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A national surveillance of eosinophilic meningitis in Thailand

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ABSTRACT

Introduction: Eosinophilic meningitis (EOM) is an emerging infectious disease worldwide. The most common cause of EOM is infection with *Angiostrongylus cantonensis*. One possible method of monitoring and control of this infection is surveillance and prediction. There are limited data on national surveillance and predictive models on EOM. This study aimed to develop an online surveillance with a predictive model for EOM by using the national database.

Methods: We retrospectively retrieved reported cases of EOM from all provinces in Thailand and quantified them by month and year. Data were retrieved from Ministry of Public Health database. We developed a website application to explore the EOM cases in Thailand including regions and provinces using box plots. The website also provided the Autoregressive Integrated Moving Average (ARIMA) models and Seasonal ARIMA (SARIMA) models for predicting the disease cases from nation, region, and province levels. The suitable models were considered by minimum Akaike Information Criterion (AIC). The appropriate SARIMA model was used to predict the number of EOM cases.

Results: From 2003 to 2021, 3330 EOM cases were diagnosed and registered in the national database, with a peak in 2003 (median of 22 cases). We determined SARIMA(1,1,2)(2,0,0)[12] to be the most appropriate model, as it yielded the fitted values that were closest to the actual data. A predictive surveillance website was published on <http://202.28.75.8/sample-apps/NationalEOM/>.

Conclusions: We determined that web application can be used for monitoring and exploring the trend of EOM patients in Thailand. The predictive values matched the actual monthly numbers of EOM cases indicating a good fit of the predictive model.

1. Introduction

Eosinophilic meningitis (EOM) is defined by presence of cerebrospinal fluid eosinophils in over 10% of white blood cells. The most

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common cause of EOM is infection with *Angiostrongylus cantonensis* (Sawanyawisuth and Chotmongkol, 2013). Many humans report getting infected with this parasite by consuming raw or uncooked freshwater snails, slugs, or shrimp (Khamsai et al., 2020; Wang et al., 2008). Patients with EOM suffer from severe headache which may last for months (Khamsai et al., 2020).

Although EOM can be found all over the world, it is most prevalent in northeast Thailand. A review published in 2008 reported that 47.33% out of 2827 EOM cases were from Thailand (Wang et al., 2008), underscoring the need for intervention/monitoring strategies to control EOM in Thailand which may be applied to other countries. One possible method of monitoring infection is web-based surveillance and prediction, which has been used in various other infectious diseases such as influenza (Christaki, 2015). Prediction modelling is also a tool for the progression of epidemics of infectious disease. It may be used for forecasting of disease spreading in the future (Huppert and Katriel, 2013; Yadav and Akhter, 2021). Although EOM is common in Thailand, there are limited data on national surveillance and predictive models. This study aimed to develop a web surveillance system and predictive model for EOM using a national database.

2. Materials and methods

This is a retrospective study based on data retrieved from the Department of Disease Control's national database of reported EOM cases in Thailand. The study period was between 2003 and 2021. Cases of EOM in all provinces in Thailand (77 provinces) were quantified by month and year.

2.1. Data analysis and model development

All numbers of EOM during the study period were imported to R programming language (R Core Team, 2021). Medians with interquartile ranges (IQRs) were used to describe the number of EOM cases in each year and month. The nation, regions and provinces data were fitted using the Autoregressive Integrated Moving Average (ARIMA) models and Seasonal ARIMA (SARIMA) model, and minimum Akaike Information Criterion (AIC) were calculated and used to select the appropriate models. Root mean square error (RMSE) of the selected models were also calculated by using all nation data for comparing actual number of EOM cases and predicted values from the model. The models were used to predict the number of EOM cases over the next 6 months. Point estimated values of predictions with their 95% Confident Intervals (CI) were calculated and compared with actual numbers of EOM cases for the last three years.

