A web-based surveillance model of eosinophilic meningitis: future prediction and distribution patterns

Noppadol Aekphachaisawat [1,4], Kittisak Sawanyawisuth [2,4], Chalongchai Phitsanuwong [5], Sittichai Khamsai [2], Paiboon Chattakul [2], Verajit Chomtmongkol [2], Somsak Tiamkao[2], Panita Limpawattana [2], Vichai Senthong [2], Jarin Chindaprasirt [2], Chetta Ngamjarus [3,4]

(1) Central Library, Silpakorn University, Bangkok, Thailand
(2) Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand
(3) Department of Epidemiology and Biostatistics, Faculty of Public Health, Khon Kaen University, Khon Kaen, Thailand
(4) Sleep Apnea Research Group, North-eastern Stroke Research Group, Research Center in Back, Neck and Other Joint Pain and Human Performance, Research and Training Center for Enhancing Quality of Life of Working Age People, and Research and Diagnostic Center for Emerging Infectious Diseases (RCEID), Khon Kaen University, Khon Kaen, Thailand
(5) University of Chicago Pritzker School of Medicine, Chicago, Illinois, USA

CORRESPONDING AUTHOR: *Chetta Ngamjarus Department of Epidemiology and Biostatistics, Faculty of Public Health, Khon Kaen University, Khon Kaen, Thailand, email: nchett@kku.ac.th*

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ABSTRACT

Background: web-based surveillance is a useful tool for predicting future cases of various emerging infectious diseases. There are limited data available on web-based surveillance and patterns of distribution of eosinophilic meningitis (EOM), which is an emerging infectious disease in various countries around the world.
Methods: this study applied web-based surveillance to the prediction of EOM incidence and the analysis of its distribution pattern by using a national database, which may be used for future prevention and control. The number cases of EOM in each month over a period of 12 years (between 2006 to 2017) from Loei province were retrieved from the National Disease Surveillance (Report 506) website, operated by Thailand's Public Health Center.
Results: we developed autoregressive integrated moving average (ARIMA) models and seasonal ARIMA (SARIMA) models. The best model was used for predicting numbers of future cases. The forecast values from the SARIMA (1, 1, 2)(0,1,1)6 model were close to actual values and were the most valid, as they had the lowest RMSE and AIC. The predictive model for future cases of EOM was related to previous numbers of EOM cases over the past eight months. The disease exhibited a seasonal pattern during the study period.
Conclusions: web-based surveillance can be used for future prediction of EOM, that the predictive model applied here was valid, and that EOM exhibits a seasonal pattern.

Key words: Angiostrongylus cantonensis, epidemiology, seasonal

INTRODUCTION

Eosinophilic meningitis (EOM) is an emerging disease in various regions around the world, the main cause of which is the nematode, *Angiostrongylus cantonensis* [1]. It is a food-borne disease that causes long-lasting, severe headaches and, in cases of encephalitis, can be fatal [2, 3]. Comatose patients or those with a severe form of the disease have poor prognoses. Rats are the definitive host, while freshwater snails and slugs are intermediate hosts [4]. Consumption of an uncooked intermediate or paratenic host is the main route of EOM transmission. Several other transmission routes have been reported, such as handling infected slugs, or consuming contaminated produce.

There were 2,827 reported EOM cases worldwide [5]. Of those, 1,337 (47.33%) cases were from Thailand. Although Thailand is the country in which EOM is the most prevalent [5], cases of this disease have been reported on every continent. Rats and snails infected with A. *cantonensis*, for example, have been reported in North and South America [1, 3, 6]. EOM is believed to be underdiagnosed or misdiagnosed, due to its non-specific symptoms (i.e., headache without any neurological abnormalities) [1]. Additionally, people traveling to endemic areas or being exposed to infected rats or larva-contaminated produce may increase the risk of EOM around the globe [7].

Several factors have been reported to be associated with emergence of infectious diseases such as population density and climate change [8]. Web-based or internet-based surveillance is currently used to predict and control infectious diseases [9-11]. Two previous studies that employed internet-based surveillance found a high correlation between found high a correlation between dengue or influenza incidence and surveillance data, with coefficients between 0.82-0.99 [11, 12]. However, there has yet been no study conducted to predict future numbers of EOM patients or their distribution using an internet database. Thus, this study will apply web-based surveillance to the prediction of EOM incidence and the analysis of its distribution pattern, which may be used for future prevention and control.

METHODS

We reviewed the annual EOM report issued by the Bureau of Epidemiology's National Disease Surveillance Division, part of Thailand's Ministry of Public Health Department of Disease Control [13]. The website received a report under the National Disease Surveillance form 506 from provincial public health offices, government hospitals, and public health centers throughout Thailand. Eosinophilic meningitis is one of 52 communicable diseases reported via this system. The numbers of patients with EOM were reported by month and province. The study period was between January 2006 and December 2017. Data from Loei province was used for the study due to its having the highest prevalence of EOM in Thailand.

