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GENERALIZED LINEAR MODEL APPROACH TO ASSESS THE INFLUENCE OF CLIMATIC FACTORS ON THE CHIKUNGUNYA INCIDENCE DURING AN EPIDEMIC IN MYSORE DISTRICT

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ABSTRACT

Objective: The geographic expansion of the chikungunya outbreak has given rise to a global interest in identifying the influential factors that cause the spread of the disease. The aim of this paper was to recognize by negative binomial models using climatic conditions from 2006 to 2019, the environmental factors and climatic factors which are associated with the incidence of chikungunya, in the chikungunya epidemic region of Mysore, Karnataka. **Methods:** Various Climatic factors were considered as predictor variables while Chikungunya cases were considered as response variable. Spearman correlation was assessed between Chikungunya cases and climatic factors to identify the most preceding months (lag period) on the occurrence of Chikungunya cases. Lag period of one to three months were considered. **Results:** The occurrence of chikungunya was significantly influenced by the minimum temperature at lag 1 and the maximum relative humidity at lag 2. The variable minimum temperature at lag 1 has a coefficient of 0.394 which implies that for each one degree Celsius increase in Minimum temperature at lag 1 month, the expected log of chikungunya cases increases by 0.394 %. Similarly for Maximum Relative humidity with a coefficient of 0.104, one degree increase in Maximum Relative humidity of the corresponding month, the expected log of dengue cases increase by 0.104%. The vector control and chikungunya management programme should be introduced at least three months in advance of the chikungunya epidemic season, taking into account the impact of maximum temperatures in previous months on the incidence of chikungunya.

Keywords: Chikungunya, Negative binomial model, Maximum temperature, Rainfall, Relative humidity

INTRODUCTION

An unusual epidemic of chikungunya virus (CHIKV) infection recently emerged in countries of the Indian Ocean area resulting in a debilitating and acute syndrome with strong fever, asthenia, skin rash, polyarthritis, and lethal cases of encephalitis **[1]**. It's a mosquito-borne arboviral disease spread by aedes mosquitos. Chikungunya virus belongs to the Alphavirus genus and the Togaviridae family. Fever, rash, and incapacitating arthralgia are general symptoms of the disease **[2]**. During 2006-2007, India was struck by a major outbreak of chikungunya fever caused by the Chikungunya virus (CHIKV). During the year 2020, there were approximately 11783 suspected and 1095 confirmed Chikungunya cases in Karnataka **[3]**. This paper looked at the effects of climatic variables and their lag periods on the incidence of chikungunya in the Mysore district. This paper aims to provide insights into how to strengthen the chikungunya control plan and, as a result, take action before the lag time for the public sector.

METHODS

Study Area and Climatic Conditions

Mysore, which is known for its heritage buildings and palaces. The district forms the southern part of Karnataka, with Tamil Nadu to its southeast, the district of Kodagu to its west, the district of Mandya to its north, the district of Hassan to its northwest, and the district of Bangalore to its northeast. It occupies a surface of 6854 sq. Km, which is 3.57 per cent of the total geographical area of the state.

Geographical Location and Area: A total geographical area of 6,76,382 hectares is occupied by the district, of which 62,851 hectares are forestland. As of 2011, Mysore

City had an estimated population of 920,550, consisting of 461,042 men and 459,508 women, making it Karnataka's third most populous city.

Climatic Condition: Mysore has a tropical savanna climate (*Aw*) bordering on a hot semi-arid climate (*BSh*) under the Köppen climate classification. Main seasons are summer from March to June, the monsoon season from July to November and winter from December to February **[4]**. The temperature Ranges from 39.4^0 to 46^0 F.

Data and Climatic Factors: Monthly Chikungunya cases from 2006 to 2019 were collected from District Health office, Public sectors and government agencies, Mysore Karnataka. Monthly records of Maximum temperature (°C), Minimum temperature (°C), Mean temperature (°C), Maximum rainfall (mm), and Minimum rainfall(mm), Mean rainfall(mm), Relative humidity (Maximum, Minimum and Mean)(%), Velocity daily mean (km) Vapor pressure (Maximum, Minimum, Daily mean)(%), Evaporation (Maximum, Minimum, Total, Daily)(mm) and Average sunshine were collected from the district between 2006 to 2019 from Indian Meteorological Department (IMD), India.

