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Impact of Climatic Fluctuation on Dengue Virus Etiology

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Abstract

Aedes mosquito-body is the favored habitat for the member of *Flaiviridae*, the most famous member of the family, formerly known as Dengue virus (DENV). Dengue virus infection induces high fever in human and responsible for associated symptoms like skin rashes. In literature, it has been noted that the onset of dengue fever usually occurs in monsoon and winter seasons, which gradually declines with onset of summer. This season-coordinated trend has suggested positive association towards the climate and proliferation of Dengue virus. To investigate this hypothesis, this study has been proposed. In this study, the date-wise data for Dengue positive cases were obtained from the Government hospitals across Gujarat region. The data were further correlated with the climatic parameters for that date. The investigation suggests the strong correlation between climatic fluctuations. The correlation analysis of obtain data suggests the fluctuations in relative humidity, temperature and pressure during day and night has strong impact. We proposed Poisson regression model and Negative Binomial model for prediction.

Keywords: Dengue fever; Climate fluctuation; Poisson regression

Introduction

Aedes mosquitoes render shelter to Dengue virus. The virus brood in mosquitoes and transmitted in the human through mosquito bites. It belongs to the family *Flaviviridae* [1], consist single stranded RNA as their genome and induces fever like symptoms that usually threatens life. Though, dengue fever affecting the mankind since ages, there is little information on virus structure and its replication inside the host [2]. Few vaccines against dengue virus are recently introduced in market however no commercially available vaccine targets all the five serotypes of Dengue virus. Present dengue prevention and control strategies involve the use of insecticidal agents that kills the vector [3].

In Developing countries, especially like India where ¼ of the world population resides the spread of vector borne disease is obvious [1,4]. Asian climate is as diverse as its culture. An India climate is divided in mainly two types of climatic regions: tropical rainy, that oversee the warm climate where temperature normally do not fall below 18 °C. The other region represents the tropical wet or the dry climate [5]. Due to its diverse environmental and geographical heritage India is an ideal destination for conducting the climate impact assessment of particular disease [4,5].

Vector transmitted diseases are accounted for more than 10% of death in a year. Indian government has instituted the National Vector Borne Disease Control Programme (NVBDCP) that vigilantly records the occurrence of vector- transmitted diseases [6]. According to the information available in public domain through NVBDCP, dengue is one of the endemic vector-borne diseases that have affected 35 states of India [6,7]. From them Gujarat ranked fourth in 2016 in list of dengue affected states. The numbers of DENV affected patients are increasing continuously in the state in subsequent in the year 2017. The similar studies have performed in other Asian countries, Thailand, Philippines and Bangladesh have suggested that the maximum cases of DENV induced fever were observed during the winter season [2,8]. Indicating the direct impact of climate on Dengue vector transmission and thereby the spread of Dengue virus.

An impact of climatic fluctuations on other vector-borne diseases, such as Malaria is well- documented by large groups of researchers [9]. Contrasting to this, no region-specific document is available for the association of climatic fluctuations on Dengue virus transmission. Current development in remote sensing technology has facilitated the region-specific measurement of climatic parameters [10]. Remote-sensing based weather forecasting platforms, Earth System Research Laboratory and European Centre Medium-range weather forecast (ECMWF), records the temperature, humidity and pressures four times in a day [10,11].

The presented study was conducted for one of the large state of India, covering around 196,024 km^2 region of Indian subcontinent. In this study the day- wise detail for various climatic parameters were obtained. In parallel set of survey, the details for the Dengue patients were obtained from the hospitals across the Gujarat region. The details for 2,920 dengue affected patients were obtained and processed further for correlation analysis. In addition to that a statistically validated model was developed for forecasting. Through analysis, strong correlation of selected environmental factors with dengue occurrence was established. The obtained results were transformed in to a statistical model developed through Poisson regression methodology. The developed model is statistically significant and realistic.

