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Original Research Article

Prediction of dengue outbreaks in Kerala state using disease surveillance and meteorological data

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ABSTRACT

Background: Dengue is one of the most serious and fast emerging tropical diseases. Its incidence of is influenced by many meteorological factors such as rain fall in mm, temperature, humidity etc. Information about these factors can be used to forecast the incidence of dengue fever cases in the next coming months.

Methods: The current study was an analytical study using retrospective secondary data from Kerala state. The annual integrated disease surveillance reports of dengue fever cases. Rain fall data and mean monthly temperatures for a period of twelve years from 2006 to 2017 were used. Best fitted model was developed and accuracy of the prediction was tested. All analyses were performed in R software using the mgcv package and nlme package.

Results: A total of 144 months study period from January 2006 to December 2017 was used for analysis. Five different models developed for prediction of dengue cases among them, best fitted model including optimal combination of meteorological variables and recent and long term transition of dengue was selected. Out of 84 months predictions in the training period, 68 months prediction was correctly negative, 5 months prediction was correctly positive, 2 months prediction was incorrectly negative and 9 months prediction was incorrectly positive.

Conclusions: A better predictive generalized additive model can be developed using the optimal combination of meteorological predictors and dengue fever counts. It will enable the health care administrators to forecast future out breaks and to take better precautionary measures.

Keywords: Dengue fever, Forecast analysis, Predictive analysis, Surveillance

INTRODUCTION

Dengue is one of the most serious and fast emerging tropical diseases which in certain socio-ecological settings exacts disease burden (465,000 DALYs across the globe) that can only be paralleled with that of malaria.[1] Dengue infection in humans results from four dengue virus serotypes (DEN-1, DEN-2, DEN-3, and DEN-4) of *Flavivirus* genus which are single-stranded positive polarity ribonucleic acid (RNA) viruses. *Aedes aegypti* is the principal vector for both Dengue virus (DENV) and chikungunya viruses (CHIKV). Dengue virus is maintained in a human-mosquito-human cycle. It is also transmitted by *Aedes albopictus*.[1–3] It poses an increasingly perilous situation due to lack of specific antiviral drugs or vaccine.[4] The global incidence of dengue fever has increased in recent decades.[5] The World Health Organization estimates that 50 to 100 million infections occur yearly, including 500,000 DHF cases and 22,000 deaths, mostly among children.[6] In India, over the past decade, dengue fever increased in frequency and in geographical extent.[7] High dengue incidence, ranging between 21 and 50 per million, was reported for the states of Punjab, Gujarat, Karnataka, Kerala, Tamil Nadu and

Orissa.[8] Among them Kerala is one of the high risk state reporting more number of cases every year.[7]

Since 2007, diagnosis and data assimilation for dengue and chikungunya in India have been facilitated by the National Vector Borne Disease Control Programme.[3,9] Integrated disease surveillance program is providing the day wise and district wise data of dengue fever cases in Kerala state.[10] However only the number of cases is available, and they are not presented as epidemiological parameters such as epidemic curves or incidence rates. Incidence of dengue fever is influenced by many meteorological factors such as rain fall, temperature, humidity etc. Information about these factors can be used to forecast the incidence of dengue fever cases in the next coming months.[11] This enables the health systems for better preparedness to plan and allocate resources for effective control of future outbreaks.

Several attempts were made in different countries to create a best fitted forecast model suitable to their own environmental conditions to predict dengue fever incidence in the next coming months.[11–13] But environmental conditions in India are different from those countries.

Some studies were already conducted in India to develop a suitable forecast model for dengue fever incidence using Auto regression integrated moving averages (ARIMA) analysis based on the past incidence of dengue fever cases.[14,15] But these ARIMA models are based on only time series data of dengue fever incidence. They have not included any meteorological factors in their predictive models. Time series analysis such as ARIMA derives a trend across time, which might be used to predict future values. But, a generalized additive model (GAM) predicts future values by identifying the predictors and summing of their influence which results in a trend line that best fits the data.[16]

Based on this background, an attempt was made to predict dengue fever incidence in Kerala state using Generalized additive model with the help of meteorological and surveillance data. The objectives of this study are to assess the correlations between predictors on subsequent dengue incidence, to create a best fitted forecast model and to estimate predictive ability of that model.