Table 1: Climatic variables, Variable label and Units of measurement

S. No	Climatic Variables	Variable Label	Units of measurements
1	Maximum temperature	TEMP MAX	°C
2	Minimum temperature	TEMP MIN	°C
3	Mean temperature	TEMP MEAN	°C
4	Maximum rainfall	RAIN MAX	mm
5	Minimum rainfall	RAIN MIN	mm
6	Mean rainfall	RAIN MEAN	mm
7	Total rainfall during month	RAIN TOTAL	mm
8	Wind velocity daily mean	VELOCITY DAILY MEAN	Km/hr
9	Maximum relative humidity	RH MAX	%
10	Minimum relative humidity	RH MIN	%
11	Mean relative humidity	RH MEAN	%
12	Maximum vapor pressure	VP MAX	millibars
13	Minimum vapor pressure	VP MIN	millibars
14	Vapor pressure daily mean	VP DAILY MEAN	millibars
15	Maximum evaporation	EVA MAX	mm
16	Minimum evaporation	EVA MIN	mm
17	Total evaporation	EVA TOTAL	mm
18	Daily evaporation	EVA DAILY	mm
19	Average sunshine	AVG SUNSHINE	hours

Statistical analysis

Temperature (Maximum, Minimum, Mean), Rainfall (Maximum, Minimum, Total during month, Mean), Wind velocity daily mean, Relative humidity (Maximum, Minimum and Mean), Vapor pressure (Maximum, Minimum, Daily mean), Evaporation (Minimum, Maximum, Total, Daily), Average Sunshine were considered as predictor variables while chikungunya case was considered as response variable. Spearman correlation analysis was assessed between chikungunya cases and climatic factors to identify the most preceding months (lag period) on the occurrence of chikungunya. The predictor variable of 1 month earlier was considered lag 1 and the month corresponding to that of chikungunya case was lag 0. Lag period of 1 to 3 months were considered for preceding months.

Chikungunya cases were considered as count variable, this could fit either as Poisson or Negative binomial distribution. In Modeling Poisson regression model, one of the major assumptions is equality of the mean and variance. If this assumption is violated, an over dispersion problem can arise. In order to overcome the over dispersion, this study considered the generalization of Poisson model that is Negative Binomial regression model. However, chikungunya cases were over-dispersed that means variance greater than mean, **(Mean=3.52, Variance=37.774)** Thus we considered negative binomial regression for chikungunya cases as a response variable which seemed to be appropriate for modeling.

$$P(y) = P(Y=y) = \frac{r(y+\frac{1}{\alpha})}{r(y+1)r(\frac{1}{\alpha})}\left(\frac{1}{1+\alpha\mu}\right)^{\frac{1}{\alpha}}\left(\frac{\alpha\mu}{1+\alpha\mu}\right)^{y}$$

Where μ>o is the mean of Y and α is the heterogeneity parameter. It can derive this parameterization as a Poisson-gamma mixture or alternately as the number of failures were the predicted variables, X_1, X_2, …., $X_p$are given, and the population regression coefficients $\beta_0, \beta_1, \beta_2, \beta_3, \ldots\ldots \beta_p$ are to be estimated **[5]**. The study used the maximum likelihood ratio statistics or commonly known as Deviance (D) statistics to test for the goodness of fitted model for Negative Binomial model **[5, 6, 7]**. The best fit model was selected and interpreted. Similarly, incidence rate ratio (IRR) between chikungunya case and climatic factors was assessed to consider the relative risk of chikungunya incidence in relation to climatic factors. The statistical analyses were conducted using SPSS software version 22.

Maximum Likelihood method (MLE) was used for parameter estimation and negative binomial regression technique was used to analyze the MLE method. The general model was as followed;

$$\text{Log (DHF)} = a + b_1 X_1 + b_2X_2 + b_3X_3 + \ldots + b_kX_k$$

$$\text{DHF} = \exp\,[a + b_1 X_1 + b_2X_2 + b_3X_3 + \ldots + b_kX_k]$$

$$\text{DHF} = e^{a}\, e^{b_1 x_1} e^{b_2 x_2} e^{b_3 x_3} \ldots\, e^{b_k x_k}$$

Where DHF was number of chikungunya hemorrhagic fever cases, a, b_1, b_2, b_3,…..b_k were constants in model and X were independent variables **[5, 6, 7]**.

