보건학 석사 학위논문

Association between Infectious Diseases and Weather Variables in Lao People's Democratic Republic

국내 만성질환자에서의 독감예방접종과 관련 특성

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보건학과 통계전공

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이 논문을 보건학 석사 학위논문으로 제출함

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Prima Lydia의 석사학위논문을 인준함

2014 년 2 월

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Abstract

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Background: Existing studies and models of the effect of climate condition on the incidence of infectious diseases have been conducted to examine the association between infectious diseases and weather variables. Infectious diseases incidences are still high in tropical and subtropical zones, which most of them are developing countries, and remain as major health problems due to economically challenged situations. Our aim is to investigate the association between infectious diseases and weather variable (local and global) in Lao People's Democratic Republic, a tropical and developing country, where infectious diseases are still the major health problem.

Method: We analyzed the incidence of three diseases data (dengue fever, typhoid fever, and total hepatitis) and five weather variables (mean temperature, relative humidity, rainfall, DMI, and NINO3) using Generalized Additive Models (GAMs) analysis, to conduct a fitted model that shows the association between infectious diseases and weather variables.

Conclusion: The association is the strongest in dengue fever, followed by typhoid fever, and total hepatitis. For Lao People's Democratic Republic, both local and global weather variables (mean temperature, relative humidity, and NINO3) showed strong association with dengue fever. For typhoid fever, global weather variable (DMI) showed the strongest association. For total hepatitis, local weather variable (relative humidity) showed the strongest association in Northern and Southern regions but showed no association in Central region.

Key words: Dengue fever, DMI, Generalized Additive Models, Infectious diseases, Lao, NINO3, Rainfall, Relative humidity, Temperature, Total hepatitis, Typhoid fever

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Chapter 1. Introduction

The effect of climate and the environment on infectious diseases has been a subject of debate, speculation, and serious study for centuries (Shape, 1991). Infectious diseases may be classified into two categories based on the mode of transmission: from person to person (through direct contact or droplet exposure) and those spread indirectly through an intervening vector organism (mosquito or tick) or a non-biological physical vehicle (soil or water). Infectious diseases also may be classified by their natural reservoir as anthroponoses (human reservoir) or zoonoses (animal reservoir) (Patz et al. 2003).

Many infectious diseases of humans are restricted to, or more prevalent in, tropical and subtropical zones (Ostfeld, 2009). Infectious diseases incidences are still high in tropical and subtropical zones, which most of them are developing countries, and remain as major health problems due to economically challenged situations.

Dengue fever is a viral illness caused by infection of the dengue virus that spread by the bite of an infected dengue mosquito (usually the *Aedes aegypti* species), and occurs in tropical and sub-tropical areas of the world (CDC). The outbreak of dengue can occur anytime as long as the mosquitos are active, however high temperature and humidity are the conditions that favor the survival of mosquito (WHO). *Aedes aegypti* prefer to lay its eggs in human-made container around homes that collected rainwater. *Aedes aegypti* females will often feed on several persons during a single blood meal and may transmit dengue virus to multiple persons in a short time, so it is common that several members in a household become ill with dengue fever (Gubler, 1998).

Typhoid fever is an infectious disease that is caused by the bacteria *Salmonella enterica* serotype typhi (*S. typhi*) (Bhan, 2005) that spread by eating or drinking contaminated food (Sharma, 2009) and water (Mermin, 1999). Typhoid fever's risk factor are also including poor sanitation (Karkey, 2010) and flooding (Vollaard, 2004). The incidence of typhoid fever has decline in Europe and America as clean water and good sewage system are developed. However, the incidence remains high in developing countries as sanitation and water in those countries are still in poor condition. *S typhi* is restricted to human beings (Bhan, 2005).

Hepatitis is an inflammation of liver, commonly caused by viral infection, with five main hepatitis viruses, type A, B, C, D, and E. Hepatitis A and E typically caused ingestion of contaminated food or water, whereas hepatitis B, C and D usually occur as a result of parenteral contact with infected body fluids, such as receipting of contaminated blood or blood products, invasive medical procedures using contaminated equipment and for hepatitis B transmission from mother to baby at birth, from family member to child, and also by sexual contact (WHO).