METHODS

The current study was an analytical study using retrospective secondary data from Kerala state. Department of Director of Public Health of Kerala state is providing annual reports of month wise incidence of communicable disease in Kerala state.[10] The annual reports for a period of twelve years from 2006 to 2017 were downloaded and data of dengue fever cases was extracted from the downloaded pdf files. In the current study data of suspected dengue fever cases was used for analysis. Rain fall data was obtained from the Indian Institute of Tropical Meteorology department report.[17] Records of mean monthly temperature readings (°C) were obtained from World weather online website.[18] Lag data was created using dengue fever incidence data and meteorological factors data with MS Excel software. Lag means a period of time between one event and another. Lag0 means actual data, Lag1 means one month delay, lag2 means 2 months delay, lag3 means 3 months delay and lag24 means 24 months delay from the original month.

A model was developed and validated by dividing the data file into two datasets: seventy percent of the data i.e., from January 2006 to December 2014 was used to train a model, and the remaining thirty percent of data i.e., from January 2015 to December 2017 was used for testing and validate the fitted model. There were no missing data.

The data was analyzed to find out the relationship of meteorological variables to the dengue time series, and relationship within the dengue time series itself. Some studies revealed a relationship between meteorological factors and dengue transmission with up to a 16-20 weeks delay between the variability in the weather factors and corresponding influences on the dengue cases.[12] Thus a lag of 0-3 of the meteorological variables were used for analysis.

The influence of most recent dengue transmission on the dengue fever cases was estimated using the same lags as for the meteorological variables i.e., lag1-3. Lag0 of dengue cases was excluded as it is the outcome variable. In a similar way, influence of dengue fever counts 24 months back i.e., lag24 was estimated to know the impact of cyclic pattern of the disease. R software was used to assess the correlation of meteorological variables and dengue time series on dengue count and to develop a best fitted predictive model. Five different prediction models developed in Kerala state using the meteorological variables, and the surveillance data on its own and together. These models were evaluated based on the adjusted R-squared initially, and later on by prediction performance according to Root mean square error (RMSE) and Standardized root mean square error (SRMSE) for continuous predictions. Model having high R-squared adjusted and low RMSE, SRMSE values was selected as best fitted model.[19,20]

Outbreak predictions and validation

Best fitted model was used for prediction of dengue transmission. Accuracy of the prediction was tested. Average number of dengue fever cases in the study period was selected as cut-off point. Prediction accuracy according to sensitivity, specificity, and positive and negative predictive values were calculated for training period i.e., from January 2006 to December 2014. Later best fitted model was used for prediction in the forecast period i.e., from January 2015-December 2017. The predicted number of dengue cases for the forecast period was compared with observed number of cases in this period. All analyses were performed in R software using the mgcv package and nlme package.[21,22]

RESULTS

A total of 144 months study period from January 2006 to December 2017 was used for analysis. Table 1 depicts that, monthly average of dengue fever cases in this period was 386 cases ranged from 7 cases to 5555 cases. The mean temperature in Kerala state was 27.67 degree centigrade with a range from 27 to 29 degree centigrade. Monthly average rain fall in Kerala state was 2085mm with a minimum of zero mm rain fall and maximum of 10680 mm rain fall.

Table 1: Descriptive statistics of monthly dengue fever incidence and meteorological variables during 2006 to 2017.

Variable	Minimum	Maximum	Mean	S.D.
Monthly dengue fever cases	7	5555	386.12	762.579
Monthly average temperature in degree centigrade	27	29	27.67	0.853
Monthly rain fall in mm	0	10680.0	2085.387	2188.6917

Table 2: Cumulative monthly incidence of dengue fever and meteorological variables during 2006 to 2017.

