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Original Contribution

El Niño, Climate, and Cholera Associations in Piura, Peru, 1991–2001: A Wavelet Analysis

Iván J. Ramírez[1,2] and Sue C. Grady[3]

[1]*Interdisciplinary Science Program, The New School, 65 W 11th Street, New York, NY 10011*
[2]*Tishman Environment and Design Center, The New School, New York, NY*
[3]*Department of Geography, Michigan State University, East Lansing, MI*

Abstract: In Peru, it was hypothesized that epidemic cholera in 1991 was linked to El Niño, the warm phase of El Niño–Southern Oscillation. While previous studies demonstrated an association in 1997–1998, using cross-sectional data, they did not assess the consistency of this relationship across the decade. Thus, how strong or variable an El Niño–cholera relationship was in Peru or whether El Niño triggered epidemic cholera early in the decade remains unknown. In this study, wavelet and mediation analyses were used to characterize temporal patterns among El Niño, local climate variables (rainfall, river discharge, and air temperature), and cholera incidence in Piura, Peru from 1991 to 2001 and to estimate the mediating effects of local climate on El Niño–cholera relationships. The study hypothesis is that El Niño-related connections with cholera in Piura were transient and interconnected via local climate pathways. Overall, our findings provide evidence that a strong El Niño–cholera link, mediated by local hydrology, existed in the latter part of the 1990s but found no evidence of an El Niño association in the earlier part of the decade, suggesting that El Niño may not have precipitated cholera emergence in Piura. Further examinations of cholera epicenters in Peru are recommended to support these results in Piura. For public health planning, the results may improve existing efforts that utilize El Niño monitoring for preparedness during future climate-related extremes in the region.

Keywords: El Niño, El Niño–Southern Oscillation, cholera, climate, wavelet, mediation

INTRODUCTION

Since 1991, epidemic cholera has emerged twice in the western hemisphere, contributing to approximately 2 million cases in the region (Pan American Health Organization 2008, 2014). The first emergence began in Peru in 1991, spread to South and Central America, and lasted approximately a decade. The second emergence, which is ongoing, spread from Haiti in 2010 to the Dominican Republic, Cuba, and Mexico (Moore et al. 2014). In Peru, similar to in Haiti (Jutla et al. 2013), studies suggested that cholera emergence was triggered by climate impacts. In Peru, it was hypothesized that epidemic cholera was linked to El Niño, the warm phase of El Niño–Southern Oscillation (ENSO) (Epstein et al. 1993; Colwell 1996). ENSO is a climatic cycle in the equatorial Pacific Ocean that affects global to local weather patterns every 2–7 years.

To date, most studies examining this hypothesis have focused on the 1997–1998 El Niño, finding positive correlations between local climate and cholera incidence. For

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Correspondence to: Iván J. Ramírez, e-mail: ramirezi@newschool.edu

example, Speelmon et al. (2000) and Gil et al. (2004) showed that elevated coastal air and sea temperatures were associated with cholera epidemics in Lima, the capital of Peru. More recently, Ramirez (2015) demonstrated that rainfall, in addition to air and sea temperatures, increased cholera at a district level in Piura, Peru (900 km north of Lima). While these studies demonstrated an association with El Niño using cross-sectional data, i.e., at one point in time, they did not assess the consistency of this relationship across the decade. Furthermore, previous studies have not investigated the impact of El Niño on cholera in the early 1990s. Understanding these years is important because it represents a period when cholera emerged, and reportedly, when El Niño's timing and effects were unclear (Ramirez et al. 2013). Thus, how strong or variable an El Niño–cholera relationship was in Peru or whether El Niño triggered the epidemic in 1991 remains unknown. Such temporal information may be critical for public health planning in the region, where El Niño monitoring is important.

The objective of this study was, therefore, to estimate the temporal relationships among El Niño, climate, and cholera incidence from 1991 to 2001. We focused on the northern region of Piura, Peru where index cases were reported in 1991 (Ries et al. 1992). To examine El Niño–cholera associations, we employed wavelet analysis to characterize bivariate temporal patterns between climate variables and cholera cases. Wavelet analysis is a method used in geophysical studies to examine the oscillating components and frequency of relationships between ocean and atmospheric processes, including ENSO (Torrence and Compo 1998). In particular, it is useful to study complex relationships, whose temporal properties exhibit non-stationarity, meaning their periodic components and associations change over time (Cazelles et al. 2007). Wavelet analysis provides an advantage over traditional time-series approaches, such as regression and Fourier analyses, which assume consistent associations (Cazelles et al. 2007). Non-stationarity in climate–disease relationships has been reported in several global studies, including cholera in Ghana (Constantin de Magny et al. 2006) and Bangladesh (Hashizume et al. 2013), dengue in Thailand (Cazelles et al. 2005), and Leishmaniasis in Costa Rica (Chaves and Pascual 2006). This study will differ from previous studies by not only using a wavelet time-series approach but also combining wavelet with mediation analysis to estimate impacts of local climate variables on El Niño–cholera associations in Piura. Mediation analysis is a method employed in psychology and public health to estimate the effects of intervening variables through which a causal factor affects a health outcome (Frazier et al. 2004; Grady and Ramirez 2008). As studies in Peru (Gil et al. 2004; Ramirez 2015) and Bangladesh (Pascual et al. 2000, 2002; Cash et al. 2008) suggest, El Niño's effect on cholera is interconnected via local climate influences, known as teleconnections (Glantz 1991). In this research, our overarching hypothesis is that a potential El Niño–cholera link in Piura was transient and mediated by local climate variables, specifically rainfall, river discharge, and air temperature.

METHODS

Study Area

The study area is Piura, located in the Department of Piura in northwestern Peru. Piura is a health administrative region that borders the Pacific Ocean and the foothills of the Andes (Fig. 1). Piura's climate varies from semi-arid on the low-lying coast to subtropical conditions in the mountainous east (PAEN/GTZ 2003). Figure 2 shows air temperature and rainfall at the Miraflores meteorological station, located in the capital city of Piura. The annual average air temperature is 24°C, and median rainfall is 43 mm,[1] except during El Niños, when record estimates are reported (e.g., 1849 mm—1998) (Takahashi 2004). Approximately 68.0% of the population lived on the coast during the study period (Institute of National Statistics and Information [INEI] 2000).

Data

Weekly cholera data including probable and confirmed cases from 1991 to 2001 were obtained from the Departments of Epidemiology at the Ministries of Health (MINSA) in Lima and Piura, Peru. The case definition for probable cholera was "a person of any age who developed acute watery diarrhea, with or without vomiting, with severe dehydration or shock or died from acute watery diarrhea" (MINSA 2005). A confirmed case of cholera was defined as a laboratory isolate of *Vibrio cholerae 01* from a patient's blood specimen. If a probable case was confirmed within 2 weeks following the initial diagnosis the case was changed from probable to confirmed. In this study, weekly

[1]Estimate based on Miraflores data from 1971–2003 without El Niño years.

