

El Niño Southern Oscillation, monsoon anomaly, and childhood diarrheal disease morbidity in Nepal

Nicholas Adams^a, Meghnath Dhimal^b, Shifali Mathews^a, Veena Iyer^c, Raghu Murtugudde^d, Xin-Zhong Liang^d, Muhiuddin Haider^a, Raul Cruz-Cano^e, Dang Thi Anh Thu^f, Jamal Hisham Hashim^g, Chuansi Gao^h, Yu-Chun Wangⁱ and Amir Sapkota^{a,*}

^aMaryland Institute for Applied Environmental Health, University of Maryland School of Public Health, College Park, MD 20742, USA

^bHealth Research Section, Nepal Health Research Council, Kathmandu 44600, Nepal

^cIndian Institute of Public Health Gandhinagar (IIPHG), Gandhinagar 382042, Gujarat, India

^dDepartment of Atmospheric and Oceanic Science, University of Maryland, College Park, MD 20742, USA.

^eDepartment of Epidemiology and Biostatistics, University of Maryland School of Public Health, College Park, MD 20742, USA.

^fInstitute for Community Health Research, Hue University of Medicine and Pharmacy, Hue City 52000, Vietnam

^gDepartment of Health Sciences, University Selangor Shah Alam Campus, Selangor 40000, Malaysia

^hDivision of Ergonomics and Aerosol Technology, Faculty of Engineering, Lund University, Lund 223 62, Sweden

ⁱDepartment of Environmental Engineering, Chung Yuan Christian University, Taoyuan City 320314, Taiwan.

*To whom correspondence should be addressed: Email: amirsap@umd.edu

Edited By: Sandro Galea.

Abstract

Climate change is adversely impacting the burden of diarrheal diseases. Despite significant reduction in global prevalence, diarrheal disease remains a leading cause of morbidity and mortality among young children in low- and middle-income countries. Previous studies have shown that diarrheal disease is associated with meteorological conditions but the role of large-scale climate phenomena such as El Niño-Southern Oscillation (ENSO) and monsoon anomaly is less understood. We obtained 13 years (2002–2014) of diarrheal disease data from Nepal and investigated how the disease rate is associated with phases of ENSO (El Niño, La Niña, vs. ENSO neutral) monsoon rainfall anomaly (below normal, above normal, vs. normal), and changes in timing of monsoon onset, and withdrawal (early, late, vs. normal). Monsoon season was associated with a 21% increase in diarrheal disease rates (Incident Rate Ratios [IRR]: 1.21; 95% CI: 1.16–1.27). El Niño was associated with an 8% reduction in risk while the La Niña was associated with a 32% increase in under-5 diarrheal disease rates. Likewise, higher-than-normal monsoon rainfall was associated with increased rates of diarrheal disease, with considerably higher rates observed in the mountain region (IRR 1.51, 95% CI: 1.19–1.92). Our findings suggest that under-5 diarrheal disease burden in Nepal is significantly influenced by ENSO and changes in seasonal monsoon dynamics. Since both ENSO phases and monsoon can be predicted with considerably longer lead time compared to weather, our findings will pave the way for the development of more effective early warning systems for climate sensitive infectious diseases.

Keywords: climate change, extreme event, diarrhea, Nepal, ENSO, El Niño

Significance Statement:

Climate change is impacting burden of infectious diseases across the globe. Using Nepal as a case study, here we show how large-scale weather phenomenon such as ENSO and monsoon anomaly can negatively impact the burden of diarrheal disease among young children. Since both ENSO and monsoon anomaly can be predicted with considerably longer lead time compared to weather—our findings may inform future development of early warning system with a longer lead time and enhance community resilience to threats of climate change in such resource limited settings.

Background

Diarrheal diseases are the leading causes of morbidity and mortality among young children, accounting for half a million deaths (1–3). Diarrhea causes dehydration and undernutrition due to a lack of nutrient absorption in intestinal cells, leading to a weakened immune system that may increases risk of infectious diseases in the short term, while enhancing susceptibility to chronic diseases over the lifespan (4, 5). Most recent estimates suggest that 88% of diarrhea-associated deaths are attributed to a lack

of proper water sanitation and hygiene (6). Despite a significant decline in burden across the globe since 1990, diarrheal diseases still remain a leading cause of childhood morbidity and mortality, particularly in low- and middle-income countries (LMICs) including Nepal (2, 3, 7–11). Overall burden of diarrheal diseases is expected to be worsened by ongoing climate variability and change (12, 13). Recent epidemiological studies and meta-analysis have linked higher temperature and precipitation as well as large-scale weather phenomenon such as El Niño-Southern Oscillation

Competing Interest: The authors declare no competing interest.

Received: October 26, 2021. **Revised:** February 2, 2022. **Accepted:** March 25, 2022

© The Author(s) 2022. Published by Oxford University Press on behalf of the National Academy of Sciences. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (<https://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact journals.permissions@oup.com



(ENSO) with burden of diarrheal diseases, particularly in the LMIC settings (12, 14–19).