Month	Mean dengue fever incidence	Mean average temperature in degree centigrade	Mean rain fall in mm
January	162	28	65.2
February	128	28	151.4
March	121	29	548.6
April	196	29	1009.2
May	463	29	1929.4
June	974	27	5626.0
July	979	27	5200.4
August	666	27	3296.4
September	302	27	2720.6
October	252	27	2655.8
November	187	27	1497.6
December	204	27	324.1

Table 2 depicts that the incidence of dengue fever gradually rose from April to July and declined thereafter. High temperatures were reported during March, April and May in every year. Rain fall gradually rose from March to July every year and decreased thereafter.

Table 3: Correlation of dengue fever cases with lag of dengue fever cases, temperature and rain fall.

Dengue	Correlation (r)
Dengue lag0	1
Dengue lag1	0.8406101
Dengue lag2	0.6356488
Dengue lag3	0.4417069
Dengue lag24	0.3597232
Temperature lag0	-0.3782293
Temperature lag1	-0.1934203
Temperature lag2	0.05995751
Temperature lag3	0.2761873
Rain fall lag0	0.3215773
Rain fall lag1	0.3462091
Rain fall lag2	0.2835589
Rain fall lag3	0.06645689

Observation of average of monthly cumulative rainfall and the average of monthly dengue fever cases revealed that, a phase difference of two months in their distribution pattern. The average of monthly cumulative rainfall was lowest in January (65.2 mm), while the average of monthly dengue cases was lowest in March (121 cases). Similarly the average of monthly cumulative rainfall was the highest in June (5626 mm), while the average of monthly cases was the highest in July (979 cases).

Table 3 shows the correlation of dengue fever cases with lag of dengue fever cases, temperature and rain fall. Correlation of dengue fever incidence in the current month with incidence of dengue fever cases in the lag1, lag2, lag3 and lag24 was tested. Correlation of dengue fever incidence in the current month with meteorological factors such as temperature and rain fall, in the last month, two months back and three months back was tested. Dengue fever cases positively correlated to lag1 and lag2 of dengue fever count. At lag24, dengue fever cases were positively auto correlated indicating the cyclic pattern of dengue fever cases. The correlation of various meteorological variables such as temperature and rain fall at different lag levels with incidence of dengue fever was tested. Temperature was negatively correlated to dengue fever at lag0 and lags 1, not correlated at lag2 and positively correlated at lag3. Rain fall was correlated to dengue fever cases at lag0, 1 and 2 and not at 3.

Relative risk of occurrence of dengue fever was measured for all meteorological variables and different lags of dengue fever incidence are shown in Figure 1. First panel shows the graphical representation of association between log of relative risk of dengue fever occurrence and temperature at lag0, lag1, lag2 and lag3. Second panel shows the association with rainfall and third panel shows association with dengue incidence. In the first panel it was observed that, among the different lag levels of temperature, relative risk of dengue fever incidence was high at lag3 when compared to lag0, 1 and 2. In the second panel it was observed that, all the graphs are showing j shaped curves. It revealed that, up to a moderate rain fall dengue fever relative risk is decreasing, but later it is in increasing trend. All the four graphs showing high relative risk at high rain fall. Third panel revealed the relation between numbers of dengue fever cases at different lag levels with relative risk of dengue fever. Relative risk of dengue fever is showing raising trend at lag1 and 24 of dengue fever cases and declining trend at lag2 and 3 of dengue fever cases. It indicates that the current incidence of dengue fever cases in the present month depends upon, three months back temperature, rain fall in the current month and in the previous month, incidence of dengue fever cases in the previous month and incidence of dengue fever cases before 24 months These variables can be considered as predictors of future incidence of dengue fever cases.

