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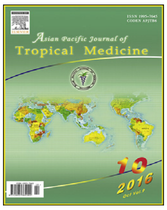

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Meteorological influences on dengue transmission in Pakistan

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ABSTRACT

Objective: To identify the influences of local and regional climate phenomena on dengue transmission in Lahore District of Pakistan, from 2006 to 2014.

Methods: Time-series models were applied to analyze associations between reported cases of dengue and climatic parameters. The coherence trend of regional climate phenomena (IOD and ENSO) was evaluated with wavelet analysis.

Results: The minimum temperature 4 months before the dengue outbreak played the most important role in the Lahore District ($P = 0.03$). A NINO 3.4 index 9 months before the outbreaks exhibited a significant negative effect on dengue transmission ($P = 0.02$). The IOD exhibited a synchronized pattern with dengue outbreak from 2010 to 2012. The ENSO effect (NINO 3.4 index) might have played a more important role after 2012.

Conclusions: This study provides preliminary results of climate influences on dengue transmission in the Lahore District of Pakistan. An increasing dengue transmission risk accompanied by frequent climate changes should be noted. Integrating the influences of climate variability into disease prevention strategies should be considered by public health authorities.

1. Introduction

Dengue fever is one of the most prevalent vector-borne diseases in tropical and sub-tropical regions. Dengue virus (DENV) is mainly transmitted by two species of *Aedes* mosquito: *Aedes aegypti* (*Ae. aegypti*) as the major vector and *Aedes albopictus* (*Ae. albopictus*) as the secondary vector [1]. DENV has been classified into four serologically distinct types (DEN-I, DEN-II, DEN-III, and DEN-IV), which can cause flu-like clinical outcomes, including fever, headache, muscle and joint pain, or retro-orbital pain [2]. Type-specific antibodies can be produced against infection by the same serotype of DENV; however, severe dengue hemorrhagic fever and dengue shock syndrome mediated by an antibody-dependent enhancement mechanism might occur if subsequent infection is caused by different serotypes [3].

The disease burden of dengue has increased dramatically since 1970, and recent estimates indicate 390 million infections annually and approximately 100 million people with clinical symptoms [4]. Dengue fever is dominant in Latin America, South-East Asia, and Pacific Asia; however, countries in South Asia, including Pakistan, India, and Bangladesh, have also reported an increasing number of outbreaks and brought significant impacts on public heath [4–6].

The ecological changes in dengue transmission are attributable to multifactorial causes with complicated interactions. *Ae. aegypti* and *Ae. albopictus* are well-adapted to urban

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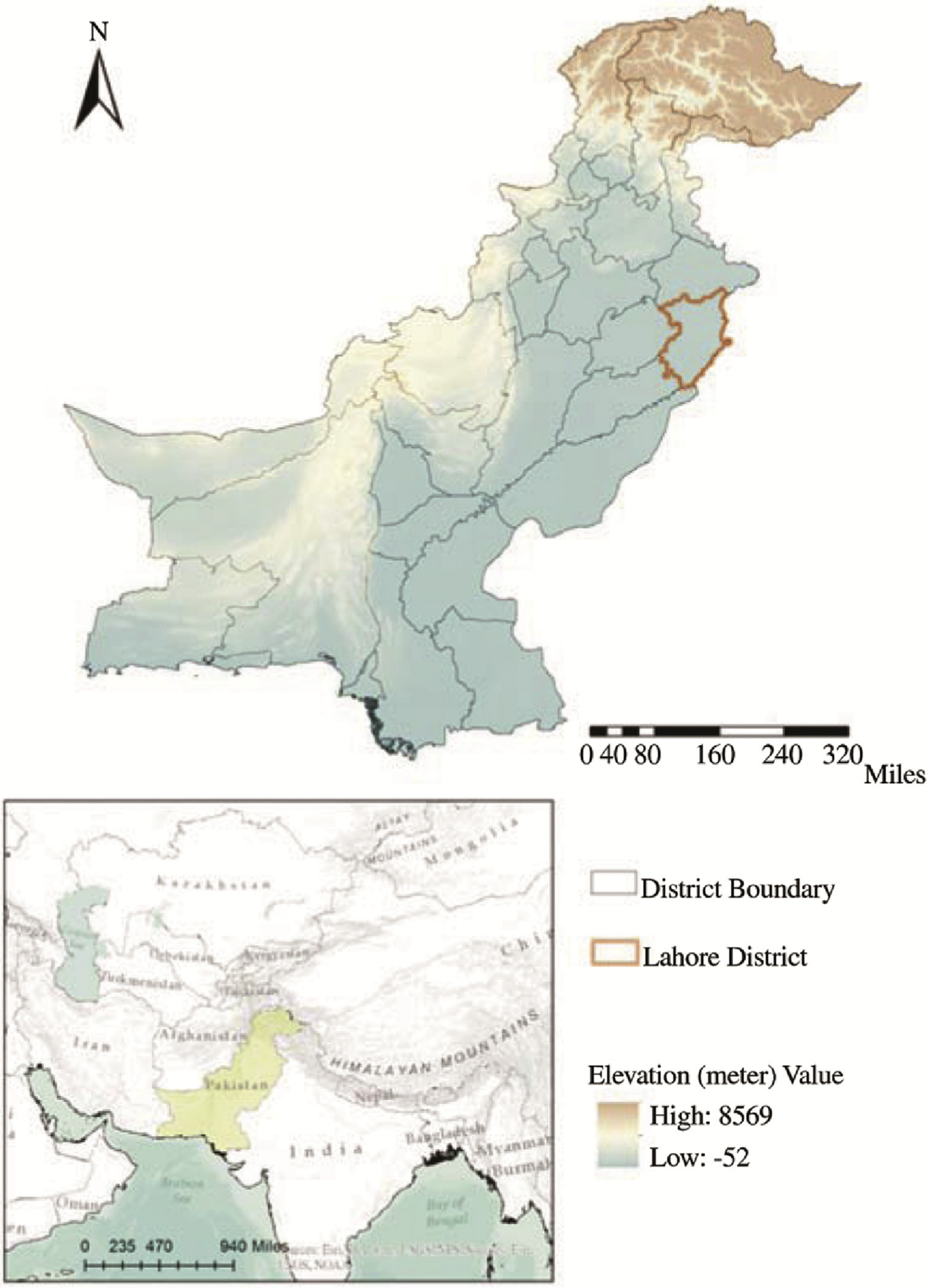