Data analysis and model development

Median and interquartile range (IQR) were used to describe the number of patients from each year. The decomposition method was used to investigate long-term trends and seasonality of the data. The data were separated into two parts: 1) training data (January 2006 to December 2016), used to create a time series model, and 2) test data (January 2017 to December 2017), used to evaluate the models. We plotted an autocorrelation function (ACF) and partial autocorrelation function (PACF) for identifying potential ARIMA and SARIMA models. The minimum root mean square error (RMSE) and Akaike information criterion (AIC) were used to identify the best model for forecasting numbers of EOM patients over the following 12 months. Fitting and predicting values with their 95% confidence interval (CI.) were calculated from the best model. All analyses were conducted using R program and forecast, tseries packages on R [14-17]. An online tool of the predictive model was created.

RESULTS

During the study period, there were 1,126 EOM patients reported to the surveillance database. The median number of EOM patients in each month was seven (IQR 4.8, 11). The year with the highest number of EOM patients was 2009, in which there were143. The median number of EOM patients per month in 2009 was 11 (IQR 7.8, 14.5), as shown in Table 1. As the decomposition time series graph below demonstrates, the number of EOM patients did not increase over the course of the study period. However, it might be a seasonality because line graph in the seasonal part has a similar pattern during the period of time (Figure 1). The months with the highest numbers of EOM cases were from June to November.

We found that SARIMA(1, 1, 2) (0,1,1) $_6$ without constant (Model 12) best predicted the monthly numbers of EOM patients due to its having the smallest AIC and RMSE for training data and small RMSE for test data (Table 2). The parameter estimates of the best model are ϕ_1=0.7721, ϕ_1=-1.4226, ϕ_2=1.4226 and ϕ_1=-1. Where ϕ_1 is a coefficient of autoregressive model of order 1, ϕ_2 is a coefficient of moving average (MA) model of order 1, ϕ_2 is a coefficient of MA model of order 2, and ϕ_1 is a coefficient of seasonal MA of order 1. The best model can be expressed as

$$(1 - B)(1 - B^6)(1 - \phi_1 B)y_t =$$

TABLE 1. Number of eosinophilic meningitis patients in Thailand's Loei province between 2006 and 2017.

Year	Monthly patients Median (IQR)	Total patients/ year
2006	9 (6.8, 11.2)	114
2007	6 (6, 10.2)	102
2008	5.5 (4, 11.5)	85
2009	11 (7.8, 14.5)	143
2010	8 (3.5, 8.2)	78
2011	2 (0, 4)	28
2012	7 (4.5, 10.8)	98
2013	7.5 (5.8, 10.5)	94
2014	6 (3, 8)	68
2015	7 (5.8, 9.5)	93
2016	7.5 (4.8, 9.2)	94
2017	10.5 (6.8, 13.8)	129
Total	7 (4.8, 11)	1,126

$$(1 + \Theta_1 B^6)(1 + \theta_1 B + \theta_2 B^2)w_t$$

When B is the backshift operator and defined as $B^s y_t = y_{(t-s)}$, s is a period to shift the data back, y_t is the number of cases at time t and w_t is a white noise series.

Thus, the best model is

$$(1 - B - B^6 + B^7)(1 - \phi_1 B)y_t =$$

$$(1 + \theta_1 B + \theta_2 B^2 + \Theta_1 B^6 + \theta_1 \Theta_1 B^7 + \theta_2 \Theta_1 B^8)w_t$$

or

$$y_t = y_{t-1} + y_{t-6} - y_{t-7} + 0.7721y_{t-1} - 0.7721y_{t-2}$$

$$- 0.7721y_{t-7} + 0.7721y_{t-8} + w_t$$

$$- 1.4226w_{t-1} + 1.4226w_{t-2} - 1.4226w_{t-6}$$

$$+ 1.4226w_{t-7} - 1.4226w_{t-8}$$

Figure 2 reveals the series of the actual values (black solid line), fitting values (red dashed line), and forecasted values (blue solid line) from the best model bounded by its 95% CI. Both actual values and fitting values had almost identical pattern throughout the study period. The prediction in 2018 showed similar pattern with most previous years.

The predicted and actual numbers of EOM patients in 2018 are shown in Table 3. The actual numbers of all months fell within the 95% CI of the predicted model. The total actual number of EOM patients in the year 2018 was also closed to the predicted value (130 vs 134.51). An online tool of the predictive model can be found at http://202.28.75.8/sample-apps/EOM/

FIGURE 1. The trend and seasonality of numbers of eosinophilic meningitis patients by time series analysis.