2.2. Website creation

We created the web application that provided the automatic box-plots, suitable SARIMA models, and predicted values for all regions and provinces in Thailand. The website was conducted using R programming language (R Core Team, 2021) and Shiny (Chang et al., 2019), R Markdown (Allaire et al., 2019), forecast (Hyndman et al., 2019), tseries (Trapletti et al., 2018), dplyr (Wickham et al., 2019) packages on RStudio software (RStudio Team, 2022).

3. Results

The predictive model was published online at <http://202.28.75.8/sample-apps/NationalEOM/>. From 2003 to 2021, 3330 EOM cases were diagnosed and registered in the national database. The data form all provinces, regions, and country levels were shown by using box plots on the website. The box-plot of national data (Fig. 1) revealed that the highest number of EOM cases was in 2003 (median of 22 and IQR 18.8 to 31.8 patients), and the lowest number was in 2021 (median of 3 and IQR 2 to 3.3 patients). Most patients were reported in January (median of 17 and IQR 12 to 27 patients) and October (median of 17 and IQR 10 to 19.5 patients) as shown in

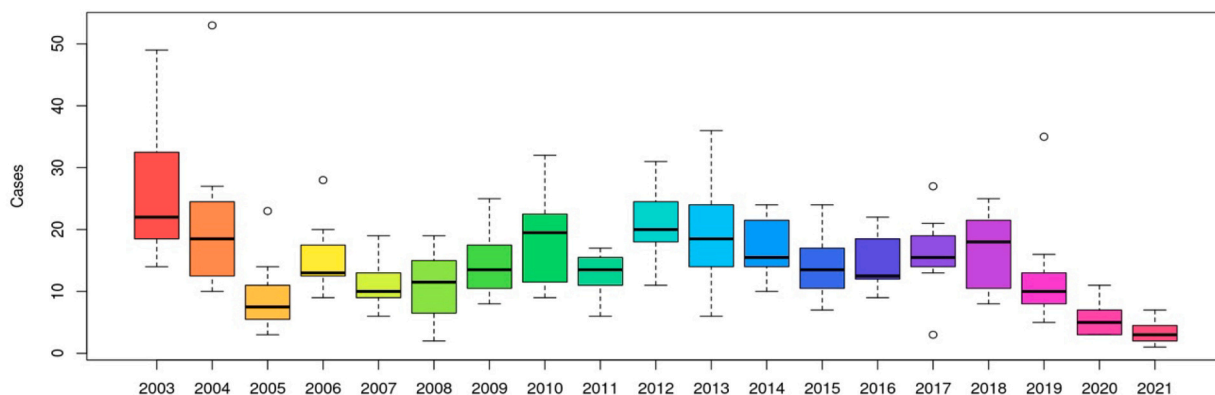
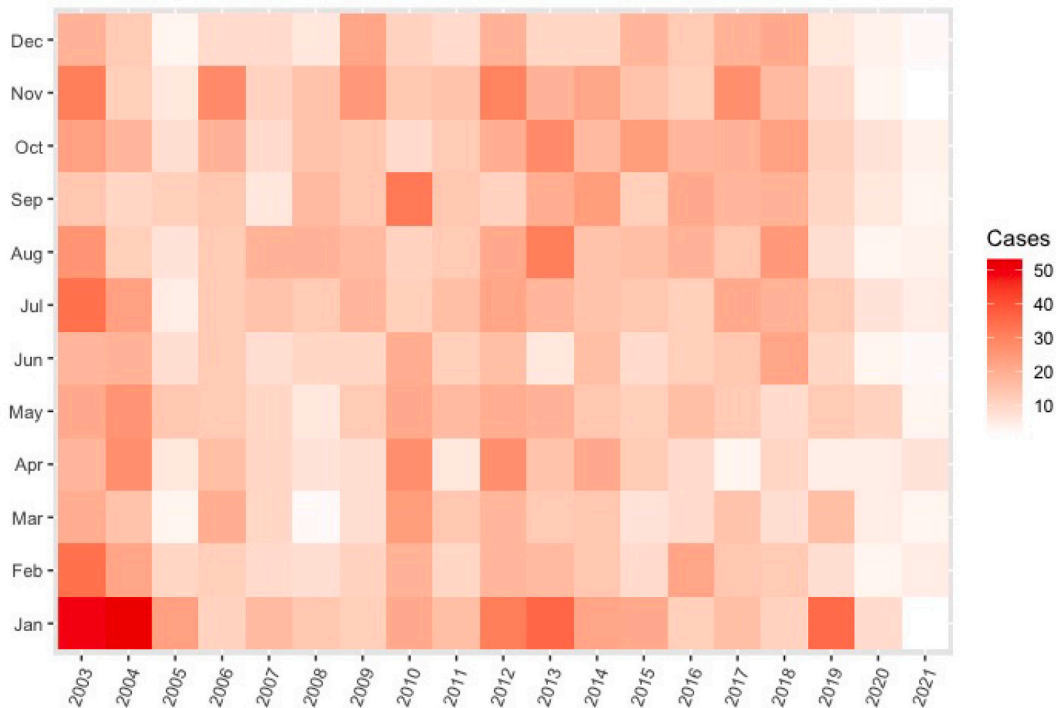