Figure 1. Location of the Lahore District, Pakistan.
The elevation map of Pakistan was acquired from ASTER Global Digital Elevation Map Version 2.

environments; thus, the urbanization triggered by economic development may create more artificial breeding sites preferred by disease vectors [7–9]. Globalization accompanied with frequent international and domestic traveling also enhances the transmission probability of dengue [10,11]. Climate is another important driver, and diverse interactions have been reported among local meteorological parameters (temperature, precipitation, and humidity) and vector population dynamics, virus circulation, and transmission probability [12–14].

More frequently, regional climate changes can cause extreme weather conditions that might influence dengue transmission. The El Niño Southern Oscillation (ENSO) effect is a widely known phenomenon of climate change and is related to the rising sea surface temperature across the tropical Pacific Ocean in 2–7 year cycles [15]. ENSO typically causes regional climate turbulence associated with heavy rainfall and temperature anomalies; however, there is substantial uncertainty regarding the future prediction of these effects [16]. Different synchronized patterns between ENSO and dengue outbreaks have been reported in many studies [17–19]. The Indian Ocean Dipole (IOD) is another ENSO-like climate phenomenon that occurs in the Indian Ocean [20]. Recent studies have demonstrated associations between the IOD and malaria in eastern Africa and dengue in Bangladesh [21,22].

Pakistan has reported few dengue cases before 2006, and most cases occurred in the southern region; however, large outbreaks have been identified and expanded to different parts of the country since then [23]. Whether the rapidly increased dengue incidence is a result of regional or local climate variations is not well understood. Dengue prevention relies highly on vector control and community health education because effective vaccines and drugs are not currently available. It is critical to understand environmental changes and their effects on dengue transmission. Thus, the main goal of this study is to investigate climate variables on dengue transmission in the Lahore District, Pakistan.

2. Materials and methods

2.1. Data collection

The Lahore District is located at the northeastern part of Pakistan and is characterized as a flat plain with low elevation (Figure 1). The largest city within this district is Lahore City, which has a population of over 1 000 000 (2009 census). Lahore District belongs to the subtropical climate zone, in which both *Ae. aegypti* and *Ae. albopictus* can co-exist in urban and suburban settings. The annual temperature ranges from 15 °C to 40 °C, and the cumulative precipitation is 1 000 mm per year, which mainly occurs during the monsoon season in the summer.

Data on dengue cases from 2006 to 2014 were provided by the Health Department, Lahore District. Positive cases were confirmed by detecting nonstructural protein 1 or anti-dengue IgM by an enzyme-linked immunosorbent assay or by determining the nucleotide sequence by means of RT-PCR by following a standard protocol [24]. Gender and age information were also included during the reporting process. Because of the unstable political situation in Pakistan, precise population estimates in the Lahore District were not available after 1998. The dengue case number was used in the analysis instead of the incidence rate, which is commonly applied in epidemiology. The bias should be limited because we did not compare dengue transmission in different locations. Dengue cases were summarized on a monthly basis for further analysis.