Overall burden of diarrheal disease in Nepal is higher during the summer monsoon season (typically June–September), which is critical for agricultural productivity in the region (20). Typical summer monsoon season is characterized by warmer temperature that can promote bacterial growth and higher precipitation that can enhance fecal-oral route of exposure to these pathogens among communities lacking access to safe drinking water (13, 21, 22). Over the past century, there have been more frequent dry spells within a monsoon season (referred to as monsoon breaks) that give rise to short, frequent, and more intense wet spells (23). Recent data suggest that monsoon onset and withdrawal timings and rainfall distributions within the season are shifting, with the frequency of wet spells moving toward the latter part of the season and dry spells moving earlier (23). The solar dimming due to air pollution and aerosol loading have been blamed for the land not warming faster than the ocean as expected, resulting in a decrease in the Indian monsoon (24). However, the faster warming of land compared to oceans may have commenced impacting monsoon circulation, leading to stronger summer monsoons and weaker winter monsoons, thereby altering spatiotemporal variations in rainfall (25, 26). Yet, very few studies have investigated how ongoing anomalies in monsoon onset, withdrawal, and duration are driving the burden of diarrheal diseases.

In addition to the monsoon, large-scale phenomena such as ENSO are known to impact rainfall and temperature anomaly across South Asia including Nepal (20). For example, a positive Southern Oscillation Index (SOI) was associated with higher rainfall while negative SOI and more intense El Niño led to decreased rainfall (20). A recent study has reported an increasing temporal trend in total rainfall during the summer monsoon season in the Bagmati River Basin of Nepal (27), as well as the overall rainfall over Nepal (28).

Based on these prior observations, we hypothesize that both monsoon anomaly and phases of ENSO influence burden of childhood diarrheal disease burden in Nepal and that such burden vary by geographic region. Since anomalies in ENSO and the seasonal monsoon evolution can be forecasted with considerably longer lead times (months–seasons) as opposed to weather (1–10 days), we argue that findings from such studies will pave the way for the development of early warnings systems with longer lead time.

Methods

The study site consists of all 75 administrative districts in Nepal, which can be broadly categorized into 3 elevation-based regions encompassing altitudes that range from 60 to 8,848 m above sea level: the plains, hilly regions and mountainous regions. As a result of the large range of elevation throughout the country, there are many microclimates throughout Nepal, which greatly influence local temperature and precipitation patterns (28–30).

We obtained district level under-5 diarrheal disease data for the 2002–2014 period from Nepal's Health Management Information System (HMIS: <http://dohs.gov.np/>) operated by the Department of Health Services within the Ministry of Health and Population. Currently, the operational definition of diarrhea in Nepal consists of passage of 3 or more watery stools per day that are related to either bacterial, parasitic, or viral infections (31). We obtained meteorological data, including daily maximum temperature (TMAX) and precipitation from Nepal's Department of Hydrology and Meteorology for the period of 2002–2014. We also obtained monsoon information including its onset and withdrawal

dates for the country during 1984–2014 (32). We obtained information on the ENSO categories (Normal, El Niño, and La Niña) from NOAA that were derived based on Oceanic Niño Index (ONI) values, which measures the sea surface temperature anomalies in the Niño 3.4 region of the equatorial Pacific (33).

Statistical analysis

To ensure temporal alignment of the exposure and outcome variables, we converted all district level daily meteorological data to monthly scale to match the health data. We defined monsoon as the months of June, July, August, and September (Figure S1, Supplementary Material). We also established local climatology for temperature, and precipitation (by month and district), as well as monsoon onset and withdrawal dates (by year and country level) using a 30-year average (1984–2014). We calculated anomaly in monsoon onset, withdrawal, and duration by subtracting yearly values from their respective long-term averages. We categorized the anomaly in monsoon onset and withdrawal as early (< 30th percentile value), normal (30th–70th percentile value), or late (> 70th percentile value). Likewise, we categorized the temperature, and monsoon precipitation as above normal, normal, and below normal using the 30th and 70th percentile cutoff, determined based on their respective climatology.

We used a negative binomial Generalized Estimating Equations (GEE) (34) to estimate the associations between exposure variables and diarrheal disease risk in 75 districts in Nepal as described previously (13, 22, 35, 36). First, we conducted a univariate analysis to estimate the effects of total monthly precipitation, TMAX, monsoon, ENSO phases, elevation categories as well as categories of monsoon rainfall, onset, withdrawal, and duration. We then conducted a multivariate analysis that included total monthly precipitation, TMAX, season, ENSO phases, and elevation category using diarrheal disease data for the whole year (Model 1). We further stratified the analysis by elevation categories to investigate if the association varied across these categories. We performed additional analysis restricting the dataset to monsoon months alone (June–September) to investigate how changes in monsoon duration (Model 2), and monsoon onset and withdrawal (Model 3) impacted burden of diarrheal diseases. These models were adjusted for monthly rainfall (mm) and TMAX (°C).