Experimental Procedure

Dengue positive patient details

Gujarat provenance is sub-divided in 33 districts; the data were obtained from the Central Government Hospital repository that maintains the records for Gujarat Region. Data for positive Dengue cases were obtained from the hospitals representing 8 different zones of Gujarat. The particulars are presented in Table 1. Only those positive cases were taken in account which have analyzed through immunodiagnostic techniques.

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Data-mining for climatic parameters of Gujarat region

European Centre for Medium-Range Weather Forecast (ECMWF) provides accurate medium-range global weather forecasts and the date-wise record for temperature, pressure and relative humidity [10]. The data was obtained towards providing the region-specific longitude and latitude; it measures and subsequently records these parameters for every 10 km radius. The data were collected for four-time zones, 12 A.M., 6 A.M., 12 P.M. and 18 P.M. respectively. The readings were obtained as net CDF files that further decoded through MATLAB analysis tools, workflow for the process presented in Figure 1. The obtained climatic data were further sorted as minimum and maximum values for each parameter for particular day. As an example, on the day 26th January, 2016, there were four records for Temperature, 14°C (12 A.M.), 22°C (6 A.M.), 30°C (12 P.M.), 20°C (18 P.M.) for analysis minimum temperature (14°C) and maximum temperature (30°C) were taken in account. The temperature difference was calculated towards subtracting the value of day high and night-low.

Correlation analysis

Daily record of minimum and maximum value of climatic data was plotted against the number of dengue patient recorded for that particular day across various regions of Gujarat. For the preparation of prediction model [12,13] the patient details and the climatic data for the year 2016 were considered. The Indians states; Sikkim and Arunachal Pradesh have observed lowest positive cases. These States were considered as negative control for the analysis. West Bengal and Gujarat have observed highest positive cases for the year 2016. These States were considered as positive control for analysis.

Development of prediction model

SAS statistical package was used to develop the model for climate-based forecasting of Dengue instances. The sorted data were subjected to multiple regression analysis. Temperature, Pressure, and Relative humidity are three independent variables [14,15] affecting the Dengue spread, hence the count of dengue patients was considered as dependent variable.

Equation-1 represents the model for simple multiple regression. In which Y expressed as dependent variables (Dengue patients), while X_1, X_2, and X_3 represents independent variables Temperature, Pressure, and Relative humidity respectively.

$$y = B_0 + B_1 X_1 + B_2 X_2 + B_3 X_3 + e \quad (1)$$

Assessing the data towards multiple regression analysis has demonstrated the strong interrelationship leading to wrong interpretation. Hence a need of more specific statistical analysis was observed, and the data were further transformed to Poisson regression. Poisson regression is used when the dependent variable is a count [16-22]. For modelling of over-dispersion in count data, a factor representing unobserved heterogeneity was added to a model. That leads towards the negative binomial regression model.

The details of variables for Poisson regression model represented towards (Tables 2 and 3) while the negative binomial regression model are represented towards (Table 4). Each model was fitted to zero-inflated and Zero-non-inflated probabilities.

Results

Province-wide distribution of dengue in India

India has diverse culture and geographical conditions; each province exhibits uniqueness in life style, food habits and environment. Reflecting into occurrence of particular disease, (Figure 2) shows the number of positive dengue cases in province across India. During 2016, Gujarat provenance has observed highest number (7896) of dengue positive cases in its history [6]. While the states like West Bengal (WB) and Punjab has high number of dengue cases since last 5 years. Therefore, it is interesting to recognize the underlining factors for the sudden rise in Dengue cases in Gujarat. In a study for the Gujarat and other provenance a common pattern for dengue endemic was observed. The steep rise in Dengue patients were observed in Month of September, October and November (Figure 3). West Bengal provenance has observed highest Dengue cases after Gujarat provenance, in the same months. However, both states have different climatic condition during these two months. Unlikely to this, in a study conducted for Mexico has shown the more number of incidences of Dengue cases were during the monsoon season [8,17]. Indicating the role of other climatic factors, beyond the temperature fluctuations, many other factors are associated here. No cases of dengue fever were reported for the month of January and March. West Bengal as reference province, a comparative analysis was performed (Table 5) to study the associated factors. The mean difference of day-night climate fluctuations is tabulated in Table 5. It Indicates that the states like Sikkim and Arunachal Pradesh which has lowest reported Dengue cases, has less pressure fluctuation during day-night compared to the dengue affected states Gujarat and WB. In other observations, relatively low temperature at night reduces the instances of Dengue fever. For abstracting this relationship for better prediction, the data sets were subjected to statistical analysis.