The DMI index is an indicator that represent the difference in SST anomaly between the tropical western Indian Ocean (50°E - 70°E, 10°S - 10°N) and the tropical south-eastern Indian Ocean (90°E - 110°E, 10°S - Equator) (Saji, 1999). A positive IOD period is characterized by cooler than normal water in the tropical eastern Indian Ocean and warmer than normal water in the tropical western Indian Ocean and a negative IOD period is characterized by warmer than normal water in the tropical eastern Indian Ocean and cooler than normal water in the tropical western Indian Ocean.

The Nino3 SST anomaly index is an indicator of eastern tropical Pacific El Nino conditions, calculated with SSTs in the box 150°W -

90°W, 5°S – 5°N (NOAA). During El Nino phase, there is a warming in the eastern equator Pacific and during La Nina phase, there is a cooling in the eastern equator Pacific (Lipp, 2002).

Some studies have been conducted to examine the association between infectious diseases and weather variables. A study in China shows that temperature has correlation with changes of spatial and temporal distribution of dengue fever (Bai et al. 2013). A study in Taiwan shows that extreme precipitation events were associated with the occurrence of 8 infectious diseases (including hepatitis A and dengue fever) with lags of 0-70 days (Chen et al. 2012). Study in 14 island nations of the South Pacific shows that there were positive correlations between global climate variable (SOI index) and dengue fever in 10 countries (Hales et al. 1999). A study in Dhaka (Dewan et al. 1998) did not show a strong association between rainfall and typhoid fever however it showed that the risk of the disease is high during monsoon.

Chapter 2. Methods

2-1. Study design and setting

Lao People's Democratic Republic is a landlocked country located in the Indochina Peninsular (Mekong Region). Lao PDR belongs to WHO's Western Pacific region (Kimball, 2008), bordered to the northwest by Myanmar and China, to the east by Vietnam, to the south by Cambodia, and to the west by Thailand. Lao PDR has a tropical monsoon climate which causes significant rainfall and high humidity, with a pronounced rainy season from May through October, a cool dry season from November through February, and a hot dry season in March and April (Savada, 1994). The average annual rainfall in the country is about 1,300 - 3,000 mm and average temperature is 26.5°C.

Fig. 1. Geographical location of Lao People's Democratic Republic
(Source: http://en.wikipedia.org/wiki/Provinces_of_Laos)

Lao People's Democratic Republic can be considered to consist of three geographical regions: northern, central, and southern. This study will cover all three regions in Lao. Geographical location of Lao People's Democratic Republic is shown in Fig. 1, and the list of provinces based on regions is shown in Table 1.

Table 1. Provinces in Lao People's Democratic Republic

Region	Province
Northern	Phôngsali
	Luang Namtha
	Oudômxai
	Bokèo
	Louangphabang
	Houaphan
	Xaignabouli
	Xiangkhouang
Central	Vientiane(CAPITAL)
	Vientiane Province
	Bolikhamxai
	Khammouan
	Savannakhét
Southern	Salavan
	Xékong
	Champasak
	Attapu

2-2. Data collection and processing

All cases of diseases reported from January 2005 to December 2010 were obtained from the Center for Laboratory and Epidemiology Department of Hygiene and Prevention. The cases of diseases were monthly reported by all health post and center, also region hospital to Center for Laboratory and Epidemiology Department of Hygiene and Prevention, Ministry of Health of Lao PDR (Kim, 2011). From 21 diseases available, 3 infectious diseases were selected to this study based on potential association with climate change. The 3 diseases selected are dengue fever (ICD-10, A90), typhoid fever (ICD-10, A01.0), and total hepatitis (ICD-10, B15–B19, K75.9).

All meteorological data were obtain from Department of Meteorology and Hydrology, Ministry of Natural Resources and Environment (Lao PDR). All the data were provided in daily basis and we use the variables as follows: Mean Temperature (°C), Humidity (Mean Humidity of air in %), and Total Daily Rainfall (mm) for each province. Daily weather data was converted into monthly basis. For the analysis data was grouped according to the regions (Northern, Central, and Southern) of Lao PDR.

Daily basis data of DMI and NINO3 was publicly accessible from the National Oceanic and Atmospheric Administration (NOAA), United State Department of Commerce (http://www.noaa.gov/). DMI and NINO3 data was converted into monthly basis data for the purpose of analysis.

2-3. Statistical Analysis

Descriptive analysis and monthly time series approach were calculated for all diseases and weather variables to investigate the distribution of the data and the association between all infectious diseases with weather variables. Pearson correlation and p-value were calculated to examine the significance of the association between diseases and weather variables. Monthly mean incidences were calculated to examine the quality of correlation.

