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## ABSTRACT

**Introduction:** Enteric Fever (EF) affects over 14.5 million people every year globally, with India accounting for the largest share of this burden. The water-borne nature of the disease makes it prone to be influenced as much by unsanitary living conditions as by climatic factors. The detection and quantification of the climatic effect can lead to improved public health measures which would in turn reduce this burden.

**Methodology:** We obtained a list of monthly Widal positive EF cases from 1995 to 2017 from Ahmedabad and Surat Municipalities. We obtained population data, daily weather data, and Oceanic Niño Index values from appropriate sources. We quantified the association between extreme weather events, phases of El Niño Southern Oscillations (ENSO) and incidence of EF.

**Results:** Both cities showed a seasonal pattern of EF, with cases peaking in early monsoon. Risk of EF was affected equally in both cities by the monsoon season -- Ahmedabad (35%) and Surat (34%). Extreme precipitation was associated with 5% increase in EF in Ahmedabad but not in Surat. Similarly, phases of ENSO had opposite effects on EF across the two cities. In Ahmedabad, strong El Niño months were associated with 64% increase in EF risk while strong La Niña months with a 41% reduction in risk. In Surat, strong El Niño was associated with 25% reduction in risk while moderate La Niña with 21% increase in risk.

**Conclusions:** Our results show that the risk of EF incidence in Gujarat is highly variable, even between the two cities only 260 kms apart. In addition to improvements in water supply and sewage systems, preventive public health measures should incorporate variability in risk across season and phases of ENSO. Further studies are needed to characterize nationwide heterogeneity in climate-mediated risk, and to identify most vulnerable populations that can benefit through early warning systems.

**Key words:** Typhoid and climate; Typhoid and ENSO; Enteric Fever and El Niño; Climate and Typhoid; El Niño and Typhoid in India

## INTRODUCTION

Enteric Fever (EF) is a systemic disease caused due to infection by *Salmonella enterica* serovars Typhi and Paratyphi. Despite considerable progress made over the past few decades, EF remains a major disease burden, particularly in the low and middle income countries (1). Most recent data suggest that there were over 14.5 million cases of EF in 2017 alone, resulting in over 135.9 thousand deaths. The largest population burden of EF in the world is in India (2). Studies have suggested that ongoing climate variability and change may negatively impact the burden of EF (3,4). EF is a systemic infection, exclusive to humans, which is caused by gram-negative bacterium, *Salmonella enterica*, belonging to serovars *Typhi* and *Paratyphi* (also known as typhoidal *Salmonella*). Their presence in the environment is maintained through cases and carriers (5). EF is transmitted from person to person through fecal-oral route involving contaminated food and water (3). Eighty-five percent of the global burden of EF is contributed collectively by Pakistan, India, and Bangladesh (6,7). While the Global Burden of Disease (GBD) estimates the incidence of Typhoid and Paratyphoid in South Asia at 550 cases per 100,000 individuals (2), a recent Indian review arrived at a pooled community level incidence of 377 cases per 100,000 based on three studies reporting culture-confirmed cases (8). In these haphazardly urbanizing countries, the disease mostly afflicts the poor, living in slums. The traditional public health measures of reducing EF burden, namely, safe water and basic sanitation, require large infrastructural investment. In addition, available vaccines are not suitable for mass administration, and are not expected to be deployed any time soon (6,9,10). A clearer and more comprehensive elucidation of the seasonal nature of EF could lead to less demanding and more efficient public health measures to reduce its burden.

A recent systematic review assessed the seasonal and spatial dynamics of EF across the globe. This study analyzed 114 datasets from 33 countries and found a clear seasonal pattern of EF, which became markedly pronounced at latitudes away from the equator (11). Three other studies have explored the association of EF incidence with climatic factors in Asian countries. Kelly-Hope et al. (2007) identified humidity to be positively associated with EF in Vietnam from 1991 to 2001 (3). Subsequent study by the same authors concluded a year later that although climate factors - hotter, wetter and more humid climate - define high-risk periods, these are only one component of a multitude of complex interactions that exacerbate the disease (12). Wang et al (2012) observed that the incidence of EF in Guizhou district of China during 1984-2007 was closely associated with a hotter (temperature) and wetter (rainfall) climate, but not with relative humidity (13). Unlike the Vietnamese study, the disease peak in this Chinese study occurred after a month of hot and wet weather. Dewan et al. (2013) reported similar findings in Dhaka city of Bangladesh, but for a shorter time period (2005-2009). They observed an increase in EF incidence in a hotter and wetter climate at time lags ranging from three to five weeks.(4) The definition of a case varied in the three settings. In Vietnam and China, clinically diagnosed and laboratory confirmed cases were combined and treated as EF, while in Bangladesh only those cases that had been diagnosed through culture or Widal test were classified as EF cases.