Climate data were collected from the Lahore City weather station (31°35′ N, 74°24′ E), which records maximum temperature, minimum temperature, precipitation, and relative humidity on an hourly basis. The index was summarized on a monthly basis. To evaluate regional climate phenomena, we also included the NINO 3.4 index and the IOD index in the analysis. The Nino 3.4 region is located from 120°W to 170°W and 5°N to 5°S, where the anomaly average sea surface temperature has been used to evaluate the ENSO effect [25]. A positive NINO 3.4 index usually indicates a warm ENSO phase (El Niño event), whereas a negative value reflects a cold ENSO phase (La Niña event). The IOD is considered to have an effect similar to ENSO on the Indian Ocean, and its anomaly might result in extreme weather conditions around this region, including in Pakistan [26]. The monthly NINO 3.4 index was acquired from the Global Climate Observing System, which is supported by the National Oceanic and Atmospheric Administration (www.ncdc.noaa.gov/teleconnections/enso/). The IOD index was retrieved from the Japan Agency for Marine-Earth Science and Technology (www.jamstec.go.jp).

Table 1

Gender and age distributions of dengue infection in Pakistan from 2006 to 2014 [*n* (%)].

Year		2006	2007	2008	2009	2010	2011	2012	2013	2014	Total
Gender	Male	137 (63.72)	170 (61.82)	937 (67.80)	73 (60.83)	3 012 (68.64)	14 532 (68.26)	171 (66.28)	1 758 (66.57)	944 (67.72)	21 734 (68.00)
	Female	78 (36.28)	105 (38.18)	445 (32.2)	47 (39.17)	1 376 (31.36)	6 758 (31.74)	87 (33.72)	883 (33.43)	450 (32.28)	10229 (32.00)
Age	<20	66 (32.51)	73 (27.97)	244 (17.66)	47 (39.83)	842 (19.19)	4 710 (25.80)	111 (43.02)	768 (29.08)	425 (30.51)	7286 (25.21)
	20–60	131 (64.53)	175 (67.05)	1 114 (80.61)	63 (53.39)	3413 (77.78)	12337 (67.57)	136 (52.71)	1 774 (67.17)	930 (66.76)	20073 (69.45)
	>60	6 (2.96)	13 (4.98)	24 (1.74)	8 (6.78)	133 (3.03)	1 212 (6.64)	11 (4.26)	99 (3.75)	38 (2.73)	1 544 (5.34)
Total		215	275	1 382	120	4 388	21 290	258	2 641	1 394	31 963

2.2. Statistical analysis

This study sought to evaluate climate influences on dengue transmission in the Lahore District of Pakistan. Cross-correlation function was used to analyze the correlation between the number of dengue cases and climate parameters. Seasonal autoregressive integrated moving average (SARIMA) models were developed to analyze the time-series structure of dengue outbreaks and climate parameters. The simplified formula of SARIMA is presented below:

$$\text{ARIMA}\ (p,\ d,\ q) \times (P,\ D,\ Q)\ S,$$

in which p indicates the non-seasonal autoregressive (AR) order, d is the non-seasonal differencing, and q indicates the non-seasonal moving average (MA) order. P, D, and Q represent the same notations for the seasonal part, respectively. S indicates the time span of the seasonal patterns, which is 12 because monthly data were used in this study. We applied SARIMA models to evaluate the importance of different climatic variables by comparing the Akaike Information Criteria (AIC). A lower AIC indicates better model performance, and the AIC difference indicates the importance of the variables [27]. Both monthly local weather variables (temperature, rainfall, and relative humidity) and regional climate indices (NINO 3.4 and IOD) were included in the analysis. Because minimum and maximum temperatures exhibited very similar patterns and a high correlation, only minimum temperature was included as the thermal indicator in the analysis.

Because of the nonstationary characteristic and inter-annual variability of regional climate phenomena, we applied cross-wavelet coherence analysis to identify the synchronized patterns between regional climate index and dengue transmission. This technique can determine whether the two time-series share similar oscillation patterns over time [28,29]. The map of the study area in Pakistan was generated in ArcGIS 10.3 (ESRI, Redlands, CA). Statistical analysis and modeling were performed with R 3.25.

3. Results

A total of 31 963 dengue cases were reported in the Lahore District, Pakistan from 2006 to 2014 (Table 1). Males were affected more frequently than females (68% *vs.* 32%). Approximately 90% of the cases occurred among individuals younger than 60. The annual reported case numbers ranged from a few hundred to more than twenty thousand in 2011. The temperature in the Lahore District exhibited consistent seasonality, and increased precipitation has occurred since 2010 (Figure 2). The anomaly of IOD exhibited more fluctuation than the NINO 3.4 index.