Generalized Additive Models (GAMs) for time series (Wood. 2006) were used to model the simultaneously non-linear structure in the association between monthly diseases data and weather variables. Lag models were used to examine the lag structure of the weather effects with lag up to 6 months for local variables (Mean Temperature (°C), Humidity (%), and Rainfall (mm)). For global weather variables (DMI (Dipole Mode Index in °C) and NINO3 (ENSO index in °C)) lag up to 12 months were used.

Sensitivity Analysis was used to show the sensitivity of the model over small changes into the model. We conducted the sensitivity analysis by omitting a variable from the model and by changing the lag of variables.

The Microsoft Excel and R statistical software was used for the analysis the contributed package MGCV used to fit the GAMs. The MGCV package uses generalized cross-validation to select the degree of freedom for each smooth (non-linear) term (Wood. 2006). The lag models were fit using MGCV and DLNM package.

2-3. Limitation

There was limitation in the data available, especially in disease and meteorological data. The diseases reported just the number of cases and lack more detail clinical information. The quality of the data was not very good especially in the Total Hepatitis cases data. Total hepatitis was used in the analysis because the possibility of association with seasonal variable, especially Hepatitis A (Villar, 2002) and Hepatitis E (Previsani, WHO, 2001). Even though the data available for Hepatitis was not specified by the types, but this analysis was expected to see an association with seasonality.

Another limitation occurred in the meteorological data, where there were substantial missing values. There were some problems in some provinces, especially in the Southern region (et. some values above 100% for Humidity). The limitation in the data made the whole data unstable and not very reliable, but it expected that it could reflect the association.

Chapter 3. Results

Descriptive statistics for all variables are shown in Table. 2. The average numbers of monthly cases of dengue fever from 2005 to 2010 were 104.33, 369.93, and 206.03 for Northern, Central, and Southern region, respectively. These result showed that the cases of dengue fever was the highest in Central region, followed by Southern region, and Northern region has the lowest incidence. For typhoid fever, the average numbers of monthly cases from 2005 to 2010 were 130.51, 61.71, and 1.86 for Northern, Central, and Southern region, respectively. These result showed that the cases of typhoid fever was the highest in Northern region, followed by Central region and the lowest in Southern region. For total hepatitis, the average numbers of monthly cases from 2005 to 2010 were 16.92, 24.43, and 12.08 for Northern, Central, and Southern region, respectively. These result showed that the cases of total hepatitis was the highest in Central region, followed by Northern region and Southern region was the least among all regions.

Average of mean temperatures for Northern, Central, and Southern region from 2005 to 2010 were 23.30°C, 26.64°C, and 27.52°C, respectively. Averages of mean humidity were 75.18%, 74.13%, and 73.26% for Northern, Central, and Southern region from 2005 to 2010, respectively. Average of mean rainfall for Northern, Central, and Southern region from 2005 to 2010 were 23.30mm, 26.64mm, and 27.52mm, respectively. Average of Dipole Mode Index (DMI) and ENSO index (NINO3) from 2005 to 2010 were -0.45°C and 25.74°C, respectively.

Table 2. Descriptive statistics for the study regions from 2005 - 2010

Variable	Northern				Central				Southern			
	Min	Mean	Max	SD	Min	Mean	Max	SD	Min	Mean	Max	SD
Diseases												
Dengue Fever	0.00	104.33	1160.00	184.74	5.00	369.93	2788.00	547.38	0.00	206.03	1567.00	258.91
Typhoid Fever	0.00	130.51	380.00	82.30	0.00	61.71	308.00	59.68	0.00	1.86	11.00	2.83
Total Hepatitis	0.00	16.92	56.00	9.74	0.00	24.43	336.00	38.55	0.00	12.08	38.00	8.07
Weather Variables												
Mean Temp (°C)	17.09	23.30	27.46	2.89	20.57	26.64	30.19	2.36	23.31	27.52	31.09	1.72
Mean RH (%)	59.82	75.18	84.30	6.00	61.19	74.13	86.30	6.96	57.51	73.26	87.83	8.87
Mean Rainfall (mm)	0.31	123.31	386.00	106.98	0.00	193.22	672.62	197.13	0.00	157.06	697.83	173.45
DMI	−1.82	−0.45	1.27	0.64	−1.82	−0.45	1.27	0.64	−1.82	−0.45	1.27	0.64
NINO3	23.17	25.74	28.05	1.28	23.17	25.74	28.05	1.28	23.17	25.74	28.05	1.28