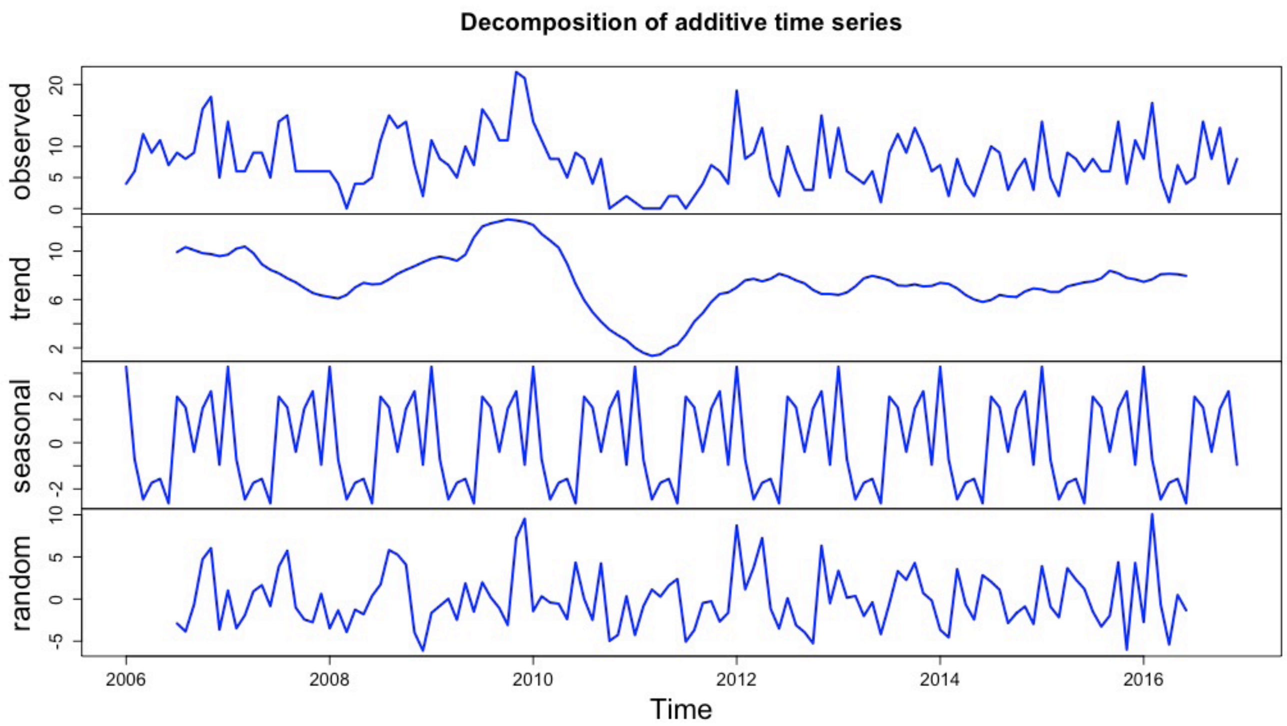

FIGURE 2. Fitting and predicting values from SARIMA(1, 1, 2)(0,1,1)6 to predict numbers of eosinophilic meningitis patients.

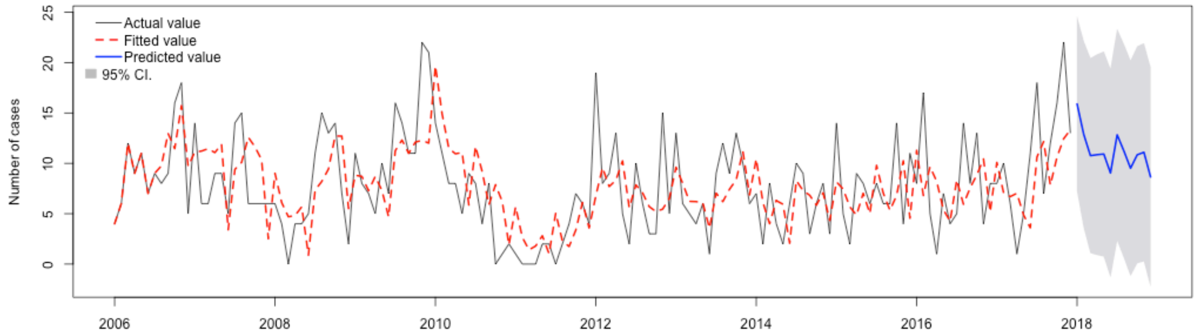

TABLE 2. Summary of model fitting parameters to predict numbers of eosinophilic meningitis patients using various models.