The results of the cross-correlation plot indicated that both maximum and minimum temperatures exhibited delayed positive correlations with dengue incidence (lag = 4 months) (Figure 3). Elevated precipitation in the previous two months was correlated with dengue occurrence; however, relative humidity showed relatively weaker associations. Both IOD and NINO 3.4 indices demonstrated negative associations with

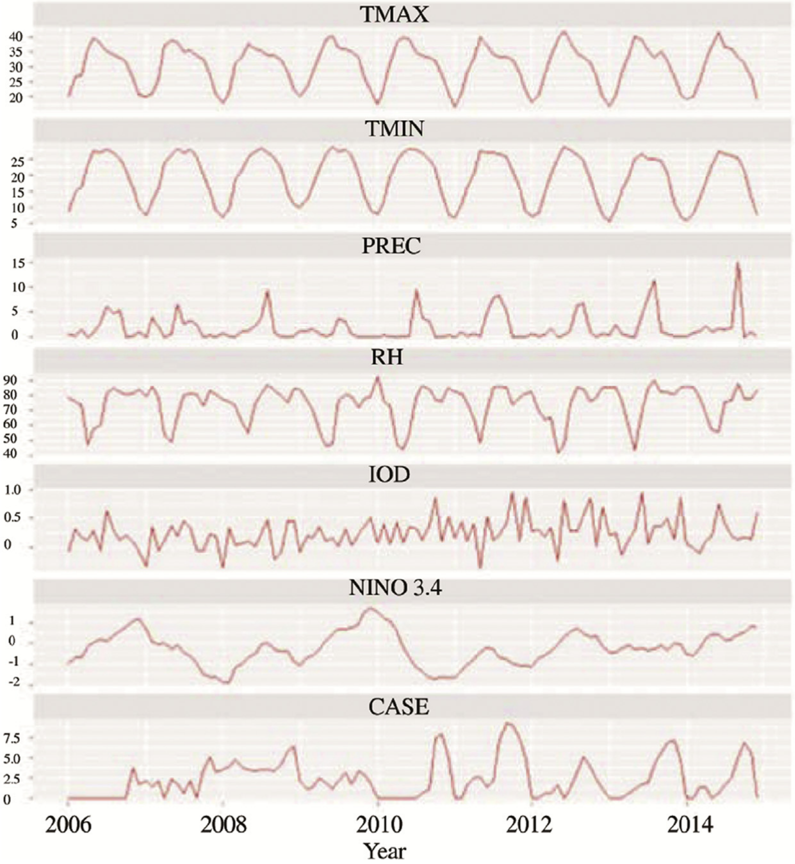

Figure 2. Monthly meteorological parameters and the number of dengue cases in the Lahore District, Pakistan, 2006–2014. The number of reported dengue cases was transformed by the natural log.