Despite the known positive relation between climatic factors ( temperature and precipitation) and risk of EF, no studies to date have explored how extreme weather events, which are projected to increase in response to climate change, impact burden of EF in a high risk country like India. Likewise, to the best of our knowledge, no studies to date have investigated how large scale weather phenomenon such as the El Niño Southern Oscillations (ENSO) impact the risk of EF on the Indian subcontinent. ENSO is an anomaly in sea surface temperature in the Niño 3.4

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4 85 region of the deep tropical Pacific that oscillates between positive (warmer: El Niño) and the  
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6 86 negative (cooler: La Niña) phase. These phases of ENSO are known to affect weather regimes  
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9 87 across the globe and impact human health outcomes (14). Numerous infectious diseases (vector-  
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11 88 borne and enteric) have been found to vary with weather in regions that experience such ENSO-  
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14 89 driven weather anomalies (11). The incidence rate of cholera in Bengal over the last century has  
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16 90 shown a definite, though weak correlation with ENSO cycles between 1893 to 1920, but a very  
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19 91 strong correlation from 1980 to 2001 (12). Recent publications have reported that in Africa, during  
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21 92 El Niño years, cholera incidences shift to the eastern part of the continent while in the United  
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24 93 States, the incidence of enteric diseases increases markedly in the Northeastern region (15,16).  
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26 94 Since the relationship between ENSO and intensity of the Indian monsoon is well established, one  
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29 95 would expect that ENSO may indirectly drive the risk of EF in India (17). Anthropogenically  
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31 96 forced warming is now shown to affect not only the land and ocean warming with associated  
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34 97 humidity changes, but also the pattern and life cycle of ENSO itself (18,19). The net impact of  
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36 98 these cascading manifestations of greenhouse gas warming on human health outcomes will  
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42 100 Enteric fever , controlled quite effectively in developed countries, continues to pose a grave  
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44 101 public health challenge in Asia, Africa and Latin America (20). India bears the highest burden of  
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47 102 (EF). Although, EF is endemic to India, there is a paucity of data regarding how the ongoing  
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50 103 climate variability and change are impacting burden of EF in India. To address this, we  
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52 104 investigated the association between extreme weather events, phases of ENSO and EF in cities of  
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54 105 Ahmedabad and Surat in the western state of Gujarat.  
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## METHODS

We collected EF cases, daily weather, and population data for Ahmedabad and Surat cities, both located in the state of Gujarat, India. Ahmedabad city, with a population of 6 million is the seventh largest metropolis of the country (21), while Surat with a population of 4.4 million, is the fastest growing city in the country (22). Although the two cities are only 260 kms apart, significant differences exist in their weather patterns. Ahmedabad is an inland city with a semi-arid hot climate with Sabarmati river bisecting the city (Figure 1a). Surat is a coastal city with a tropical sub-humid climate that experiences moderately abundant rainfall and is located beside the river Tapi (23). The 2001 census showed that the slum populations comprised 12.5% of Ahmedabad's and 16.7% of Surat's population (24). A 2008-09 survey showed that both cities had very similar water supply infrastructure with 85% of the households in the service area possessing direct water connections. The sewerage and toilet coverage in Surat was marginally better than in Ahmedabad. However, in slums, access to individual/community toilets and a sewerage connection was 65% in Ahmedabad, but only 41% in Surat (25).

We obtained aggregated monthly numbers of Widal positive, address-confirmed, EF cases of past 23 years (January 1995 to December 2017), totaling up to 20,544 cases, reported to the Epidemic control cell of the Health Department of the Ahmedabad Municipal Corporation (AMC). We also obtained 8,692 monthly EF cases from Surat Municipal Corporation (SMC). We obtained decadal population count from 1961 to 2011 within the official city limits, as well as the recasted population of the expanded city limits during the previous census years for both cities from the Gujarat State Census department. The decadal population growth in Ahmedabad for the years 1991, 2001 and 2011 was 22%, 26%, and 50% respectively. The sharp increase of the city's census population in 2011 was due to the expansion of the city limits in 2006 with the addition of 158.86

sq. kms of peri-urban area, composed of 21 wards and a population of 1.1 million (Figure 1a). In Surat the decadal growth rate for the years 1991, 2001 and 2011 was 93%, 62% and 83%, respectively (Figure 1b). We interpolated mid-year populations from a line fitted to the recasted population to calculate monthly-normalized EF case rates (NEF) for both the cities for our preliminary analysis.

