extremely low temperature is associated with lower risk of WB

Table 13 RRs of extreme atmospheric conditions

Extreme atmospheric condition	WB hospitalization				VB hospitalization				Renal disease hospitalization			
	RR	95% confidence interval		*p* value	RR	95% confidence interval		*p* value	RR	95% confidence interval		*p* value
		Lower	Upper			Lower	Upper			Lower	Upper	
Extremely hot	1.053	1.044	1.062	0.000	.973	.941	1.005	0.098	1.024	0.999	1.050	0.060
Heavy rain	1.051	1.035	1.067	0.000	1.050	1.020	1.080	0.001	0.962	0.922	1.003	0.072
High humidity	1.028	1.014	1.043	0.000	1.096	1.054	1.141	0.000	1.068	1.030	1.108	0.000
High wind	1.067	1.057	1.077	0.000	1.084	1.050	1.119	0.000	0.932	0.903	0.961	0.000
Extremely cold	0.984	0.974	0.995	0.005	0.952	0.917	0.988	0.010				
No rain	0.952	0.948	0.956	0.000	0.946	0.934	0.959	0.000	0.974	0.965	0.984	0.000
Low humidity	1.046	1.037	1.056	0.000	0.891	0.855	0.929	0.000	1.029	1.003	1.056	0.030
Low wind	1.069	1.060	1.079	0.000					0.929	0.904	0.956	0.000

Extremely high values are values above 95% percentile and extremely low values are below 5% percentile

(0.984), VB (0.952) disease hospitalizations but higher risks in case of heart disease hospitalization (1.012) and WB & VB disease deaths (1.092). Heavy rainfall is associated with higher risks of WB (1.051) and VB (1.050) disease hospitalizations but lower risk (0.962) of renal disease hospitalization. Moreover, dry days are associated with lower risks in WB, VB, and renal disease hospitalizations with RRs 0.952, 0.946, and 0.974, respectively. Similarly, dry days are also associated with lower risk of WB and VB disease deaths with 0.979 RR. Extremely humid days are associated with higher risks of WB (1.028), VB (1.096), and renal disease hospitalizations (1.068) and all-cause mortality (1.007) and disease-specific (WB and VB) deaths (1.098). Similarly, extremely non-humid days are associated with less risks of VB (0.891), heart disease (0.977), and WB and VB disease mortality (0.931) but higher risks in WB (1.046) and renal disease (1.029) hospitalizations. Lastly, high winds are associated with higher risks in WB (1.067), VB (1.084), heart disease (1.026), and WB and VB deaths (1.037) but lower risks in renal disease hospitalizations (0.932). Similarly, days with very low wind are associated with higher risks in WB (1.069), heart disease (1.083), and WB and VB disease deaths (1.044) but lower risks in renal disease hospitalization (0.929) (Tables 13 and 14).

4 Conclusions

Analysis of climate-sensitive and health effect data through statistical modeling demonstrated that rise in atmospheric temperature is associated with rise in WB and VB disease hospitalizations and deaths associated with these diseases as well as hospitalization of renal-related diseases with relative risks varying in between 1.03 and 1.10 resulting in substantial proportions of the considered disease and death burdens attributed to rise in temperature. One of the main findings revealed that even though average temperature is positively associated with WB, VB, and renal disease hospitalizations as well as WB- and VB-related deaths, this is not found true with

Table 14 RRs of extreme atmospheric conditions

Parameter	RR	95% confidence interval			RR	95% confidence interval			RR	95% confidence interval		
		Lower	Upper	*p* value		Lower	Upper	*p* value		Lower	Upper	*p* value
	HD hospitalization				All-cause mortality				Water- and vector-borne deaths			
Extremely hot	1.019	.999	1.040	0.063	1.012	0.996	1.028	0.137	0.926	0.865	0.991	0.026
Heavy rain												
High humidity					1.007	0.997	1.017	0.199	1.098	1.041	1.158	0.001
High wind	1.026	1.017	1.034	0.000	1.014	1.007	1.021	0.000	1.037	0.981	1.096	0.198
Extremely cold	1.012	1.001	1.024	0.030					1.092	1.010	1.181	0.027
No rain									0.979	0.966	0.993	0.002
Low humidity	0.977	0.954	1.000	0.052					0.931	0.884	0.980	0.006
Low wind	1.083	1.059	1.107	0.000					1.044	1.012	1.077	0.006