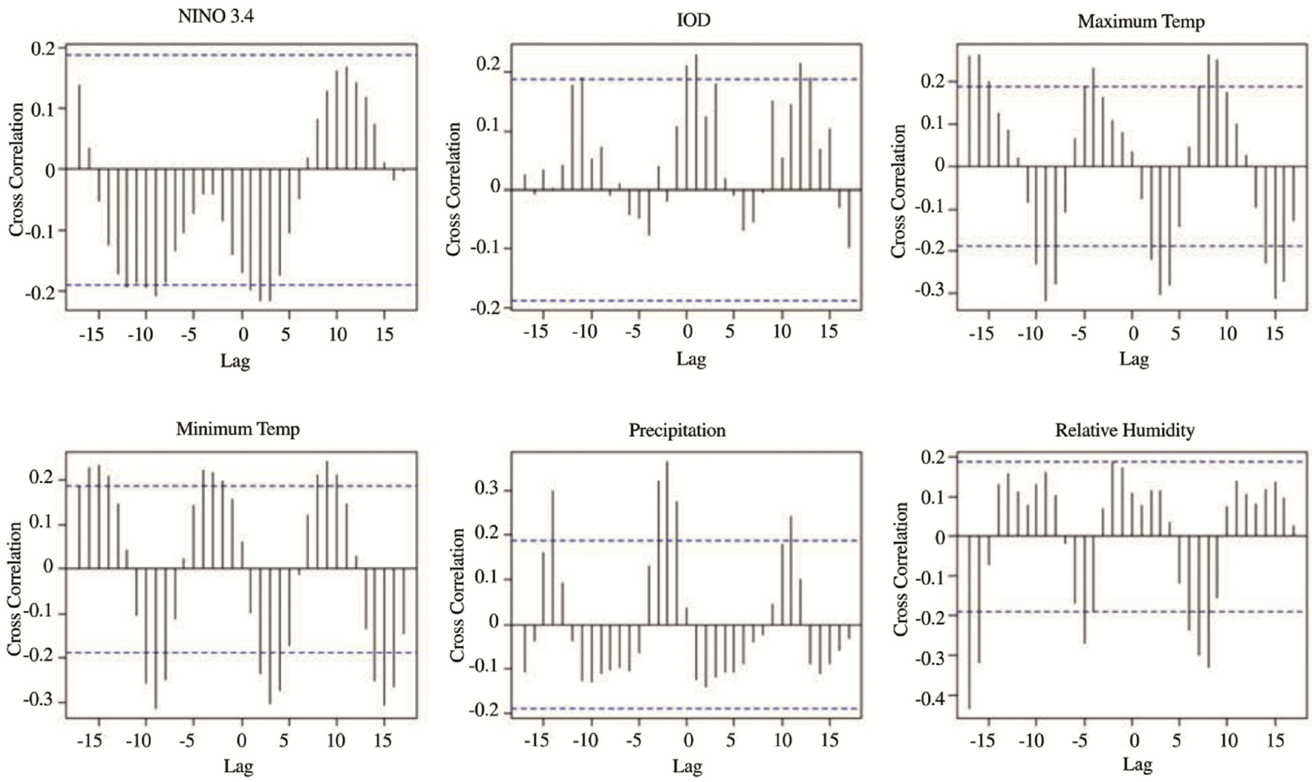

Figure 3. Cross-correlation function of dengue incidence and meteorological parameters.
Dashed lines (blue) indicate the 95% confidence interval.

Table 2

SARIMA results of each meteorological parameter.

Variables	SARIMA*	AR(1)	AR(2)	AR(3)	AR(4)	MA(1)	MA(2)	SAR(1)	SAR(2)	SMA(1)	SMA(2)
Dengue	(1,0,1)	0.288	–	–	–	0.560	–	–	–	–	–
IOD	(4,1,2) (2,0,0)12	−0.847	−0.065	−0.013	0.174	−0.071	−0.894	0.867	−0.296	–	–
NINO 3.4	(2,0,0)	1.428	−0.518		–	–	–	0.717	–	–	–
TMIN	(3,0,1) (0,0,2)12	1.413	−0.496	−0.242	–	−0.642	–	0.429	0.249	0.449	0.508
PREC	(2,0,0)12	–	–	–	–	–	–	0.154	0.554	–	–
RH	(1,0,0) (1,0,0)12	0.398	–	–	–	–	–	0.701	–	–	–

Note: *SARIMA (p,d,q) (P,D,Q)s model.

dengue infection. The negative effect of the NINO 3.4 index may be the result of the influences of the cold phase of ENSO (La Niña events). A univariate SARIMA model decomposed the time-series structure of each variable (Table 2). Dengue cases were more relevant to the case number in the previous month (AR = 1) without a seasonal component. All of the climate parameters from the ground-level weather station and IOD had seasonality structures with different orders. The NINO 3.4 index was captured using an autoregressive model (lag = 2 months).

A multivariate SARIMA analysis was used to evaluate the importance by integrating each climate variable into the dengue ARIMA (1,0,1) model as covariates. The NINO 3.4 index (*AIC* difference = −140.94, $P = 0.02$) and minimum temperature (*AIC* difference = −65.08, $P = 0.03$) were the two most significant parameters related to dengue infection at different lags (Table 3).

A cross-wavelet analysis was applied to detect the synchronized patterns between regional climate phenomena and dengue infection. The IOD and NINO 3.4 indices demonstrated different coherence patterns for dengue transmission (Figure 4). The

Table 3

Model comparisons of different meteorological parameters.

Model[a]	Coefficients	SE	*P*	*AIC*	*AIC* Difference
Null model				1802.88	–
NINO 3.4 (lag = 9)	−338.0621	243.8423	0.02[b]	1661.94	−140.94
IOD (lag = 0)	−200.7605	340.5834	0.36	1804.17	1.29
TMIN (lag = 4)	50.1855	23.6326	0.03[b]	1737.80	−65.08
Precipitation (lag = 2)	34.8775	35.9552	0.33	1772.62	−30.26
Relative humidity (lag = 2)	7.6733	10.6518	0.47	1773.07	−29.81

[a] The lag is determined by the cross-correlation analysis. [b] $P < 0.05$.

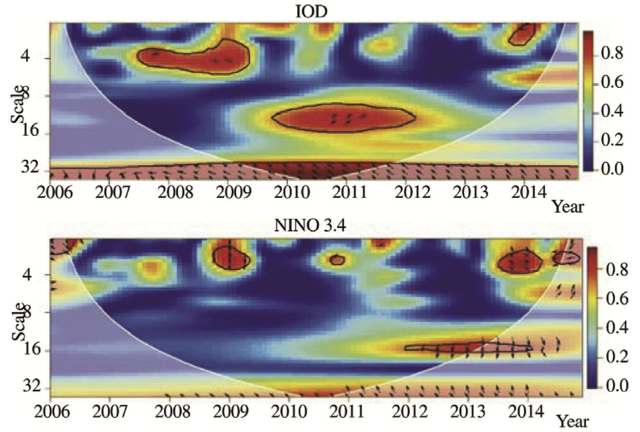

Figure 4. Cross wavelet coherence analysis of dengue incidence and the Indian Ocean Index and NINO 3.4 index.