Factor-based impact analysis and climatic association

In Gujarat, no positive dengue cases have been reported for the month of March and January. Henceforth the climatic conditions for those months were used as control. It has been observed that, high number of dengue cases was observed when the difference in Day-Night temperature is above or equal to 2°C (Figure 4). In the month like January and March this difference is very less, sometimes below 1°C, indicating the role of relatively low night temperature in reducing the dengue instances. The other crucial factor, atmospheric pressure had great impact when the day-night difference is above 200 Pascal (Figure 5). Relative humidity is the third major factor that positively affects the growth of Dengue virus (Figure 6). The study conducted by other group have shown the large impact of monsoon on Dengue incidence, as it logically connected with the breeding of Dengue host in stored rain water [17]. However, In Indian Climate the maximum number of cases were observed post monsoon, suggesting the breeding of vector in stored water in relatively less humid environment [2,18]. In an analysis encompassing the association of dengue fever incidences with climate fluctuations for past six years, indicates the strong effect of temperature and relative humidity. In general, following two trends were observed (Table 6) in a research that triggers dengue virus spread.

1. Warm day-cool night.
2. Warm day- cool night and high humidity.

Prediction modeling

As mentioned in section 3.1 and 3.2, these climatic factors have strong positive impact on dengue outbreak; this correlation can be transformed to statistical modelling [19,20]. The first attempt was made to establish a relationship among variables Temperature, Pressure and Humidity using simple linear regression [21]. The predictor variables have shown high interdependence hence leading to biased estimates of dengue incidence (Figures 7 and 8).

Serial no	Region/District	Name of hospital/s	No of patients	Sample size/year	Females	Males
1	Ahmedabad Latitude: 23.03 Longitude: 72.40	B J Medical College, Ahemdabad,	1033	1,221 (2016)	310	723
2	Nadiad Latitude: 22.92 Longitude: 72.99	Government Civil Hospital, Nadiad	162	641 (2016)	70	92
3	Nadiad Latitude: 22.92 Longitude: 72.99	Sanjay Hospital, Nadiad	90	90 (2016)	37	53
4	Godhra Latitude: 22.80 Longitude: 73.55	Government Civil Hospital, Godhra	8	293 (2016)	1	7
5	Changa Latitude: 22.56 Longitude: 72.92	Charusat Hospital, Changa	72	72 (2016)	39	33
6	Surat Latitude: 21.17 Longitude: 72.83	Surat Municipal Institute of Medical Education and Research (SMIMER)	458	458 (2016)	179	279
7	Dahod Latitude: 22.83 Longitude: 74.25	Government Hospital, District Dahod	40	40 (2016)	21	19
8	Vadodara Latitude: 22.30 Longitude: 73.18	Dhiraj Hospital, Vadodara	105	105 (2016)	47	58

Table 1: Details for dengue patients obtained from hospitals.

Criterion	Df	Value	Value/ Df
Deviance	8	620.6194	77.5774
Scaled Deviance	8	620.6194	77.5774
Pearson Chi-Square	8	750.7658	93.8457
Scaled Pearson X2	8	750.7658	93.8457
Log Likelihood	--	4047.661	--
Full Log Likelihood	--	-342.668	--
AIC (smaller is better)	--	693.3361	--
AICC (smaller is better)	--	699.0503	--
BIC (smaller is better)	--	695.2757	--

Table 2: Criteria for assessing goodness of fit.