Time series trends were used to examine the trend of all variables (diseases and weather variables). Fig. 2, Fig. 13, and Fig. 14 showed there was increasing of dengue fever cases in three regions in 2010 (Fig. 13 and Fig. 14 were presented in the Appendix). The trend of increasing in mean temperatures was also seen for the last 3 years. Mean rainfall decreased in northern and southern region, but showed an increasing on 2010 in central region. This trend also could be seen in relative humidity trend. There is a slightly decrease in northern and southern region, but showed a slightly increase on 2010 in central region. Fig. 15 (see appendix) showed monthly trend of dengue fever cases from 2005 to 2010. This figure showed that there is an increase in dengue fever cases on rainy season, and showed a decrease on dry season. This figure showed a high quality of correlation between dengue fever and seasonal variables.

Fig. 16, Fig. 17, and Fig 18 (see appendix) showed there was increasing of typhoid cases in all three regions for the last 3 years, which also could be seen in mean temperature trends. In the southern region, Fig. 18 showed an increase in the incidence of typhoid fever after the flooding event in 2009, as flooding is one of the risk factor of the disease (Vollaard, 2004). Fig. 19 (see appendix) showed monthly trend of typhoid fever cases from 2005 to 2010. This figure showed that there is an increase in dengue fever cases on rainy season, and showed a decrease on cool dry season. Typhoid fever showed the least cases on hot dry season. This figure also shows a high quality of correlation between typhoid fever and seasonal variables.

Fig. 20 and Fig. 21 (see appendix) showed an outbreak of total hepatitis cases in 2008 in northern and central region, but in southern region from Fig. 22 (see appendix), the outbreak could be seen in

2007 and there is a slightly increase in the beginning of 2009 and the midyear of 2010. Fig. 23 (see appendix) showed monthly trend of total hepatitis cases from 2005 to 2010. This figure showed that there is no significant increase in monthly total hepatitis cases, but an outbreak of total hepatitis case was shown on November in central region caused by the disease outbreak in November 2008. This figure showed a low quality of correlation between total hepatitis and seasonal variables.

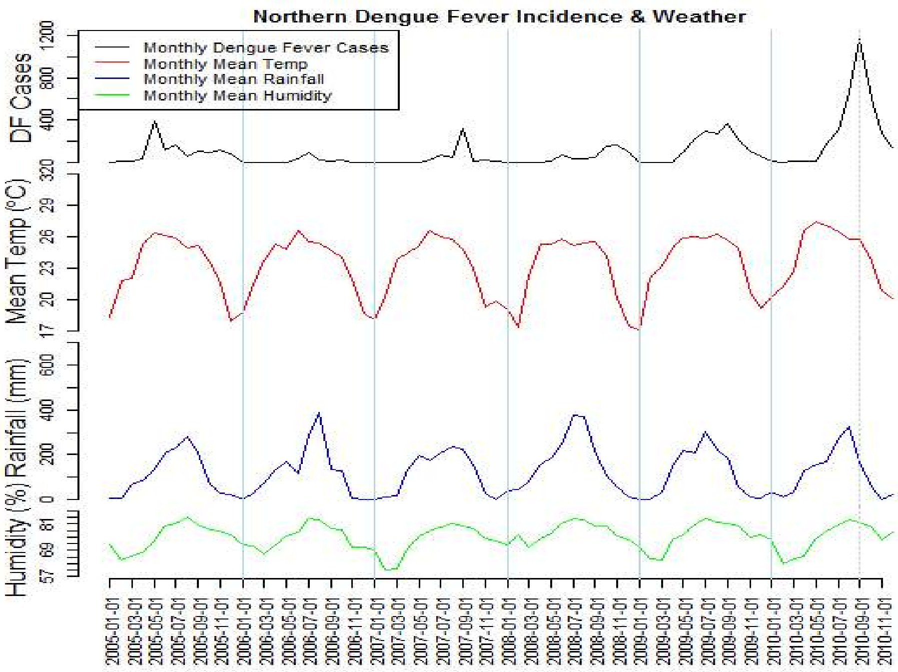

Fig. 2. Time series trend of dengue fever cases, mean temperature (°C), mean rainfall (mm), and mean relative humidity (%) for Northern region from 2005 to 2010.