The cross-wavelet coherence scale ranges from 0 (blue) to 1 (red). The cone of influence (in which results are not influenced by the edges of the data) and the significantly coherent time-frequency regions ($P < 0.05$) are indicated by solid black lines. The arrow indicates the lead/lag relations. For the IOD, arrows moving to the upper-right direction indicate that the IOD leads the dengue case. For the NINO 3.4 index, the arrows at the zero phases indicate that both time-series moved together.

results revealed that the IOD might have been associated with the outbreaks mainly in 2010 and 2011, whereas the NINO 3.4 index exhibited a synchronized pattern with dengue transmission after 2012.

4. Discussion

Dengue transmission in southern Asia, including in Pakistan, is rarely discussed, in contrast to the outbreaks that occurred in Latin America and South East Asia. The scale and geographical distribution of emerging dengue infection in South Asia appears to be increasing [23,30]. Pakistan is one of the countries in this region that has experienced elevated dengue transmission since 2006. Many studies have focused on describing the clinical and epidemiological aspects of dengue transmission in different districts of Pakistan [30]. We conducted the first time-series study to investigate the influences of climate variability on local and regional scales on dengue transmission in the Lahore District of Pakistan. The 9-year (2006–2014) time-series data not only highlight the large outbreak in 2011 but also reveal the gradually increasing annual case number reported after the outbreak.

Climate is an important driver that alters the behavior of mosquito abundance, virus propagation, and transmission to humans. We revealed the importance of minimum temperatures on dengue transmission, which corresponds to findings from other dengue studies [31–33]. Higher temperatures can shorten the interval of larvae development and extrinsic incubation period of DENV, which might enhance the transmission probability [34]. The annual minimum temperatures in the Lahore District range between 5 °C and 27 °C. According to previous experiments, *Ae. aegypti* cease being active when the temperature is below 17 °C [35]. These findings indicate that warming temperatures might extend the period of mosquito activity and the duration of disease transmission.

Bushra *et al.* have analyzed various environmental factors associated with dengue infection in major cities, including Lahore City, in Pakistan. The higher temperatures and heavy rainfall that occurred in 2011 have been proposed to be the cause of the dengue outbreak in 2011 [36]. However, the study focused on the outbreak in only a single year, and no further statistical methods were applied to examine the time-series relationships. Our study also indicated that precipitation during the prior 2 months was positively associated with dengue transmission. Precipitation may play either a positive or negative role on the transmission of mosquito-borne diseases. Appropriate rainfall might produce more water pools or fill containers in the field, which serve as breeding sites of immature mosquitoes. However, extremely heavy rainfall might flush away mosquito larvae or pupae in the breeding sites or directly kill adult mosquitoes [37,38]. The effect of precipitation might have an arbitrary and non-linear pattern. Thus, mosquito development and survival are expected to remain in an appropriate climatic niche, for which appropriate interactions between temperature and precipitation are critical.

The wavelet coherence analysis demonstrated that regional climate phenomena also played a role in dengue transmission. The IOD effect exhibited a synchronized pattern that corresponded to the dengue outbreak from 2010 to 2012. A moderate La Niña effect (also referred to as the cold phase of ENSO) occurred from 2010 to 2012. The interaction between the IOD and La Niña effect was observed after 2007, and a strongly synergized effect of the IOD and La Niña is believed to be the cause of flooding in Queensland, Australia [39]. This interaction might also have contributed to the flooding disaster in Pakistan and may have caused the dengue outbreak in 2011. The effect of ENSO and the IOD on dengue transmission has also been identified in Bangladesh, thus highlighting the importance of IOD in South Asia [22]. Dengue transmission coherence with the NINO 3.4 index after 2012 should also be assessed carefully in the future. The complicated interaction between regional climate phenomena and dengue transmission requires longer time-series data for clarification of these findings.

The lack of mosquito data is a limitation in our study. Knowledge about spatial distribution and the abundance of *Ae. aegypti* and *Ae. albopictus* in the Lahore District is scarce. Fatima *et al.*, through applying an ecological niche model, have found that *Ae. aegypti* distributions are associated with population density and urban structure [40]. More studies about vector ecology and population dynamics should be conducted in the Lahore District to enhance the efficiency of vector surveillance and disease control.

The dengue incidence was higher in males than in females; however, the reason for this difference remains unclear. A similar sex ratio has been reported in other epidemiological studies conducted in different regions of Pakistan [30,41]. Mohsin *et al.* have assessed dengue infection among 400 asymptomatic children under 12 years of age in Lahore and have observed no difference in prevalence between males and females [42]. However, the study focused on younger children; thus, the serological evidence in the total population is not clear. The gender difference in dengue infection in Pakistan might be a result of different culture, behaviors or medical accessibility between genders, and this hypothesis requires further investigation.

Pakistan has recently encountered various natural disasters because of climate change, including flooding and heatwaves, which might increase the transmission risk of dengue fever. Our study revealed the influences of local and regional climate variability on dengue transmission in the Lahore District. This information may provide basic knowledge for developing an early warning system in the future. The system might help public health authorities modify their strategy for dengue prevention under different environmental conditions. Furthermore, there is a strong need to integrate vector control, case management, epidemiological investigation, and health education to combat the growing threat of multiple mosquito-borne diseases, such as dengue, Zika, and chikungunya, which are prevalent in the South Asia region.