Model	Fit		Predict
	RMSE	AIC	RMSE
1) ARIMA(1, 0, 0)	4.32	766.87	5.1
2) ARIMA(2, 0, 0)	4.24	763.94	5.01
3) ARIMA(0, 0, 1)	4.4	771.98	5.11
4) ARIMA(0, 0, 2)	4.33	769.9	3.93
5) ARIMA(0, 0, 3)	4.21	764.15	3.77
6) ARIMA(1, 1, 2)	4.22	761.6	5.3
7) ARIMA(2, 1, 1)	4.24	762.78	5.12
8) ARIMA(2, 0, 3)	4.19	766.82	3.49
9) ARIMA(2, 1, 3)	4.21	764.7	3.41
10) ARIMA(3, 1, 0)	4.46	772.62	4.16
11) SARIMA(1, 1, 2)(0,0,1)6	4.2	761.98	3.27
12) SARIMA(1, 1, 2)(0,1,1)6	3.96	741	3.27
13) SARIMA(1, 1, 2)(0,0,2)6	4.19	763.88	3.21
14) SARIMA(1, 1, 2)(1,0,2)6	4.08	762.32	2.45

Remark: ARIMA(p, d, q) and SARIMA(p, d, q) (P, D, Q) where p is the order (number of time lags) of the autoregressive (AR) model, d is the degree of differencing, q is the order of the moving average (MA) model, P is the seasonal of AR, D is the degree of seasonal differencing and Q is the seasonal of MA model(4); RMSE: root-mean-square error; AIC: Akaike information criterion.

DISCUSSION

This study provides a predictive model to forecast future cases of EOM that was developed based on monthly numbers of EOM patients. Data from the previous eight months were required for this model. The correlation between future prediction and actual numbers of patients was high, as it has been in other studies that have employed web or internet-based surveillance to predict future epidemics [11, 12]. Both fit and predicting values of the model had small RMSEs, indicating model validity.

This study also showed that EOM exhibits seasonal variation, similar to several other infectious diseases such as seasonal flu, measles, or dengue [18-20]. Figure 2 shows the typical waxing and waning pattern of seasonal transmission or sinusoidal force. Measles exhibits similar seasonal variation, primarily based on the beginning and end of the school term [21]. In the case of EOM, the seasonal variation may be primarily due to the effects of weather and climate variations on the growth cycles or number of transmission vectors. For example, the population of giant African snails (*Achatina fulica*), an intermediate host for A. *cantonensis*, is significantly affected by temperature and rainfall [22]. Another study also found that a higher proportion of *Pomacea canaliculata*, another intermediate host, are infected in the months of April and October (60.7% and 68.4%, respectively) [23, 24]. High numbers of vectors may increase risk of larva exposure in humans, particularly in northeast Thailand, where people often eat raw or uncooked snails [25].

As shown in Table 3, the predicted numbers of EOM patients in 2018 were valid compared with the actual numbers of EOM patients reported to the surveillance system (Table 3). Therefore, there are at least three advantages of this EOM predictive model for the public health system. First, the web surveillance may change the attitude of persons who are at risk for EOM including those who habitually consume raw freshwater snails [25, 26]. Second, it may be a useful tool to detect an outbreak of EOM [27]. Third, the web-based surveillance found that the endemic months for EOM were between June and November. Therefore, preventive strategies such as health education may be performed prior to the peak of EOM. Finally, it may be used as a monitoring tool after the intervention for disease control [28].

There are three main limitations to this study. First, in order to calculate future numbers of EOM patients, data regarding the numbers of EOM patients were required from at least the past eight months. However, one advantage

TABLE 3. Predicted and actual of numbers of eosinophilic meningitis patients in 2018.

Months	Predicted numbers	Lower 95% CI	Upper 95% CI	Actual numbers
Jan-2018	15.89	7.24	24.55	9
Feb-2018	12.87	3.61	22.13	10
Mar-2018	10.76	1.09	20.44	5
Apr-2018	10.86	0.89	20.82	6
May-2018	10.92	0.75	21.10	5
Jun-2018	9.04	-1.30	19.37	11
Jul-2018	12.83	2.33	23.33	15
Aug-2018	11.23	0.63	21.84	21
Sep-2018	9.51	-1.18	20.20	12
Oct-2018	10.85	0.08	21.61	14
Nov-2018	11.10	0.27	21.92	14
Dec-2018	8.65	-2.23	19.53	8
Total	134.51			130

Note. CI: confidence interval.

of this model is that no other factors (such as clinical or weather factors) needed to be included. Second, the predictive model does not show any causal relationship of EOM. Finally, the model is based on the natural occurrence of EOM. It may become less reliable if any kind of prevention intervention is implemented. The model may be limited by the weaknesses of the surveillance system including underreporting or underdiagnosed. However, diagnosis of EOM requires evidence of eosinophils in cerebrospinal fluid. Therefore, an underdiagnosis issue may be less likely.

Competing interests

None.

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