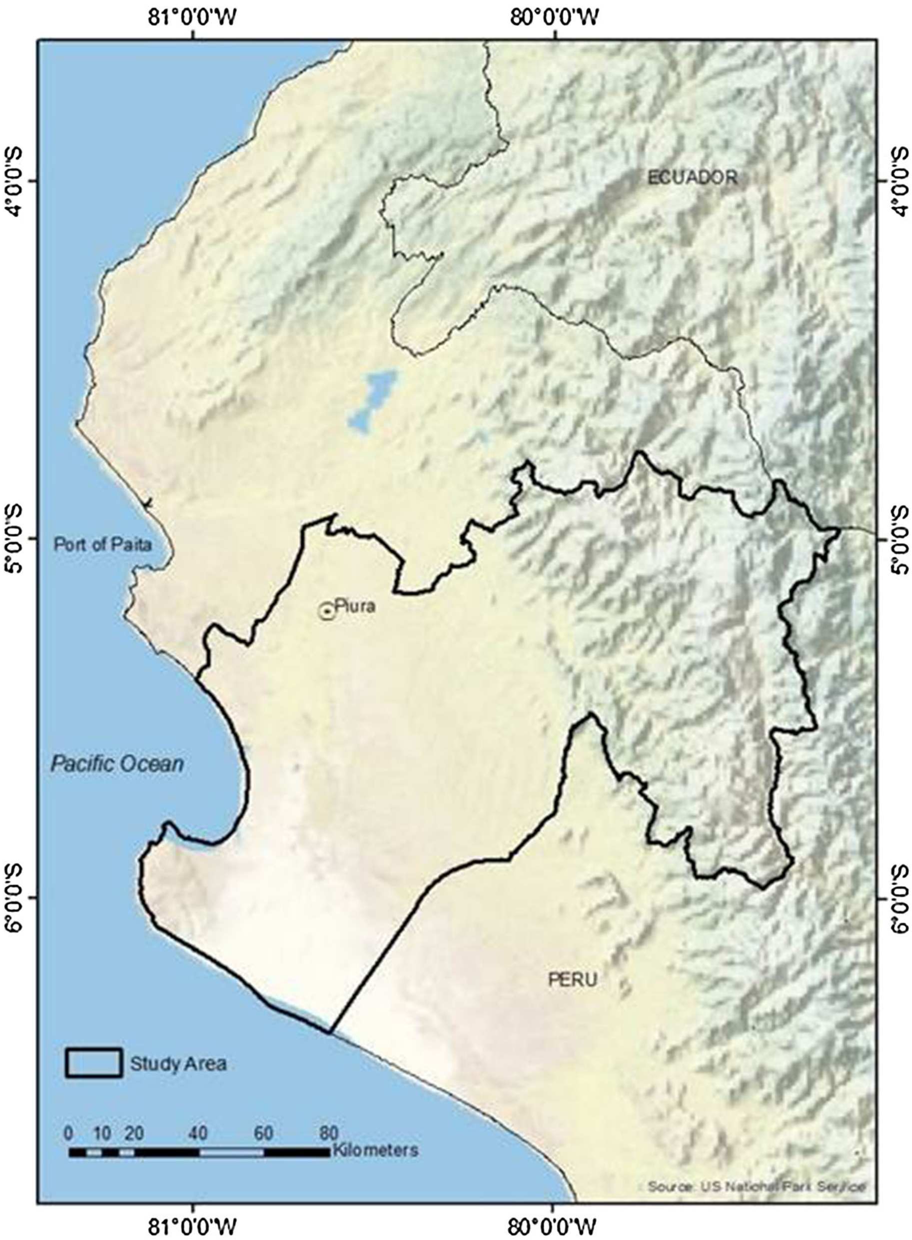


Figure 1. Map of Piura health administration region in Peru.

cholera probable and confirmed cases were aggregated by month over the study time period (n = 132 months) and square-root transformed to dampen positive extreme values prior to wavelet analysis (Cazelles et al. 2005).

Monthly sea surface temperature (SST) anomaly data representing ENSO in the Niño Regions 3.4 and 1+2 were obtained from the National Oceanic and Atmospheric Administration (NOAA 2015) (http://www.cpc.ncep.noaa.gov/data/indices/). These SST regions were selected because of proximity to the Peruvian coast (Niño 1+2) and areas of convection (Niño 3.4) in the equatorial Pacific Ocean. To interpret our results, we identified El Niño episodes based on the commonly used ONI-index associated with Niño 3.4 (http://www.cpc.ncep.noaa.gov/products/analysis_monitoring/ensostuff/ensoyears.shtml). Local climate data collected included monthly average Paita SST anomaly, air temperature anomaly (T_{mean}), rainfall, and river discharge (proxy for river flow). These data come from a monitoring station in the Port of Paita, and the Miraflores station, mentioned earlier. All climate data were collected beginning in 1971 in order to capture temporal trends prior to the 1991 cholera epidemic. For a further description of these data, see Ramirez (2015). Rainfall and river discharge data were also square-root transformed prior to analysis.

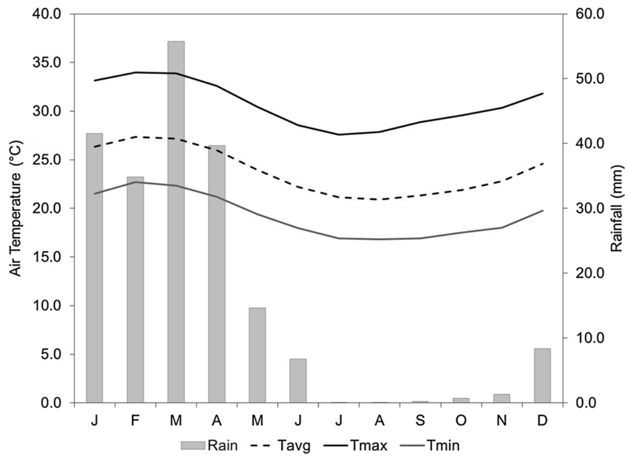


Figure 2. Monthly averages of air temperature and rainfall parameters for 1971–2001 at the Miraflores meteorological station located in the capital city of Piura.

Wavelet Analysis

To characterize El Niño, local climate, and cholera relationships, three types of wavelet analyses were implemented. First, each time series was characterized using continuous wavelet transform (CWT) to decompose each series into time–frequency space and identify areas of high/low periodicity, i.e., variability and frequency, according to period (scale by year[s]) and time interval(s) (Torrence and Compo 1998). Second, to understand the relationship between two time series, cross-wavelet transform (XWT) and wavelet coherence (WTC) were employed. The XWT estimated common areas where two series co-varied and shared high/low periodicity, while the WTC measured the strength of covariance and identified areas of linear correlation. Both XWT and WTC analyses estimated direction of relationships (e.g., in-phase or out-of-phase) and temporal lags (indicated by arrows in the wavelet figures). To address serial correlation, autoregressions were controlled for using a first-order autoregressive term, a process commonly used to model geophysical time series (Torrence and Compo 1998). Wavelet analyses were performed in Matlab R2013a using scripts written by Grinsted et al. (2004, 2008) and Ng and Kwok (2012).

Mediation Analysis

Following the wavelet analysis, significant time intervals of coherence were explored further for mediating effects of local climate on El Niño–cholera relationships. First, temporal lags (0–12 months) were explored to identify the best

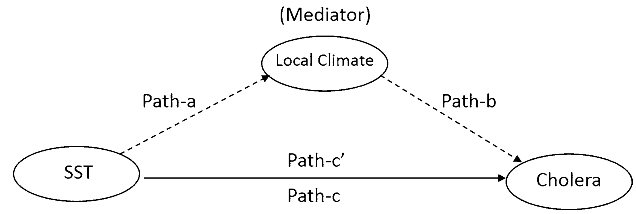


Figure 3. Pathways (a–c, and c') in the mediation model of the SST and cholera relationship adapted from Barron and Kenny (1986).

climate variable-predictors of cholera. The Barron and Kenny's (1986) model to test for mediating effects was implemented (Fig. 3). The first step was to show that there was a significant relationship between SST and cholera (Path c). Path c was used as a reference model from which subsequent models were compared. The second step was to show that SST was significantly associated with local climate (Path a). The third step was to show that local climate was significantly associated with cholera (Path b), controlling for SST. Finally, Path c' measured the mediating (reduced) effect of SST on cholera after local climate was added to the model. To determine if the reduced effect was significant, the Aroian version of the Sobel test recommended by Preacher and Hayes (2004) was implemented. Mediation analyses were conducted using ordinary least squares (OLS) regression models in SPSS v. 22 (IBM-SPSS 2015).

Results

From 1991 to 2001, there were 38,040 cases of cholera reported in Piura, Peru, representing 5.2% of all cases in Peru. A majority (83.0%) of these cases were reported in the first 2 years of the epidemic. Of the remaining cases ($n = 6406$), a majority (64.7%) were later reported in 1998. Figure 4a–g shows the time-series (left panel) and CWT analyses (right panel) of climate variables and cholera cases. Wavelet analysis of cholera (Fig. 4a) revealed moderate to high periodicity during the onset of the epidemic at periods of 1 year and less from 1991–1993. Significant periodicity, however, was confined to 1992–1993, due to edge effects (discontinuities) at the margins of the wavelet power spectrum (black curve delimits the cone of influence). Thereafter, low periodicity (decline in cholera cases) was observed, followed distinctly by moderate periodicity in 1997–1998 at periods less than 1.5 years. Although cholera periodicity at this interval was not statistically significant,