Criterion	Df	Value	Value/Df
Deviance	--	685.3361	--
Scaled Deviance	--	685.3361	--
Pearson Chi-Square	7	750.7658	107.2523
Scaled Pearson X2	7	750.7658	107.2523
Log Likelihood	--	4047.661	--
Full Log Likelihood	--	-342.668	--
AIC (smaller is better)	--	695.3361	--
AICC (smaller is better)		705.3361	--
BIC (smaller is better)	--	697.7606	--

Table 3: Criteria for assessing goodness of fit when model subjected to zero inflated data.

Hence, the Poisson model was introduced for the count data of Dengue patients assuming the equal mean and variance. The data

Criterion	Df	Value	Value/ Df
Deviance	8	12.2404	1.53
Scaled Deviance	8	12.2404	1.53
Pearson Chi-Square	8	14.7951	1.8494
Scaled Pearson X2	8	14.7951	1.8494
Log Likelihood	--	4333.865	--
Full Log Likelihood	--	-56.4636	--
AIC (smaller is better)	--	122.9272	--
AICC (smaller is better)	--	132.9272	--
BIC (smaller is better)	--	125.3517	--

Table 4: Criteria for assessing goodness of fit negative binomial model.

for dengue patients contains too many zero counts leading towards underestimating the variance. Therefore, here, we are presenting four models for count data with many zero (Tables 7 and 8), following four models were tested for the count data.

1. Poisson model
2. Zero Inflated Poisson
3. Negative Binominal
4. Zero Inflated Negative Binominal

In Poisson model, a log-linear relationship between the mean (μ) and the variables was specified as

$$log(\mu) = log(n) + intercept \ + temperature \ + pressure \ + \ relative\ humidity$$

The unknown parameters for intercept, temperature, pressure, and relative humidity were estimated by the GENMOD procedure in

Indian States	Total number of Patients (2016)	Geographic distance*	Month	Climatic parameters		
				Temperature	Pressure	Relative Humidity
West Bengal			October	0.58	170.71	-0.52
	17702	2150 km	November	0.53	134.37	0.71
			December	0.51	170.72	0.03
			March	0.55	188.93	-1.2
			October	0.96	226.06	0
Gujarat	7869	2150 km	November	1.07	201.49	0.39
			December	1.84	200.02	0.91
			March	3.02	263.14	0.31
			October	-2.12	-51.16	0.59
Sikkim	8	508 km	November	-1.7	-46.31	0.71
			December	-0.28	-34.91	0.39
			March	-0.66	-66.36	1.51
			October	1.2	78.02	-0.6
			November	0.89	104.96	0.1
			December	0.22	135.05	-0.04
Arunachal Pradesh	13	901 km	March	1.19	83.48	-0.17

Table 5: Comparative analysis for various states of India.

Year	Total Number of Dengue Patient in Gujarat (October)	Climatic Parameter of March Month			Climatic Parameter of October Month		
		Temperature	Pressure	Relative humidity	Temperature	Pressure	Relative humidity
2010	142	**2.9637**	**151.17**	**0.4482**	**0.8454**	**115.08**	**-0.3571**
2011	62	2.7877	133.83	0.3448	1.2131	115.08	-1.2834
2012	98	3.3349	131.36	0.5305	1.4623	124.74	0.3167
2013	275	**3.2518**	**150.6603**	**0.2305**	**0.9956**	**82.04**	**-1.50215**
2014	178	3.053	157.64	0.4351	0.8204	127.018	0.109
2015	288	**2.57**	**19.47**	**0.9238**	**-0.6578**	**124.03**	**-0.1793**
2016	378	**2.65**	**263.14**	**0.31**	**0.96**	**226.06**	**0**

Table 6: Year-wise analysis of dengue cases, wherein no significant number of cases was detected in month of March.

	Possion Regression			ZIP		
Parameters	Estimates	Standard Error	Pr>Chisq	Estimates	Standard Error	Pr>Chisq
Intercept	11.3835	9.3191	0.2219	11.3835	0.962	<0.0001
Temperature	-0.0819	0.1214	0.5	-0.0819	0.0125	<0.0001
Pressure	-0.0248	0.0202	0.2193	-0.0248	0.0021	<0.0001
Humidity	1.168	1.0377	0.2601	1.168	0.1071	<0.0001
Scale	9.6874	0	--	1	0	--
Intercept		--		-21.2029	11602.71	0.9985

Table 7: Poisson regression and zero inflated Poisson model for Gujarat region.

