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The Effect of Climate and Intervention Methods on Malaria Incidence : A Time Series Analysis

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ABSTRACT

Background : Climate has been considered as an influential factor related to Malaria casesin several previous research. However,there are still contradiction results in several countries. It is also interesting to find out the effect ofmalaria intervention methods when information about theinfluenced variables are still limited.
Purpose: The aim of this research was to analyse the effect of climate and intervention method using model prediction.
Methods : This research was an analytic study with time series analysis in Menoreh ecosystem, Central Java, Indonesia. Some variables were collected such as temperature, rainfall, intervention methods (the use of mosquito nets, Indoor Residual Spraying, Mass Blodd Survey and number of malaria cases). Data were collected during the period of 2005-2015 (10 years). Data analysis useda poisson regression to assess correlation between variables, and a quasi poisson and negative binomial to determine the best model.
Results : Theresult of this study showed that malaria incidences were influenced by case finding through mass blood survey, and the number of malaria cases in previous month. While climate variables such as temperature and rainfall had no significant correlation with malaria incidence.
Conclusion: This modelling framework revealed that mass blood survey and the number of malaria cases influenced the malaria incidence. Therefore, it is important to conduct routine mass blood survey and active surveillance to monitor and predict the malaria cases.

Keywords : Climate, Malaria, Mass blood survey

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INTRODUCTION

Malaria is a public health problem globally. Nowadays, there is developed a conceptual model or modelling in controlling malaria. A mathematical modelling of malaria is the best method to synthesize information, measure uncertainty, and extrapolate knowledge (1). Modelling of malaria used a factor of climate has been undertaken in some countries like Nigeria, Bangladesh, Brazil, Kenya, Ethiopia, China, West Africa, Burundi,and Bhutan (2)(3)(4)(5)(6)(7)(8)(9)(10)(11). Climate plays an important role in malaria transmission particularly in a highland tropical area. Social economics factor such as land use, population growth, urbanization, migration, and economic development also need to be paid attention in risk assessment of malaria in the future (12).A climate change will directly affect to a transmission of vector-borne disease by changing a geographical distance of vector, increase reproduction and biting rate, and shorten incubation period of pathogen(13). The other factors like temperature, rainfall, and humidity influence a population of Anopheles and a malaria incidence(14)(15). Warm temperature or hotter can reduce duration of an extrinsic cycle (a sporogonic cycle) by which mosquitoes will be more infective and spread widely(16)(17)(11). Temperature, rainfall, and humidity relate to dynamic population of malaria vector and spread of malaria disease. Suitable temperature for mosquito lifespan ranges from 16°C to 36°C with life sustainability equal to 90%. Higher proportion in incubation period of mosquitoes occurs in temperature of 28°C – 32°C (18).Even though rainfall does not directly affect on parasites, it plays an important role in a transmission of malaria. Rain will form water as a breeding place of Anopheles. High rainfall also increase humidity and prolong age of adult mosquitoes. For example, in sub-Saharan area, a transmission of malaria occurs more frequent during rainy season(18). The increase of rainfall and humidity is linear with density of Anopheles mosquitos(19). A study in India demonstrated the higher rainfall, the more cases of malaria (20). Another study in Tibet showed that rainfall and temperature were important environmental factors in a transmission of malaria even though the influence of these both factors were not linear (15).The results of a scoping reviewabout a prediction model of malaria byZinszer et al (21), besides climate factors, other intervention variables like the use of mosquito net and spraying can also be used in modelling. An effort of intervention in controlling malaria is made by controlling vector and providing medicines for patients. Vector control includes Indoor Residul Spraying (IRS) andLong-lasting Insecticidal Nets (LLIN). Some previous studies demonstrated that the use of IRS and LLIN can reduce density of mosquitos and an incidence of malaria cases(22)(23)(24).One of the areas that still has high cases of malaria in Indonesia is Menoreh hills. During 11 years from 2005 to 2015, there had been reported 3,812 cases of malaria. Area of covers Districts of Purworejo and Kulonprogo(25). The results of buffering analysis showed that malaria sufferers at Menoreh hills lived nearby breeding places of mosquitos like river stream, water springs, puddle, ditch, and pond (26).The results of research in Purworejo revealed that climate factors such as humidity and rainfall influenced the occurrence of malaria (27). Climate factors which were collaborated with intervention factors at Menoreh will be examined in accordance with suggestion by Zinzser 2012.