Significance test: In the current paper, the maximum likelihood ratio statistics or commonly known as deviance (D) statistics to test for the goodness of fitted model for negative binomial model. Deviance in the normal linear regression was similar to R^2 or coefficient of determination which was used to provide the descriptive information about the model fit and was calculated by

$$R^2 = \frac{\Sigma\,(\hat{y} - \bar{y})^2}{\Sigma\,(y - \bar{y})^2}$$

Where y was the observed value of y, $\hat{y}$was the value of y predicted from the model and $\bar{y}$ is the mean value of y. The log likelihood ratio statistics (deviance) was introduced to check the appropriateness of a chosen response distribution when explanatory variables were added or excluded from the model. The deviance value was defined as:

$$\text{Deviance (D)} = 2\ \{\ \Sigma_i [y_i \ln\left(\frac{y_i}{\hat{\mu}_i}\right) - (y_i - \hat{\mu}_i)]\}$$

For a well fitted model with appropriate link function, error distribution and functional form, the expected value of residual deviance should approximately be equal to the number of degree of freedom regardless of the value of μ. In SPSS, we used to estimate the parameter by considering from mean deviance, the mean deviance close to 1 was the optimal model.

Residual analysis: In order to check for model fit, residual analysis is important as it can be thought of as the error associated with predicting or estimating outcomes using predictor variables **[5, 6, 7]**.

RESULTS

During the 14 years period, a total of 558chikungunya cases have been reported with the smallest number being 0 per month and highest value of 35 cases per month. The mean is 3.519 and the variance is 37.7738. Since Variance was found to be greater mean, the data was considered to be over dispersed. In **Figure 1**, Yearly and monthly distribution of chikungunya cases showed a Seasonal pattern.

A clear seasonal pattern of chikungunya occurrence was observed during April to October. In 2015, 2016 and 2017, Mysore was considered to have a substantially increased incidence of chikungunya. The peak in chikungunya cases was observed in the year 2016 with total of 158 cases. Mysore thus became a chikungunya endemic district of Karnataka.

Spearman correlation analysis showed temperature and relative humidity have some significant correlation with chikungunya cases. Minimum temperature was significantly correlated with chikungunya cases through lag month 1 with P value of ($P<0.05$) **(Table 2)**. The effect of minimum temperature was significant through lag 1-3 with moderate correlation. Maximum rainfall was significant ($P<0.01$) but showed a negative correlation for lag 0 and lag 1 ($p<0.05$). Mean rainfall was significant ($P<0.01$) but showed a negative correlation for lag 0 and lag 1 ($p<0.05$). Maximum relative humidity showed significant ($P<0.05$) and moderate correlation at lag 0 to 2. Vapor Pressure (VP) minimum, VP daily mean and Average sunshine were also significant through lag 0 to 2.

Negative binomial regression model was fitted for response variables on given predictor variables based on the fitting criteria. Both deviance test and omnibus test supported that eight models were well fitted to the data. The criteria of lowest value of AIC (or BIC) and mean deviance (-2LL/df) close to one were used to select a better model. The first model included all 56 predictor variables but none were significant under Wald Chi square test ($P<0.05$). Thus, it did not satisfy the condition those only significant predictors from the fitting of negative binomial regression of chikungunya case **(Table 3)**.

Highly significant predictors in Model under the Wald Chi square test ($P<0.05$) were Minimum temperature at lag 1 month (Temp Max_1) and Maximum Relative humidity at lag 2 (RH Max). In order to make the interpretation simple, partial regression coefficients were expressed in the exponential form, i.e., exp (bi). Exponential value greater than one indicated more effect of the predictor on the response variable and less than one indicated less effect, while one indicated no effect. The variable Min Temp_1 has a coefficient of 0.394 which implies that for each one degree Celsius increase in Minimum temperature at lag 1 month, the expected log of chikungunya cases increases by 0.394. Similarly for Maximum Relative humidity with a coefficient of 0.104, one degree increase in Maximum Relative humidity of the corresponding month, the expected log of dengue cases increase by 0.104. Further from **Figure 2**, the mean predicted value of the response variable and standard deviance Residual were plotted on the scatter plot, to check whether the preferred model is the best model.