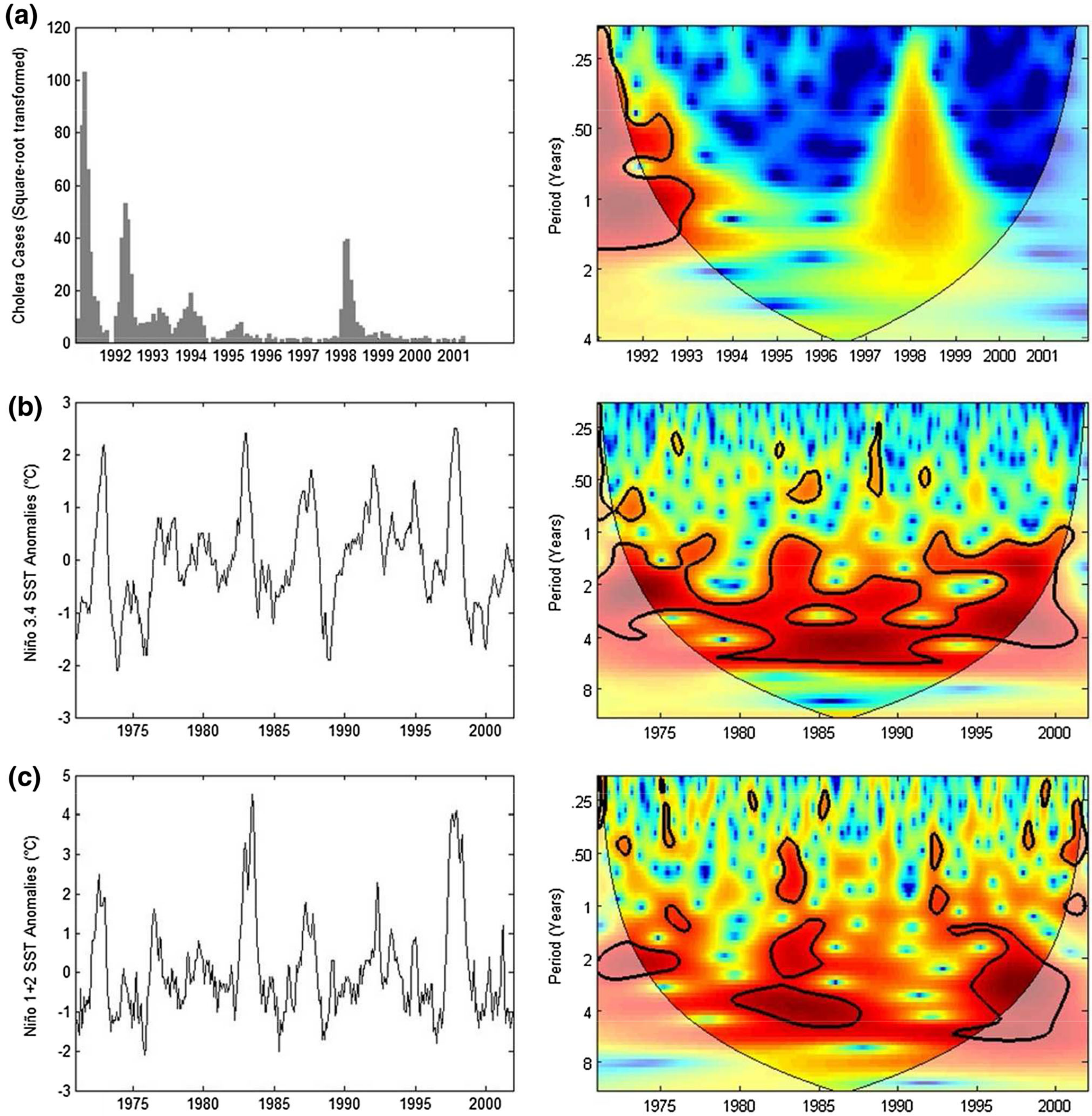
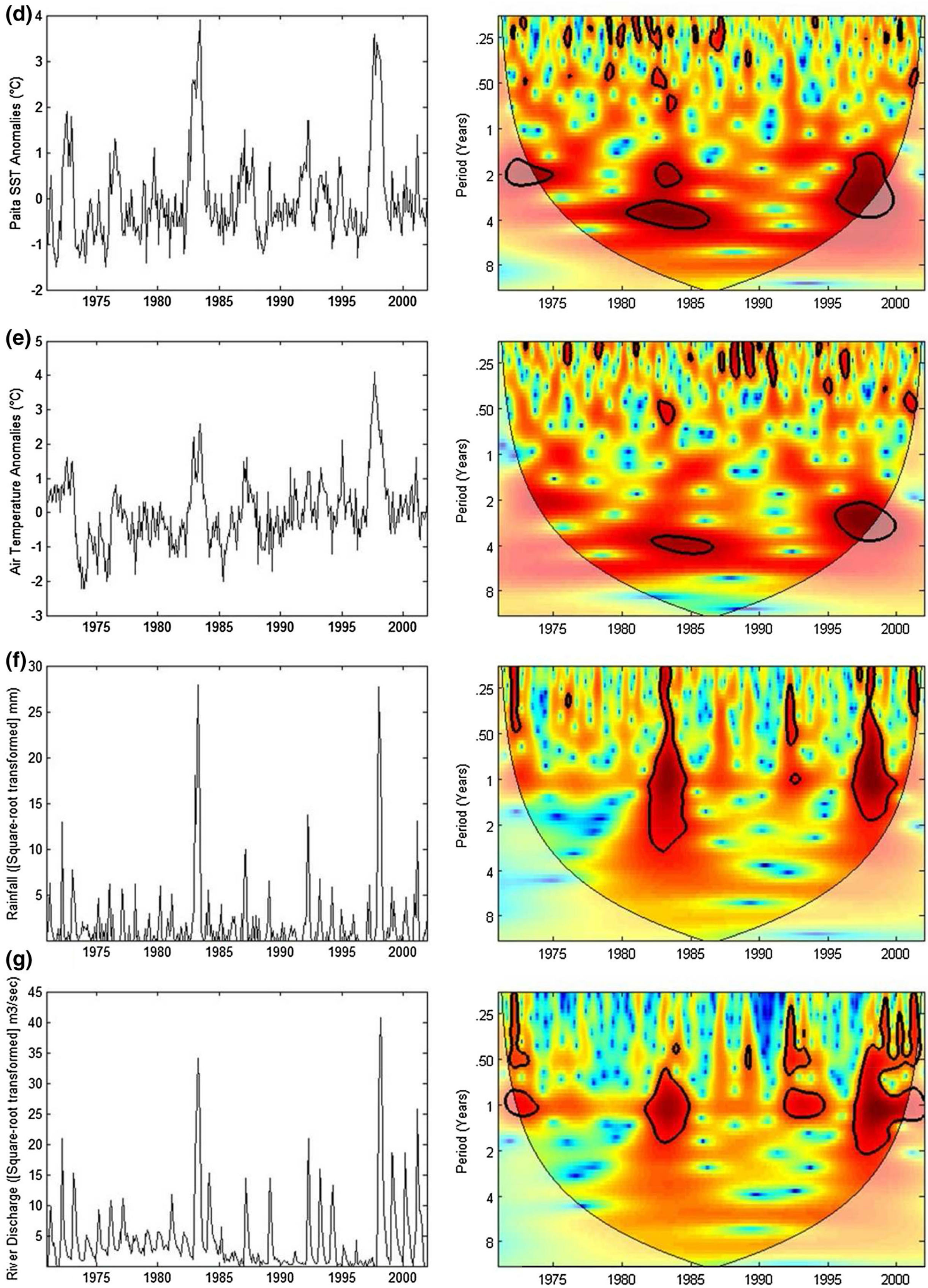


Figure 4 . a–g Monthly time series (*left panel*) and continuous wavelet transform analyses (*right panel*) of cholera and climate variables: **a** cholera cases (square-root transformed); **b** Niño 3.4 sea surface temperature (SST) anomaly; **c** Niño 1+2 SST anomaly; **d** Paita SST anomaly; **e** air temperature (T_{mean}) anomaly; **f** rainfall (square-root transformed); and **g** river discharge (square-root transformed). The continuous wavelet transform is denoted by period (scale by year) and across time intervals. The *color code* for power values increases from *dark blue* (low) to *dark red* (high), and statistical significance (95.0% confidence level) is indicated by areas within *thick black outlines*. The *black curve* delimits the cone of influence (COI), a region influenced by edge effects.

the shape of the spectra captured the major epidemic reported in 1998. Why cholera activity from 1997 to 1998 was not significant was surprising and interesting given it was the third largest epidemic in Piura in the 1990s.