METHODS

This was an observational study with a time series spatial analysis method using data of malaria, climate factors, and monthly intervention during 10 years. Independent variables consisted of average temperature, average rainfall, number of mosquito nets, IRS, and MBS. A dependent variable wasnumber of monthly cases of malaria for 10 years. All variables were measured every month. Data of average temperature and average rainfall were collected from climate station of Tegal Kalibawang in Kulonprogo District of Yogyakarta Province. Data of malaria cases and intervention (mosquito nets, IRS and MBS)per month were obtained from District Health Office and Public Health Centers (PHC) namely Bagelen, Dadirejo, Kaligesing, Kokap I, and Kokap II. Furthermore, data were analyzed using count data. Then, these data were examined in three kinds of analyses namely poisson regression, quasi-poisson, and negative binomial in order to result the best model. After obtaining the best model, it was continued by analysis of a time series model in the following steps:model identification (a transient predictive model), estimation (estimation of model parameters), diagnostic check (verification of model suitability),forecasting (using a model to forecast). Software R was used to perform data analyses.

RESULTS

Malaria cases and API rate in Menoreh ecosystem fluctuated during the period of 11 years. API rate tended to decline until 2009 but it increased gradually until 2015. API rate significantly rose in the last five years. The highest number of malaria cases and API occurred in 2015.Climate conditions and intervention during the period of 2005-2015 in the research site were as follows:

Table1. The results of multivariate analysis for variables of climate and malaria intervention in Menoreh ecosystem in the period of 2005-2015

Variable	Year										
	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Temperature											
- Mean	24.1	23.4	24.3	23.9	24.1	25.0	23.6	24.6	24.8	24.6	24.7
- Min	22.1	20.5	22.2	21.1	21.1	24.1	20.3	21.9	22.0	22.6	21.0
- Max	25.1	26.0	26.4	25.4	26.2	25.4	26.8	26.5	26.3	25.8	26.6
Rainfall											
- Mean	130.8	192.5	231	226.8	271.3	276.2	263.5	229.4	244.2	181.4	208.2
- Min	0	0	0	0	104	104	0	0	0	0	0
- Max	404	521	698	595	461	519	691	555	538	525	554
Mosquito Nets											
- Mean	92	83	86	107	21	44	147	133	218	36	91
- Min	0	0	0	0	0	0	0	3	4	3	2
- Max	1050	950	1002	540	150	425	1264	663	2367	123	307
IRS											
- Mean	0	0	0	0	0	0	1	1	0	0	0
- Min	0	0	0	0	0	0	0	0	0	0	0
- Max	0	3	1	0	0	1	2	4	3	2	4
MBS/MFS											
- Mean	0	0	0	0	0	0	1	1	1	1	1
- Min	0	0	0	0	0	0	0	0	0	0	0
- Max	3	2	1	0	0	2	3	3	4	4	3
Malaria case											

- Mean	17	25	6	6	4	10	77	46	48	49	80
- Min	1	1	0	1	0	0	1	12	18	8	16
- Max	44	42	12	17	8	38	259	126	92	149	162

Average annually temperature during the period of 2005-2015 ranged from 23.4°C-25.0°C with the lowest temperature was 20.3°C and the highest temperature was 26.8°C. In addition, average monthly rainfall during the same period ranged from 130.8 – 276.2 mm with the highest rainfall occurred in 2010.Average mosquito nets distributed in Menoreh ecosystem varied, ranging from 100 to 200. The most of mosquito nets was distributed in 2013 and the lowest number of mosquito nets distribution was in 2009. Number of mosquito nets distributed in the area during 11 years ranged from 150 to 2367 pieces. The activity of IRS was rare. In sub district of Kokap, IRS was no longer undertaken in the last five years. Average MBS/MFS was only one village per year in the last five years even though the Menoreh ecosystem had 43 villages.Malaria cases tended to increase in the last 11 years. The highest average malaria cases occurred in 2015 (80 cases/month) and the lowest average malaria cases occurred in 2009 (4 cases/month).

A predictive model of malaria case

The results of time series analysis to create a predictive model of malaria case based on the variables of average temperature, rainfall, mosquito nets, IRS, MBS/MFS are shown in Table 2. A time series model used for making the predictive model was poisson, quasi-poisson, and negative binomial.