Results

Of the 75 districts in Nepal, more than half are located in the hilly regions (39), followed by the plains (20) and mountain regions (16). The mean under-5 district-level population size is significantly larger in the plain region (83,964), compared to the hilly (37,089) or the mountain (16,829) regions ($P < 0.05$). Between July 2002 and June 2014, there were 13,580,925 diarrheal disease cases among < 5-y-olds in the 75 districts of Nepal. Median case rates (per 1,000) were significantly higher in the mountain region than in the hilly and plain regions during all ENSO phases (Table 1). Median case rates were highest during La Niña phases (30.5), compared to ENSO-neutral (25.7) and El Niño (15.7) phases.

The majority of the study months were categorized as having late monsoon onset (45.8%), followed by normal onset (37.5%) and early onset (16.7%; Table 2; Figure S2, Supplementary Material). Roughly, half of the study years were characterized as having normal monsoon withdrawals, while 45.8% and 4.1% were characterized as having early and late monsoon withdrawals, respectively. Likewise, the majority of the years witnessed normal monsoon duration (62.5%), while additional 33.4% and 4.1% of the years

Table 1. Distribution of under-5 diarrheal disease cases (median) in Nepal during 2002–2014, stratified by elevation categories. The values in the parenthesis represent the 25th and 75th percentiles.

Characteristics		Total	Plains	Hills	Mountains
Districts		75	20	39	16
Population under-5		38,772 (23,553–66,313)	83,964 (73,663–96,227)	37,089 (25,065–44,989)	16,829 (6,700–20,695)
Cases					
	Total	13,580,875	6,620,722	5,704,588	1,255,565
	Monthly	844 (372–1,728)	2,209 (887–3,471)	808 (421–1,391)	384 (108–779)
Monsoon cases					
	Total	5,512,079	2,499,730	2,451,073	561,276
	Monthly	1,125 (542–2,122)	2,431 (1,102–3,946)	1,080 (607–1,813)	551 (180–1,080)
Case rate/1,000					
	Overall	25.7 (10.7–45.4)	25.3 (9.0–41.3)	23.9 (11.0–44.7)	29.1 (12.5–57.9)
	La Niña	30.5 (18.1–46.2)	32.1 (19.8–43.7)	27.2 (16.0–43.1)	37.5 (21.3–60.3)
	El Niño	15.7 (8.1–32.0)	16.7 (7.9–32.0)	14.4 (7.9–29.1)	19.4 (9.6–42.4)
	Monsoon season				
	Neutral	32.0 (17.8–53.3)	29.9 (16.2–44.7)	30.4 (17.2–53.3)	41.4 (23.5–69.8)
	La Niña	40.5 (21.9–63.5)	36.1 (19.2–50.1)	38.2 (20.5–63.6)	50.8 (32.9–81.7)
	El Niño	22.4 (8.3–55.3)	17.8 (6.7–45.7)	21.5 (9.0–54.1)	33.2 (10.8–79.1)

Table 2. Meteorological data stratified by phases of ENSO.

Characteristics		Total	ENSO neutral	La Niña	El Niño
District-months		10,768	5,309 (49.3%)	3,221 (29.9%)	2,238 (20.8%)
Monsoon onset					
	Normal	37.50%	32.40%	44.20%	40.00%
	Early	16.70%	14.10%	21.00%	16.80%
	Late	45.80%	53.50%	34.80%	43.20%
Monsoon withdrawal					
	Normal	50.10%	56.40%	34.80%	56.80%
	Early	4.10%	0.00%	0.00%	19.90%
	Late	45.80%	43.60%	65.20%	23.20%
Monsoon duration					
	Normal	62.50%	63.40%	60.40%	63.30%
	Short	4.10%	0.00%	0.00%	19.90%
	Long	33.40%	36.60%	39.60%	16.80%
TMAX (Celsius), median (25th–75th %ile)					
	Plains	31.9 (26.7–33.9)	33.1 (30.2–35.0)	30.2 (25–32.8)	29.8 (24.8–32.8)
	Hills	26.1 (22.2–30.2)	28.1 (23.7–31.2)	24.7 (21.0–28.8)	24.0 (20.6–28.6)
	Mountains	22.6 (18.5–25.7)	23.6 (20.1–26.8)	21.3 (17.2–24.7)	20.6 (16.5–24.4)
Median monthly rainfall (25th–75th %ile), mm					
	Plains	40.5 (0.9–212.1)	81.8 (11.8–234.8)	7.9 (0–148.9)	28.1 (0–182.4)
	Hills	56.4 (8.0–218.5)	94.1 (23.6–246.6)	22.0 (0–152.7)	40.1 (4.3–188.0)
	Mountains	40.7 (7.2–133.4)	55.0 (16.8–162.9)	24.9 (2.0–96.7)	28.9 (4.0–107.3)
Median monsoon monthly rainfall (25th–75th %ile), mm					
	Plains	314.8 (190.1–471.1)	297.0 (176.0–438.0)	380.5 (263.3–552.5)	276.2 (173.0–524.1)
	Hills	311.9 (190.9–455.6)	296.4 (181.6–429.5)	368.6 (239.5–523.9)	283.3 (169.6–479.7)
	Mountains	209.6 (63.2–393.5)	189.9 (60.2–358.3)	278.6 (107.7–476.3)	180.6 (58.2–408.5)
Precipitation category					
	Below average	29.80%	32.10%	19.60%	34.80%
	Average	39.80%	41.30%	40.10%	35.50%
	Above average	30.40%	26.60%	40.30%	29.70%

were classified as having long and short monsoon season, respectively. We observed that monsoon duration was driven largely by timing of monsoon withdrawal. La Niña monsoons brought in significantly higher rainfall compared to monsoons during ENSO-neutral or El Niño phases (Table 2).