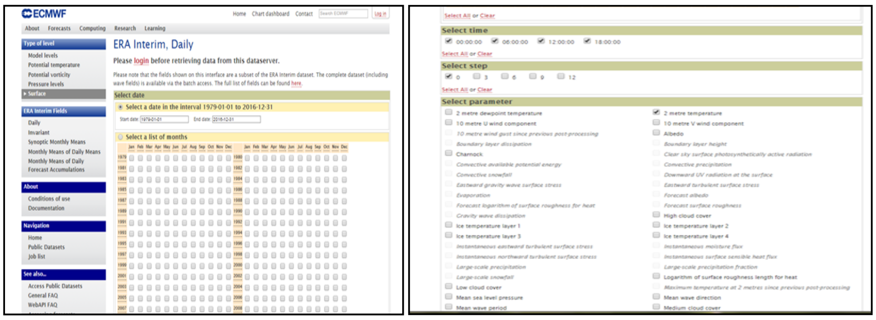
Parameters	Negative Binomial			ZINB		
	Estimates	Standard Error	Pr>Chi-sq	Estimates	Standard Error	Approx Pr>|t|
Intercept	11.6349	3.7909	0.0021	11.63492	3.790142	0.0021
Temperature	-0.0293	0.0931	0.7529	-0.02931	0.093105	0.7529
Pressure	-0.0267	0.0084	0.0015	-0.02665	0.008405	0.0015
Humidity	1.1581	0.471	0.0139	1.158112	0.471081	0.014
Dispersion	0.4849	0.1912	--		--	--
Inf-Intercept	--	--	--	96.42425	--	--
Inf-Temperature	--	--	----	-120.68	--	--
Alpha	--	--	--	0.484925	0.191242	0.0112

Table 8: Negative binomial and zero inflated negative binomial model for Gujarat region.

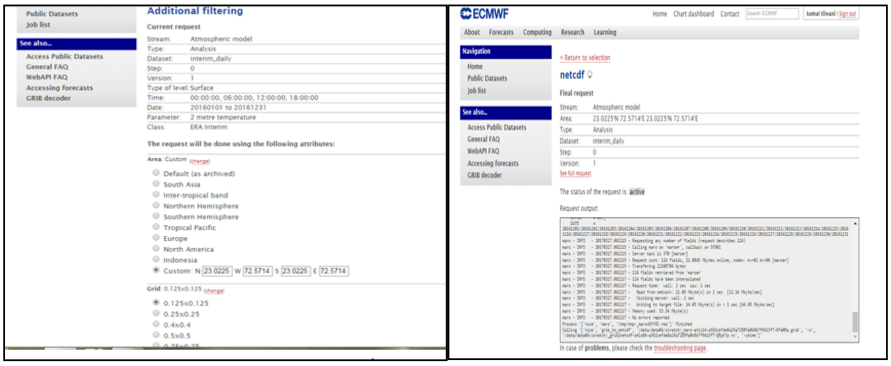
SAS. In zero inflated Poisson model, the scale parameter was fixed for model –fitting. The model illustrates the scale value 1, suggesting its appropriateness for the prediction. Poisson model and the negative-binomial model components within each of ZIP (Zero Inflated Poisson) and ZINB (Zero Inflated Negative Binomial), the intercept for three covariates, were estimated (Tables 7 and 8).

Discussion

The growth of host and thereby the residing Dengue virus is positively correlated towards environmental fluctuations. The high impact of pressure drop and relative increment in humidity during the night time can be seen as one of the key factor. The tested four model shave shown the significant impact of predictor variables (*p*-value



a. Time selection **b**. Parameter selection



c. Insertion of geographic information **d**. Results generated in net CDF

Figure 1: Workflow for ECMWF for climate data mining.