### **Figure 1 a and b here**

We obtained monthly maximum and minimum temperatures (Tmax and Tmin), relative humidity (RH) and rainfall data for Ahmedabad and Surat from the Indian Institute of Tropical Meteorology (IITM). The monthly Oceanic Niño Index (ONI) values, used to define phases of ENSO, were obtained from the NOAA (26). We also calculated monthly Extreme Heat Events (EHE) and Extreme Precipitation Events (EPE) for both cities, following Jiang et al (27). We used 20 years (1980-1999) of baseline data to compute city and calendar day-specific 95th percentile thresholds for maximum temperature and precipitation. We compared the daily maximum temperature and rainfall values during the study period to their location and calendar day-specific 95th percentile thresholds. Days where the Tmax exceeded 95th percentile temperature thresholds were coded as “1” and defined as extreme heat events (EHE) while those exceeding the precipitation thresholds were defined as extreme precipitation events (EPE). Both EHE and EPE were summed over calendar months to obtain monthly EHE and EPE events for each city. We used descriptive statistics and anomaly graphs to examine the monthly trend of EF cases, cumulated by months during a year and across the study period of 23 years. We calculated descriptive statistics to detect effects of ENSO categories on monthly and annual case incidences, climate variables and extreme heat and precipitation events. We used negative binomial generalized estimating equations to quantify the association between extreme weather events,

phases of El Niño Southern Oscillations and incidence of EF (28,29). The full model consisted of EHE, EPE, phases of ENSO (strong El Niño, moderate El Niño, neutral, moderate La Niña, strong La Niña), and monsoon season (yes/no). First, we performed the analysis for Ahmedabad, and Surat separately, and then repeated it by combining the cases from both cities together.

## RESULTS

Normalized EF (NEF) cases for Ahmedabad ranged from 0.03 to 4.6 monthly cases per 100,000 population (Figure 2). Inter-annual variability of cases showed a decadal pattern. Between 1995 to 2005, cases reduced and maintained a steady seasonal pattern, while in the recent decade (2005-17) cases increased. For Surat, NEF case incidence ranged from 0.05 to 2.89 per 100,000 populations. Within this narrow range, there is a seasonal pattern but no obvious long term trend. An initial drop in cases in 2000, was followed by a steady rise from 2003 to 2010, after which there was a gradual drop again (Figure 2). The graphs of these two cities over the 23 years, in large parts curved in opposite directions. There were three main episodes of strong El Niño months, largely before 2000 and after 2015, and four of strong La Niña months, largely within this period. However, the clustering of these ENSO events and the opposing directions of the NEF curves do not visually suggest a strong association. The correlation between the NEF and Oceanic Nino Index was not significant for Ahmedabad (Spearman Rank Correlation Coefficient ( $r_s$ ) = 0.114,  $p$  = 0.06) but was very weak and significant for Surat ( $r_s$  = 0.166,  $p$  = 0.006).

### Figure 2 here

In both cities, highest incidence of EF was observed during the monsoon season from June to September (Figure 3). A sharp downward tapering begins in September, leading to lowest incidence in the post-monsoon months. Cases again rise steadily in the pre-monsoon months. In Ahmedabad, monthly distribution of NEF cases follows a bi-modal distribution with a prominent



peak in June and a minor second peak in August-September. The first NEF peak in June lags the Tmax peak in May by a month and the second minor NEF peak in August coincides with a dip in both Tmax and Tmin when diurnal temperature is the least (Fig 3 a) and humidity is the highest (3b). The dip between the two NEF peaks coincides with the rainfall peak in July. Both cities showed significant correlation between NEF and rainfall (Ahmedabad 0.237,  $p < 0.0001$ ; Surat 0.251,  $p < 0.0001$ ). The drop in incidence follows the decrease in minimum temperature and humidity (Fig 3c). In Surat, monthly mean NEF case peaked in the month of July. This peak coincided with the drop in Tmax, lowest diurnal temperature, and peak humidity-and rainfall (Fig 4 a, b, c). The cases taper off in parallel to the fall in minimum temperature and humidity.

### **Figures 3. a, b, c and Figures 4. a, b, c**

EF Cases: Monthly NEF of Ahmedabad (1.5) during the study period was nearly double that of Surat (0.81) (Table 1). Interestingly, during the monsoon months, considerably higher number of EF cases are observed in Ahmedabad during strong El Niño months compared to Neutral months (150 vs 62,  $p = 0.01$ ) and strong La Niña months (95 vs 62) (Table 1). In Surat, EF cases during strong El Niño months are comparable to ENSO neutral months (40 vs 38) but cases during strong La Niña months are lower (40 vs 23). Median monthly EF cases in Ahmedabad during strong El Niño monsoon months is very high (150), compared to all other ENSO groupings of monsoon months (Mostly less than 70).

Maximum Temperature: In general, Ahmedabad has higher temperatures while Surat receives more rainfall during the monsoon season. In Ahmedabad, temperature during ENSO neutral phase was 0.5 to 1.5°C higher than El Niño or La Niña phases; while in Surat, this difference was not more than 0.5°C. Although Ahmedabad has the lowest average temperatures during strong El Niño months, the monthly EHEs in Ahmedabad during these months is at least

double of that during other ENSO months in both Ahmedabad and in Surat. NEF showed significant correlation with EHE in Surat ( $r_s = 0.13$ ,  $p=0.03$ ) but not in Ahmedabad ( $r_s = 0.028$ ,  $p=0.64$ ).