Conflict of interest statement

We declare that we have no conflicts of interest.

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References

[1] Lambrechts L, Scott TW, Gubler DJ. Consequences of the expanding global distribution of *Aedes albopictus* for dengue virus transmission. *PLoS Negl Trop Dis* 2010; **4**(5): e646.

[2] WHO. Dengue: guidelines for diagnosis, treatment, prevention and control. Geneva 2009. Available from: http://apps.who.int/iris/bitstream/10665/44188/1/9789241547871_eng.pdf.

[3] Simmons CP, Farrar JJ, Nguyen VV, Wills B. Dengue. *N Engl J Med* 2012; **366**(15): 1423-1432.

[4] Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. The global distribution and burden of dengue. *Nature* 2013; **496**(7446): 504-507.

[5] Anders KL, Hay SI. Lessons from malaria control to help meet the rising challenge of dengue. *Lancet Infect Dis* 2012; **12**(12): 977-984.

[6] Stanaway JD, Shepard DS, Undurraga EA, Halasa YA, Coffeng LE, Brady OJ, et al. The global burden of dengue: an analysis from the global burden of disease study 2013. *Lancet Infect Dis* 2016; **16**(6): 712-723.

[7] Li Y, Kamara F, Zhou G, Puthiyakunnon S, Li C, Liu Y, et al. Urbanization increases *Aedes albopictus* larval habitats and accelerates mosquito development and survivorship. *PLoS Negl Trop Dis* 2014; **8**: e3301.

[8] Gubler DJ. Dengue, urbanization and globalization: the unholy trinity of the 21(st) century. *Trop Med Health* 2011; **39**(4 Suppl): 3-11.

[9] Wu PC, Lay JG, Guo HR, Lin CY, Lung SC, Su HJ. Higher temperature and urbanization affect the spatial patterns of dengue fever transmission in subtropical Taiwan. *Sci Total Environ* 2009; **407**(7): 2224-2233.

[10] Wesolowski A, Qureshi T, Boni MF, Sundsoy PR, Johansson MA, Rasheed SB, et al. Impact of human mobility on the emergence of dengue epidemics in Pakistan. *Proc Natl Acad Sci USA* 2015; **112**(38): 11887-11892.

[11] Raut CG, Rao NM, Sinha DP, Hanumaiah H, Manjunatha MJ. Chikungunya, dengue, and malaria co-infection after travel to Nigeria, India. *Emerg Infect Dis* 2015; **21**(5): 908-909.

[12] Misslin R, Telle O, Daude E, Vaguet A, Paul RE. Urban climate versus global climate change-what makes the difference for dengue? *Ann N Y Acad Sci* 2016; http://dx.doi.org/10.1111/nyas.13084.

[13] Morin CW, Comrie AC, Ernst K. Climate and dengue transmission: evidence and implications. *Environ Health Perspect* 2013; **121**(11–12): 1264-1272.

[14] Cheng Q, Jing Q, Spear RC, Marshall JM, Yang Z, Gong P. Climate and the timing of imported cases as determinants of the dengue outbreak in Guangzhou, 2014: evidence from a mathematical model. *PLoS Negl Trop Dis* 2016; **10**: e0004417.

[15] Climate.gov [Internet]. Available from: https://www.climate.gov/enso.

[16] Kim BH, Ha KJ. Observed changes of global and western Pacific precipitation associated with global warming SST mode and mega-ENSO SST mode. *Clim Dyn* 2015; **45**: 3067-3075.

[17] Thai KT, Cazelles B, Nguyen NV, Vo LT, Boni MF, Farrar J, et al. Dengue dynamics in Binh Thuan province, southern Vietnam: periodicity, synchronicity and climate variability. *PLoS Negl Trop Dis* 2010; **4**: e747.

[18] Fuller DO, Troyo A, Beier JC. El Nino Southern Oscillation and vegetation dynamics as predictors of dengue fever cases in Costa Rica. *Environ Res Lett* 2009; **4**: 140111-140118.

[19] Tipayamongkholgul M, Fang CT, Klinchan S, Liu CM, King CC. Effects of the El Nino-southern oscillation on dengue epidemics in Thailand, 1996–2005. *BMC Public Health* 2009; **9**: 422.

[20] Saji NH, Goswami BN, Vinayachandran PN, Yamagata T. A dipole mode in the tropical Indian Ocean. *Nature* 1999; **401**: 360-363.

[21] Hashizume M, Terao T, Minakawa N. The Indian Ocean Dipole and malaria risk in the highlands of western Kenya. *Proc Natl Acad Sci USA* 2009; **106**(6): 1857-1862.