Min temp [exp(0.394)=1.483], RHMax [exp(0.104)= 1.109] have values greater than one. That means these Predictors have greater influence on the Chikungunya cases.

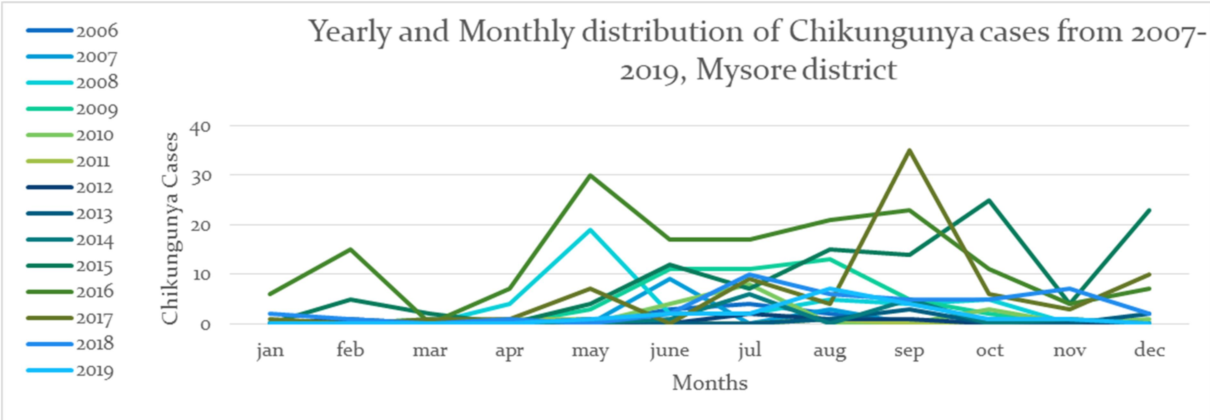

Figure 1: Yearly and Monthly distribution of chikungunya cases in Mysore district from 2006 to 2019

Table 2: Correlation analysis between Chikungunya cases and climate factors with lag effects of 0-7 month's period

Climate variable	Lag month	Correlation	*P*-value
Maximum temperature	0	-0.115	0.153
	1	0.012	0.882
	2	0.166*	0.038
	3	0.300**	0.000
Minimum temperature	0	0.207**	0.010
	1	0.332**	0.000
	2	0.356**	0.000
	3	0.318**	0.000
Mean temperature	0	0.038	0.641
	1	0.195*	0.015
	2	0.312**	0.000
	3	0.378**	0.000
Maximum Rainfall	0	0.208**	0.009
	1	0.183*	0.022
	2	0.095	0.239
	3	-0.022	0.783
Minimum Rainfall	0	0.035	0.662
	1	-0.013	0.868
	2	0.069	0.392
	3	0.022	0.786
Mean Rainfall	0	0.208**	0.009
	1	0.181*	0.024
	2	0.098	0.225
	3	-0.021	0.796
Maximum Relative humidity	0	0.195*	0.015
	1	0.189*	0.018
	2	0.176*	0.028
	3	0.064	0.425
Minimum Relative humidity	0	0.225**	0.005
	1	0.171*	0.032
	2	0.117	0.146
	3	-0.046	0.569
Mean Relative humidity	0	0.312**	0.000
	1	0.270**	0.001
	2	0.117	0.146
	3	0.014	0.866
EVA Max	0	0.089	0.268
	1	0.138	0.086
	2	-0.015	0.848
	3	-0.066	0.416
EVA Min	0	0.135	0.094
	1	0.038	0.637
	2	-0.001	0.990
	3	-0.046	0.565
EVA Total	0	-0.172*	0.032

	1	-0.068	0.376
	2	-0.020	0.803
	3	0.014	0.860
EVA daily	0	-0.183*	0.022
	1	-0.077	0.340
	2	-0.030	0.710
	3	0.020	0.808
Rain total during month	0	0.162*	0.043
	1	0.178*	0.026
	2	0.150	0.061
	3	-0.007	0.926
Velocity Daily Mean	0	-0.001	0.992
	1	0.057	0.481
	2	0.044	0.582
	3	-0.007	0.933
VP max	0	0.005	0.952
	1	0.040	0.623
	2	0.054	0.505
	3	0.040	0.618
VP min	0	0.354**	0.000
	1	0.303**	0.000
	2	0.213**	0.008
	3	0.175*	0.029
VP Daily mean	0	0.194*	0.015
	1	0.192*	0.016
	2	0.159*	0.047
	3	0.133	0.098
Average Sunshine	0	-0.348**	0.000
	1	-0.280**	0.000
	2	-0.191*	0.018
	3	-0.007	0.927