**Precipitation:** Precipitation was higher in Surat, particularly during La Niña months. During strong La Niña month, precipitation was much higher than during neutral months in Surat, but much lower in Ahmedabad. Phases of ENSO had minimal impact on EPEs in Ahmedabad. Highest frequency of EPEs was observed during the strong La Niña month in Surat. NEF did not show significant correlation with EPEs in either of the cities.

**Table 1 here**

Results from an adjusted Negative Binomial Generalized Linear Model (GLM) of 23 years of disease and climate data, show that monsoons increased the risk of EF equally in both cities, in Ahmedabad by 35% (Incident Rate Ratio (IRR): 1.35; 95% Confidence Interval (CI): 1.17-1.55) and in Surat by 34% (IRR: 1.34; 95% CI: 1.16-1.56) (Table 2).

**Table 2 here**

During strong El Niño months, the risk of EF increased by 64% in Ahmedabad (IRR: 1.64; 95% CI 1.26-2.14), and reduced by 25% in Surat (IRR: 0.75; 95% CI: 0.58-0.96). During strong La Niña months, the risk of EF decreased by 31% in Ahmedabad (IRR 0.69; 95% CI: 0.50-0.95). Such a reduction in risk was also observed in Surat, however the results were not statistically significant (IRR: 0.90; 95% CI: 0.66-1.08). Results for moderate El Niño was not statistically significant but moderate La Niña was associated with 21% increase in incidence in Surat. In the combined analysis, EF incidence increased by 16% only during Moderate La Niña months.

Extreme precipitation events (EPE) increased the risk of EF by 5% (IRR: 1.05, 95% CI: 1.00-1.10) in Ahmedabad (Table 2). However, such a risk was absent in Surat. Higher monthly

frequency of EHEs did not increase the risk of EF, either in the combined or city specific analysis.

## DISCUSSION

Extreme weather events tied to ongoing climate variability and change are on the rise across the globe, and are leading to exacerbation of infectious diseases outbreaks (18,19,30). We examined how extreme events and phases of ENSO affect the incidence of EF in Ahmedabad and Surat, an inland and a coastal city respectively in Gujarat, in central western India. We found that the monsoon was clearly associated with increase in the risk of EF in both the cities. Rapid urbanization, poor water supply and sanitation systems have a well-known role to play in transmission of typhoidal *salmonellae* (6). Conceivably, these effects are exacerbated during the monsoon season, leading to an unequivocal and equivalent rise in cases in both cities. Additionally, we observed opposite effect of Strong El Niño in inland Ahmedabad vs coastal Surat. One possible explanation is the relatively higher frequency of monthly EPE in Ahmedabad (1.22) during strong El Niño compared to Surat (0.44), and apparent lack of association between EPE and EF in Surat (Table 1). However, future studies with larger geographic coverage and longer temporal duration is needed prior to drawing a definitive conclusion regarding this issue.

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During the study period, EF cases increased in the latter decade in Ahmedabad, but not in Surat, when there was a higher frequency of El Niño months. Contrastingly, there was a slight drop of cases in Ahmedabad and a slight rise in Surat between 2000 to 2015, when there was a larger frequency of La Niña months. The possibility of local factors like failing water quality or other environmental factors causing rise in Ahmedabad after 2010 cannot be ruled out. Future studies are needed to investigate if this observation is indeed tied to the higher frequency of El

Niño months after 2015. There are indications that ENSO may have different patterns and the teleconnections of ENSO on remote regions may depend on the flavor of ENSO (31). Such details are beyond the scope of the present study but will be a focus of further studies. In both cities we found that the cases began rising in February, well before the pre-monsoon months. With the beginning of the monsoons in June, the cases peaked, and then quickly dropped in July/August, completing their run by the end of the monsoons in November. December and January were low incidence months.

Our preliminary analysis (Figs 3 and 4) indicates that the increase in temperatures coincide with the increase in NEF incidence in Ahmedabad and Surat . Similar findings have been reported in Bangladesh and China with a one month lag (4,13). One plausible explanation for this early rise in cases with temperature, is the exponential growth of *Salmonella* in the seasonally warming temperatures from March to May (11). Typhoidal Salmonellae are obligate human pathogens and are transmitted from humans to humans. Increasing temperature likely enhances multiplication of *Salmonellae* excreted by humans in the environment and increases the risk of transmission through unhygienic food handling (32). Likewise, increased precipitation associated with monsoon season facilitates the spread of *Salmonella* through contaminated water (33) and food (34). Our findings regarding the increasing risk of EF in pre-monsoon months and the highest risk in the monsoon season is in agreement with published literature. Studies in Vietnam, Bangladesh and China have shown that not only does EF variability follow seasonal variability (12,13,35), but also that the core mechanisms that determine seasonality of this disease depend on the local context (11).