In the SST analysis, significant high periodicity was evident at periods of approximately 3 years and 5 years. There were some differences to note, however. For example, a quasi-continuous cycle was observed in the Niño 3.4 region



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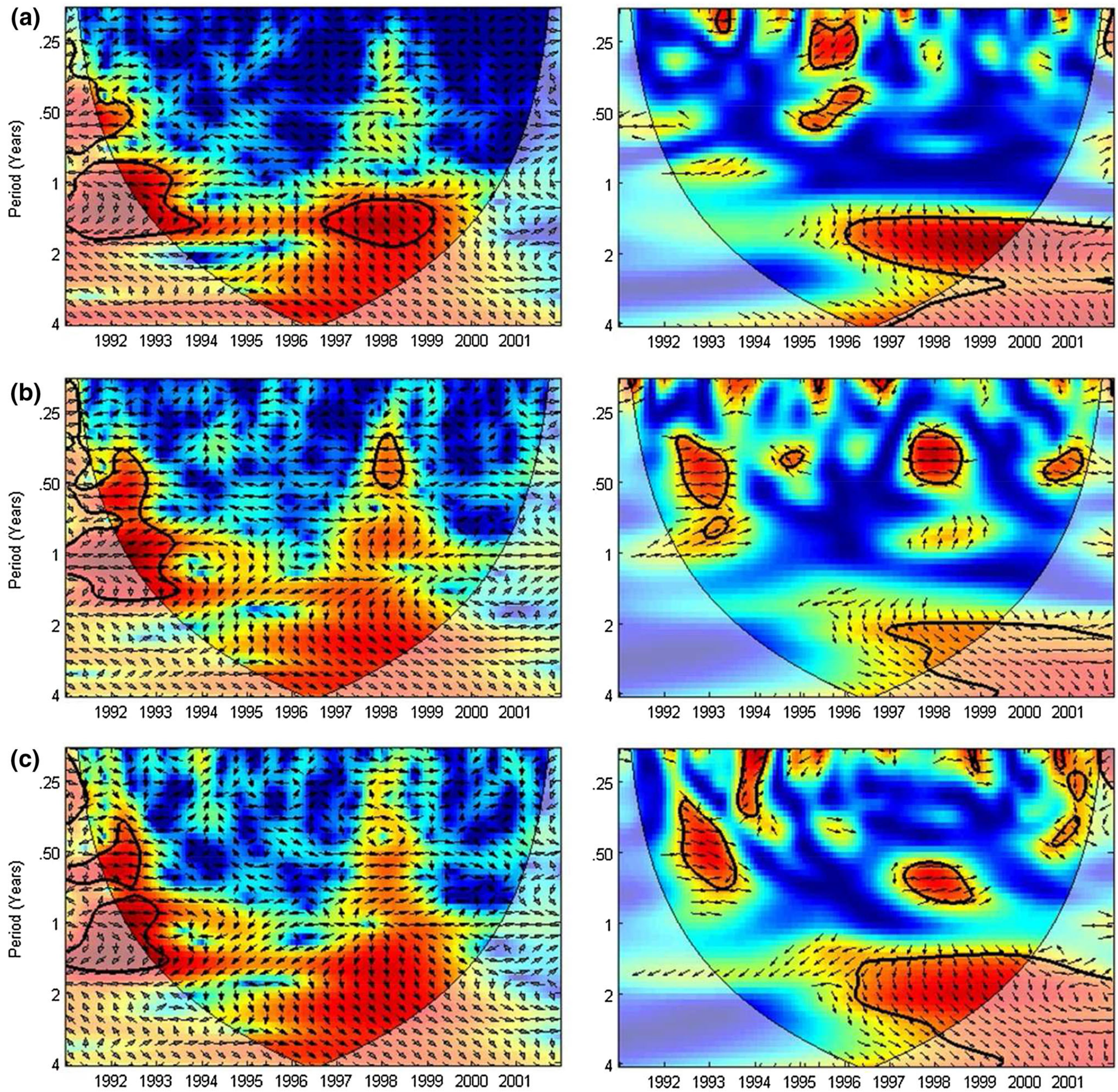

Figure 5. **a**–**f** Cross wavelet transform (*left panel*) and wavelet coherence (*right panel*) analyses between climate variables and cholera: **a** Niño 3.4 SST anomaly; **b** Niño 1+2 SST anomaly; **c** Paita SST anomaly; d air temperature (T_{mean}) anomaly; **e** rainfall (square-root transformed); and **f** river discharge (square-root transformed). Both analyses are denoted by period (scale by year) and across time intervals. The color code shows power values (cross wavelet) and coherence values (wavelet coherence) that increase from *dark blue* (low) to *dark red* (high). The direction (phase) of relationships is indicated by arrows, as such: *up* (climate lags); *down* (climate leads); *right* (climate-cholera in-phase); and *left* (climate-cholera out of phase). Statistical significance (95.0% confidence level) is indicated by areas within thick *black outlines*. The *black curve* delimits the cone of influence (COI), a region influenced by edge effects.

(Fig. 4b), particularly from 1980 to 1992 (5-year period). While in the Niño 1+2 region and coastal Paita (Fig. 4c, d), ENSO's influence was transient but distinguished during significant El Niños (e.g., 1972–1973, 1982–1983, and 1997–1998). In addition, there was also significant high periodicity in the Niño 3.4 series (e.g., 1972–1973; 1982–1984; and 1992–1999) and to some degree in the Niño 1+2 series (1983–1984) at the 1.5-year period. For air temperature

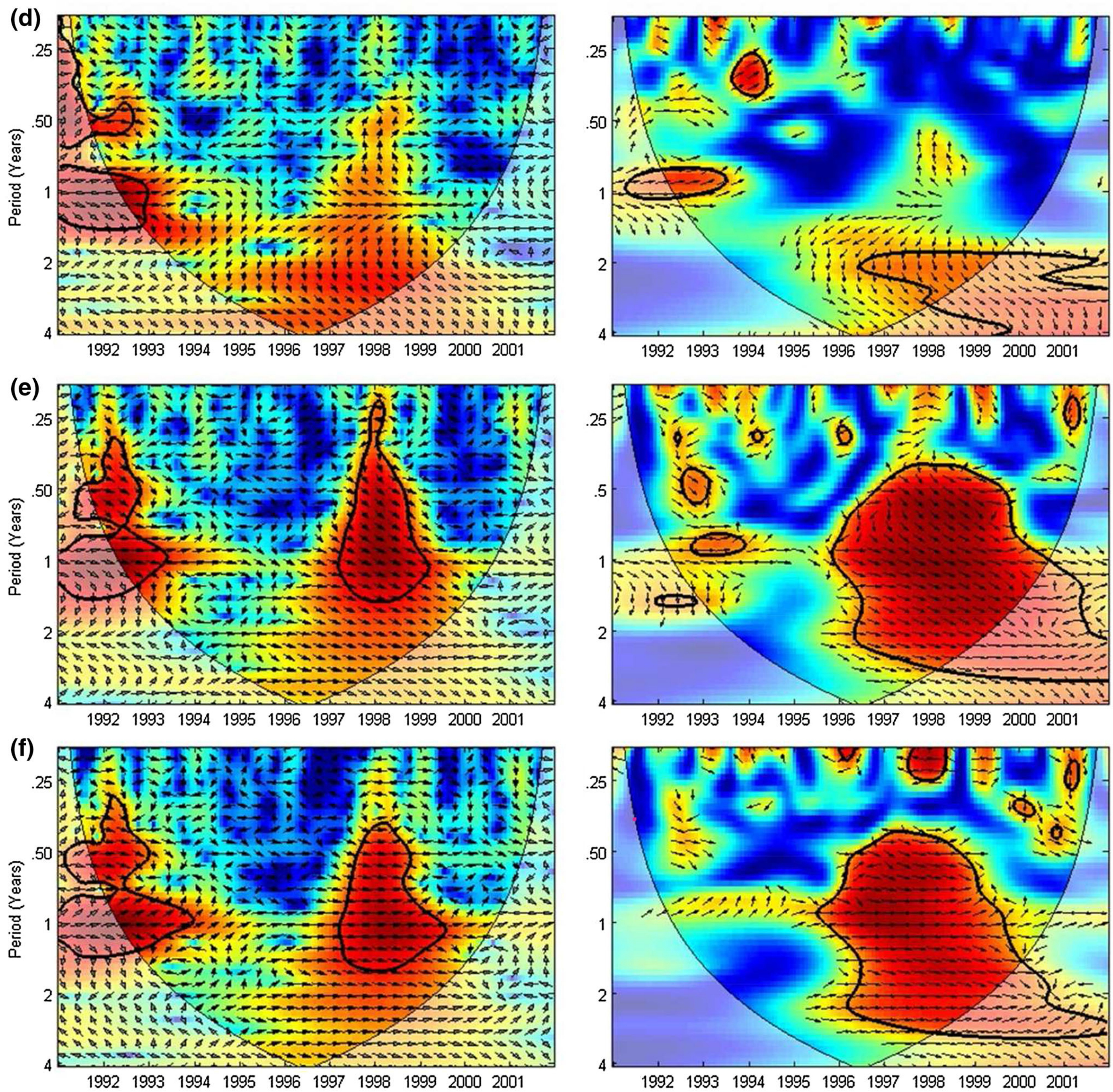

Figure 5. continued

(Fig. 4e), areas of significant high periodicity were limited to two ENSO-related intervals: 1997–1999 and 1983–1985 at periods of 2–3 years and 4 years. The wavelet analyses of rainfall and river discharge (Fig. 4f, g) revealed a distinct pattern of significant high periodicity coinciding with ENSO-related intervals (1972–1973; 1982–1984; and 1997–1999), as well as in 1993–1994. Periodicity at these intervals was evident across multiple periods at less than 2 years.