Fig. 1. Box-plots of number of eosinophilic meningitis cases in Thailand from 2003 to 2021.

Fig. 2. The numbers of EOM patients were decreasing in 2020 and 2021 as shown in the heat map (Fig. 2A). Northeastern region had the highest EOM cases during the study periods (Fig. 2B). In this region, the highest number of cases was in 2003 (289 cases). In 2021, there were only 28 cases in this region.

A. by month



B. by region

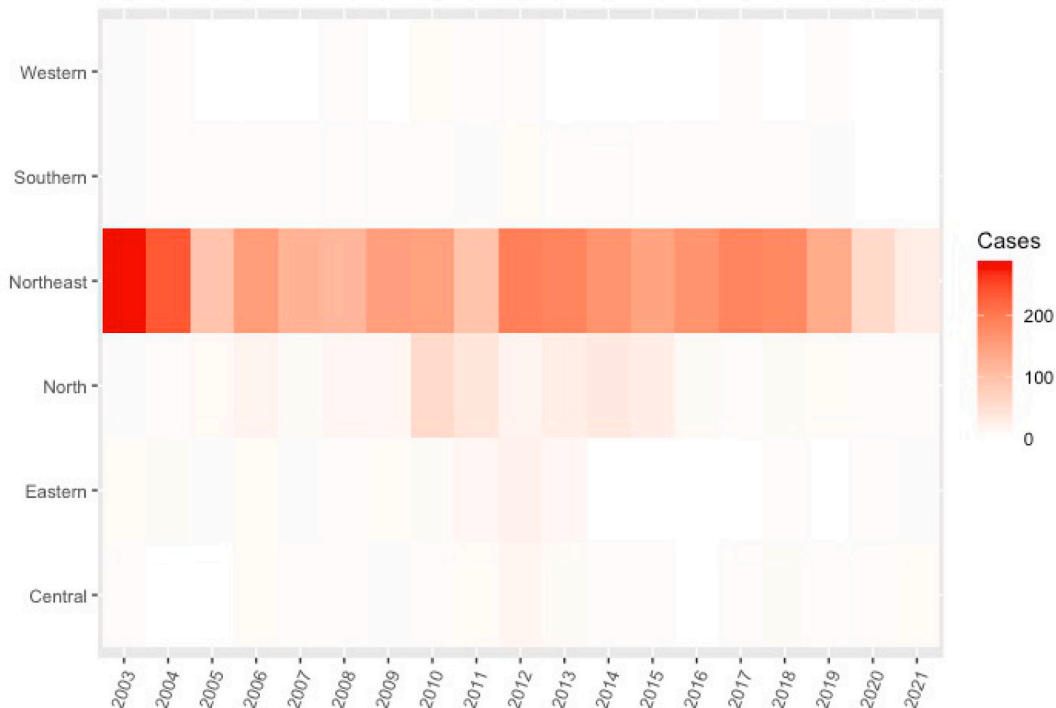


Fig. 2. Heat maps of median numbers of eosinophilic meningitis cases in Thailand by month and region from 2003 to 2021.