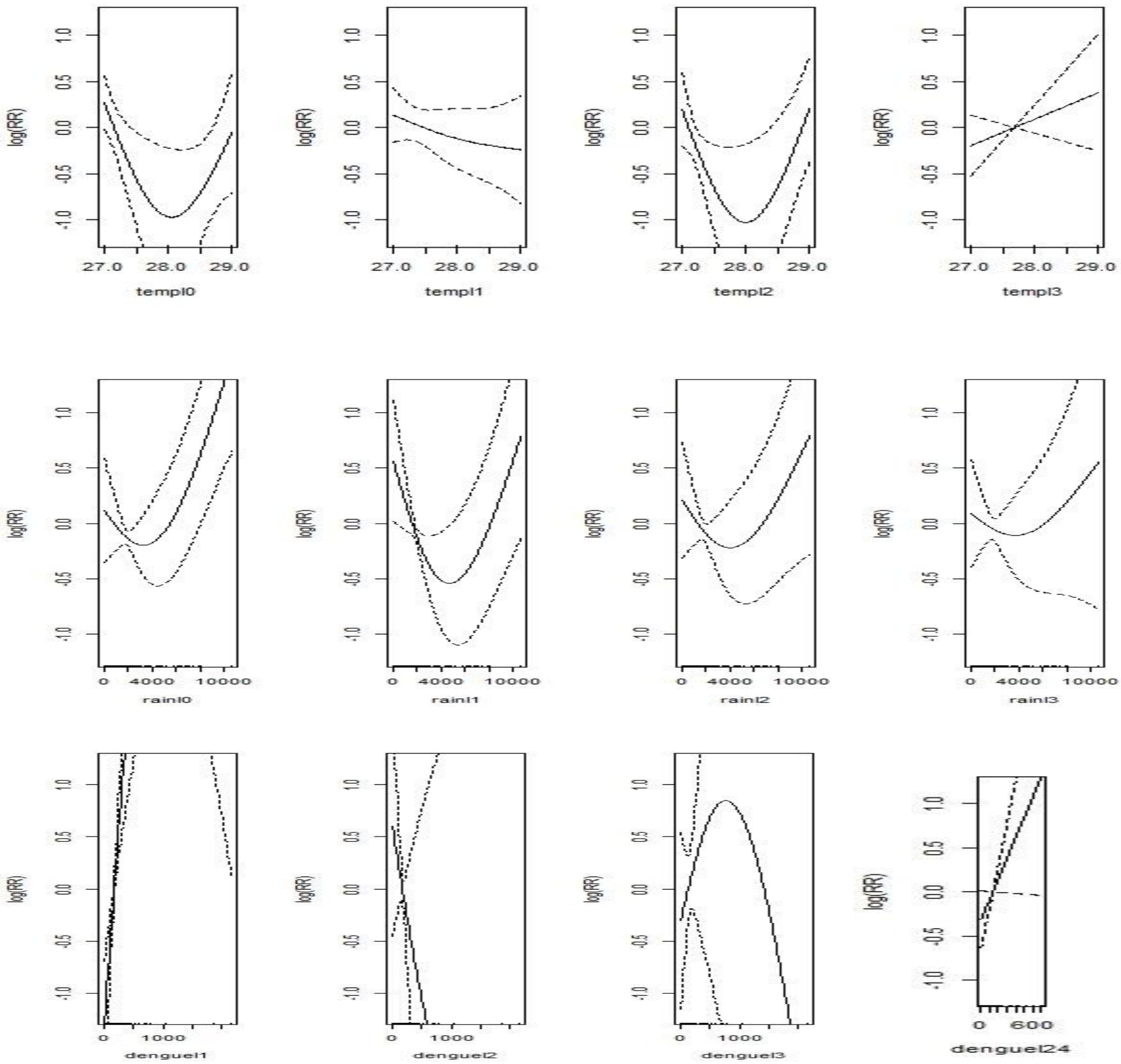

Figure 1: Association between meteorological variables and dengue over lag0-3. Solid lines represent relative risks of dengue cases and dotted lines depict the upper and lower limits of 95% confidence intervals.