Figure 5a–f displays the XWT (left panel) and WTC (right panel) analyses between climate variables and cholera cases. Overall, the results revealed patterns associated with two sets of climate parameters: (a) Niño 1+2 SST, Paita SST, and T_{mean}; and (b) Niño 3.4 SST, rainfall, and river discharge. Set (a) shared a common area of periodicity with cholera in 1992–1993; while set (b) shared common areas of periodicity with cholera in the time intervals, 1992–1993 and 1996–1999. Once these patterns were examined further, the WTC analyses identified significant coherency with cholera in one time interval, 1996–1999, with all climate variables at periods that differed by set: set (a) was coherent at intraannual to annual scales of .5–1.5 years, whereas, set (b) was coherent at annual to interannual scales of 1–3 years. The phase relationships suggest positive associations where rainfall and river discharge variables were closely synchronized with cholera (in-phase, 0°), while SST and T_{mean} variables led cholera by approximately 45°–90°, suggesting a time delay of several months.

In addition, we examined SST-local climate associations from 1971 to 2001 to illustrate potential links in a mediation analysis (see Fig. 10 in Appendix). In general, SST had strong positive coherent associations with rainfall, river discharge, and T_{mean}. The interannual signal, namely ENSO, was clearly evident in the coherency patterns (e.g., periods >2.5 years).

Wavelet Summary

Independently, cholera periodicity was detected during the initial epidemic years (1992–1993) in Piura. Once this pattern was examined in relation to climate, coherency was observed in 1996–1999, which includes the resurgence of cholera in 1998, at periods that ranged from 0.5–3 years. No significant climate–cholera coherency was observed in other time intervals, including 1991–1993 (cholera emergence). Overall, the strongest coherencies in 1996–1999 were associated with rainfall and river discharge indicated by strong correlations and consistent phase relationships across multiple periods. In general, rainfall and river discharge links were in-phase (0- to 1-month lag) with cholera, compared to sea and air temperature associations with cholera which had longer temporal lags ($\sim$several months).

Mediation Results

Informed by the wavelet analysis, the interval 1996–1999 was selected to explore mediation factors in El Niño–cholera relationships. Tables 1, 2, 3, 4, and 5 show the OLS statistical summaries, including the temporal lags for each predictor. Figures 6, 7, and 8 illustrate mediation pathway results. The effects of Niño 3.4 SST ($\beta = 0.674$, P value = 0.000), Niño 1+2 SST ($\beta = 0.620$, P value = 0.000), and Paita SST ($\beta = 0.673$, P value = 0.000) on cholera were significant and positive (Path c). In Path a, all SST variables were significantly and positively associated with rainfall, river discharge, and T_{mean} (P value = 0.000). Rainfall ($\beta = 0.936$, P value = 0.000), river discharge ($\beta = 0.894$, P value = 0.000), and T_{mean} ($\beta = 0.702$, P value = 0.000) were also significantly associated with cholera. Of these local climate parameters, the strongest mediators in the SST–cholera relationships were *rainfall* [Niño 3.4 ($\beta = 0.833$, P value = 0.000); Niño 1+2 ($\beta = 0.840$, P value = 0.0000); and Paita ($\beta = 0.809$, P value = 0.0000)] and *river discharge* [Niño 3.4 ($\beta = 0.755$, P value = 0.000); Niño 1+2 ($\beta = 0.818$, P value = 0.0000); and Paita ($\beta = 0.766$, P value = 0.0000)], controlling SST (Path b). T_{mean} was a significant mediator only in the Niño 3.4 SST–cholera relationship ($\beta = 0.453$, P value = 0.013). The Sobel Test results (Path c') are shown in Table 6. The decrease in the effects of SST was statistically significant and supported the observations described above. In general, the optimal temporal lags identified in the OLS models support the trends in the wavelet findings: sea and air temperatures led cholera by several months (Niño 3.4 SST—4-month lag; Niño 1+2 SST—6-month lag; Paita SST—6-month lag; T_{mean}—6-month lag), whereas rainfall and river discharge were synchronized (rainfall—1-month lag; and river discharge—zero-month lag).

Table 1. Path c: Effect of SST (Lag-Months) on Monthly Cholera Cases, Piura, 1996–1999.

Predictor (lag)	β	SE	t-ratio	P value
Niño 3.4 SST (4)	0.674	0.778	6.189	0.000
Niño 1+2 SST (6)	0.620	0.499	5.365	0.000
Paita SST (6)	0.673	0.616	6.165	0.000

Table 2. Path a: Effect of SST (Lag-Months) on Local Climate Variables, Piura, 1996–1999.

	β	SE	t-ratio	P value
Outcome				
Rainfall				
Predictor (lag)				
Niño 3.4 SST (3)	0.609	0.609	5.209	0.000
Niño 1+2 SST (4)	0.525	0.393	4.186	0.000
Paita SST (4)	0.570	0.504	4.701	0.000
Outcome				
River discharge				
Predictor (lag)				
Niño 3.4 SST (4)	0.570	1.029	4.701	0.000
Niño 1+2 SST (6)	0.605	0.602	5.158	0.000
Paita SST (5)	0.618	0.779	5.332	0.000
Outcome				
Air temperature				
Predictor (lag)				
Niño 3.4 SST (0)	0.854	0.087	11.136	0.000
Niño 1+2 SST (0)	0.952	0.031	20.978	0.000
Paita SST (0)	0.932	0.050	17.391	0.000

Table 3. Paths b and c′: Mediating Effect of Local Climate Variables (Lag-Months) on the Niño 3.4 SST (Lag-Months) and Monthly Cholera Relationship, Piura, 1996–1999.

	β	SE	*t*-ratio	*P* value
Outcome				
Cholera				
Path c′: Predictor (lag)				
Niño 3.4 SST (4)	0.170	0.435	2.781	0.008
Path b: Mediator (lag)				
Rainfall (1)	0.833	0.083	13.669	0.000
Path c′: Predictor (lag)				
Niño 3.4 SST (4)	0.244	0.519	3.356	0.002
Path b: Mediator (lag)				
River Discharge (0)	0.755	0.061	10.384	0.000
Path c′: Predictor (lag)				
Niño 3.4 SST (4)	0.307	1.250	1.754	0.086
Path b: Mediator (lag)				
T_{mean} (6)	0.453	1.072	2.588	0.013

Table 4. Paths b and c′: Mediating Effect of Local Climate Variables (Lag-Months) on the Niño 1+2 SST (Lag-Months) and Monthly Cholera Relationship, Piura, 1996–1999.

	β	SE.	*t*-ratio	*P* value
Outcome				
Cholera				
Path c’: Predictor (lag)				
Niño 1+2 SST (6)	0.185	0.237	3.384	0.001
Path b: Mediator (lag)				
Rainfall (1)	0.840	0.075	15.322	0.000
Path c’: Predictor (lag)				
Niño 1+2 SST (6)	0.125	0.353	1.528	0.133
Path b: Mediator (lag)				
River discharge (0)	0.818	0.069	9.997	0.000
Path c’: Predictor (lag)				
Niño 1+2 SST (6)	0.765	0.611	5.401	0.000
Path b: Mediator (lag)				
T_{mean} (6)	−0.241	0.461	−1.701	0.096

Table 5. Paths b and c′: Mediating Effect of Local Climate Variables (Lag-Months) on the Paita SST (Lag-Months) and Monthly Cholera Relationship, Piura, 1996–1999.