In our setting, the increased risk in Ahmedabad is surprising, since Surat is the less affluent (GDP USD 60 billion) city and has a considerably higher percentage of population living in slums (10.5%), compared to Ahmedabad (USD 68 billion, slum population of 4.5%) (36,37). Surat's

unique history of clean-up in 1994 (35) and its sustained pioneering efforts at improved sewage management (39) may explain the fact that baseline case incidence is lower in Surat and extreme precipitation does not lead to increased risk of EF cases there. In the last decade too, Surat, the smaller city, received 25% more funds for “urban renewal” than Ahmedabad, and Surat spent 65% of this allocation on water and sewerage while Ahmedabad spent only 32% (40,41). However, there is no baseline data available on water supply and sewerage systems of these two cities before our study period in order to contrast them quantitatively with the present data. Possibly, Ahmedabad already had relatively many more human reservoirs of typhoidal *Salmonellae* than Surat historically.

In both cities, extreme heat events were not associated with EF risk. This is different than the findings of Jiang et al (2015), whose findings regarding non-typhoidal salmonellosis risk in Maryland, United States were contrary to our findings (27). The null findings associated with extreme heat events in our analysis may be associated with the fact that EHEs may not be an influencer of bacterial growth in our already hot tropical climate. The maximum temperature remains relatively high throughout the year ranging from 27<sup>0</sup>C in January to 42<sup>0</sup>C in May for Ahmedabad and 30<sup>0</sup>C to 37<sup>0</sup>C for Surat. Jiang et al. (2015), found that both EHEs and EPEs led to increased risk of non-typhoidal salmonellosis, with higher risk observed in coastal areas. The authors hypothesized that higher prevalence of large scale poultry operations as well as increased recreational activities in contaminated water bodies that receive runoff from fields with presence of poultry litter during warmer months may explain high risk in coastal areas. They further hypothesized that consumption of improperly cooked barbecue meat product during warmer days may enhance exposure to *Salmonella*, contributing to higher risk. Because of our limited geographic focus (just two cities) we were unable to further investigate such underlying

mechanisms in our study. Further studies with larger geographic focus are needed to 1) conform our findings regarding the phases of ENSO and risk of EF in India, and 2) characterize the underlying mechanism that explain the relationship between ENSO and EF risk over the Indian subcontinent.

To the best of our knowledge, ours is the first such study to compare the influence of ENSO and extreme weather events on the burden of EF in two neighboring cities in India. We observed that while EF risk rose in both Ahmedabad and Surat during the monsoon season, the rest of the climate effects on EF incidence were contrasting in nature -- strong El Niño phase was associated with an increased risk of EF in Ahmedabad, but a decreased risk in Surat; strong La Nina with a decreased risk of EF incidence in Ahmedabad, and moderate La Niña with an increased risk in Surat. We also found that although the strong El Niño months coincide strongly with higher monthly frequency of EHEs, the EHEs themselves did not affect EF incidence in the city.

India accounts for the highest burden of EF in the world, ranging between 377 to 550 cases/100,000 population (2,8). The total annual treatment costs for all lower and middle income countries (LMICs) together is estimated to be \$141 million in direct costs and 1.2 billion in productivity loss (42). Our finding of significant effect of El Niño on EF incidence needs to be investigated further with more data from across India and the globe. If confirmed, public health measures that address such a climate effect on EF can be effective in reducing the burden of this disease, at least in those parts of the world where this burden is unacceptably high.

There are several strengths to our study. Our outcome measure spans over two decades. This enabled us to sufficiently sample the role of a large scale weather phenomenon such as ENSO. We used the frequency of extreme weather events as our exposure metric, as opposed to daily weather (e.g., daily precipitation, temperature). This is important because extreme weather events

are increasing in frequency, duration, and intensity, and are widely accepted as attributes of changing climate (43). Our study site represents one of the highest risk areas for EF across the globe. That our analysis showed contrasting effects of strong El Niño on EF incidence in the two cities is noteworthy because it comes on the back of our finding of uniform rise in cases with rainfall in both cities. Our study has limitations as well. Our study focused on only two cities from Gujarat, so our findings may not be generalizable across India which has a very heterogeneous rainfall distribution. The data was available to us only as monthly case incidence, not daily. As a result, we were unable to look for finer lag effects at weekly/fortnightly intervals, nor adjust for individual level confounders. Although this study establishes the association between ENSO and EF incidence in Ahmedabad, the local climate factors that must be mediating this effect directly or indirectly have not been adequately elucidated. The EF cases reported to the city's epidemic cell were based on Slide and/or Tube Widal positive tests. Each of the case addresses had been visited, and the patient confirmed to be ill by public health inspectors of the municipality. Our analysis assumes that the surveillance mechanisms in both cities independently maintained consistent rigor throughout the study period. To minimize impact of missing weather data, future studies may consider gathering data from multiple weather stations and incorporate river flow data that may indirectly provide increases in precipitation at a regional level. Future studies may also consider alternate metric for extreme heat including tropical nights or those that incorporate relative humidity (44).