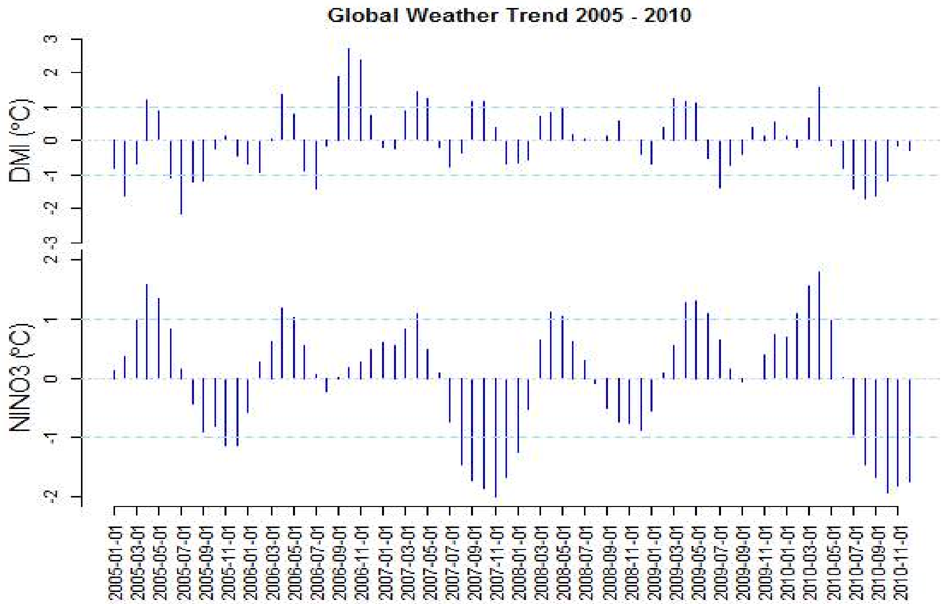

Fig. 3. Standardization-Time series trend of Dipole Mode Index (DMI) and ENSO Index (NINO3), 2005 - 2010

Fig. 3 showed time series trend of Dipole Mode Index (DMI) and ENSO Index (NINO3) from 2005 to 2010. Dipole Mode Index (DMI) showed negative value, characterized by warmer than normal water in the tropical eastern Indian Ocean and cooler than normal water in the tropical western Indian Ocean. In reverse, Dipole Mode Index (DMI) showed positive value, characterized by cooler than normal water in the tropical eastern Indian Ocean and warmer than normal water in the tropical western Indian Ocean. As for Lao PDR, negative phase means warmer weather and heavy rainfall, in contrast positive phase means colder weather and can lead to dry season (low rainfall). ENSO Index (NINO3) showed that there are some El Niño conditions (positive value, warmer) and La Niña (negative value, cooler).

3-1. Dengue fever

Table 3 showed Pearson correlation between dengue fever and local weather variables (mean temperature, relative humidity, and rainfall) for all regions. Table 4 showed Pearson correlation between dengue fever and global weather variables (DMI and NINO3) for all regions. The tables showed that for all local weather variables, maximum lags are up to 4 months, but for global weather variables, DMI and NINO3 showed different pattern. DMI has correlation at up to 2 months as NINO3 up to 7 months. This result showed that DMI has faster effect on dengue fever that NINO3.

Table 3 and table 4 showed the significantly correlation between dengue fever and weather variables (p-value < 0.05). Lag models were used to examine the lag structure of the weather effects, using GAM (Generalized Additive Model) analysis. For local weather variables lagged up to 6 months data were used, and up to 12 months (a year) for global weather variables. Each region has different demographic characteristic and weather condition, so the analysis will be conducted partly. Model that have the best fit for describing association between dengue fever and weather variables are,

$$f(dengue\_fever)_{north} = \beta_0 + s(time, df) + s(meantemp_{-4}, df) + s(humid_{-4}, df) + s(rain_{-4}, df) + s(dmi_{-2}, df) + s(nino3_{-5}, df)$$

for northern region,

$$f(dengue\_fever)_{central} = \beta_0 + s(time, df) + s(meantemp_{-3}, df) + s(humid_{-3}, df) + s(dmi_{-12}, df) + s(nino3_{-5}, df)$$

for central region, and

$$f(dengue\_fever)_{south} = \beta_0 + s(time, df) + \beta_1 meantemp_{-4} + s(humid_{-1}, df) + s(rain_{-1}, df) + s(dmi_{-5}, df) + s(nino3_{-5}, df)$$

for southern region.