Overall, higher monthly temperature was significantly associated with increases in diarrheal disease rate (Table 3) among < 5-y-olds (Incident Rate Ratio [IRR]: 1.02; 95% CI: 1.02–1.03), with a slightly higher rate of diarrheal disease in the hilly and mountain regions (4%) compared to the plains region (1%). Likewise, the

monsoon season was associated with a 21% increase in diarrheal disease (IRR: 1.21; 95% CI: 1.16–1.27), which was fairly consistent across the 3 elevation categories, ranging from 17% to 21% increases (Table 3). Compared to the ENSO neutral phase, the El Niño phase was characterized by an 8% reduction in the under-5 diarrheal disease cases (IRR: 0.92; 95% CI: 0.88–0.95) while the La Niña phase was associated with a 32% increase (IRR: 1.32; 95% CI 1.28–1.37). The increased risk of diarrheal disease associated with La Niña periods was higher in the mountain region (IRR: 1.53; 95% CI 1.39–1.68) than in the hilly (IRR: 1.31; 95% CI 1.24–1.38) or

Table 3. IRR and 95% CI depicting association between meteorological variables, ENSO phases, and diarrheal disease risk in Nepal during 2002–2014.

	Overall			Plain			Hill			Mountain		
	IRR	LCL	UCL	IRR	LCL	UCL	IRR	LCL	UCL	IRR	LCL	UCL
Rainfall	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Tmax	1.02	1.02	1.03	1.01	1.00	1.02	1.04	1.03	1.04	1.04	1.03	1.05
Monsoon	1.21	1.16	1.27	1.19	1.07	1.32	1.21	1.13	1.30	1.17	1.04	1.32
ENSO phase	Neutral	1.00	—	—	1.00	—	1.00	—	—	1.00	—	—
	La Niña	1.32	1.28	1.37	1.32	1.22	1.42	1.31	1.24	1.38	1.53	1.39
	El Niño	0.92	0.88	0.95	0.90	0.83	0.99	0.91	0.86	0.97	0.94	0.84

Table 4. Association between monsoon duration, rainfall, phases of ENSO, and district level under-5 diarrheal disease cases in Nepal during 2002–2014, stratified by elevation categories.

	Overall			Plain			Hill			Mountain		
	IRR	LCL	UCL	IRR	LCL	UCL	IRR	LCL	UCL	IRR	LCL	UCL
Duration												
ENSO	Normal	1.00	—	—	1.00	—	—	1.00	—	—	1.00	—
	Short	1.32	1.16	1.50	0.79	0.60	1.04	1.60	1.32	1.94	2.86	2.09
	Long	0.99	0.93	1.05	1.08	0.94	1.23	0.93	0.85	1.01	1.00	0.86
Monsoon rainfall (percentile)	Neutral	1.00	—	—	1.00	—	—	1.00	—	—	1.00	—
	La Niña	1.17	1.10	1.26	1.13	0.98	1.31	1.19	1.07	1.31	1.30	1.10
	El Niño	0.87	0.80	0.94	0.91	0.76	1.09	0.84	0.75	0.95	0.75	0.62
	< 30th	1.00	—	—	1.00	—	—	1.00	—	—	1.00	—
	30th–70th	1.02	0.95	1.10	0.97	0.84	1.13	1.01	0.91	1.12	1.30	1.05
	> 70th	1.10	1.02	1.20	1.03	0.87	1.21	1.07	0.94	1.21	1.51	1.19

plains regions (IRR: 1.32; 95% CI 1.22–1.42; Table 3). The decreases in diarrheal disease rates observed during the El Niño periods was consistent across the 3 regions, with the reduction in risk ranging from 6% in mountain region to 10% in the plain region (Table 3).

To further investigate the role of the seasonal monsoon anomalies on diarrheal disease burden, we conducted a subanalysis restricted to the monsoon season alone (Table 4). During the study period, a short monsoon duration was associated with increased incidence of diarrheal disease in the nationwide model (IRR: 1.32; 95% CI: 1.16–1.50). When stratifying the analysis by elevation category, a short monsoon duration remained significantly associated with increased diarrheal disease incidence in the hilly (IRR: 1.60; 95% CI: 1.32–1.94) and mountain (IRR: 2.86; 95% CI: 2.09–3.91) regions, but a negative nonsignificant association was observed in the plain region. Longer monsoon duration was not associated with diarrheal disease rates in the nationwide or the stratified analysis (Table 4).