Creating predictive models

Based on the observations from correlation and relative risk calculations, five different predictive models were created. Model A was created using the months of the year including all meteorological variables. Model B was created using the optimal combination of meteorological factors i.e., only temperature at lag3, rainfall at lag0 and rainfall at lag1. Model C was created using the dengue count time series at lag1, Model D was created using dengue at lag1and lag24. Model E was created by combining Model B and Model D i.e., using the combination of optimal combination of meteorological factors and dengue time series at lag1 and lag24. R square adjusted value was calculated for all the models for trained data. Table 4 depicts that, among all the models, model E had high R square adjusted value and low RMSE and SRMSE values and it is considered as best fitted model.

Table 4: Comparison of different predictive models.

Model	R square adjusted	RMSE	SRMSE
A- Including all meteorological variables	0.229	0.287	0.785
B- Including optimal combination of meteorological variables	0.143	0.303	0.844
C- Including recent dengue transmission	0.311	0.277	0.770
D- Including recent and long term dengue transmission	0.371	0.287	0.799
E- Combining both B and D	0.593	0.222	0.617

Figure 2 shows the plotted graphs for observed and predicted number of dengue fever cases for all five different models for the trained data period i.e., from 2006 to 2014. Model A and B were based on metereological factors thus started prediction after one month from observed data. Model C used the surveillance data at lag1, thus started prediction after one month from observed data. But Model D and E includes the surveillance data at lag24, thus started prediction after 24 months of observed data. Among the five models, Model E shows less deviation between observed and predicted cases.

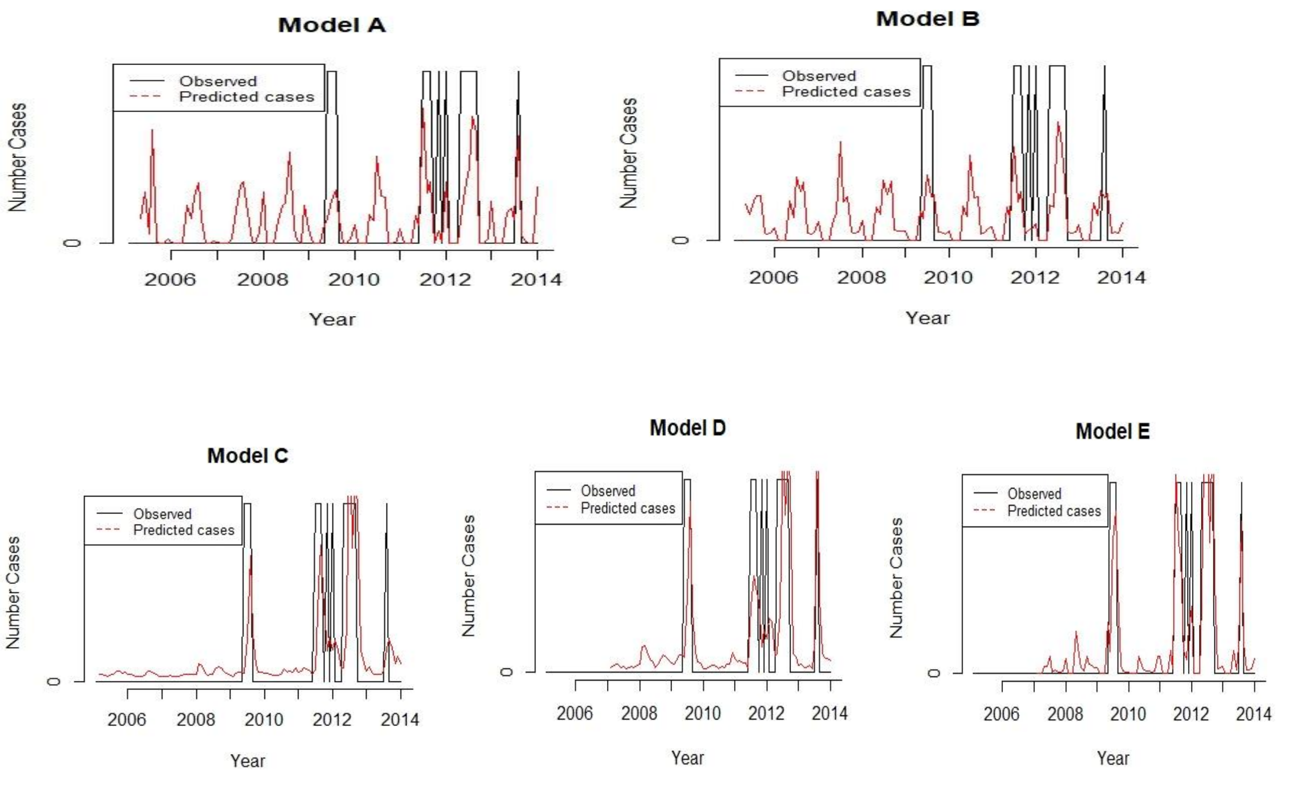

Figure 2: Plots of different predictive models.

After fitting the model, Model E was examined for residuals to check normality in their distribution pattern and to check the residual autocorrelation. Residual is the difference between observed value and predicted value. The histogram of residuals in Figure 3 revealed that, the pattern had only one peak and had almost symmetrical pattern. But it had peak is in the negative side i.e., in between -0.5 to 0. It indicates that actual numbers of dengue fever cases are less than the predicted number of cases. The Quantile-Quantile plot (Q-Q plot) in Figure 3 for deviance of residuals showed a reasonably straight line. It suggests that, residuals had almost normal distribution pattern. Partial auto correlation factor (PACF) plot in Figure 3 shows insignificant autocorrelation in the residuals as none of the lines crossed the 95% confidence limits. It indicates that series of predicted numbers of cases is not correlated to the series of observed number of cases at different lag levels, suggesting that the selected predictive model is a good fit.

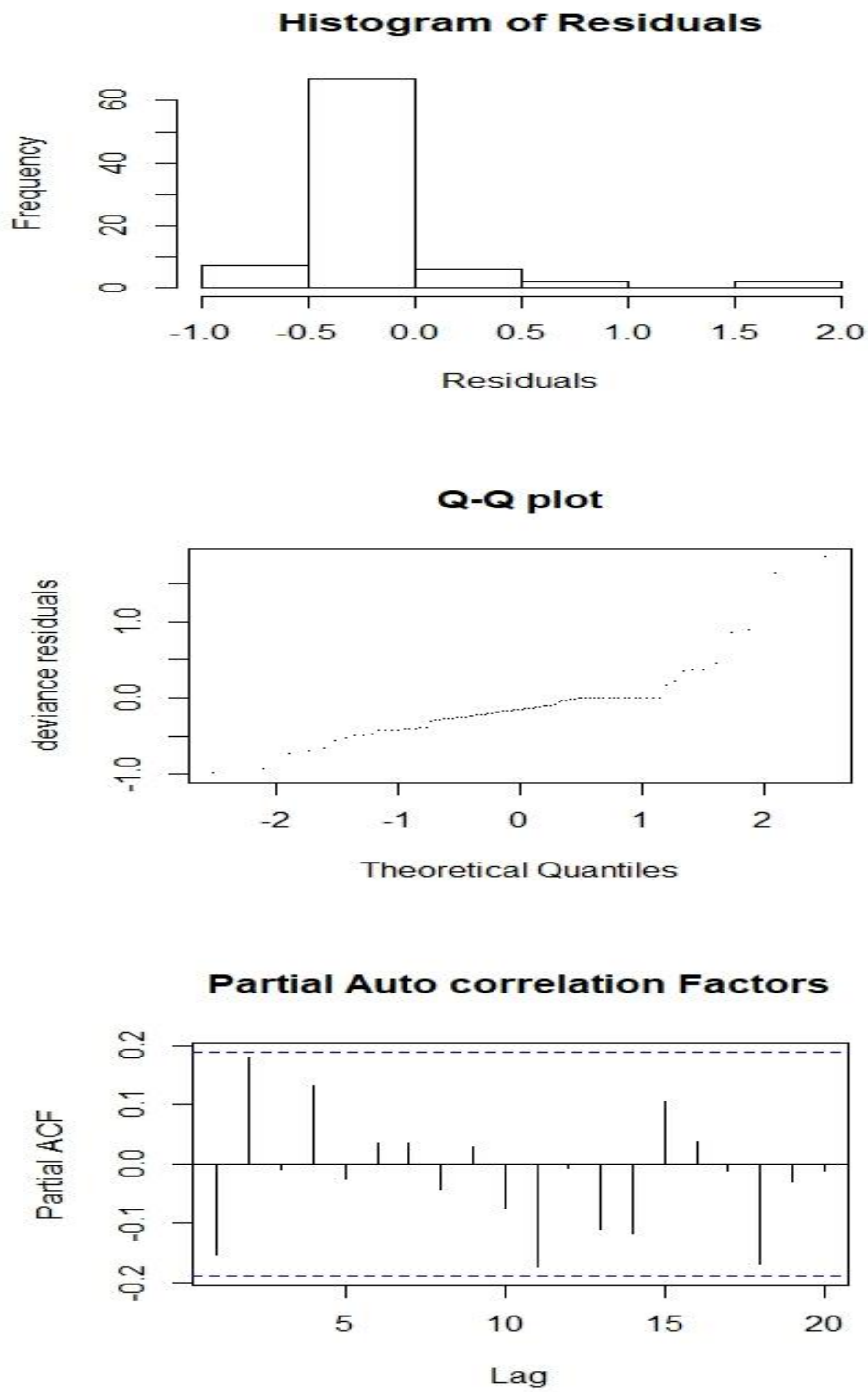

Figure 3: Residuals examination of best fitted model.

Model E was used for the prediction of dengue fever cases. Figure 4 shows the observed dengue fever cases and predicted number of cases during the period 2006 to 2018. Average monthly number of cases 385 was chosen as cut-off point to test the selected predictive model. Predictions showed a relative good discriminating ability to separate transmission months above and below 386 cases.

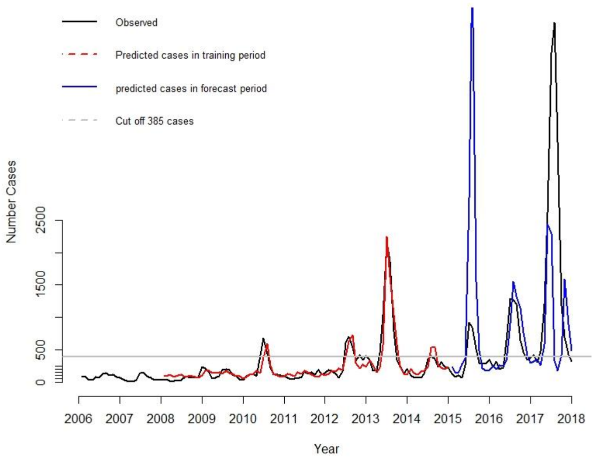

Figure 4: Observed and predicted dengue fever cases for best fitted model.

Out of 84 months predictions in the training period, 68 months were correctly negative, 5 months were correctly positive, 2 months were incorrectly negative, and 9 months were incorrectly positive. The total error rate of the prediction was 8.33% and accuracy of prediction was 91.67%. The sensitivity of detecting the outbreaks was estimated to 97.14% and the specificity to 64.29%. In addition, the positive and negative predictive value respectively was estimated to 93.15% and 81.82%. During the forecast period i.e., for 2015-2017, out of 36 months, 14 months were correctly negative, 14 months were correctly positive, 5 months were incorrectly negative and 3 months were incorrectly positive, error rate is 22.22% and accuracy rate is 77.78%. Sensitivity of detecting the outbreaks was estimated to 82.53% and the specificity to 73.68%, positive and negative predictive values were estimated to 73.68% and 82.35% respectively.

DISCUSSION

Surveillance data of the communicable diseases is very useful to the administrators for monitoring trends of incidence daily with the help of statistical analysis to know the loopholes in the reporting system and to know the peak period of incidence of disease. Apart from these benefits, predictive analysis gives us a scope to predict the future burden of disease also i.e., to predict an epidemic early.[23-26] In the current study, the dengue incidence was predicted by using a best fitted predictive model which was developed by combining disease surveillance and meteorological data.

Correlation analysis revealed that, temperature and rainfall are associated with dengue incidence. This result is in consistence with the evidence of several studies which showed correlation of weather and dengue transmission with up to four months delay.[13] In the current study short term lag of disease counts and lag of two years was correlated with dengue incidence. After a period of two years, disease counts increased showing the cyclic pattern of the diseases. The same result stated by another studies showing that the risk of re-current outbreaks in the same location can occur after a few years.[27-29] Herd immunity in the community reduces the severity of burden in the society, but after a period because of exposure to new strain there might be a chance of occurring outbreak. Apart from the herd immunity changes in weather patterns might cause cyclic inter-annual pattern.[30]

The present study identified that, temperature with three-month lag and rainfall of the same month and one-month lag are the best predictors for dengue incidence patterns in Kerala state. The time delay between temperature and rainfall on the dengue incidence have shown in other studies.[31-33] This time delays are likely to represent biological processes in the vector lifecycle.[34,35]

In the current study predictors in the final model includes lag3 of temperature, lag0 and lag1 of rain fall and lag1 and lag24 of dengue series. In the study conducted by Ramadona, lag3 of temperature, lag2 and lag3 of rain fall, lag2 and lag24 of dengue fever count were included in the best fitted predictive model.[11] This difference might be attributed to geographical conditions in two different study settings.

The model correctly predicted 14 out of the 19 epidemic months in the period 2015-2017.There are 5 false predictions regarding the outbreak of dengue fever i.e., more than 386 cases during 2015-2017. R square value of the best fitted model is 0.593. That indicated that, the best fitted predictive model explain only 60 per cent of the variation in the dengue cases incidence. The remaining 40 per cent unexplained variation might be due to the influence of other factors. In the forecast period, i.e., in between 2015 to 2017, two peaks were observed in the forecasted incidence. It might be because of peak in incidence of dengue fever cases before 24 months as lag24 of dengue fever cases was included as predictor in this model.

Administrators can use this model to predict the future occurrence of dengue cases. As temperature provides a three month lag and rainfall a one month lag it would be feasible to predict the upcoming epidemic and carry out control measures. Further, the effectiveness of the control measures could be evaluated- a much needed tool for administrators to justify the expenditure on control measures.[36]

Limitations

There were certain limitations in the study such as quality of data entry and missing of the actual data. The current study was based on the secondary data collected from reports of IDSP. There might be some chances of errors in data entry while preparing the reports. In the earlier years under reporting could have been higher one of the reasons being an evolving surveillance and data capture system. The study was based on the number of suspected dengue fever cases not the laboratory confirmed cases. Number of cases from private hospitals might be missed. Further, the data are for the whole state. There are wide variations in all the parameters across the state. Data at district or sub district level, inclusion of other parameters such as elevation would provide a more robust model. In-spite of these limitations, the predictive model identifies the high risk periods, when health education and public health interventions should be taken to curb the epidemic. In the predictive model weather forecasts can be used instead of observed weather records. It extends forecast period. Same predictive models can be developed for smaller geographical areas, such as districts or sub districts based on the availability of the data for accurate predictions of dengue fever outbreaks.

CONCLUSION

A better predictive generalized additive model can be developed using the optimal combination of meteorological predictors such as temperature and rain fall and recent and long term dengue fever counts. It will enable the health care administrators to forecast future out breaks and to take better precautionary measures.

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