	β	SE	*t*-ratio	*P* value
Outcome				
Cholera				
Path c′: Predictor (lag)				
Paita SST (6)	0.234	0.293	4.525	0.000
Path b: Mediator (lag)				
Rainfall (1)	0.809	0.071	15.616	0.000
Path c’: Predictor (lag)				
Paita SST (6)	0.212	0.437	2.741	0.009
Path b: Mediator (lag)				
River discharge (0)	0.766	0.065	9.905	0.000
Path c’: Predictor (lag)				
Paita SST (6)	0.123	1.714	0.406	0.686
Path b: Mediator (lag)				
T_{mean} (6)	0.586	1.857	1.932	0.060

Discussion

Using wavelet analysis, correlations between cholera incidence and El Niño and local climate were found at multiple time scales (0.5–3 years) in the latter half of the 1990s, but no other-related links were observed at the beginning of the epidemic or other time intervals. Specifically, the analysis showed that rainfall and river discharge were strongly associated with cholera in Piura in 1996–1999. This finding supports a recent study (Ramirez 2015) that found rainfall associations (1-month lag) with cholera incidence ($r^2 > 0.80$; P value = 0.000) across several coastal districts in Piura in 1998. More broadly, the findings agree with a wavelet study in Ghana, where cholera and rainfall were synchronized at approximately a low temporal lag (Constantin de Magny et al. 2006). The impacts of rainfall on cholera incidence are well documented (Ruiz-Moreno et al. 2007; Hashizume et al. 2008; Rinaldo et al. 2012). In low-lying areas, such as Piura, heavy rains can lead to flooding in city streets, which may overwhelm sewer and drainage systems. Consequently, sewage waste can surface and be transported via flood waters, which may contaminate water supplies (Curriero et al. 2001; Saskai et al. 2009). In the city of Piura, sewer overflows in city streets are chronic environmental hazards (El Tiempo 1992). Thus, during the 1997–1998 El Niño, it is plausible that torrential rains exacerbated existing infrastructural problems. Furthermore, heavy rains may have increased the flow and level of the Piura River, which in turn contributed to floods and increased human exposure to cholera.

While rainfall associations suggest flooding as a mechanism for exposure, the impact of rainfall extremes on emerging cholera is a much more complex pathway.

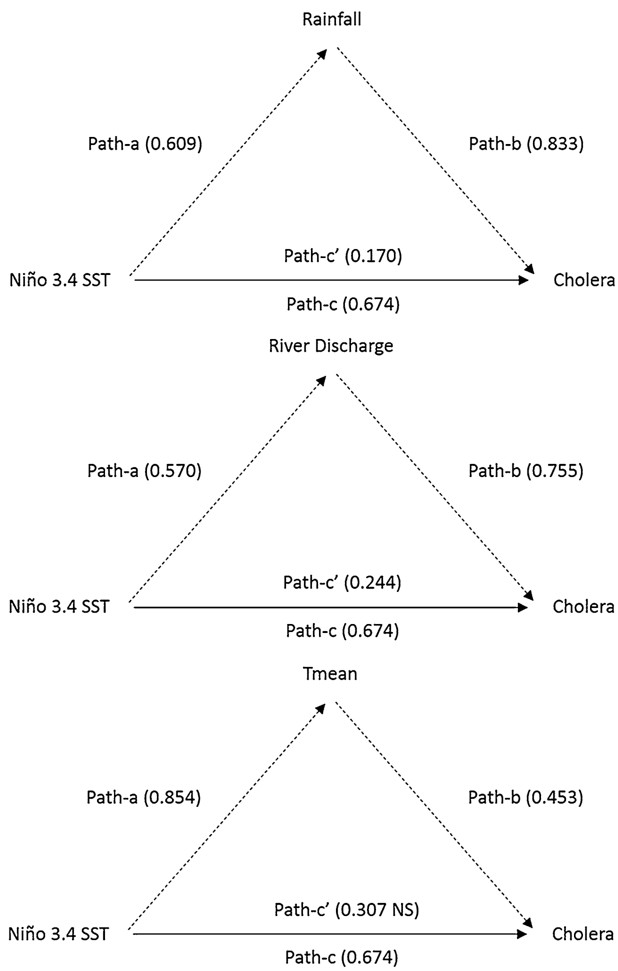

Figure 6. Mediating effects (standardized coefficients) of rainfall, river discharge, and T_{mean} in the Niño 3.4 SST and cholera relationship, Piura, Peru, 1996–1999.

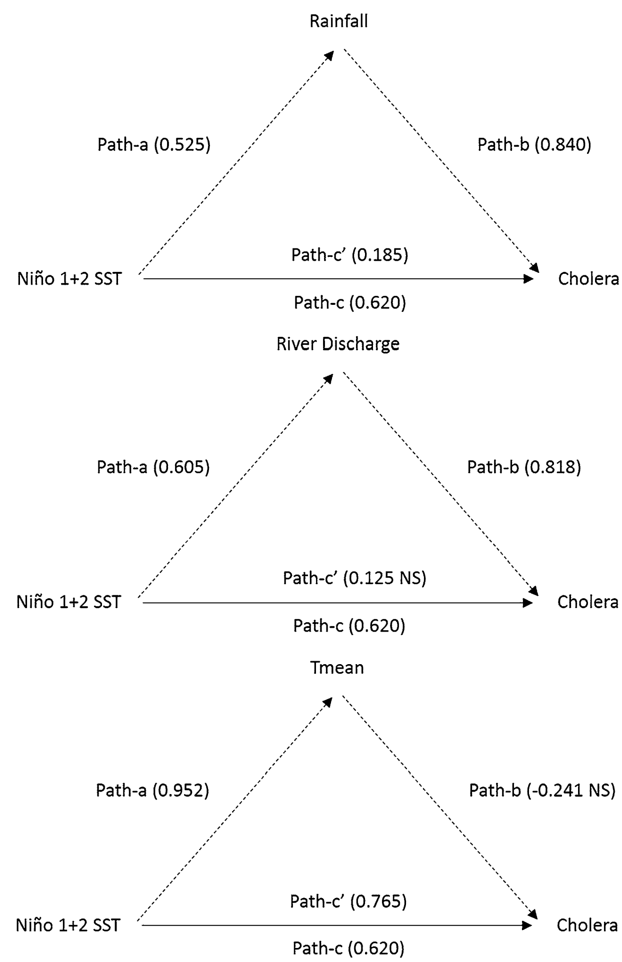

Figure 7. Mediating effects (standardized coefficients) of rainfall, river discharge, and T_{mean} in the Niño 1+2 SST and cholera relationship, Piura, Peru, 1996–1999.

According to Ruiz-Moreno et al. (2007), rainfall can play a dual role in cholera transmission, whereby exposure can decrease due to a dilution effect on bacterial concentrations in water bodies or exposure can increase as flooding contaminate water supplies. It has also been suggested that heavy rainfall can wash away predators of *V. cholerae*, which enables the bacteria's survival, and enhances the potential for exposure (Hashizume et al. 2008). More recently, it has been proposed that increased river discharge may not only contribute to flooding exposure but also transport nutrients into coastal bays that impact the reproduction of vibrios and aquatic reservoirs (Jutla et al. 2011). This is important because these authors found evidence that disputes the role of SST in cholera epidemics, specifically, in the Bay of Bengal, Bangladesh. In Piura, river discharge associated with the Piura River was a significant mediator in the SST–cholera relationship ($\beta > 0.750$; P value = 0.00), and thus, nutrient run-off into coastal areas may also have been an important pathway for transmission in 1998.