We further investigated how the timing of the monsoon onset and withdrawal may influence the burden of diarrheal disease during summer months (Fig. 1). In the nationwide analysis, early onset of monsoon was associated with a 7% decrease in diarrheal disease (IRR: 0.93, 95% CI: 0.85–1.01) and the hilly region (IRR 0.85, 95% CI: 0.75–0.96). However, a positive association was observed for mountain region. Late onset of monsoon was associated with increases in burden of diarrheal disease in the national as well as regional analysis (Fig. 1). Both early and late onset of monsoon withdrawals were associated with a consistent increase in diarrheal disease risk in the nationwide as well as regional analysis.

As with the overall analysis using the whole year data (Table 3), phases of ENSO were significantly associated with the diarrheal disease burden in the monsoon only analysis with a noted

differences in magnitude. For example, the La Niña phase was associated with a 17% increase, while the El Niño phase was associated with a 13% reduction in rates of diarrheal diseases nationally during monsoon season. The most pronounced influence of ENSO was observed in the mountain region where the La Niña was associated with a 30% increase (IRR: 1.30, 95% CI: 1.05–1.60) while the El Niño phase was associated with a 25% reduction (IRR: 0.75; 95% CI: 0.62–0.92) in rates of diarrheal diseases during the monsoon season.

Rainfall anomaly during the monsoon season was associated with the burden of diarrheal disease in Nepal (Table 4). Compared to a low monsoon rainfall (< 30th percentile value), high (> 70th percentile value) rainfall was associated with 10% (IRR: 1.10; 95% CI: 1.02–1.20) increase in rates of diarrheal disease nationally. This was considerably higher in the mountain region with the high monsoon rainfall associated with 51% increases in risk (IRR: 1.51, 95% CI: 1.19–1.92).

Discussion

As compared to weather, large-scale climate phenomena, such as ENSO phases and monsoon evolutions, can be reasonably predicted with subseasonal to seasonal lead times. As such, early warning systems based on such large-scale phenomena have the potential to provide public health professionals the critical lead time necessary to prepare for increases in climate-sensitive disease burden, including diarrheal diseases. The first essential step to building such a warning system is to better characterize the empirical relationship between these climate phenomena and human health outcomes. To that end, our study provides the first ever quantitative assessment of how anomalies in monsoon

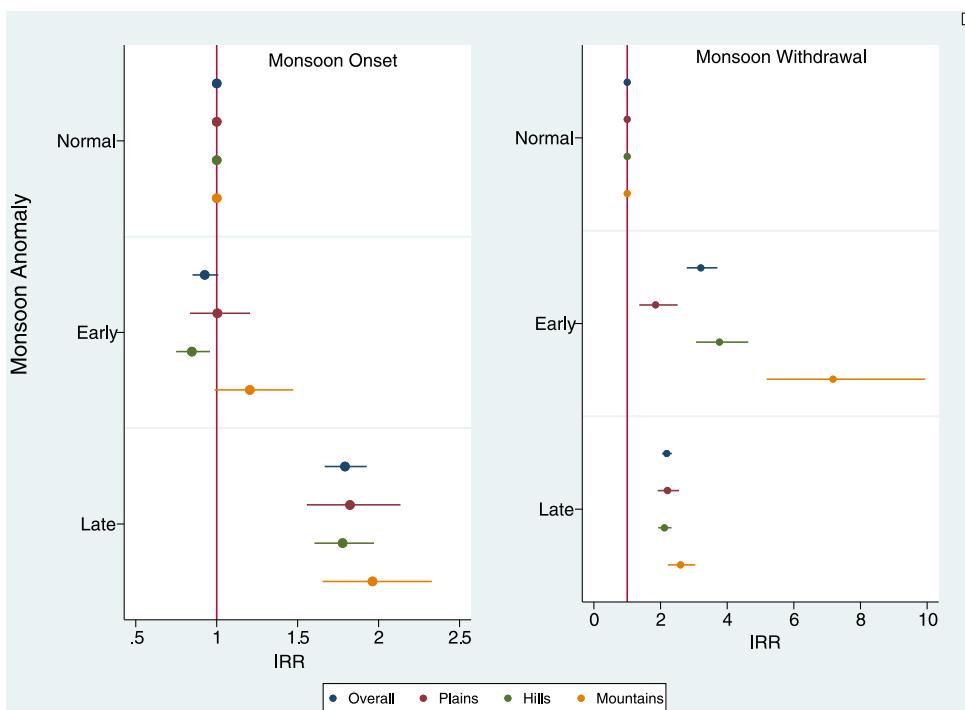


Fig. 1. IRR and 95% CI for monsoon anomaly (early: < 30th percentile, late: > 70th percentile, vs. normal: 30th–70th percentile values) and risk of diarrheal disease.

rainfall, onset, withdrawal, and duration as well as phases of ENSO impact childhood diarrheal disease burden in Nepal and how this relationship vary by elevation categories.