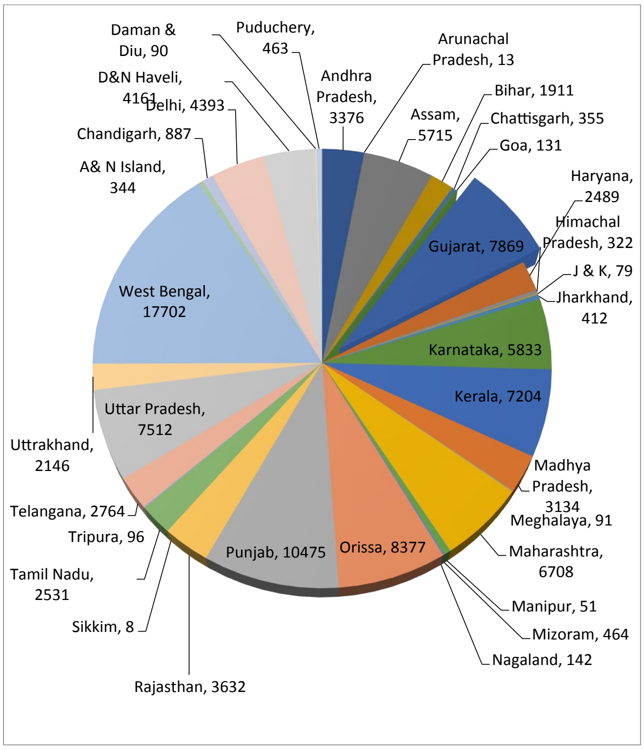


Figure 2: Distribution of dengue cases among the states of India in 2016.

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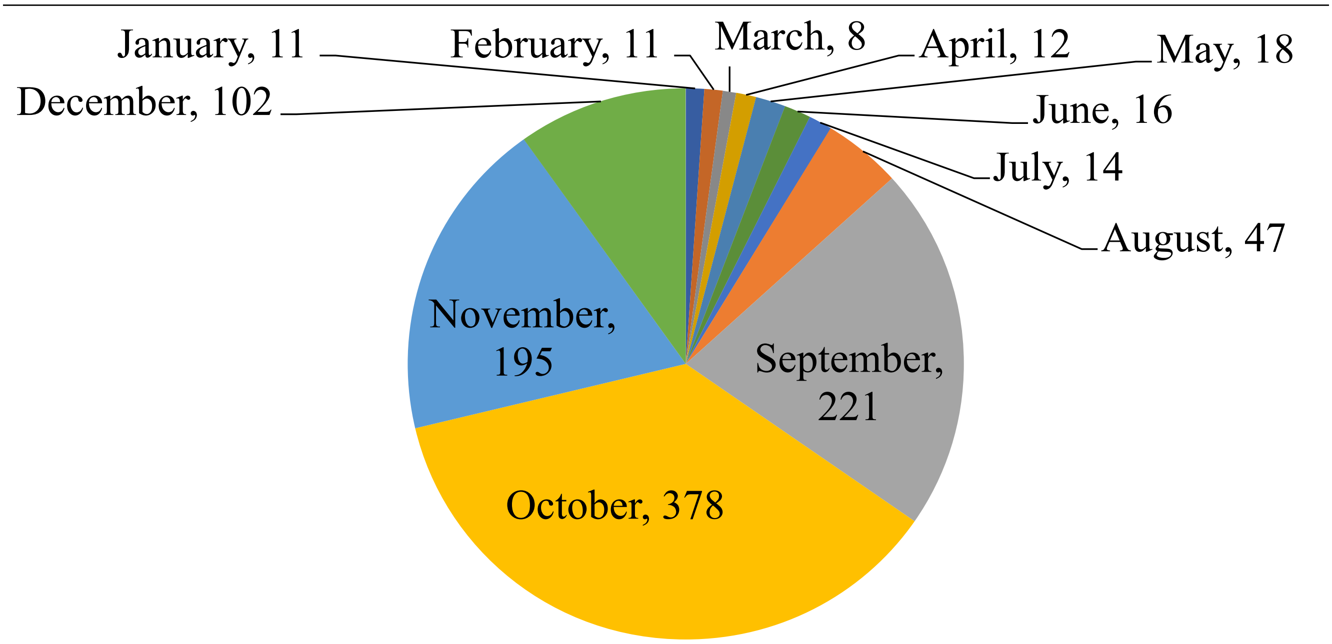

Figure 3: Occurrence of dengue cases in Ahmedabad (Gujarat) region during 2016.