Table2. The results of analysis of climate factors and intervention correlated with the occurrence of malaria using three models (poisson regression, quasi-poisson, andnegative binomial)

No	Variabel	Model 1	Model 2	Model 3
1	Intercept	$-1.001x10^{-1}$ 0.92098	$-1.001x10^{-1}$ 0.98296	$-2.613x10^{-1}$ 0.9407
2	Temperature	$2.538x10^{-2}$ 0.19958	$2.538x10^{-2}$ 0.78242	$3.248x10^{-2}$ 0.6882
3	Temperature_lag1	$-5.125x10^{-2}$ 0.03684^{*}	$-5.125x10^{-2}$ 0.65324	$-1.249x10^{-1}$ 0.1878
4	Temperature_lag2	$-1.857x10^{-1}$ $2.60\ x10^{-12***}$	$-1.857x10^{-1}$ 0.13463	$-9.399x10^{-2}$ 0.3424
5	Temperature_lag3	$2.107x10^{-1}$ $< 2\ x10^{-16***}$	$2.107x10^{-1}$ 0.07736	$1.480x10^{-1}$ 0.0961
6	Temperature_lag12	$9.77x10^{-2}$ $1.80\ x10^{-6***}$	$9.77x10^{-2}$ 0.30552	$1.205x10^{-1}$ 0.0998
7	Rainfall	$-1.463x10^{-3}$ $6.83\ x10^{-16***}$	$-1.463x10^{-3}$ 0.08506	$-1.358x10^{-5}$ 0.9835
8	Rainfall_lag1	$6.007x10^{-4}$ 0.00269^{**}	$6.007x10^{-4}$ 0.51867	$5.230x10^{-4}$ 0.4459
9	Rainfall_lag2	$-5.896x10^{-4}$ 0.00398^{**}	$-5.896x10^{-4}$ 0.53564	$-2.873x10^{-4}$ 0.6735
10	Rainfall_lag3	$-1.341x10^{-4}$ 0.47226	$-1.341x10^{-4}$ 0.87699	$7.620x10^{-4}$ 0.1996
11	Rainfall_lag12	$1.303x10^{-3}$ $1.87\ x10^{-13***}$	$1.303x10^{-3}$ 0.11598	$-2.101x10^{-4}$ 0.7572
12	Mosquito nets	$-1.770x10^{-4}$ 0.03161^{*}	$-1.770x10^{-4}$ 0.64370	$-2.654x10^{-4}$ 0.4524
13	Mosquito nets_lag1	$-3.575x10^{-4}$ $4.41\ x10^{-5***}$	$-3.575x10^{-4}$ 0.38022	$-3.969x10^{-4}$ 0.2293
14	Mosquito nets_lag2	$1.262x10^{-4}$ 0.21517	$1.262x10^{-4}$ 0.78958	$6.923x10^{-5}$ 0.8270
15	Mosquito nets_lag3	$3.587x10^{-4}$ $8.59\ x10^{-8***}$	$3.587x10^{-4}$ 0.25090	$3.187x10^{-4}$ 0.2637
16	Mosquito nets_lag12	$-3.035x10^{-5}$ 0.70902	$-3.035x10^{-5}$ 0.93595	$-1.225x10^{-4}$ 0.7060

17	IRS	2.063×10^{-1} $4.03\times10^{-10***}$	2.063×10^{-1} 0.18065	2.626×10^{-1} 0.0477^{*}
18	IRS_lag1	2.095×10^{-1} $6.05\times10^{-11***}$	2.095×10^{-1} 0.16149	1.141×10^{-1} 0.4097
19	IRS_lag2	-2.350×10^{-1} $6.31\times10^{-10***}$	-2.350×10^{-1} 0.18554	-6.225×10^{-2} 0.6802
20	IRS_lag3	2.775×10^{-1} $< 2\times10^{-16***}$	2.775×10^{-1} 0.04260^{*}	2.858×10^{-1} 0.0332^{*}
21	IRS_lag12	-1.241×10^{-1} 0.00239^{**}	-1.241×10^{-1} 0.51366	-8.805×10^{-2} 0.5465
22	MBS/MFS	2.418×10^{-1} $< 2\times10^{-16***}$	2.418×10^{-1} 0.02868^{*}	2.975×10^{-1} 0.0173^{*}
No	Variabel	Model 1	Model 2	Model 3
23	MBS/MFS_lag1	1.656×10^{-1} $5.03\times10^{-11***}$	1.656×10^{-1} 0.15976	1.469×10^{-1} 0.2101
24	MBS/MFS_lag2	1.72×10^{-1} $3.38\times10^{-10***}$	1.728×10^{-1} 0.17876	1.770×10^{-1} 0.1579
25	MBS/MFS_lag3	-7.254×10^{-2} 0.02932^{*}	-7.254×10^{-2} 0.63910	-7.748×10^{-2} 0.5925
26	MBS/MFS_lag12	-2.337×10^{-1} $8.47\times10^{-14***}$	-2.337×10^{-1} 0.11094	-1.280×10^{-1} 0.3703
27	Case_lag1	9.661×10^{-3} $< 2\times10^{-16***}$	9.661×10^{-3} $<0.00947^{**}$	1.700×10^{-2} $4.1\times10^{-6***}$
28	Case_lag2	1.854×10^{-3} 0.01650^{*}	1.854×10^{-3} 0.60592	1.543×10^{-3} 0.6840
29	Case_lag3	-6.142×10^{-4} 0.40761	-6.142×10^{-4} 0.85848	-1.498×10^{-3} 0.6765
30	Case_lag12	7.853×10^{-3} $< 2\times10^{-16***}$	7.853×10^{-3} 0.01423	6.483×10^{-3} 0.0320^{*}
	AIC	1789.8	NA	899.29