Our findings suggest that early monsoon onset is associated with decreases while late monsoon onset is associated with increases in diarrheal disease burden. We also observed that both early and late monsoon withdrawals are associated with increases in rates of diarrheal disease rates. Consistent with the findings regarding the timing of monsoon onset, we observed that shorter monsoon duration (late onset and/or early withdrawal) is associated with higher rates of diarrheal disease, while longer monsoon duration (early onset and/or late withdrawal) had no discernable impact. The exact mechanism by which changes in monsoon onset and withdrawal impact diarrheal disease rate remains unclear. While it is tempting to suggest that changes in monsoon onset and withdrawal related diarrheal disease rates must be tied to monsoon rainfall, our analysis was adjusted for the total rainfall amount. Furthermore, we investigated if anomalies in monsoon seasonal cycle were tied to rainfall amount, but we did not observe a clear pattern that could explain the observed association with diarrheal disease rates. Additional studies are needed to verify our findings regarding monsoon anomaly and under-5 diarrheal disease burden, as well as disentangle the underlying mechanism influencing this relationship. Besides overall rainfall, such studies should investigate if anomalies in monsoon onset and withdrawal impact the frequency of intense rainfall events that induce flooding and diarrheal diseases.

We observed a positive relationship between temperature and increase in diarrheal disease rates nationally, and across all regions, with a noted exception for the plain region. Higher ambient temperatures may increase the transmission of diarrheal diseases by increasing bacterial yields in drinking water and animal reservoirs, as well as leading to spoiled food that promotes diarrheal pathogen growth (37). The null association observed in the

plain region is likely because temperature is not a growth limiting factor in these low-lying areas with a tropical climate (38). In fact, the median value for monthly maximum (minimum) temperature in the plain region of Nepal during the study period was 31.9°C (20.0°C), compared to 26.1°C (14.6°C), and 22.6°C (8.9°C) in the hilly and mountainous regions, respectively. Thus, the increases in temperature that helps bacterial growth in the hilly and the mountainous regions is not associated with disease risk in the plain region, where it is not a rate limiting factor. Our findings are particularly relevant given a recent study that showed the increasing trend of temperature is more pronounced in the mid- to high-altitude regions of Nepal (39, 40). Taken together, the burden of diarrheal diseases may considerably increase in the hilly and mountain regions of Nepal in response to climate change.

Heavy rainfall and flooding can spread bacterial pathogens and increase population exposure through contamination of unprotected drinking water sources (41). Since significant proportion of the Nepali population lacks reliable municipal drinking water, fecal-oral route of exposure remains a major threat during and after extreme precipitation events (39). Our findings regarding high monsoon rainfall and increased diarrheal disease rate is consistent with study by Demitrova and Bora who found a similar association between abnormally wet monsoon months and increased childhood diarrhea, observed exclusively in the mountainous regions in India (42). Our monsoon rainfall-related findings were more pronounced in the mountain regions compared to the plain regions. This could be due, at least in part, to the fact that most of the population centers in Nepal are located in the plain region, suggesting that this area may have higher prevalence of improved water and sanitation infrastructure, which minimizes fecal-oral route of exposure to bacterial and viral pathogens.

We observed higher rates of diarrheal disease during La Niña periods, while the rates were lower during the El Niño phase. These findings could be explained, in part, by previous studies,

which found that ENSO is a key driver of precipitation in South Asia (20) and is associated with the frequency of extreme precipitation events in Nepal specifically (43). This hypothesis is supported by our data showing considerably higher median monthly precipitation during La Niña monsoon periods compared to both ENSO neutral or El Niño monsoon periods. These findings suggest that ENSO may be a key factor driving annual rainfall and extreme precipitation events in Nepal during the summer monsoon season, which could both play a significant role in the spread of diarrheal pathogens throughout the country.

There are several strengths of this study, including national level data with a long temporal coverage. This study provides the first quantitative estimate of diarrheal disease burden that is tied to anomalies in monsoon rainfall, onset, and withdrawal, as well as phases of ENSO. The anomalies were calculated using a 30-year baseline, which enabled us to estimate climatic influence on the disease burden. Since seasonal monsoon evolution and phases of ENSO can be reliably predicted with considerably longer lead times compared to 1–10 days for weather forecasts, our findings will inform early warning systems for climate sensitive infectious diseases with longer lead time, as proposed under the Ready-Set-Go framework for managing weather related health impacts (44). The concept is to ready the decision system based on the seasonal forecasts and set the assets in place based on the subseasonal forecasts (weeks 2–4). The Go step kicks in with the weather forecasts at short (days 1–3) and medium (days 3–10) range (44). Our study also has several limitations including lack of daily or weekly outcome data. Our study included a relatively short time period (2002–2014) for investigating influence of climatological phenomenon such as ENSO and monsoon anomaly. Future studies with longer time period are warranted to replicate our findings. Likewise, since we did not have individual level data, we could not investigate how the risk varied by sociodemographic factors, access to piped water as well as vaccination against diarrheal diseases. Our analysis focused on overall diarrhea as information regarding specific pathogens were not available.