Table 1 displays the selected model for all areas in Thailand. The suitable model for the country was SARIMA(1,1,2)(2,0,0)[12] with an AIC of 1489.84. The coefficient of the seasonal autoregressive model of order 1 and 2 were 0.2179 and 0.1186, respectively. The autoregressive model of order 1 was 0.9351. The coefficients of the moving average models of order 1 and 2 were -1.6563 and 0.6625, respectively. The appropriated models for each region were also presented in Table 1.

Actual number of EOM cases and predicted values in 2019 to 2021 were displayed in Table 2. Most of the fitted values from SARIMA(1,1,2)(2,0,0)[12] were closed to actual number of the disease cases and fallen within the 95% confidence interval during that period of time. The SARIMA(1,1,2)(2,0,0)[12] model gave the RMSE of 6.23 (Table 1).

Table 3 shows the point estimated value of prediction with its 95% CI in the next 6 months of 2022 of the nation and by regions. The number of EOM cases will increase slightly after 2021. The highest predicted number is in May 2022 in the northeast region (1.6 cases) as shown in Table 3. The predicted and actual values were comparable and had similar patterns (Fig. 3).

4. Discussion

Using this national surveillance method, we found that the number of EOM cases in Thailand was quite steady from 2003 to 2021 (Fig. 1). The highest number of cases was in 2003, and there was a slight decrease in 2005, but they remained steady afterward. These distribution patterns imply that some preventive strategies should be implemented.

In some circumstances, web-based surveillance may detect outbreak patterns. For example, a study by the World Health Organization used web-based surveillance to detect an outbreak in Rohingya migrants (Karo et al., 2018). However, we did not see any signs of an EOM outbreak or epidemic.

We did find, though, that the number of EOM cases is not decreasing over time. The most common months of infection were January and October (Fig. 2A). This is likely due to the fact that EOM is a food-borne disease, as these are two months in which rice is planted and harvested, and farmers tend to eat raw freshwater snails in their rice fields. Farmers in the northeast also often consume *Koi-Hoi*, a local dish that contains raw snail meat (Eamsobhana et al., 2010) as shown in Fig. 2B. Additionally, *Pomacea canaliculata*, an intermediate host of *A. cantonensis* have the highest infection rates in October (68.4%) (Banpavichit et al., 1994).

The predictive model used in this study was the SARIMA model with the lowest AIC as shown by Table 1 and Fig. 3. This model was almost perfectly fit with the actual number of EOM cases. This suggests that this kind of online tool would be useful in predicting future EOM cases and in controlling disease (Daughton et al., 2017).

Our surveillance methods may be applicable for other countries or probably outbreaks in other countries. Health policy makers and health officers may use the web for monitoring, explore the trend and find the predicted number of cases in nation, regions and provinces. However, some limitations exist. One limitation of this predictive model is that it will be valid only if no preventive intervention is implemented, in which case it may be useful for disease monitoring purposes. We also did not examine any causal relationship between EOM and other factors (Sawanyawisuth et al., 2020, 2011, 2012, 2010; Tongdee et al., 2021). Finally, unreported or undiagnosed EOM cases will be missed using retrieved data from the database.

5. Conclusions

National surveillance can be used to monitor EOM. The predictive model is available online, and fitted values were consistent with the actual numbers of EOM cases.

Table 1

Selected model for predicting eosinophilic meningitis cases in Thailand by using statistical methods by nation data and region data with their properties.