all-cause deaths and heart disease hospitalization. Statistical modeling revealed that all-cause deaths and HD hospitalizations increased with increasing hotness or coldness relative to overall average condition (20 °C) implying that extreme conditions (both hot and cold) are relatively more favorable to the occurrence of all-cause deaths and HD hospitalization compared with normal conditions. Analysis revealed that climate change in Nepal is likely to increase from 4.3% to 7.2% attributable burdens regarding WB and VB disease hospitalizations and deaths associated with these diseases as well as renal hospitalization in the period 2015–2045 compared with baseline period 1985–2014. However, the analysis showed decrease in attributable burdens for heart disease hospitalization and all-cause mortality with 1.4–2.2% decrease in attributable burdens due to climate change in Nepal since extreme cold environment is associated more with such effects compared with extreme hot environment in Nepal. The attributable burdens are estimated and compared between two scenarios assuming that total burden remains constant during the two periods. This assumption is useful to assess about the extent of effects only due to climate change with other factors like socio-economic, health facilities, population, etc. remaining constant.

Lag effects are also explored and accounted since symptoms can appear days after exposure. The main reason for accounting lag effects is due to incubation period of different bacteria and viruses which causes WB and VB diseases. Literature review showed that incubation periods in VB diseases are of much longer periods compared with WB diseases. Analysis of distributed lag effects also supported this since 45-day lag effects of meteorological variables for VB disease hospitalization was detected as against 7–15 days lag effects for WB disease hospitalization. Apart from temperature, other atmospheric conditions also play significant roles in appearance of symptoms and even death in extreme conditions. Analysis showed that relatively more rainfall increases the possibility of WB disease hospitalization which supports the fact that rainy season is actually associated with relatively higher incidence of WB disease hospitalization in Nepal with 1.02 RR. Heavy rains and occurrence of floods are found highly conducive to such diseases. In contrast, the effect of rainfall in other hospitalizations such as VB and renal-related diseases are found to be negative with 0.96 and 0.99 RRs, respectively. Studies have also shown that excessive rainfall may have catastrophic impacts on mosquito population because strong rain can sweep away their breeding sites [22]. Effects of humidity are also detected for different responses since it can affect pathogens of infectious diseases. Higher humidity is found associated with increased hospitalizations of VB and renal disease hospitalizations and all-cause mortality with 1.04, 1.01, and 1.01 RRs, respectively, whereas negatively associated with WB diseases with 0.98 RR. Higher humidity with higher water content in air could be relatively favorable to vector-borne carriers and their survival and also can have larger effects causing renal diseases including renal failure. Similarly, extreme hotness with heat waves and high humidity may have serious effects on humans particularly older people resulting in death, thus the coefficients are found to be positively associated with relative humidity. On the contrary, relative humidity is found to be negatively associated with WB disease hospitalization. One of the reasons may be due to reduced survival of WB disease pathogens due to the drying effect of surface water [14]. Increase in wind speed is found to increase WB, VB, and heart disease hospitalizations and also all-cause mortality with RRs ranging in between 1.02 and 1.05 for hospitalizations and 1.04 for all-cause deaths. However, it is found to be negatively associated with renal disease hospitalization and WB and VB deaths. Wind is found to be a principal factor affecting the pathogens of air-borne diseases since pathogen are attached with dust particles and transported from one place to another by wind [10].

Analysis of extreme weather conditions and health effects showed strong statistical associations between many extreme weather conditions and hospital morbidity and mortality of several related diseases with climatic conditions. For instance, associations of WB and renal diseases with extremely hot days; heart diseases and WB and VB mortality with extremely cold days; all-cause mortality with large deviation in average temperature compared with 20 °C; WB and VB diseases with heavy rainfall; WB, VB, and renal disease hospitalizations and all-cause mortality and disease-specific (WB and VB) deaths with extremely humid days; WB, VB, and heart disease hospitalizations and WB and VB deaths with extremely high wind, etc. These results demonstrate that Nepalese people are vulnerable to extreme climatic conditions and this warrants the need of more adaptation strategies to cope with such extreme events in Nepal. Apart from addressing the main cause of global warming, i.e., human activities that increase greenhouse gas concentration through common and widespread use of alternate renewable and eco-friendly energy technologies, Nepalese people faces the challenge and need in improving preparedness and adaptation strategies like cleaner surroundings and practices, coping effectively with diseases through improvement of infrastructure and facilities, assessing and educating the vulnerable section of our society, and enforcing regulations and laws to protect our environment as far as possible and feasible.

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Compliance with Ethical Standards

Conflict of Interests None

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