Conclusions

Our data suggest that ENSO phases and monsoon evolutions (onset and withdrawal timing, duration, as well as rainfall intensity) are significant predictor of under-5 diarrheal disease burden in Nepal. Given both ENSO phases and monsoon evolutions can be predicted with considerably longer lead times than weather forecasts, incorporating them in the early warning systems for climate sensitive health outcomes can significantly improve the prediction lead time, allowing public health professionals critical time to prepare.

Supplementary Material

Supplementary material is available at [PNAS Nexus](https://pnasnexus.pnas.org/article/1/2/pgac032/6555459) online.

Funding

This work was supported by grants from the National Science Foundation through Belmont Forum (award number (FAIN): 2025470). N.A. was supported by the NRT-INFEWS: UMD Global STEWARDS (STEM Training at the Nexus of Energy, WAtter Reuse and FooD Systems) that was awarded to the University of Maryland School of Public Health by the National Science Foundation National Research Traineeship Program (award number 1828910). Y.W. was supported by the Taiwan Ministry of Science and

Technology (MOST 109-2621-M-033-001-MY3 and MOST 110-2625-M-033-002).

Authors' contributions

Designed the research: M.D., and A.S.; performed the research: N.A., M.D., V.I., R.M., X.L., C.G., Y.W., and A.S.; analyzed the data: N.A. and A.S.; wrote the paper: N.A., M.D., V.I., R.M., X.L., M.H., R.C., T.A., J.H., C.G., Y.W., and A.S. C.G. was supported by Swedish Research Council for Health, Working Life and Welfare.

Data availability

Weather data will be shared freely. Diarrheal disease data from Nepal is restricted because of human subject concerns.

References

1. Qazi S, et al. 2015. Ending preventable child deaths from pneumonia and diarrhoea by 2025. Development of the integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea. *Arch Dis Child* 100(Suppl 1):S23–S28.
2. Troeger C, et al. 2018. Global disability-adjusted life-year estimates of long-term health burden and undernutrition attributable to diarrhoeal diseases in children younger than 5 years. *Lancet Glob Health* 6:e255–e269.
3. Walker CLF, et al. 2013. Global burden of childhood pneumonia and diarrhoea. *Lancet North Am Ed* 381:1405–1416.
4. Katona P, Katona-Apte J. 2008. The interaction between nutrition and infection. *Clin Infect Dis* 46:1582–1588.
5. Martins VJ, et al. 2011. Long-lasting effects of undernutrition. *Int J Environ Res Pub Health* 8:1817–1846.
6. CDC. 2015. Diarrhea: common illness, global killer. Global diarrhea burden. (Centers for Disease Control and Prevention).
7. Wolf J, et al. 2018. Impact of drinking water, sanitation and handwashing with soap on childhood diarrhoeal disease: updated meta-analysis and meta-regression. *Trop Med Int Health* 23:508–525.
8. Mokomane M, Kasvosve I, de Melo E, Pernica JM, Goldfarb DM. 2018. The global problem of childhood diarrhoeal diseases: emerging strategies in prevention and management. *Ther Adv Infect Dis* 5:29–43.
9. Khanal V, Bhandari R, Karkee R. 2013. Non medical interventions for childhood diarrhoea control: way forward in Nepal. *Kathmandu Univ Med J* 11:256–261.
10. Das JK, Bhutta ZA. 2016. Global challenges in acute diarrhea. *Curr Opin Gastroenterol* 32:18–23.
11. Burnett E, Jonesteller CL, Tate JE, Yen C, Parashar UD. 2017. Global impact of rotavirus vaccination on childhood hospitalizations and mortality from diarrhea. *J Infect Dis* 215:1666–1672.
12. Carlton EJ, Woster AP, DeWitt P, Goldstein RS, Levy K. 2016. A systematic review and meta-analysis of ambient temperature and diarrhoeal diseases. *Int J Epidemiol* 45:117–130.
13. Jiang C, et al. 2015. Climate change: extreme events and increased risk of salmonellosis in Maryland, USA: evidence for coastal vulnerability. *Environ Int* 83:58–62.
14. Colston J, et al. 2020. Pathogen-specific impacts of the 2011–2012 La Niña-associated floods on enteric infections in the MAL-ED Peru Cohort: a comparative interrupted time series analysis. *Int J Environ Res Public Health* 487:17.
15. Heaney AK, Shaman J, Alexander KA. 2019. El Niño–Southern oscillation and under-5 diarrhea in Botswana. *Nat Commun.* 10:5798.

16. Liang M, Ding X, Wu Y, Sun Y. 2021. Temperature and risk of infectious diarrhea: a systematic review and meta-analysis. *Environ Sci Pollut Res* 28:68144–68154.

17. Wang H, et al. 2019. Association of meteorological factors with infectious diarrhea incidence in Guangzhou, southern China: a time-series study (2006–2017). *Sci Total Environ* 672: 7–15.