This analysis also found associations between SST and air temperature and cholera in Piura, which supports previous work in Lima, Peru (Franco et al. 1997; Speelmon et al. 2000; Gil et al. 2004). Among SST parameters, Niño 3.4 and Paita had the strongest temporal links from 1996 to 1999, which agrees with Ramirez (2015), except for lag association differences (0- to 1-month lag, compared to an estimated 4- to 6-month lag in this study), which may be explained by the scale of analysis (district) and/or period of study (1998). Air temperature was also significantly coherent with cholera but weaker compared to relationships with SST. Nevertheless, concurrent impacts of anomalous temperatures in coastal and terrestrial environments are important for cholera ecology. Elevated sea

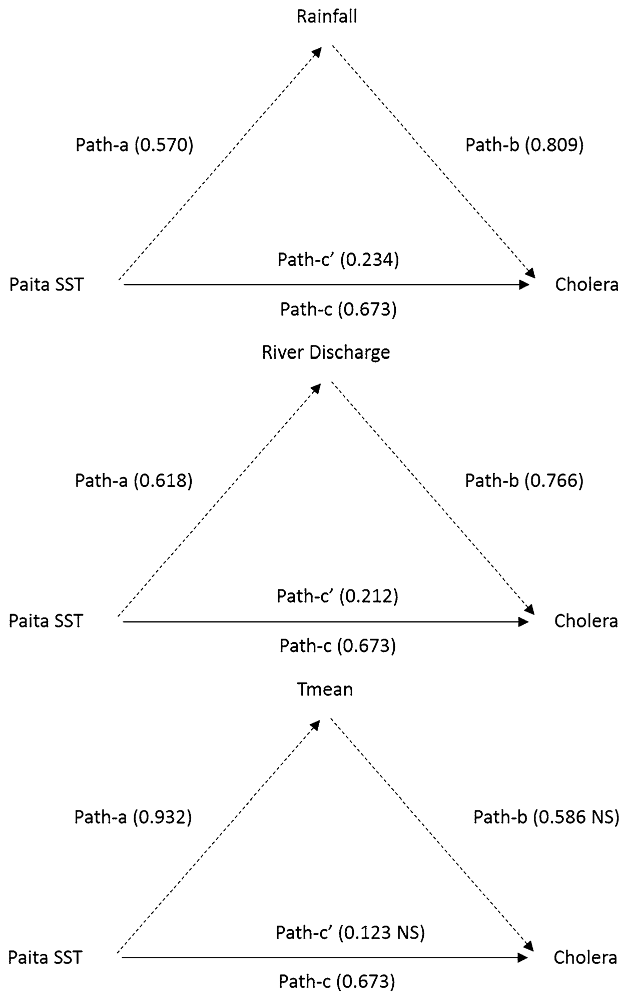

Figure 8. Mediating effects (standardized coefficients) of rainfall, river discharge, and T_{mean} in the Paita SST and cholera relationship, Piura, Peru, 1996–1999.

Table 6. Sobel's Significance Test of Mediation.

SST	Mediator	SE	*t*-ratio	*P* value
Niño 3.4	Rainfall	0.743	4.860	0.000
Niño 3.4	River discharge	0.720	4.267	0.000
Niño 3.4	T_{mean}	1.068	2.510	0.012
Niño 1+2	Rainfall	0.469	4.034	0.000
Niño 1+2	River discharge	0.468	4.564	0.000
Niño 1+2	T_{mean}	0.305	−1.693	0.090
Paita	Rainfall	0.583	4.491	0.000
Paita	River discharge	0.573	4.679	0.000
Paita	T_{mean}	1.619	1.917	0.055

and air temperatures can directly impact vibrios and aquatic reservoirs in coastal and inland water bodies (Franco et al. 1997; Lipp et al. 2003). For example, in Lima, cholera risk was associated with air temperatures above 19–20°C (Madico et al. 1996; Speelmon et al. 2000), and for every 1°C increase, diarrheal disease risk increased by ∼8.0% (Checkley et al. 2000; Lama et al. 2004). More recently, Reyburn et al. (2011) showed that cholera incidence doubled following elevated temperatures by four months in East Zanzibar. In addition, temperature changes have been shown to enhance microbial reproduction in drinking water and food stuffs (Tauxe et al. 1995). Therefore, in Piura, elevated temperatures may have enhanced the incubation of *V. cholerae* in water sources in the near shore, as well as in municipal supplies, and drinks and food products from street vendors, which were identified as vehicles for transmission in the early 1990s (Ries et al. 1992).

Although SST was shown to have a significant association with cholera, a recent study (Jutla et al. 2011), mentioned earlier, suggests that the SST link may be coincidental. According to the authors, the influx of nutrients driven by river flow may influence the abundance of phytoplankton (reservoir of *V. cholerae*), rather than SST, in the Bay of Bengal. This may explain why previous research (e.g., Lobitz et al. 2000) found that SST, which has been shown to have an inverse relationship with chlorophyll (i.e., proxy for phytoplankton), had positive relationships with plankton blooms (Jutla et al. 2011). In Piura, this explanation could be plausible, in part, because El Niños negatively affect biological productivity off the coast of Peru. However, while SST may not affect cholera directly in this coastal context, it may still be significant indirectly if one considers teleconnections. In Piura, local rainfall is strongly linked to conditions in the equatorial Pacific Ocean (Lagos et al. 2008; Takahashi 2004). Rainfall, in turn, has a strong relationship with local river discharge ($r = 0.78$; P value = 0.000). The associations are particularly evident during extreme El Niños (Lavado Casimiro et al. 2012). Based on this knowledge, we hypothesized that El Niño-related connections with cholera were mediated by local climate, particularly rainfall, which is scarce in the region, except during warm events. Indeed, using mediation analysis, we found that rainfall and river discharge were significant mediators in 1996–1999. Rainfall and river discharge at lags of 1- and zero-month had strong mediating effects across all SST–cholera associations ($\beta > 0.750$, P value < 0.05). In addition, it was shown that T_{mean} (lag of 6 months) was a mediator too, but only in the Niño 3.4 SST-cholera relationship ($\beta = 0.453$, P value = 0.013).

Taken together, our analyses suggest there is strong evidence that El Niño influenced the resurgence of cholera in Piura in 1998 yet did not impact the emergence in 1991. Our interpretation rests on the fact that we found significant climate–cholera links during one time interval associated with El Niño (1997–1998). While common areas of high variability were observed in 1992–1993 (in the cross-wavelet); there was no coherence between climate variables and cholera. While this may seem counterintuitive, the lack of coherence in the early 1990s may be explained by the order and magnitude of cholera and El Niño events. According to Ramirez et al. (2013), the onset of the 1991–1992 El Niño began in either May or November of 1991, depending on the definition and region chosen to represent an event (Niño 3.4 versus Niño 1+2). Both (regions) suggest that El Niño followed, rather than preceded epidemic cholera, which began in January 1991. Furthermore, rainfall teleconnections were not observed until the austral summer of 1992 (Fig. 9), which suggests that El Niño-related ecosystem and weather effects were likely absent during the initial epidemic. Thus, El Niño may not have been present to impact *V. cholerae* or water infrastructure in the region. Moreover, it could be argued that the magnitude of El Niño (based on SST anomalies) was weaker in 1991–1992, compared to 1997–1998 (Table 7), and therefore, its capacity for impacts on ecosystems and society was less likely.

Limitations

This study has several caveats. One limitation is that our local climate data were not representative of the entire subregion. We used meteorological stations in the low-lying coast of Piura, which may not have been representative of the highland regions in the study area. However, based on information about the epidemics in 1991 and 1998 (Ries et al. 1992; Ramirez 2015), most cases were reported in the coastal area supporting the findings of this study. Specifically, in 1991, approximately 44.0% of all cholera cases in the Department of Piura were reported in the capital city. Furthermore, in 1998, 96.2% of cases were reported in the coastal segment of the subregion. Another limitation is that we were unable to fully examine the initial cholera outbreak in the wavelet analysis because much of our data in 1991–1992 fell inside the cone of influence, which is subject to edge effects—a general limitation of the wavelet approach (Torrence and Compo 1998). A third limitation is that we were unable to incorporate socioeconomic data into this analysis to assess the potential confounding effects of income and infrastructure poverty on climate–cholera relationships (Emch et al. 2010). We obtained 1993 census data for Peru at the district level, but the next time period available was 2007; thus, an interpolation of these annual datasets would not suffice for this analysis. Lastly, we lacked data to construct a population susceptibility variable (e.g., immunity) in Piura to measure previous disease levels. According to studies in Bangladesh (Koelle et al. 2005), immunity can impact the effects of climate on cholera

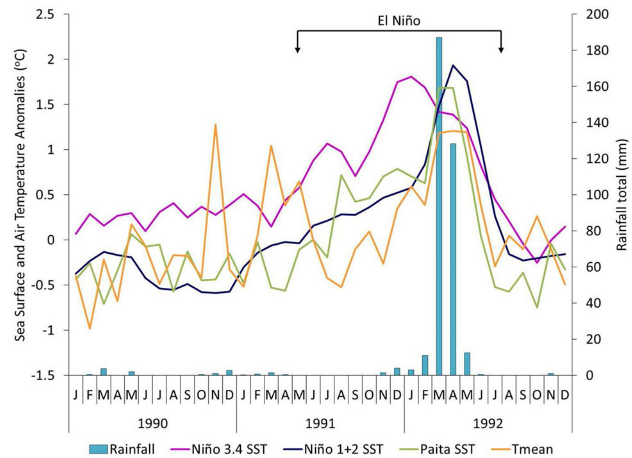

Figure 9. El Niño teleconnections (rainfall and air temperature) in Piura, Peru from 1990–1992. SST in the Niño 3.4, 1+2, and Paita coastal bay shown to illustrate the peak of El Niño.