Here some of the models are Mixed Generalized Additive Model, with linear correlation for some variables. In northern region, all variables have non-linear correlation with dengue fever incidence, with mean temperature lag 4 months, relative humidity lag 4 months, rainfall lag 4 months, DMI lag 2 months, and NINO3 lag 5 months. In central region, all significant variables have non-linear correlation with dengue fever, with mean temperature lag 3 months, relative humidity lag 3 months, Dipole Mode Index (DMI) lag 12 months, and ENSO index (NINO3) lag 5 months as variables. Rainfall showed no significant association with dengue fever in central region. In southern region, relative humidity lag 1 month, rainfall lag 1 month, Dipole Mode Index (DMI) lag 5 months and ENSO index (NINO3) lag 5 months have non-linear correlation, while mean temperature lag 4 months has linear correlation with dengue fever. The comparison between the model and the observed (the count of incidence) for dengue fever in three regions were presented in Fig. 24 (see appendix).

Table 3. Pearson correlation between dengue fever and local weather variables (without and with lag)

	Northern			Central			Southern		
time-lag (months)	Mean temperature	Relative humidity	Rainfall	Mean temperature	Relative humidity	Rainfall	Mean temperature	Relative humidity	Rainfall
0	0.281*	0.425*	0.249*	0.240*	0.532*	0.464*	0.171	0.380*	0.259*
1	0.416*	0.402*	0.414*	0.402*	0.517*	0.472*	0.317*	0.292*	0.256*
2	0.453*	0.273*	0.429*	0.497*	0.327*	0.326*	0.416*	0.106	0.130
3	0.437*	0.062	0.281*	0.495*	0.056	0.135	0.452*	−0.104	−0.027
4	0.299*	−0.165	0.124	0.385*	−0.223	−0.075	0.407*	−0.306*	−0.190
5	0.094	−0.405*	−0.072	0.146	−0.395*	−0.228	0.221	−0.432*	−0.288*
6	−0.144	−0.523*	−0.279*	−0.172	−0.455*	−0.352*	−0.029	−0.461*	−0.362*

* Statistically significant

Table 4. Pearson correlation between dengue fever and global weather variables (without and with lag)

	Northern		Central		Southern	
time-lag (months)	DMI	NINO3	DMI	NINO3	DMI	NINO3
0	-0.380*	-0.285*	-0.372*	-0.015	-0.166	-0.003
1	-0.294*	-0.110	-0.216	0.169	-0.160	0.037
2	-0.138	0.091	-0.020	0.312*	-0.110	0.127
3	-0.027	0.291*	0.013	0.362*	-0.073	0.197
4	0.059	0.400*	-0.014	0.334*	-0.007	0.258*
5	0.117	0.406*	0.035	0.243*	0.017	0.292*
6	0.100	0.310*	0.007	0.135	0.039	0.282*
7	0.120	0.156	-0.055	0.025	0.090	0.260*
8	0.100	-0.016	-0.100	-0.053	0.133	0.194
9	0.134	-0.150	-0.091	-0.085	0.113	0.142
10	0.010	-0.216	-0.111	-0.035	0.050	0.076
11	-0.078	-0.206	-0.203	0.062	-0.009	0.043
12	-0.107	-0.103	-0.186	0.182	-0.054	0.048

* Statistically significant

In northern region, mean temperature showed a rapid increase of cases for mean temperature (lag4) above 26°C. The same pattern also could be seen in ENSO index (NINO3) (lag5), which showed an increase of cases above 26°C. Fig. 4 also showed that higher number of cases associated to lower relative humidity and higher rainfall.

In central region, mean temperature showed a rapid increase of cases for mean temperature (lag3) above 27°C. The same pattern also could be seen in ENSO index (NINO3) (lag5), which showed a rapid increase of cases above 27°C. Relative humidity showed a negative correlation with dengue fever, where lower relative humidity (lag3) related to higher cases of dengue fever. In southern region, ENSO index (NINO3) (lag5) showed a rapid increase of cases for mean temperature (lag3) above 27°C. Relative humidity (lag1) showed a negative correlation with dengue fever, where lower relative humidity related to higher cases of dengue fever.