18. Watts N, et al. 2017. The Lancet Countdown: tracking progress on health and climate change. *Lancet*. 389:1151–1164.

19. Ghazani M, FitzGerald G, Hu W, Toloo GS, Xu Z. 2018. Temperature variability and gastrointestinal infections: a review of impacts and future perspectives. *Int J Environ Res Public Health* 766:15.

20. Shrestha ML. 2000. Interannual variation of summer monsoon rainfall over Nepal and its relation to Southern Oscillation Index. *Meteorol Atmos Phys* 75:21–28.

21. Rose JB, et al. 2000. Climate and waterborne disease outbreaks. *J Am Water Works Assoc* 92:77–87.

22. Iyer V, et al. 2021. Role of extreme weather events and El Niño Southern Oscillation on incidence of Enteric Fever in Ahmedabad and Surat, Gujarat, India. *Environ Res* 196:110417.

23. Vinnarasi R, Dhanya CT. 2016. Changing characteristics of extreme wet and dry spells of Indian monsoon rainfall. *J Geophys Res Atmos* 121:2146–2160.

24. Roxy MK, et al. 2015. Drying of Indian subcontinent by rapid Indian Ocean warming and a weakening land-sea thermal gradient. *Nat Commun* 6:7423.

25. Seneviratne SI, et al. 2012. Changes in climate extremes and their impacts on the natural physical environment" in managing the risks of extreme events and disasters to advance climate change adaptation. Cambridge: Cambridge University Press. p. 109–230.

26. Jin Q, Wang C. 2017. A revival of Indian summer monsoon rainfall since 2002. *Nat Clim Change* 7:587–594.

27. Shrestha R, Sthapit A. 2015. Temporal variation of rainfall in the Bagmati River Basin, Nepal. *Nepal J Sci Technol*. 16:31–40.

28. Sigdel M, Ikeda M. 2012. Summer monsoon rainfall over Nepal related with large-scale atmospheric circulations. *J Earth Sci Clim Change*. 3:112.

29. Dhimal M, Ahrens B, Kuch U. 2014. Species composition, seasonal occurrence, habitat preference and altitudinal distribution of malaria and other disease vectors in eastern Nepal. *Parasitosis* 7:540.

30. Sigdel SR, et al. 2018. Moisture-mediated responsiveness of tree-line shifts to global warming in the Himalayas. *Glob Change Biol* 24:5549–5559.

31. Bhandari D, Bi P, Sherchan JB, Dhimal M, Hanson-Easey S. 2020. Assessing the effect of climate factors on childhood diarrhoea burden in Kathmandu, Nepal. *Int J Hyg Environ Health* 223:199–206.

32. Government of Nepal. Nepal (2020) Monsoon Onset and Withdrawal Date Information. Ministry of Energy, Water Resource and Irrigation, Department of Hydrology and Meteorology, Climate Division (Climate Analysis Section).

33. NOAA. 2021. Cold & Warm Episodes by Season. (Climate Prediction Center).

34. Byers AL, Allore H, Gill TM, Peduzzi PN. 2003. Application of negative binomial modeling for discrete outcomes: a case study in aging research. *J Clin Epidemiol* 56:559–564.

35. Soneja S, et al. 2016. Extreme precipitation events and increased risk of campylobacteriosis in Maryland, U.S.A. *Environ Res* 149:216–221.

36. Morgado ME, et al.. 2021. Climate change, extreme events, and increased risk of salmonellosis: foodborne diseases active surveillance network (FoodNet), 2004–2014. *Environ Health* 20: 105.

37. Levy K, Woster AP, Goldstein RS, Carlton EJ. 2016. Untangling the impacts of climate change on waterborne diseases: a systematic review of relationships between diarrheal diseases and temperature, rainfall, flooding, and drought. *Environ Sci Technol* 50:4905–4922.

38. Hassard F, et al. 2016. Abundance and distribution of enteric bacteria and viruses in coastal and estuarine sediments - a review. *Front Microbiol* 7:1692.

39. Khatiwada KR, Panthi J, Shrestha ML, Nepal S. 2016. Hydro-climatic variability in the Karnali river basin of Nepal Himalaya. *Climate*. 4:17.

40. Shrestha AB, Aryal R. 2011. Climate change in Nepal and its impact on Himalayan glaciers. *Region Environ Change* 11:65–77.

41. Eisenhauer IF, et al. 2016. Estimating the risk of domestic water source contamination following precipitation events. *Am J Trop Med Hyg* 94:1403–1406.

42. Dimitrova A, Bora JK. 2020. Monsoon weather and early childhood health in India. *PLoS ONE* 15:e0231479.

43. Bohlinger P, Sorteberg A. 2018. A comprehensive view on trends in extreme precipitation in Nepal and their spatial distribution. *Int J Climatol* 38:1833–1845.

44. Bazo J, Singh R, Destrooper M, Coughlan de Perez E. 2019. Chapter 18 - pilot experiences in using seamless forecasts for early action: the "Ready-Set-Go!" approach in the Red Cross in sub-seasonal to seasonal prediction. In: Robertson AW, Vitart F, editors. Amsterdam: Elsevier. p. 387–398.