## CONCLUSION

We observed that EF incidence in Gujarat has a strong seasonality and is influenced by phases of ENSO and extreme precipitation events. The contrasting incidence of EF between a coastal and an inland city during strong El Niño months, located just 260 km apart highlight the need to further

characterize such geographic heterogeneity as a prerequisite for the development of critical reliable early warning systems and for evolving community specific adaptation strategies. Such solutions along with addressing long term issues such as well-maintained water supply and sewerage systems will enhance community resilience to climate change and reduce burden of EF in India.

## ACKNOWLEDGEMENTS

The research reported in this manuscript has been funded by Public Health Research Initiative (PHRI) Research grant awarded by PHFI with the financial support of Department of Science and Technology (No. PHRI LN0019). Further support (A. Sapkota, R. Murtugudde) was obtained from NSF and NOAA through Belmont Forum (Award Number (FAIN): 2025470). RM gratefully acknowledges the Visiting Faculty position at the Indian Institute of Technology, Bombay.

## CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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Figure 1 (a) Map of Ahmedabad city limits in 1986 and the wards added in 2006 (b) Map of Surat city limits in 1986 and the areas added in 2006 (Illustration based on data from Directorate of Census, not to scale)

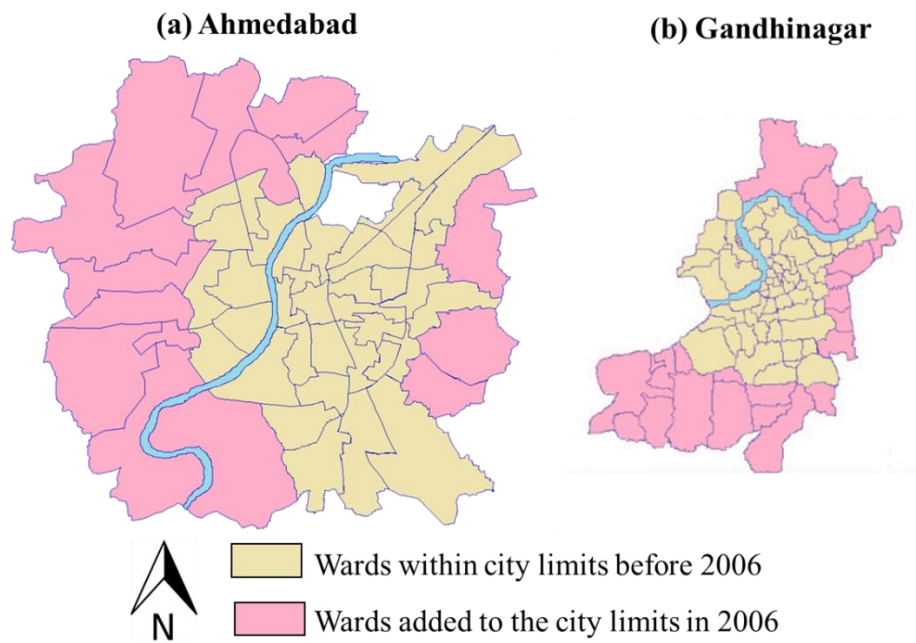


Figure 2: Temporal trend in monthly Normalised Enteric Fever (NEF) cases for Ahmedabad and Surat