The results on poisson regression (model 1) showed that there were many variables which were statistically significant. Notwithstanding, the poisson regression could not identify whether there were any over dispersion or not. Furthermore, the analysis was continued by using quasi poisson (model 2) to test parameters of over dispersion. The results of the quasi poisson demonstrated parameters of over dispersion > 1. It means that over dispersion had occurred.When over dispersion occurred, the next suitable analysis was negative binomial (model 3).The results of negative binomial analysis showed that five variables had p-value less than 0.05 namely IRS, IRS lag_3, MBS/MFS, case_lag1, and case_ lag12. The next steps was to examine these five variables in order to result two significant variables ($p<0.05$) namely MBS/MFS andcase_lag1. Then, the two variables were examined again to create the best model (appendix 3). In the resulted best model, it had been checked for error values and as the result, there were no correlation between errors and had met the required assumption.

Table3. The best model to determine a predictive model for the occurrence of malaria using negative binomial regression

	Estimate	Std. Error	Z value	Pr(>lzl)
Intercept	2,2163	0,1147	19,308	0,0001
MBS/MFS	0,2938	0,1058	2,776	0,0055
Case_lag1	0,0226	0,0024	9,152	0,0001

The last model based on analysis of negative binomial regression was as follows:

$$Y_{i=} \exp(2{,}2163 + 0{,}2938\ \text{MBS/MFS} + 0{,}0226\ \text{case\_lag1})$$

When there were no MBS/MFS and no case of malaria in the previous month, there had exp(2.2163) = 9 malaria cases. Each increase of MBS/MFS activities once would increase percentage of malaria cases equal to 29.38%. In addition, percentage of malaria cases in the previous month would increase as many as 2.26% of malaria cases in the following month. Besides creating the predictive model of malaria based on climate factors and intervention, the first sub-study had performed interpolation of temperature and rainfall that was overlaid with annual malaria cases.

DISCUSSION

Malaria had been an endemic disease in the Menoreh ecosystem since decades ago. Data from 2011 to 2015 demonstrated that malaria case tended to increase even though from 2005 to 2010 it gradually decrease in the step of pre-elimination.The high malaria cases during the period 2011-2015 indicated the target of elimination in 2018 could not be realized. In 2016, data of malaria cases in Menoreh hills declined namely 260 cases in which the proportion of P.falciparum and P.vivax was almost equal. In 2010, there was the highest average rainfall in Menoreh hills with average monthly rainfall was 276.2 mm. In addition, during 2010, rainfall equally occurred every month with the highest average monthly rainfall in January and December. Nowadays, the change of seasons is more difficult to predict. Dry season usually occurs during the period of April-September. In 2010, these period was rainy season (May-September). Climate change is caused by global warming. The transmission of diseases in a community is easy due to climate change. Bacteria, virus, and protozoa easily spread in the new environment to keep temperature of their bodies. This condition leads to transmit infectious diseases like dengue hemorrhagic fever, malaria, cholera, typhoid, and hepatitis. In the last 20 years, malaria had five-year repeat cycle in Menoreh hills. During the period of 1999-2004, malaria cases tended to be high. Then,the period of 2005-2010, number of malaria cases dramatically declined. From 2011 to 2015, malaria cases gradually increased.In 2016, number of malaria cases tended to decline. In 2010, besides the factor of high rainfall, the temperature was also relatively higher than the previous and the following years. Warm temperature would shorten a sporogonic cycle. Mosquitoes would be more infective and spread wider. The change of a rainfall pattern and temperature would increase vector-borne disease like malaria.