Table 7. Comparison of SST Anomalies (3-Month Running Means) During the 1991–1992 and 1997–1998 El Niños.

Season	1991	1992	1997	1998
DJF	0.4	**1.8**	−0.4	**2.3**
JFM	0.3	**1.6**	−0.3	**1.9**
FMA	0.3	**1.5**	0	**1.5**
MAM	0.4	**1.4**	0.4	**1**
AMJ	**0.6**	**1.2**	**0.8**	**0.5**
MJJ	**0.8**	**0.8**	**1.3**	0
JJA	**1**	**0.5**	**1.7**	*−0.5*
JAS	**0.9**	0.2	**2**	*−0.8*
ASO	**0.9**	0	**2.2**	*−1*
SON	**1**	−0.1	**2.4**	*−1.1*
OND	**1.4**	0	**2.5**	*−1.3*
NDJ	**1.6**	0.2	**2.5**	*−1.4*

El Niño (bold) and La Niña (italics) months are identified based on the ONI-index, using 1971–2000 base period incidence. For example, even if favorable climate conditions emerged, the likelihood of transmission could be low in times of high immunity because of low population susceptibility. It may, in part, explain why we only found a strong link in 1997–1998, coincidently, following large outbreaks in 1991–1992 in Piura.

Conclusion

In summary, our study provides evidence that a strong but transient El Niño–cholera link in Piura, Peru, mediated by local hydrology, existed in the latter part of the 1990s. To our knowledge, this is the first study to examine the entire period during which cholera was present in Piura, Peru. Furthermore, this study provides an approach to estimate the mediating effects of local climate on a potential El Niño–cholera relationship. Future research should examine further the mediating effects of hydrology on the El Niño–cholera link. For example, investigating river discharge in relationship to SST may provide support for a dual mechanism for SST (i.e., impacts on vibrio ecology and influence on local weather). In addition, we found no evidence of an El Niño link in the earlier part of the decade. This is important because it provides support that El Niño may not have precipitated cholera emergence in Peru (Ramirez et al. 2013). Still, before these results can be conclusive, temporal examinations of El Niño links in other cholera epicenters (e.g., Chancay and Lima) should be undertaken. Also, it will be important for these studies to also explore why El Niño was influential in 1997–1998 and not in 1991–1992. According to Capotondi et al. (2015), impacts are "highly sensitive" to the variability of ENSO characteristics from one event to another. Thus, by comparing the two events, we may learn how the diversity of El Niños impact cholera transmission. Moreover, future studies should incorporate other explanatory factors, e.g., human importation, herd immunity, socioeconomic vulnerability, public health education, or a convergence of variables, including climate.

For public health programming, this study highlights the potential utility of global to local hydro-meteorological information for disease prevention. In particular, it may inform existing efforts that utilize El Niño monitoring to mobilize health personnel and resources in anticipation of extreme weather (Sandoval 1999). At the same time, it suggests caution and careful attention to El Niño-related characteristics in decision-making. While El Niño may provide an opportunity for early warning, its development may vary in intensity and impacts (Glantz 1991), as mentioned earlier; and thus so too may its influence on weather and disease ecology. Nevertheless, concerns about reemerging cholera in the region, as well as the potential impacts of a changing climate, warrant a better comprehension of climate dynamics to improve cholera preparedness during future climate-related extremes.

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Appendix

See Fig. 10.

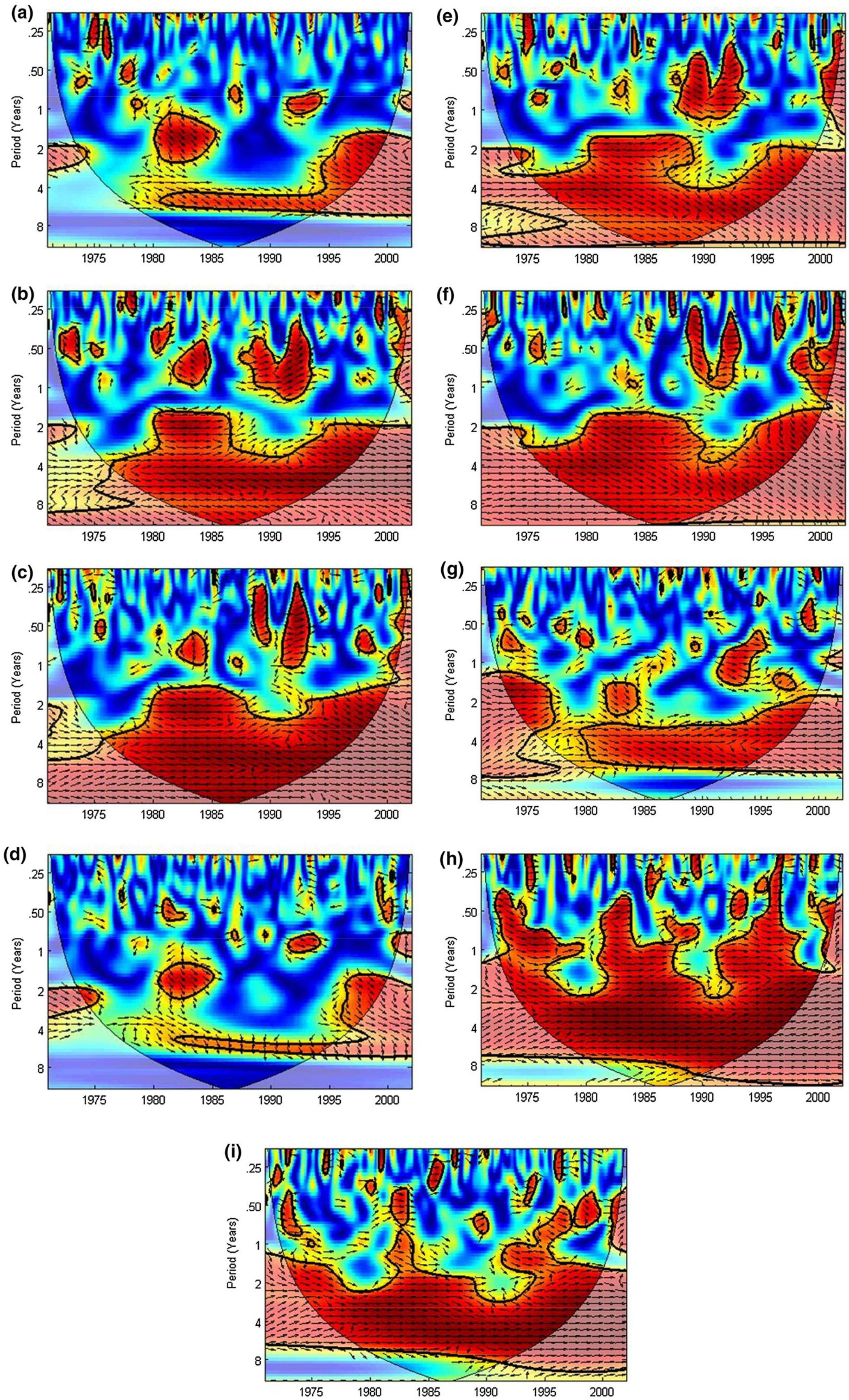

Figure 10. a-i Wavelet coherence analyses between SST and local climate variables: **a** Niño 3.4 SST anomaly and rainfall (square-root transformed); **b** Niño 1+2 SST anomaly and rainfall (square-root transformed); **c** Paita SST anomaly and rainfall (square-root transformed); **d** Niño 3.4 SST anomaly and river discharge (square-root transformed); **e** Niño 1+2 SST anomaly and river discharge (square-root transformed); **f** Paita SST anomaly and river discharge (square-root transformed); **g** Niño 3.4 SST anomaly and air temperature (T_{mean}) anomaly; h Niño 1+2 SST anomaly and air temperature (T_{mean}) anomaly; and **i** Paita SST anomaly and air temperature (T_{mean}) anomaly. The wavelet coherence analysis is denoted by period (scale by year) and across time intervals. The color code shows coherence values that increase from *dark blue* (low) to *dark red* (high). The direction (phase) of relationships is indicated by *arrows*, as such: up (climate lags); down (climate leads); right (climate-cholera in-phase); and left (climate-cholera out of phase). Statistical significance (95.0% confidence level) is indicated by areas within *thick black outlines*. The *black curve* delimits the cone of influence (COI), a region influenced by edge effects.

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