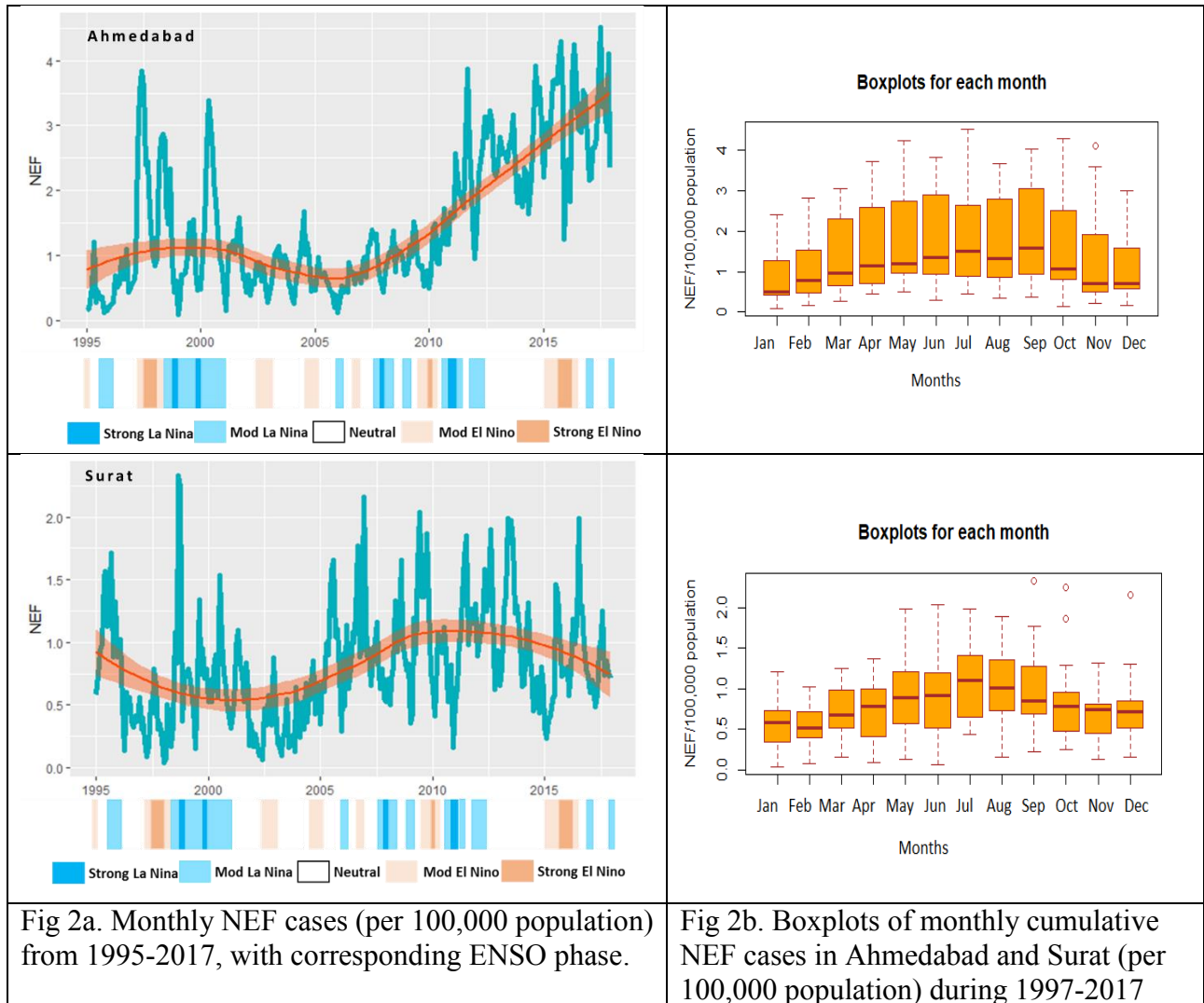


Figure 3- Monthly NEF case rates in Ahmedabad superimposed with temperatures (a), Relative Humidity (b), and monthly rainfall (c)

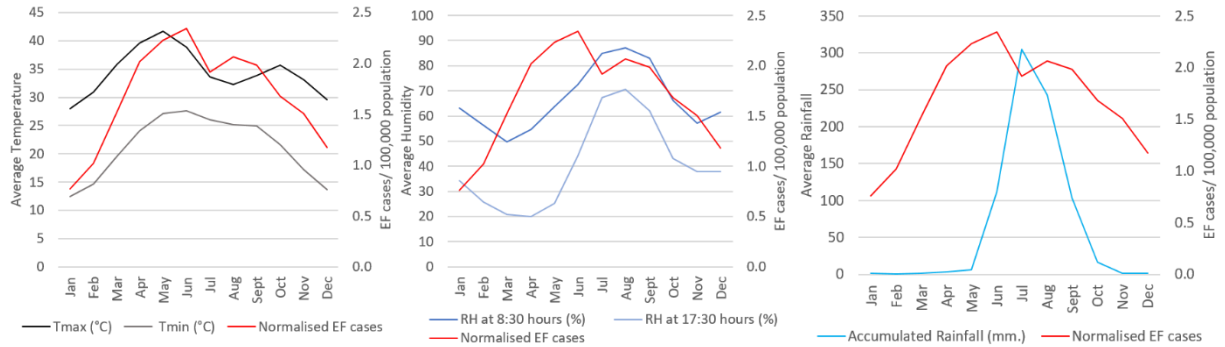


Figure 4- Monthly NEF case rates in Surat superimposed with temperatures (a), relative humidity (b)., and monthly rainfall (c)