The result of first sub-study showed the resulted predictive model as follows:

$$Y_{i} = \exp(2{,}2163 + 0{,}2938 \text{ MBS/MFS} + 0{,}0226 \text{ case\_lag1})$$

It means that when there were no MBS/MFS and no case of malaria in the previous month, there had exp(2.2163) = 9 malaria cases. Each increase of MBS/MFS activities once would increase percentage of malaria cases equal to 29.38%. In addition, percentage of malaria cases in the previous month would increase as many as 2.26% of malaria cases in the following month.This model demonstrated number of malaria in the Menoreh ecosystem was influenced by activities of MBS/MFS and number of cases in the previous month. The activities of MBS/MFS are undertaken after reporting malaria cases. A report of malaria cases was a basis of MBS/MFS action. The activity of MBS/MFS is one of the effort to find a case (case detection). This activity can be done routinely or specifically in finding malaria casesby identifying clinical symptoms or locally particular symptoms following with collecting blood samples and analyzing them at a laboratory. This activity is early case detection in order to provide medication immediately and in accordance with a standard and to prevent the transmission.Mass Blood Surveyis an effort to seek and find malaria cases massively by conducting a survey in an endemic area, suspected endemic area, higher endemic area in which cases do not have specifically clinical symptoms, an area that is not easy to access a health service unit and the increase of case number. Mass fever surveyis an activity to collect blood samples (microscopicor RDT) from all people who have fever symptoms at an area followed by providing medicines to positive cases in accordance with a kind of identified plasmodium. The activities of MBS and MFS will increase finding cases. Therefore, number of detected cases and case medication will be higher than before. The factor influencing number of malaria case was number of malaria case in the previous month. The transmission of malaria has not stopped within a month. It means that there is any influence of case in the previous month towards the case occurs in the current month.Not all malaria cases are detected due to a gamete phase spread in a community.The gamete phase is a source of transmission for the future.During the period of 2006-2012, average proportion of gametocytes stadium per year in Kulonprogo District was 33% ranging from 16%-49%.If a gamete stadium is found more than 30%, it indicated that activities of case finding are too late and activities of surveillance is not optimal. Sometimes, the gamete phase isnot found in health service or during activities of MBS. This gamete phaseis possibly submicroscopic. Until 2017, some cases with a gamete stadium was found at the research site with various rate for each public health center. Average gamete stadium in 2016 was 10.6%(28). The implementation of MBS at the research site was only sporadic, namely once a month from 43 villages (sometimes, it was only undertaken in one sub village). Criteria of a village for doing MBS activities is as follows: village/sub village that is categorized as high endemic; the activity is conducted routinely every year during high transmission;village/sub village with high endemic but there is no clinical case in a community; an area with high cases/outbreak and difficult to reach(29).

The target of village/sub village for MFS activities are village/sub village that has ever been categorized as high endemic; an receptive area of malaria; high mobility of residents; and low performance of surveillance (Kementerian Kesehatan, 2013). Determination of villages for MBS and the implementation at the research site were not appropriate. The activities of MBS were not undertaken in all endemic villages or outbreak. This condition caused the transmission of malaria continually occurred.Coverage of MBS/MFS at the research site was low about 25% (the target of coverage was 80%-100%) citizen. This low coverage led to difficulty in finding positive malaria cases. In addition, malaria cases that were not fully treated could cause carrier.Climate is a component of the environment that consisted of temperature, humidity, light, and wind. Climate is also known as weather. The factor of climate investigated in this study was only temperature and rainfall. The factor of climate was insignificant. Notwithstanding, the climate plays an important role in spreading and distributing Anopheles mosquitoes.Climate directly or indirectly influences to reproduction of vector of malaria in which it will influence number of malaria cases. In the research site, the range of temperature was narrow. Therefore, it was statistically insignificant.On the other hand, the factor of an individual risk like height of a house significantly influenced to the occurrence of malaria. Height of a house related to temperature. The higher position of a house, the lower temperature in its area.Average temperature in this study during the period of 2005-2015 ranged from 23.6^{o}C-25.0^{o}C. The results of this study were inconsistent with some studies of malaria modelling in some other countries like China, West Africa, Ethiopia, and India that found the factor of climate such as temperature, rainfall, and humidity as predictors for malaria cases (8)(9)(11). Some other studies also demonstrated various prediction models in different locations. One model could not be applied for all locations (30). Loha and Lindtjorn suggested to create a predictive model using variables other than climate. Our study had included theintervention variables like mosquito nets, IRS and MBS/MFS. However, the data of intervention during 10 years were not well documented at the research site.To sum up, the variables of mass blood survey and number of malaria cases influenced a prediction model for the occurrence of malaria. In contrast, the factor of climate did not influence.

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