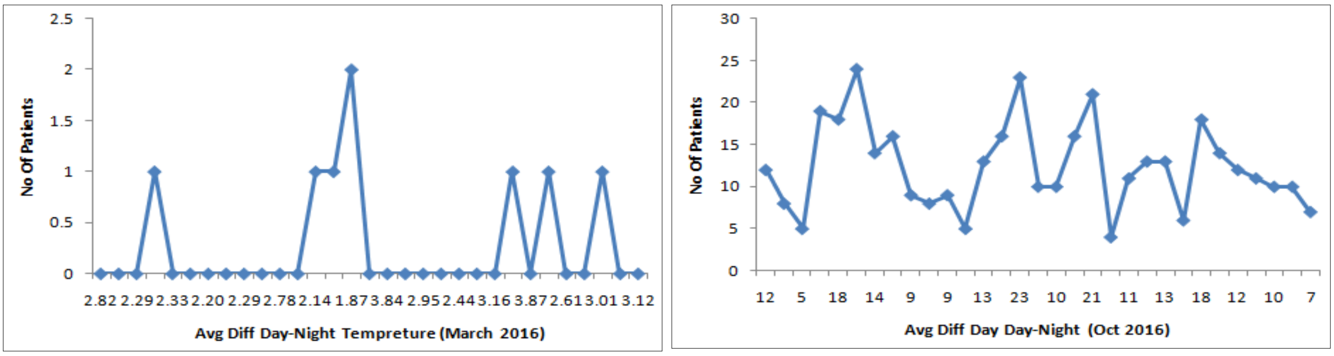

Figure 4: Correlation analysis for temperature fluctuation.

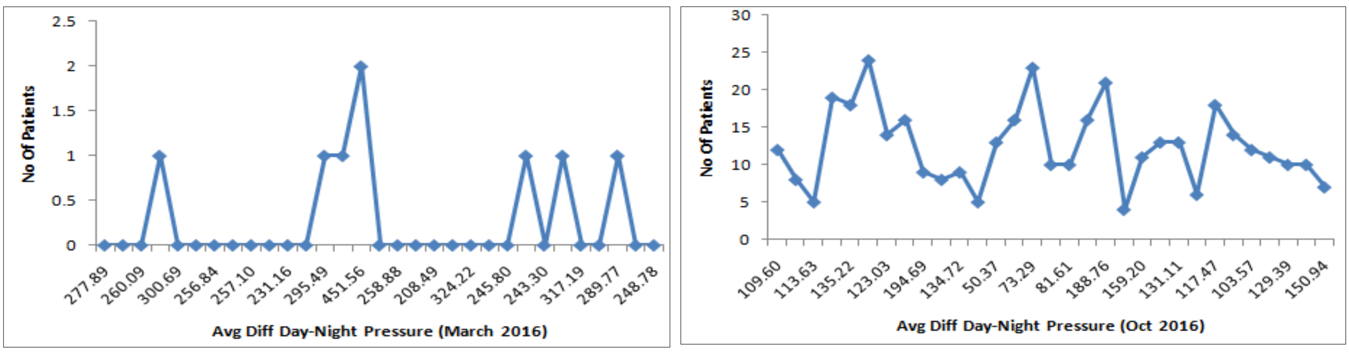

Figure 5: Correlation analysis for pressure fluctuation.