Area	Model	Coefficients	AIC	RMSE
Nation	SARIMA(1,1,2)(2,0,0)[12]	AR1 = 0.9351, MA1 = -1.6563 MA2 = 0.6625, SAR1 = 0.2179 SAR2 = 0.1188	1489.84	6.23
Northern region	ARIMA(1,1,1)	AR1 = 0.1812, MA1 = -0.8887	893.34	1.70
Western region	SARIMA(2,0,2)(1,0,2)[12]	AR1 = -1.0735, AR2 = -0.6008 MA1 = 1.3050, MA2 = 0.8003 SAR1 = -0.2671, SMA1 = 0.2658 SMA2 = 0.1279, Mean = 0.0750	59.72	0.26
Central region	ARIMA(1,0,1)	AR1 = -0.4926, MA1 = 0.7308 Mean = 0.3078	456.38	0.65
Eastern region	SARIMA(2,1,1)(1,0,0)[12]	AR1 = 0.0931, AR2 = 0.169 MA1 = -0.9008, SAR1 = 0.0228	428.32	0.61
Northeast region	SARIMA(0,1,1)(2,0,0)[12]	MA1 = -0.7039, SAR1 = 0.2621 SAR2 = 0.1276	1435.17	5.57
Southern region	SARIMA(1,0,1)(1,0,1)[12]	AR1 = -0.5659, MA1 = 0.6878 SAR1 = -0.3660, SMA1 = 0.5469 Mean = 0.1840	261.84	0.42

AR1/AR2: autoregressive models of order 1 and 2 respectively; MA1/MA2: the moving average models of order 1 and 2 respectively; SAR1/SAR2: seasonal autoregressive models of order 1 and 2 respectively; AIC: Akaike Information Criterion; RMSE: Root mean square error.

Table 2

Predicted values with their 95% confidence interval according to the model and actual cases of eosinophilic meningitis in Thailand by months and years.

Month/year	Predicted values			Actual cases
	Fitted value	Lower 95% CI	Upper 95% CI	
Jan-19	17.6	5.2	30	35
Feb-19	22.5	10.2	34.9	8
Mar-19	17.2	4.8	29.6	16
Apr-19	15.8	3.4	28.1	5
May-19	13.6	1.2	26	13
Jun-19	16.4	4.1	28.8	10
Jul-19	14.9	2.5	27.2	13
Aug-19	14.9	2.6	27.3	8
Sep-19	12.3	-0.1	24.7	10
Oct-19	12.9	0.5	25.2	11
Nov-19	12.2	-0.2	24.6	9
Dec-19	11.5	-0.9	23.8	6
Jan-20	12.3	-0.1	24.7	9
Feb-20	6	-6.3	18.4	3
Mar-20	6.7	-5.7	19	5
Apr-20	4.4	-8	16.8	5
May-20	6.5	-5.9	18.9	11
Jun-20	9	-3.4	21.3	3
Jul-20	7.8	-4.5	20.2	7
Aug-20	7.5	-4.9	19.9	3
Sep-20	6.3	-6.1	18.6	6
Oct-20	7.2	-5.2	19.6	7
Nov-20	6.3	-6.1	18.7	3
Dec-20	5.5	-6.9	17.9	4
Jan-21	7.7	-4.7	20.1	1
Feb-21	1.6	-10.8	14	5
Mar-21	4.3	-8.1	16.7	3
Apr-21	2.9	-9.4	15.3	7
May-21	6.6	-5.8	19	3
Jun-21	3.7	-8.6	16.1	2
Jul-21	4.7	-7.6	17.1	5
Aug-21	3.6	-8.8	16	4
Sep-21	4.8	-7.5	17.2	3
Oct-21	4.9	-7.5	17.3	4
Nov-21	3.8	-8.6	16.1	1
Dec-21	3.1	-9.3	15.4	2

Table 3

Predicted value for eosinophilic meningitis cases in Thailand and categorized by regions in 2022.