Table 3: Parameter Estimates of the preferred model

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test			Exp(B)	95% Wald Confidence Interval for Exp(B)	
			Lower	Upper	Wald Chi-Square	df	Sig.		Lower	Upper
(Intercept)	-16.576	3.5911	-23.615	-9.537	21.306	1	.000	6.326E-8	5.551E-11	7.210E-5
TEMPMIN_1	.394	.0729	.251	.537	29.280	1	.000	1.483	1.286	1.711
RHMAX_2	.104	.0311	.043	.165	11.160	1	.001	1.109	1.044	1.179
(Scale)	1[a]									
(Negative binomial)	2.379	.3832	1.735	3.262						

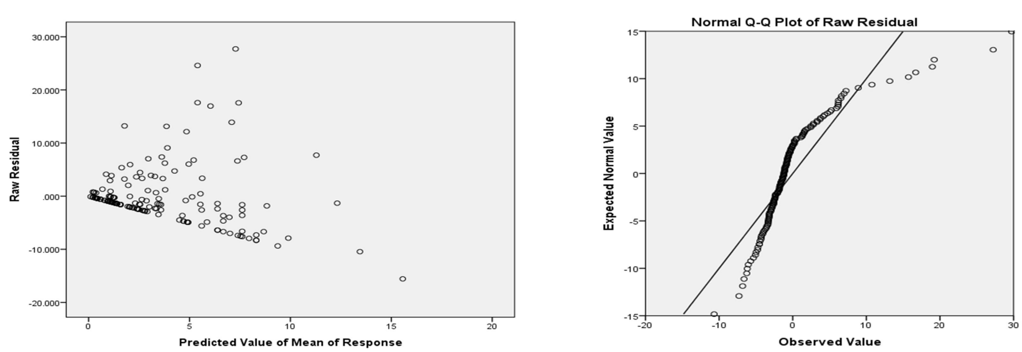

Figure 2: The relationship of the predictive value of the number of DHF cases with residuals

DISCUSSION

Cases of Chikungunya are affected by climatic factors such as temperature and relative humidity, which we observed with the aid of a correlation study of the response variable with these predictor variables, suggesting the effect of the climatic factors of the previous month, compared to other countries, at different lag times **[8, 9]**. The lag period of 1 to 3 months was chosen, taking into account the time for the adult Aedes spp. To grow from egg, extrinsic and intrinsic virus incubation period and time from the start of symptoms for patients to attend hospital **[10]**.

In order to calculate the correlation between variables, the correlation analysis is known to be one way classification, but this does not resolve the co-effect of the other climate influences, so we implemented regression analysis in order to find the true association. However, in correlation analysis, rainfall was found to be correlated with chikungunya cases; it is not included in the regression analysis as a significant predictor **[11]**. The model that included rainfall showed a low coefficient value that could have less effect on the incidence of chikungunya in the district of Mysore. Although the effect of rainfall on the incidence of chikungunya has been compared to the population of vectors. Excess rainfall, however, may have a negative effect.

In the escalation of chikungunya cases at various lag times, temperature has played an important role. Minimum temperature effect at lag 1 plays a significant role, along with Maximum relative humidity at Lag 2. We noticed that the high incidence of chikungunya occurs in the months of April to October. This transition, along with vector adaptation and human behavior, may be related to climate change.

CONCLUSION

For chikungunya incidence in Mysore district, Karnataka, we identified temperature and relative humidity as possible or significant contributors in this analysis, with Minimum temperature at lag 1 month and Maximum relative humidity at lag 2 being the most important factors influencing chikungunya incidence. We propose that the chikungunya containment vector control would be more successful if implemented from February.

Limitations

Climate conditions are not the only indicator of vector-borne diseases, like chikungunya. The relation between socio-demographic components such as population growth, travel or migration rates, water storage habits and chikungunya incidence should also be considered. This study has been confined to a single district; so many districts covering different geographical regions should be examined in the future.

Abbreviations

IRR: incident rate ratio.

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