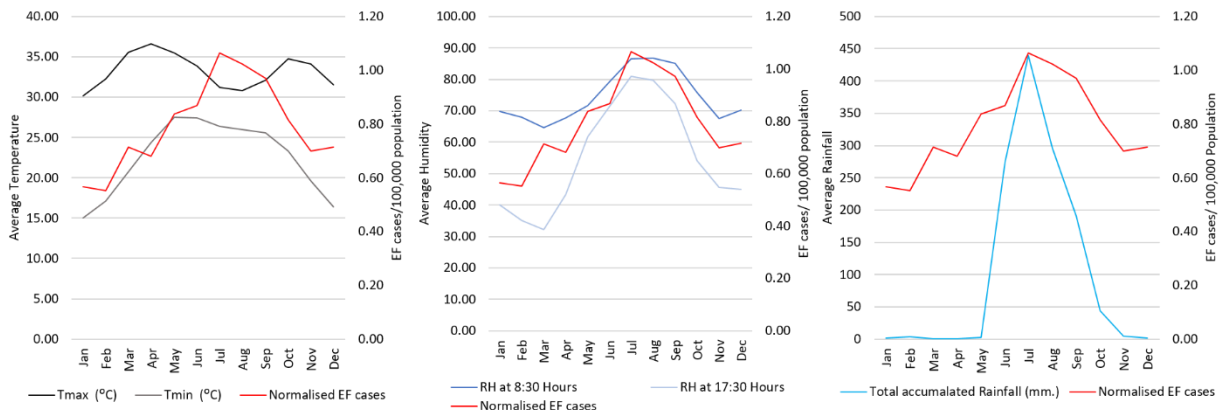




Table 1: Distribution of study population and exposure data across phases of ENSO

Study Characteristics	Ahmedabad		Surat	
Population (2011 census)	5577940		4467797	
Population density (per sq. km)	11895		13304	
No. of reported cases	20544		8692	
Monthly NEF (per 100,000)	1.5 [1.38-1.63]		0.81 [0.76-0.87]	
Median Monthly Cases during monsoon season (JJAS)				
Strong El Niño (6)	150		38	
Moderate El Niño (9)	46		17	
Neutral (57)	62		40	
Moderate La Niña (19)	69		35	
Strong La Niña (1)	95		23	
Local Climate during monsoon months (JJAS)				
	Avg	Avg	Avg	Avg
	Tmax	Precip	Tmax	Precip
Strong El Niño (6)	32.9	5.8	31.8	6
Moderate El Niño (9)	34.4	6.8	31.7	9.4
Neutral (57)	34.8	6.3	32	10
Moderate La Niña (19)	34.1	6.9	32	10.9
Strong La Niña (1)	33.4	3.7	31.5	15.4
Average of Monthly frequency of Extreme Event days during monsoon months (JJAS)				
	EHE	EPE	EHE	EPE
Strong El Niño (6)	4.78	1.22	3	0.44
Moderate El Niño (9)	2.17	1.78	1	1.11
Neutral (57)	1.26	1.48	1.16	1.18
Moderate La Niña (19)	0.29	1.58	1.33	1.83
Strong La Niña (1)	0	2	2	4

**NEF:** Normalized enteric fever **EHE:** Extreme Heat Events **EPE:** Extreme Precipitation Events

Table 2: Incident rate ratios (IRR) showing associations between climatic factors and enteric fever in Ahmedabad and Surat during 1995-2017"

Exposure Variable	Ahmedabad		Surat		All	
	IRR	95% CI	IRR	95% CI	IRR	95% CI
EHE	0.99	0.96-1.03	1.04	0.99-1.09	1.01	0.98-1.04
EPE	1.05	1.00-1.10	1.01	0.96-1.06	1.01	0.97-1.05
Monsoon	1.35	1.17-1.55	1.34	1.16-1.56	1.37	1.24-1.52
Phases of ENSO						
Neutral	1.00	-	1.00	-	1.00	-
Stong El Nino	1.64	1.26-2.14	0.75	0.58-0.96	1.13	0.93-1.36
Weak/moderate El Nino	1.19	0.98-1.44	0.97	0.82-1.16	1.06	0.93-1.22
Weak/moderate La Nina	1.13	0.97-1.32	1.21	1.04-1.41	1.16	1.03-1.29
Strong La Nina	0.69	0.50-0.95	0.90	0.66-1.23	0.79	0.63-1.01

**Role of extreme weather events and El Niño Southern Oscillation on incidence of Enteric Fever in Ahmedabad and Surat, Gujarat, India**

**Author Contributions:**

Veena Iyer	Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Roles/Writing - original draft; Writing - review & editing.
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Pradeep Umrigar	Data curation; Methodology; Resources; Supervision; Roles/ Writing - review & editing.
Raghu Murtugudde	Investigation; Methodology; Supervision; Validation; Visualization; Roles/Writing - review & editing.
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**Declaration of interests**

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: