Climatic Factors Influencing Dengue Hemorrhagic Fever in Kolaka District, Indonesia

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ABSTRACT

Dengue hemorrhagic fever in Indonesia is one of the serious health problems and requires understanding the occurrence of this disease. Climate Factors have a role that needs attention in the prevention of DHF disease. Understanding of disease patterns will benefit the health surveillance system and provide a way to tackle this problem. The records of dengue fever cases and climate data for the years 2010-2015 were obtained from the Health Office Kolaka District, southeast Sulawesi province and Meteorology, Climatology and Geophysics Agency in Southeast Sulawesi province, respectively. Data for the period 2010 to 2014 were used for model development through multiple linear regressions. The prediction model was used to forecast dengue cases in 2015 and the predicted results were compared with reported dengue cases in Kolaka in the past and forecasting period. Rainfall, humidity, temperature average, minimum temperature, and maximum temperature are significantly correlated with monthly cases of dengue fever. Predicted results showed a good performance where the model was able to predict 3 out of 5 epidemic outbreak events that occurred in January-March 2015 and November-December 2015. The sensitivity of detecting the outbreaks was estimated to be 60%, the specificity was 100%, positive and negative predictive value were estimated to be 100% and 77.8%, respectively. Climate has a major influence on the occurrence of dengue hemorrhagic fever infection in Kolaka district. Although the predictive model has some limitations in predicting the number of cases of monthly dengue fever, it can estimate the possibility of an outbreak three months in advance with a fairly high accuracy. The predictive model can be used to explain the incident rate of DHF of approximately 71%.

1. INTRODUCTION

Dengue fever is a disease caused by the dengue virus of the Flaviviridae family, with the genus of *Flavivirus* transmitted to the human body through an infected *Aedes aegypti* mosquito. The World Health Organization estimates the population affected by dengue fever has increased over the past 50 years. The incidence of dengue fever occurs in urban areas of both the tropics and subtropics, more than 100 million people are infected each year, including 500,000 cases progressing to the deadly dengue hemorrhagic fever (WHO, 2016a).

Dengue infection has a vast clinical diseases spectrum, ranging from asymptomatic, or undifferentiated febrile illness (viral syndrome), dengue fever (DF), dengue hemorrhagic fever (DHF), to dengue shock syndrome (DSS) (Horstick et al., 2014). Clinical manifestation of the primary infection of dengue fever (DF) ranges from mild febrile illness to fever, arthralgia, rash, and hemorrhage. Clinical symptoms of dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) reinfection include high fever, plasma leakage due to severe hemorrhage of skin and gastrointestinal tract, thrombocytopenia and shock (WHO, 2016b; Xiang et al., 2017; Zell, 2004). In Indonesia, dengue disease is identified based on clinical signs of dengue hemorrhagic fever (DHF) (WHO, 2016b).

Incidence rate (IR) of DHF in Southeast Sulawesi was 64.7/100,000 populations in 2015 (Tombili, 2016). In Kolaka, there is a port connecting Southeast Sulawesi and Southern Sulawesi, so all travelers going to South Sulawesi pass through Kolaka district. IR of DHF in Kolaka district was 18.76/100,000 populations in 2013 and increased to 32.17/100,000 populations in 2015 (Moeloek, 2015). Dengue hemorrhagic fever is a health problem in Indonesia. (Megawati et al., 2017). This is evident from the fact that all regions in Indonesia have a risk for contracting dengue fever (WHO, 2016b). In Indonesia, the pattern of the occurrence of the disease is somewhat different for each place due to many factors such as behavioral factors, environment, and climate (Bangs et al., 2006; Karyanti et al., 2014). Climatic factors such as rainfall, temperature and humidity are among the causes of an increase in DHF cases (Ramadona et al., 2016). The behavior of mosquitoes and the effectiveness of dengue virus transmission is determined by climatic conditions (Liu-Helmersson et al., 2014). This is because rainfall, temperature and humidity affect the interaction of biological vectors and viral vectors, through lifespan, mating age, dissemination, feeding, and faster viral replication (Bangs et al., 2006; Karyanti et al., 2014). Including temperature variables, rainfall, and humidity in a model has been used to predict a dengue outbreak in Mexico (Colón-González et al., 2011).

Research conducted in Dhaka, Bangladesh found a correlation between the temperature with the incidence of dengue fever (Sharmin et al., 2015). In Kolaka district, no research has been done to investigate and study the predictive transmission of dengue fever. Therefore, this study aims to study the predictive transmission of dengue hemorrhagic fever in Kolaka district by using meteorological and surveillance data.

2. METHODOLOGY

2.1 Study area

Kolaka district is located in the western part of Southeast Sulawesi province, extending from north to south between 3^0 36'-4^0 35' south latitude and extending from west to east between 120^0 45'-121^0 52' East longitude.

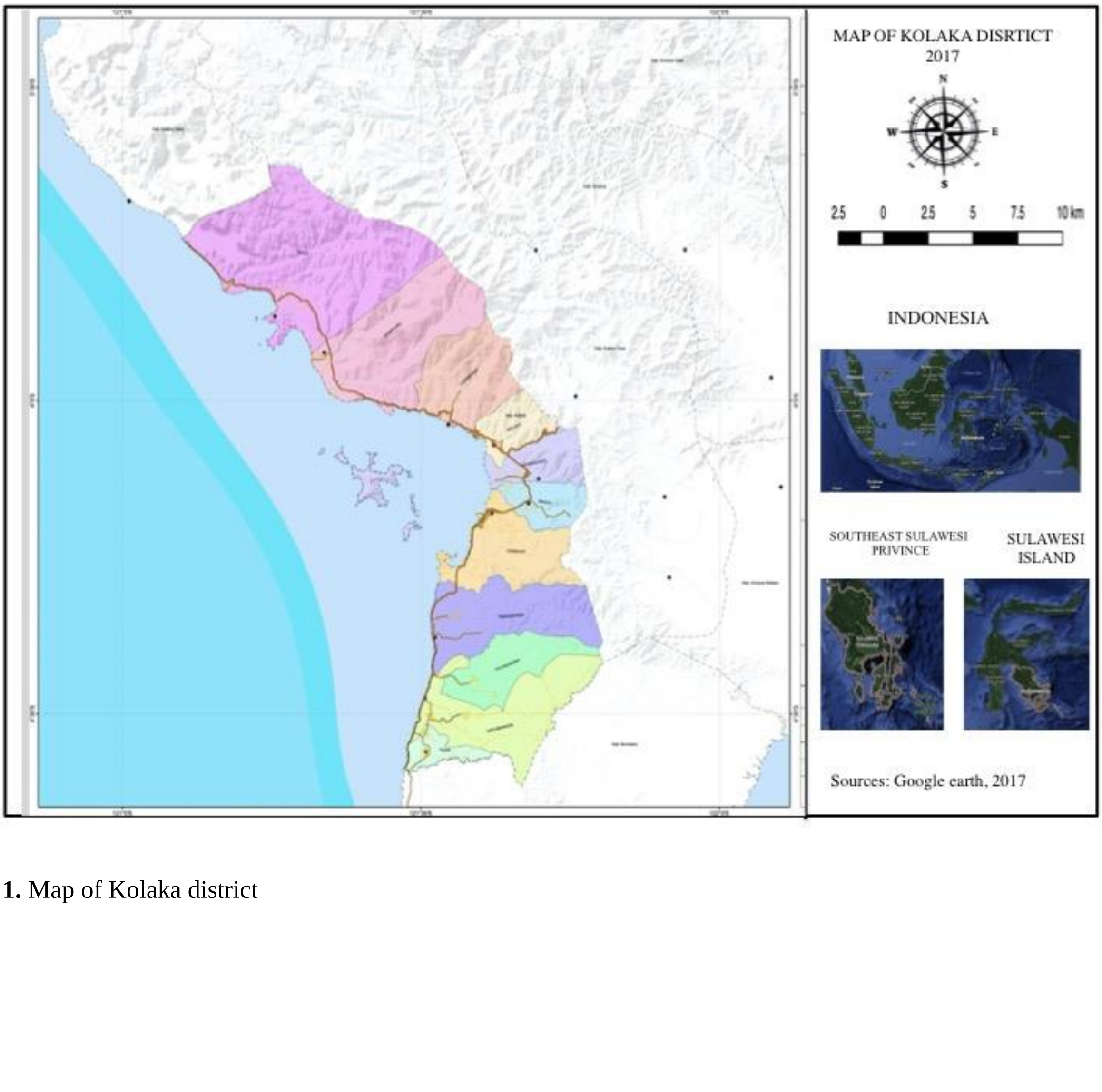

Figure 1. Map of Kolaka district

2.2 Data collection

This study used secondary data obtained from various governments of Indonesia. Data of DHF cases from 2010 to 2015 were obtained from the Health Office Kolaka. Monthly meteorological data obtained from the Meteorology, Climatology and Geophysics Agency in Southeast Sulawesi province consisted of temperature, rainfall, and humidity.

2.3 Statistical analysis

Data were cleaned and formatted by R software with R statistical language version 2.15 employed for analysis. All charts and tables were also produced in R Studio (version 3.3.2) (Lander, 2014). This study performed Spearman rank correlation tests to examine the relationship between monthly cases of DHF and meteorological variables with a lag of zero to five months. By analyzing monthly cases of DHF using a Poisson distribution, this model enables both specification of an over dispersion term and a first order autoregressive structure that accounts for the autocorrelation of monthly numbers of dengue hemorrhagic fever. A basic multivariate Poisson regression model can be written as:

$$\mathrm{In}(Y) = \beta_0 + \beta_1 \mathrm{Tmin}_{t-n} + \beta_2 \mathrm{Tmax}_{t-n} + \beta_3 \mathrm{Tmax}_{t-n} + \beta_4 \mathrm{Rain}_{t-n} + \beta_5 \mathrm{Hum}_{t-n}$$

The model that adjusts for the first order autocorrelation can be written as:

$$\ln(Y) = \beta_0 + \beta_1 \ln(Y_{t-1}) + \beta_2 \mathrm{Tmin}_{t-n} + \beta_3 \mathrm{Tmax}_{t-n} + \beta_4 \mathrm{Tmax}_{t-n} + \beta_5 \mathrm{Rain}_{t-n} + \beta_6 \mathrm{Hum}_{t-n}$$

where Tmin, Tmax, and Taverage is value of minimum, maximum and monthly temperature average, Rain and Hum are rainy and humidity variables. The t subscripts is the times and n is the time lag. Y_{t-1} is the total cases DHF in t-1 (lag 1).

3. RESULTS AND DISCUSSION

3.1 Times series of dengue hemorrhagic fever

The distributional pattern of incidence rate of dengue hemorrhagic fever and meteorological factors in Kolaka district during 2010-2015 is shown in Figure 2(a). In Kolaka, the mean and maximum incidence rates of dengue hemorrhagic fevers are 7.84 and 50.12 with 50 percent of the data in the interval of 3.29 - 16.18. The highest case of dengue occurred in 2015 and was not an outlier. This shows that Kolaka district needs to get more attention when the dengue season occurs. Seasonal patterns are also seen in annual periods corresponding to the rainy season for Indonesian territory. Dengue hemorrhagic fever season starts in December and tends to decrease after April (Figure 2 (a)).

The monthly distribution patterns of meteorological factors in Kolaka district during the years 2010-2015 are shown in Figure 2 (b-f). The variations of seasons are characterized by high rainfall from December to June (Figure 2 (b)) with the highest average volume in the range from 214-239 mm occurring in March to May. The average relative humidity in Kolaka was 76% with the highest monthly humidity average occurring in June reaching 79% (Figure 2 (c)). The average temperature in Kolaka ranged between 26.1 ºC - 29.7 ºC (Figure 2 (d)) with an average minimum temperature of 24.2 ºC (Figure 2 (e)) and an average maximum temperature of 33.6 ºC Figure 2 (f).

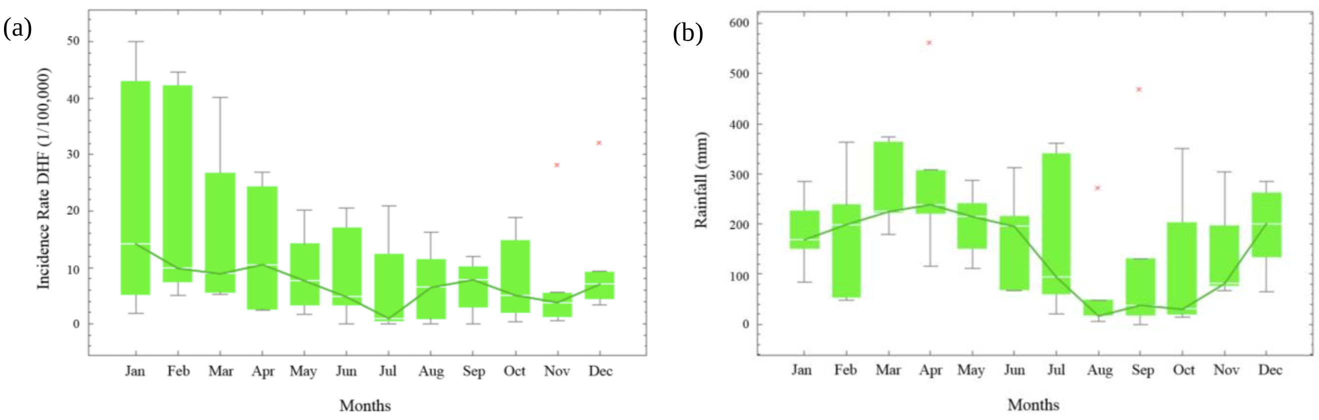

Figure 2. The spatial temporal patterns of dengue hemorrhagic fever incidence rate, during 2010 to 2015 in Kolaka

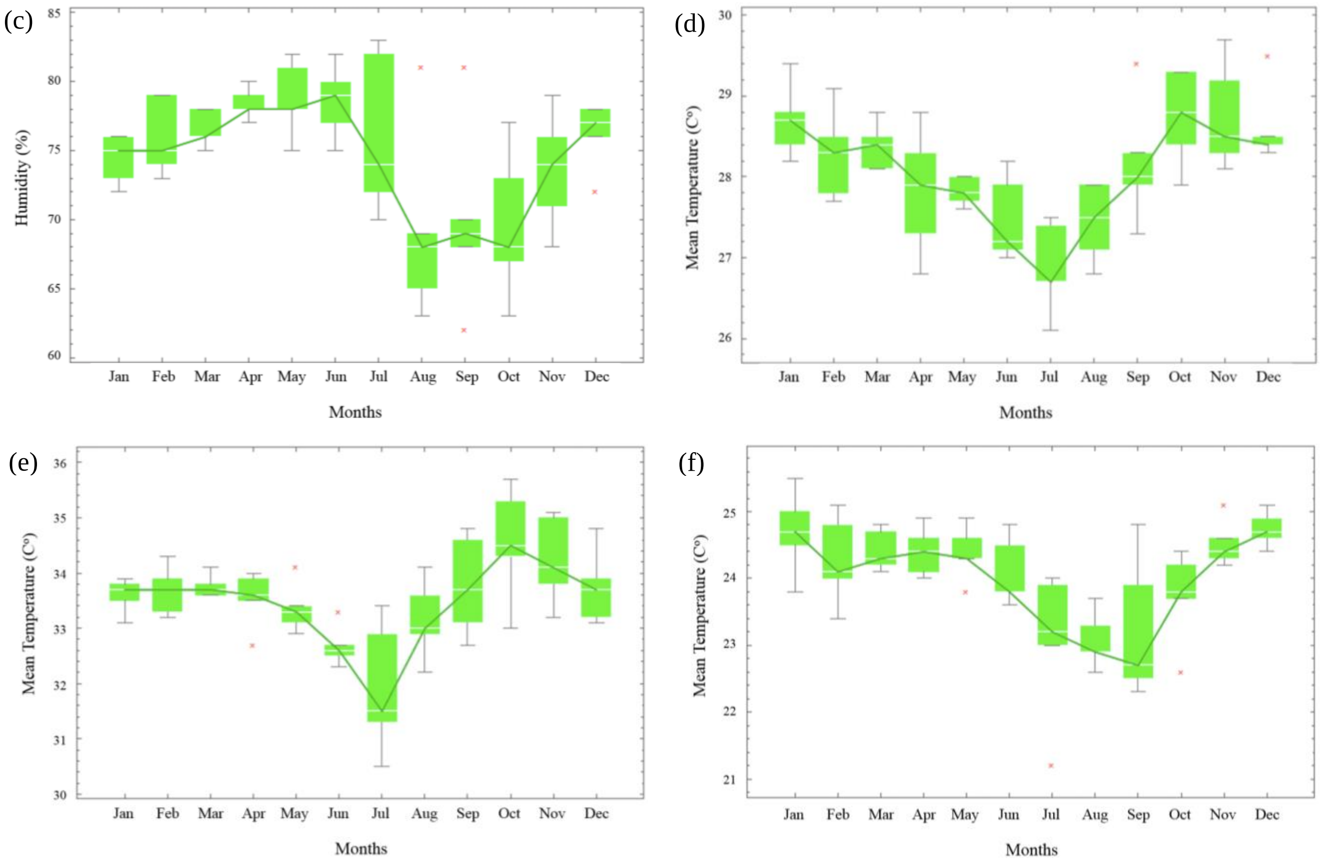

Figure 2. The spatial temporal patterns of dengue hemorrhagic fever incidence rate, during 2010 to 2015 in Kolaka (cont.)

Table 1 shows a significant relationship between dengue hemorrhagic fever events in Kolaka district with environmental factors. Positive and significant correlations of rainfall and dengue hemorrhagic fever are only found in time lag 0. DHF is significantly and positively correlated with rainfall of the same month (lag 0). For humidity, positive correlation occurs in time lag 0 and negative correlation is found in time lag 5. Analysis also revealed that there was a positive and significant impact of temperature on dengue hemorrhagic fever events. Average Temperature was significantly associated with DHF in lag 2, 3 and 4, whereas maximum temperature at lag 3 and 4 was associated. The minimum temperature was significantly associated with DHF in lag 0, 1, 2, and 3.

Table 1. Results of Spearman's rank correlation coefficient between the incidence of DHF and meteorological factors with time, time-lag ranging from 0 to 5 months, in Kolaka district

Time-lag (months)	DHF	Rainfall (mm)	Humidity (%)	Temperature (average) (°C)	Temperature (maximum) (°C)	Temperature (minimum) (°C)
0	1***	0.329*	0.27*	0.09	0.05	0.36**
1	0.58***	0.24	0.18	0.13	0.11	0.46***
2	0.4***	0.26	0.12	0.31*	0.18	0.39**
3	0.27*	0.11	0.01	0.37**	0.33*	0.37**
4	0.25	-0.07	-0.16	0.28*	0.33*	0.16
5	0.08	-0.15	-0.32*	0.29	0.32*	0.12

[a]Boldface denotes the largest value of correlation coefficient and significance with *p<0.05; **p<0.01; and ***p<0.0001.
All significance levels are assessed at α<0.05.

3.2 Predictive performance of models

- Model construction and testing

The obtained results indicated in Table 1 were used for model testing in different scenarios by using data in the period from 2010–2014. The selected models were used for dengue hemorrhagic fever prediction in Kolaka district, the concern variables in different lags are summarized in Table 2.

Table 2. Variable and time lag in Kolaka district

Variable	DHF	Rainfall	Humidity	Temperature (average) (°C)	Temperature (maximum) (°C)	Temperature (minimum) (°C)
Time lag	1	0	0. 5	2,3,4	3,4,5	0,1,2,3

We evaluated a total of 131 combinations of models in which each model included only 1 variable representing the temperature factor of 959 variations of the constructed model. The model is selected by using QICu (Quasi likelihood under the Independence model Criterion) values as well as consistent performance based on RMSE (Root Mean Square Error) and R^2 evaluations, both for data train (2010-2014) and predictive data (2015).

We ignored the 10-point difference of the model that has the highest QiCu. Table 3 shows the 5 selected models with the highest QiCu range, ie -3820.12 to -810. From table 3, it is seen entirely as a lagged time regression model where 2 models are composed of IR dengue hemorrhagic fever, rainfall, humidity and maximum temperature, 2 models without rainfall variables, and 1 model without humidity variables. The overall model using the maximum temperature variable represents the temperature factor.

Table 3. Statistical performance of models testing

Models (number)	QICu	Used data (2010-2014)		Prediction period (2015)	
		SRMSE	R^2	SRMSE	R^2
Rainfall lag 0 + humidity lag 0 .+ Tmax lag 3 (326)	-3820.12	0.478	0.593	0.415	0.333
Humidity lag 5 + Tmax lag 3 (108)	-3819.46	0.484	0.579	0.413	0.429
Rainfall lag 0 + humidity lag 5 + Tmax lag 3 (316)	-3818.31	0.488	0.572	0.422	0.431
Humidity lag 0 + Tmax lag 3 (118)	-3810.76	0.478	0.595	0.392	0.319
Rainfall lag 0 + Tmax lag 3 (98)	-3810.00	0.493	0.565	0.397	0.38

We selected model number 118 because it shows the optimal combination of consistency of performance and precision in the training period and prediction period, predicted model performance is excellent for predicting the incidence of dengue in 2015 (SRMSE, 0.392), as follows:

$$\mathrm{Log}(\mathrm{idf}_t) = \beta_0 + \beta_1 \mathrm{idf}_{t-1} + \beta_2 \mathrm{Humidity}_{t-0} + \beta_3 \mathrm{Tmax}_{t-3}$$

where IR of DHF_t is the incidence of dengue confirmed cases at time t, β_0 is the intercept and β_1 through β_3 represent coefficients of monthly incidence of dengue hemorrhagic fever, relative humidity and maximum temperature.

Table 4 shows the statistical performance of the final selected model. IR of dengue hemorrhagic fever case was significantly positive correlated with IR DHF lag 1 and maximum temperature in lag 3 had significant positive relation to monthly dengue fever cases in Kolaka. Relative humidity also contributed negatively to monthly dengue fever cases in Kolaka although it was not statistically significant.

Table 4. Statistics of best-fitting Poisson regression models of the monthly dengue cases (2010-2014) in Kolaka district

	Estimate	Std.err	Wald	Pr(>|W|)
(Intercept)	-27.4289	6.5959	17.29	3.2e-05***
IR DHF lag 1	0.5372	0.1171	21.03	4.5e-06***
Humidity lag 0	-0.0127	0.0236	0.29	0.59
Maximum Temperature lag 3	0.5233	0.2243	5.44	0.02*

*p<0.05; **p<0.01; and ***p<0.0001. All significance levels are assessed at α<0.05.

Figure 3 shows the time series of predicted results that are contrasted with reported dengue cases in Kolaka during the training period. The time series of fitted cases against actual reported cases as shown in Figure 3 exhibited a good fit of the model. Statistic performances in table 3 shows Standardized Prediction Errors (SRMSE) of the final model were 0.478 and 0.392 of the standard deviation of reported dengue cases during the model development period (2010–2014) and forecast in 2015, respectively. The SRMSE can be interpreted as the average error in the forecast of monthly dengue counts. While the R^2 of our model suggests that maximum temperature, humidity and past dengue cases explained 32 % of the variance of monthly dengue distribution.

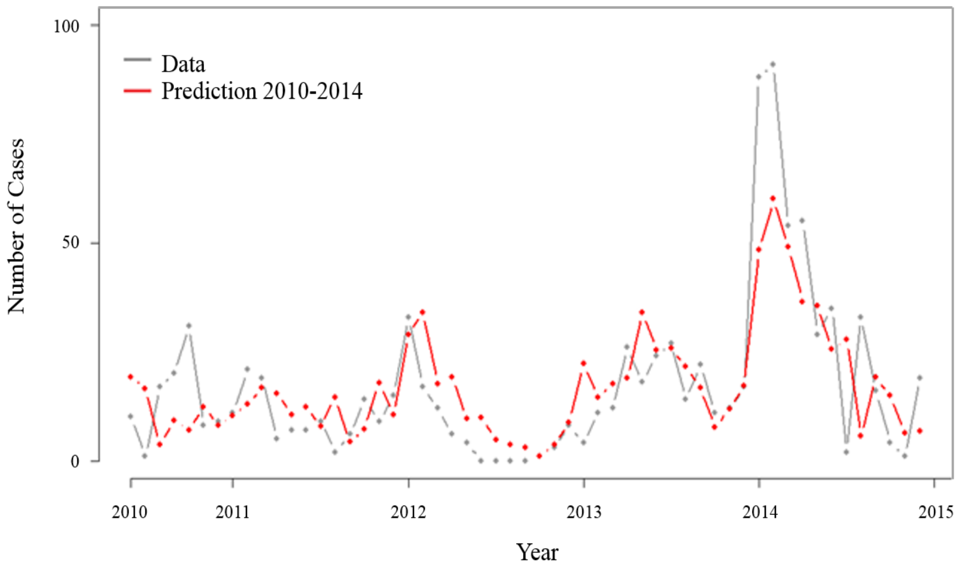

Figure 3. Fitted dengue cases versus reported dengue cases during 2010–2014 in Kolaka. Model-based predicted or fitted dengue cases were plotted against actual reported dengue cases during the model training period

Residual histograms exhibited a single modal and almost symmetrical pattern (Figure 4 (a)). Although the image was clearly visible, the right tail of the distribution was considerably longer to the other tail (Right-Skewed Histogram). From the normality test, we know that its residual distribution only followed the normal distribution based on the Lilliefors test for significance levels at α < 0.01. (Shapiro-Wilk: W = 0.9, *p*-value = 1e-04; Lilliefors: D = 0.1, *p*-value = 0.01) In addition, the Q-Q Plot for deviance residuals also shows a deviation from a straight line indicating residual data had more variability than expected under the assumed distribution (Figure 4 (b)). Meanwhile, graphical examination of Partial ACF plots shows the residual distribution is consistent about the zero value and within upper and lower limits of +/-0.2 (Figure 4 (c)). The plot of reported and predicted cases indicated a linear relation (*r*=0.712, *p*-value = 1e-11) (Figure 4 (d)).

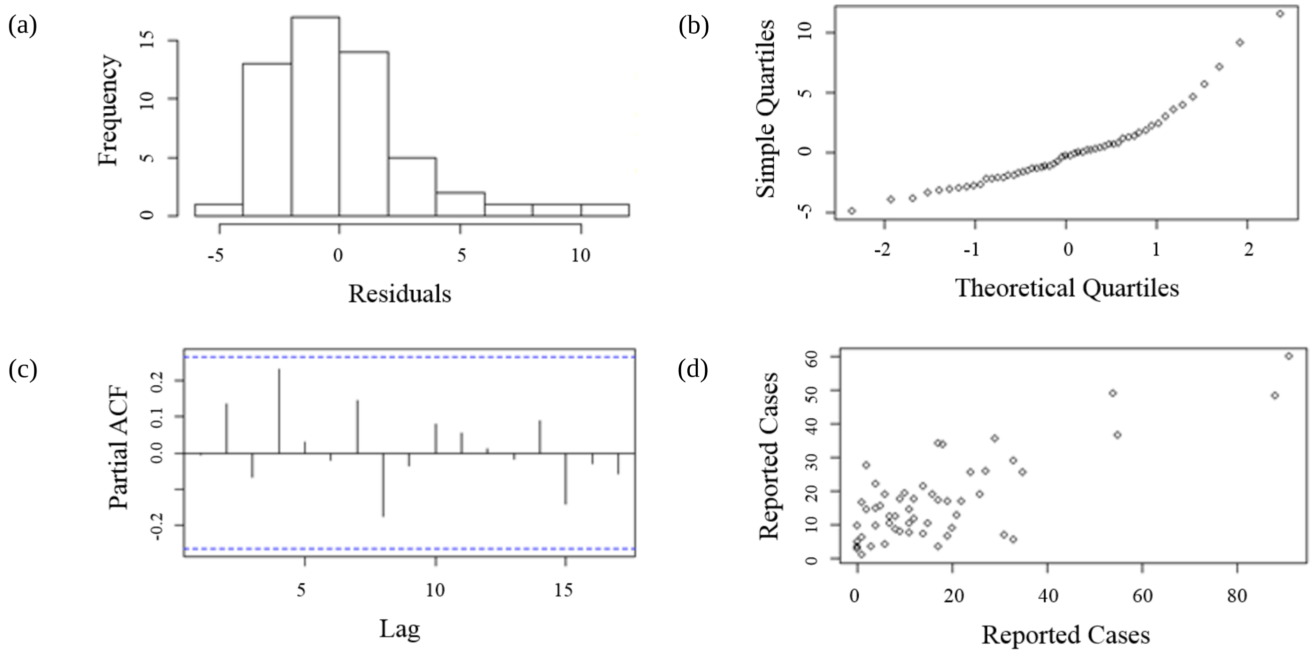

Figure 4. Residual diagnosis Kolaka. Upper panel shows (a) the residual histograms; and (b) the Q-Q plot for deviance residuals. Lower panel shows (c) the partial ACF plot; and (d) the relationship between reported and predicted cases

- Forecast of dengue cases in 2015

The final model specified in the previous section was used to predict the DHF incidence in Kolaka in 2015. Figure 5 shows the predicted time series of results in reported dengue cases in Kolaka in training and forecasting periods. Forecasted cases versus actual clinical reported dengue cases gave an average error of 0.392 of the standard deviation of reported cases.

During the training period, the incidence of DHF in Kolaka passed epidemic threshold (> 60 cases) twice in January and February 2014. The final model for Kolaka was able to predict 1 of the two outbreak events and able to predict all non-epidemic outbreak events. Performance model in the training period as follows: 53 predictions were correctly negative, 1 correctly positive, 1 incorrectly negative, and 0 incorrectly positive. Therefore, the sensitivity of detecting the outbreaks was estimated to 0.5% and the specificity to 100%. In addition, the positive and negative predictive values respectively were estimated to be 1% and 98.1%.

Meanwhile, in the forecasting period throughout 2015, predictions show a good performance in which the model was able to predict 3 of 5 epidemic outbreak events occurring in January-March 2015 and November-December 2015. The sensitivity of detecting the outbreaks was estimated to be 60%, the specificity to be 100%, positive and negative predictive values respectively were estimated to be 100% and 77.8%.

The occurrence of dengue virus transmission is very complex. Climate has an important role in the transmission. The duration of climate in every region in Indonesia is different. This is because Indonesia has a very large area and has 5 large islands (Java island, Sumatra, Kalimantan, Sulawesi, and Papua), and other smaller islands, where differences occur in moisture and temperature.

Kolaka district is geographically a tropical region composed of forests, agriculture, and seafront. The results of the study found that dengue disease increased every year. Dengue hemorrhagic fever was identified with an average temperature of 26.1 °C -29.7 °C, with a minimum temperature of 24 °C, and a maximum temperature of 33.6 °C. Moisture average was 76% relative humidity, and average monthly rainfall was 214-239 mm. These incidents occurred within six years (2010-2015). In Asian countries, dengue fever is found in urban and semi-urban areas in the tropics and subtropics (Anker and Arima, 2011). With these conditions, the temperature is considered as an optimal condition for mosquito (Kuan et al., 2010). This study is in line with research conducted in Peru, where it is at high risk for DHF, a seasonal peak occurrence occurs when the mean temperature is 26-29 °C (Campbell et al., 2015). The greatest risk of transmission of dengue fever occurs at a temperature of 28 °C (Chen and Hsieh, 2012). Minimum temperatures were not found as reliable predictors in the model, reinforcing previous studies showing that minimum temperatures are not significant variables in regional or temporal dengue distribution in Indonesia (Arcari et al., 2007). However, the minimum temperature seems to have little effect on the lags 0, 1, 2, and 3 for the occurrence of dengue fever in Kolaka district.

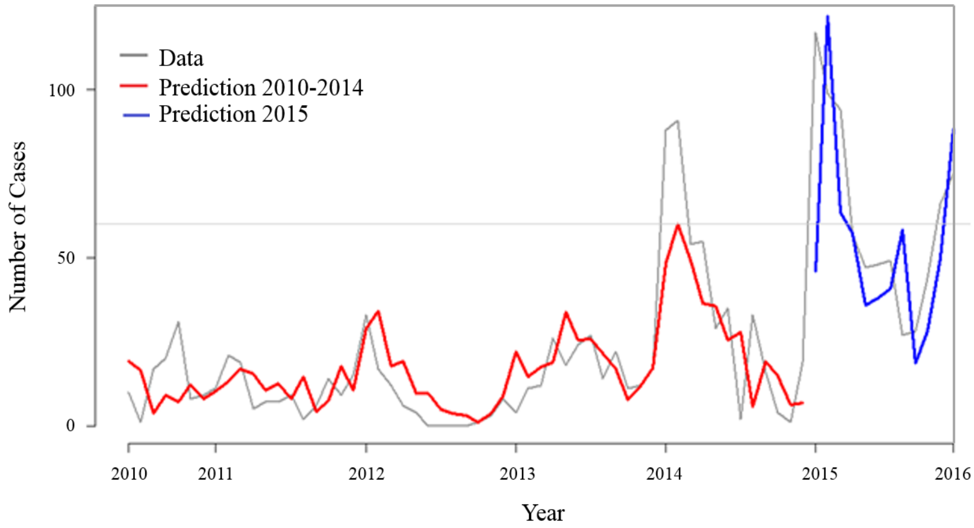

Figure 5. Predicted Dengue Cases Versus Reported Dengue Cases in Kolaka from 2010-2015. Gray line represents observed dengue cases, grey horizontal line represents the epidemic threshold, red line represents predicted cases in the training period (2010-2014), and blue line represents predicted cases in the forecasting period (2015)

The incidence of dengue was strongly influenced by meteorological variables in Kolaka district. This was based on analysis conducted using DHF surveillance data. The study was in line with the study conducted in Cordoba, Spain using a linear regression model that found a positive relationship between dengue fever and rainfall ($p < 0.01$) and humidity ($p < 0.01$) (Mattar et al., 2013). Humidity is a vapor pressure and moisture levels become high when rainfall and temperatures are high. This is a conducive condition to breeding and survival of vectors for rapid virus replication (Focks et al., 1993). Temperature and humidity are climate factors that consistently impact on dengue transmission (Naish et al., 2014). The life cycle of mosquitoes is influenced by the presence of humidity. It is known that humidity and temperature significantly affect the amount of blood food and also affect the survival rate of vector (Phung et al., 2015).

DHF cases began to rise in December and peaked in January and February, while in March it began to fall. The number of cases reached a minimum in July and November, and the lowest rainfall was in August and September. The highest occurrence of DHF cases was in Kolaka, Latambaga and Wundulako sub districts. These three sub districts are densely populated areas. Another risk factor contributing to DHF transmission is population density. The more densely populated, the more easily the *Aedes* mosquito passes the virus from one person to another. Population growth that does not have a certain pattern is one factor that plays a role in the emergence of DHF.

Climatology factors related to the 2014 and 2015 epidemics are humidity, rainfall, and temperature maximum. The predicted number of DHF cases for 2015 increases and reaches the maximum case rate in January-March. This forecasting is very beneficial for the district government of Kolaka to prevent DHF cases in the future. Prevention can be done before the peak of the cases. Forecasting models are based on cases of DHF reported at public health centers. Modeling is useful for interpreting surveillance data and case estimates to aid timely prevention and control (Allard, 1998). Forecasting cases of dengue in southern Thailand is useful to improve planning, control and prevention, and public health interventions (Promprou et al., 2006). Humidity and maximum temperature in Kolaka district increased from 2014 to 2015. Humidity and maximum temperature are factors that correlate with rising cases of DHF. These two factors are also useful in durable models to predict IR DHF.

An early prediction model of the epidemic is essential for evaluating the risk of outbreaks. Therefore, early epidemic intervention and prevention should be done, instead of the management of the epidemic. The development of a warning system should also be able to identify and quantify the risk of dengue fever in a population. In this study, DHF disease prediction models are based on data of DHF cases and climate data, using lag models as a useful model to predict the incidence of DHF, as well as to predict the occurrence of DHF occurring in Kolaka district.

4. CONCLUSIONS

The pattern of increasing incidence rate of DHF incidence in Kolaka district occurred in January and February every year. There is a correlation between climate factors (rainfall, humidity, temperature average, minimum temperature, temperature average) with dengue hemorrhagic fever. The relationship varies according to the time lag each month. The prediction model used is able to estimate the incidence of DHF in Kolaka district.

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