[22] Banu S, Guo Y, Hu W, Dale P, Mackenzie JS, Mengersen K, et al. Impacts of El Nino Southern Oscillation and Indian Ocean Dipole on dengue incidence in Bangladesh. *Sci Rep* 2015; **5**: 16105.

[23] Rasheed SB, Butlin RK, Boots M. A review of dengue as an emerging disease in Pakistan. *Public Health* 2013; **127**(1): 11-17.

[24] Lanciotti RS, Calisher CH, Gubler DJ, Chang GJ, Vorndam AV. Rapid detection and typing of dengue viruses from clinical samples by using reverse transcriptase-polymerase chain reaction. *J Clin Microbiol* 1992; **30**(3): 545-551.

[25] Rayner NA, Parker DE, Horton EB, Folland CK, Alexander LV, Rowell DP, et al. Global analyses of sea surface temperature, sea ice, and night marine air temperature since the late nineteenth century. *J Geophys Res* 2003; **108**(14): 4407.

[26] Abram NJ, Gagan MK, Liu Z, Hantoro WS, McCulloch MT, Suwargadi BW. Seasonal characteristics of the Indian Ocean Dipole during the Holocene epoch. *Nature* 2007; **445**: 299-302.

[27] Burnham KP, Anderson DR. *Model selection and multimodel inference: a practical information theoretic approach*. New York: Springer; 2002, p. 60-72.

[28] Cazelles B, Chavez M, Magny GC, Guegan JF, Hales S. Time-dependent spectral analysis of epidemiological time-series with wavelets. *J R Soc Interface* 2007; **4**(15): 625-636.

[29] Chaves LF, Chuang TW, Sasa M, Gutierrez JM. Snakebites are associated with poverty, weather fluctuations, and El Nino. *Sci Adv* 2015; **1**: e1500249.

[30] Raza FA, Rehman S, Khalid R, Ahmad J, Ashraf S, Iqbal M, et al. Demographic and clinico-epidemiological features of dengue fever in Faisalabad, Pakistan. *PLoS One* 2014; **9**: e89868.

[31] Zhang Y, Wang T, Liu K, Xia Y, Lu Y, Jing Q, et al. Developing a time series predictive model for dengue in Zhongshan, China based on weather and Guangzhou dengue surveillance data. *PLoS Negl Trop Dis* 2016; **10**: e0004473.

[32] Huang X, Williams G, Clements AC, Hu W. Imported dengue cases, weather variation and autochthonous dengue incidence in Cairns, Australia. *PLoS One* 2013; **8**(12): e81887.

[33] Gomes AF, Nobre AA, Cruz OG. Temporal analysis of the relationship between dengue and meteorological variables in the city of Rio de Janeiro, Brazil, 2001–2009. *Cad Saude Publica* 2012; **28**: 2189-2197.

[34] Tjaden NB, Thomas SM, Fischer D, Beierkuhnlein C. Extrinsic incubation period of dengue: knowledge, backlog, and applications of temperature dependence. *PLoS Negl Trop Dis* 2013; **7**: e2207.

[35] Wong MC, Mok HY, Ma HM, Lee MW, Fok MY. A climate model for predicting the abundance of Aedes mosquitoes in Hong Kong. *Meteorol Appl* 2011; **18**(1): 105-110.

[36] Khalid B, Ghaffar A. Environmental risk factors and hotspot analysis of dengue distribution in Pakistan. *Int J Biometeorol* 2015; **59**(11): 1721-1746.

[37] Chen MJ, Lin CY, Wu YT, Wu PC, Lung SC, Su HJ. Effects of extreme precipitation to the distribution of infectious diseases in Taiwan, 1994–2008. *PLoS One* 2012; **7**: e34651.

[38] Roiz D, Bousses P, Simard F, Paupy C, Fontenille D. Autochthonous Chikungunya transmission and extreme climate events in southern France. *PLoS Negl Trop Dis* 2015; **9**: e0003854.

[39] Evans JP, Boyer-Souchet I. Local sea surface temperatures add to extreme precipitation in northeast Australia during La Nina. *Geophys Res Lett* 2012; **39**(10); http://dx.doi.org/10.1029/2012GL052014.

[40] Fatima SH, Atif S, Rasheed SB, Zaidi F, Hussain E. Species distribution modelling of *Aedes aegypti* in two dengue-endemic regions of Pakistan. *Trop Med Int Health* 2016; **21**(3): 427-436.

[41] Khan E, Kisat M, Khan N, Nasir A, Ayub S, Hasan R. Demographic and clinical features of dengue fever in Pakistan from 2003–2007: a retrospective cross-sectional study. *PLoS One* 2010; **5**: e12505.

[42] Mohsin SN, Ghafoor F, Saleem M, Ghous R, Aasim M. Seroprevalence of asymptomatic dengue infection in children in Lahore. *Epidemiol Infect* 2016; **144**(11): 2276-2282.