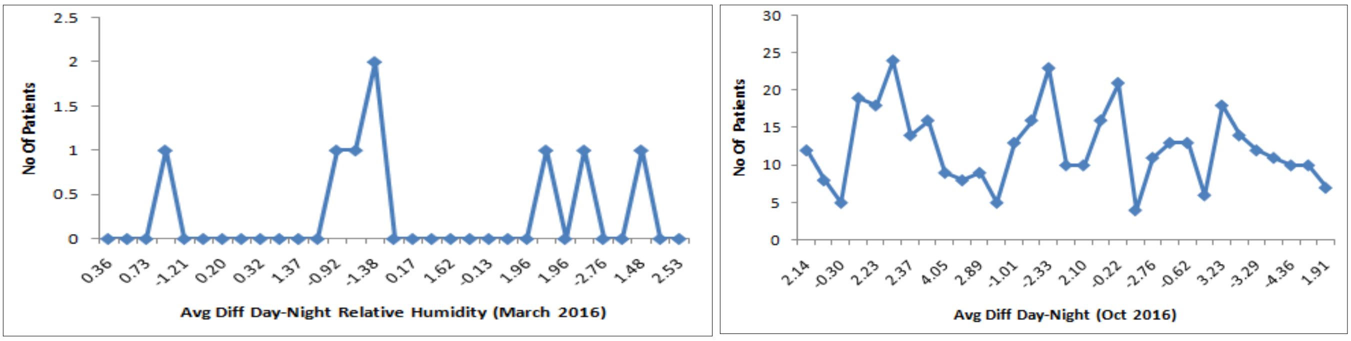

Figure 6: Correlation analysis for the factor relative humidity.

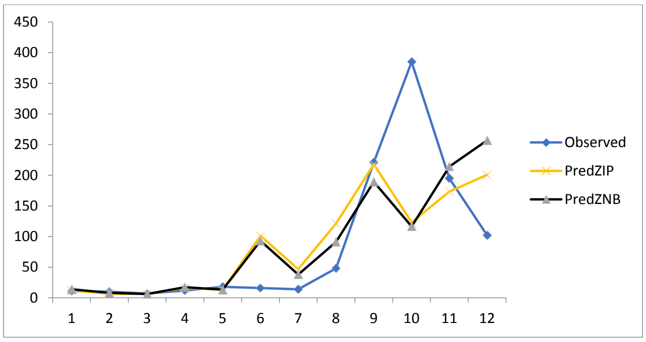

Figure 7: Showing the predicted values towards two models, ZIP and ZNB versus actual dengue incidences.

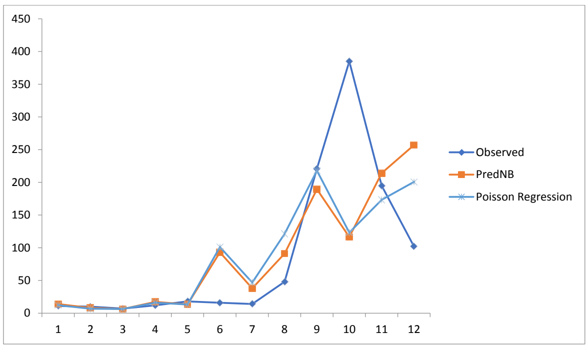

Figure 8: Showing the predicted values towards two models, poisson regression and NB versus actual dengue incidences.

>0.05). As mentioned in WHO guidelines [22], the major cause of dengue outbreak is unhygienic practices that enhance the breeding of dengue vectors. Besides confirming the WHO directives, the study furthermore emphasizes the role of climate in spread of vector borne diseases like dengue.

Conclusion

The extensive statics exercise has confirmed the climatic association in dengue transmission. Moreover, the developed statistical model is statistically significant and realistic. It predicts the dengue cases with 70% accuracy when tested for the region under study. The 30% deviation is pointing toward other environmental factors and unhygienic practices. The results of conducted statistical analysis clearly shows the impact of climatic fluctuation on dengue transmission, particularly the high impact of pressure drop and increasing relative humidity during day-night can be seen as one of the reason for dengue transmission. The laboratory research can be extended to check the viability of dengue vector towards the fluctuating climatic factors. The developed model has proven quite significant in predicting number of dengue patients; however interdependence of the studied variable has posed a constraint towards the accurate predictions.

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