Months	Predicted value (95%CI)						
	Nation	North	Western	Central	Eastern	Northeastern	South
Jan-22	2.7 (-9.7, 15.1)	0.5 (-2.9, 3.8)	0 (-0.5, 0.6)	0.4 (-0.9, 1.7)	0.3 (-0.9, 1.5)	0.8 (-10.2, 11.9)	0.1 (-0.7, 1)
Feb-22	3.1 (-9.7, 16)	0.4 (-3.1, 3.9)	0.1 (-0.5, 0.6)	0.3 (-1, 1.6)	0.2 (-1, 1.4)	1.1 (-10.4, 12.6)	0.2 (-0.7, 1)
Mar-22	3.1 (-10.1, 16.4)	0.4 (-3.2, 3.9)	0.1 (-0.5, 0.6)	0.3 (-1, 1.7)	0.2 (-1, 1.5)	1 (-11, 12.9)	0.2 (-0.7, 1)
Apr-22	4.2 (-9.4, 17.9)	0.4 (-3.2, 3.9)	0.1 (-0.5, 0.6)	0.3 (-1, 1.6)	0.2 (-1.1, 1.5)	1.1 (-11.3, 13.5)	0.2 (-0.7, 1)
May-22	4.2 (-9.7, 18.2)	0.4 (-3.2, 4)	0.1 (-0.5, 0.6)	0.3 (-1, 1.6)	0.2 (-1.1, 1.5)	1.6 (-11.2, 14.4)	0.2 (-0.7, 1)
Jun-22	3.3 (-11, 17.5)	0.4 (-3.3, 4)	0.1 (-0.5, 0.6)	0.3 (-1, 1.6)	0.2 (-1.1, 1.5)	0.7 (-12.5, 13.9)	0.2 (-0.7, 1)

CI: confidence interval.

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Declaration of Competing Interest

Authors declare that they have no conflict of interest.

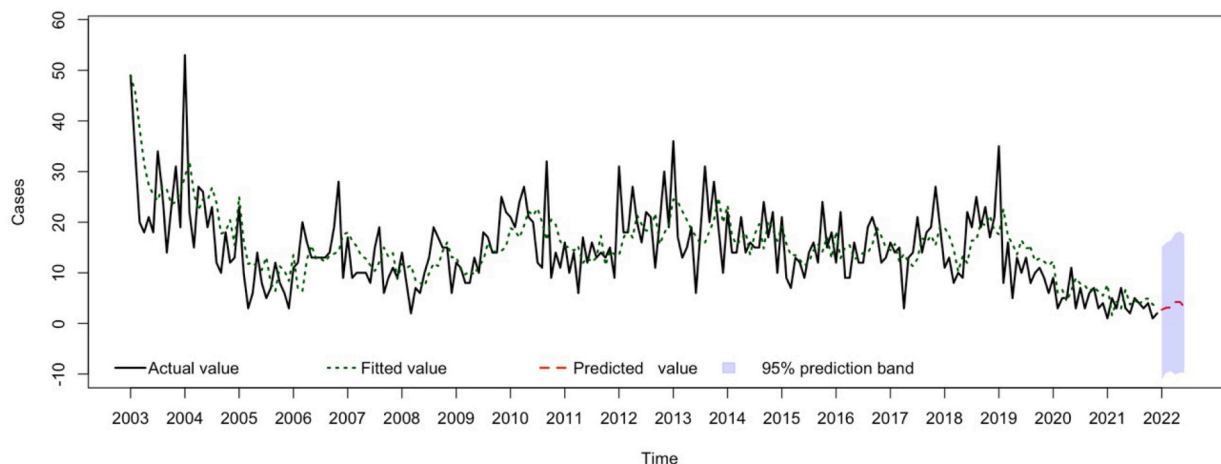


Fig. 3. Fitted, predicted values and actual value from the selected model of new cases of eosinophilic meningitis.

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