In central region, dipole mode index (DMI) (lag12) showed a significant correlation (p-value < 0.05), but smooth model that shown in Fig. 5 showed that there is no clear correlation between Dipole Mode Index (DMI) with dengue fever. The same result also could be seen in southern region. Rainfall showed a significant correlation (p-value < 0.05), but then model in Fig. 6 showed that there is no clear correlation between rainfall with dengue fever. In southern region, mean temperature showed a positive linear correlation with the incidence of dengue fever.

In three regions, mean temperature, relative humidity, and ENSO Index (NINO3) showed a strong correlation with dengue fever. Mean temperature and NINO3 showed a positive correlation (higher mean temperature and higher value of NINO3 resulted in higher number of incidence of dengue fever) and relative humidity showed negative correlation (lower relative humidity resulted in higher number of incidence of dengue fever). Since the survival of dengue mosquito prefers a high temperature (WHO), it is expected to see that higher temperature showed a high incidence of dengue. It explained why the incidence of cases was higher in higher temperature. Relative humidity decreased as the temperature increased (Valsson, 2011) explain the increase of incidence of dengue fever as the humidity lower.

The lag structure showed that local weather variables (mean temperature and relative humidity) have faster effect for the incidence of dengue fever than global variable (NINO3), except for DMI affect in northern region, where lag 2 months of DMI have a significant association with incidence of dengue fever, while all three local variables showed significant affect with lag 4 months.

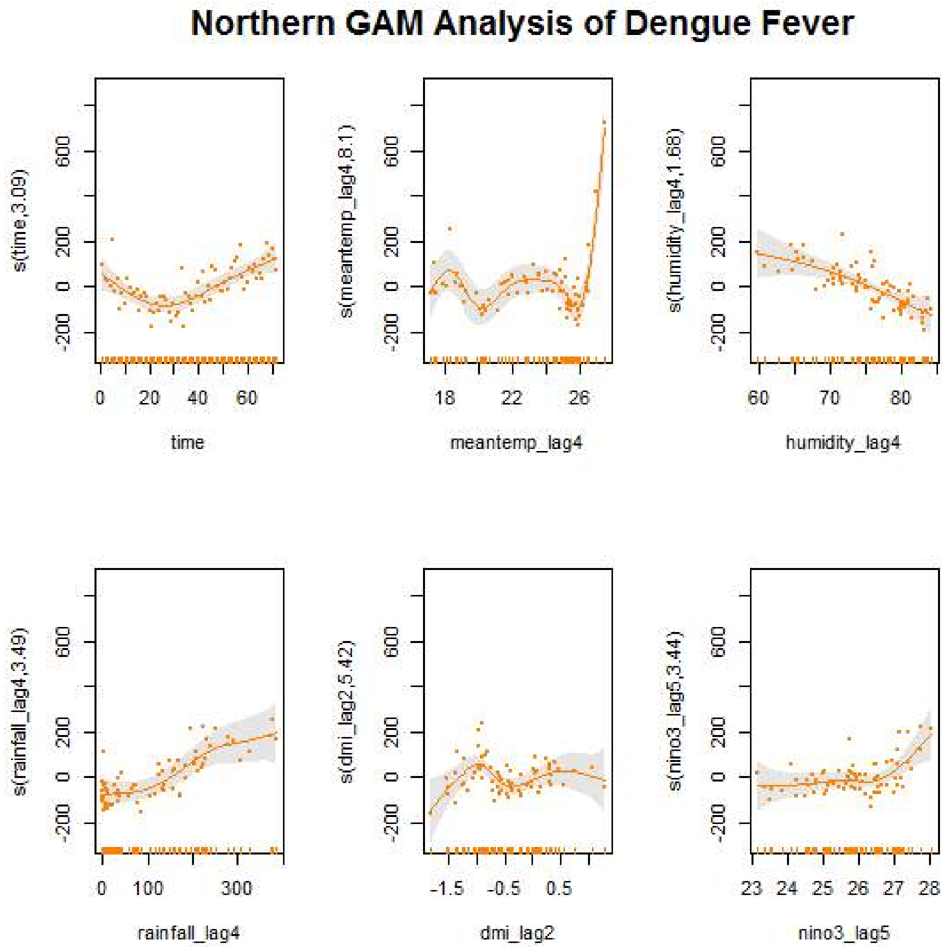

Fig. 4. The estimate of the smooth models for dengue fever in Northern region.

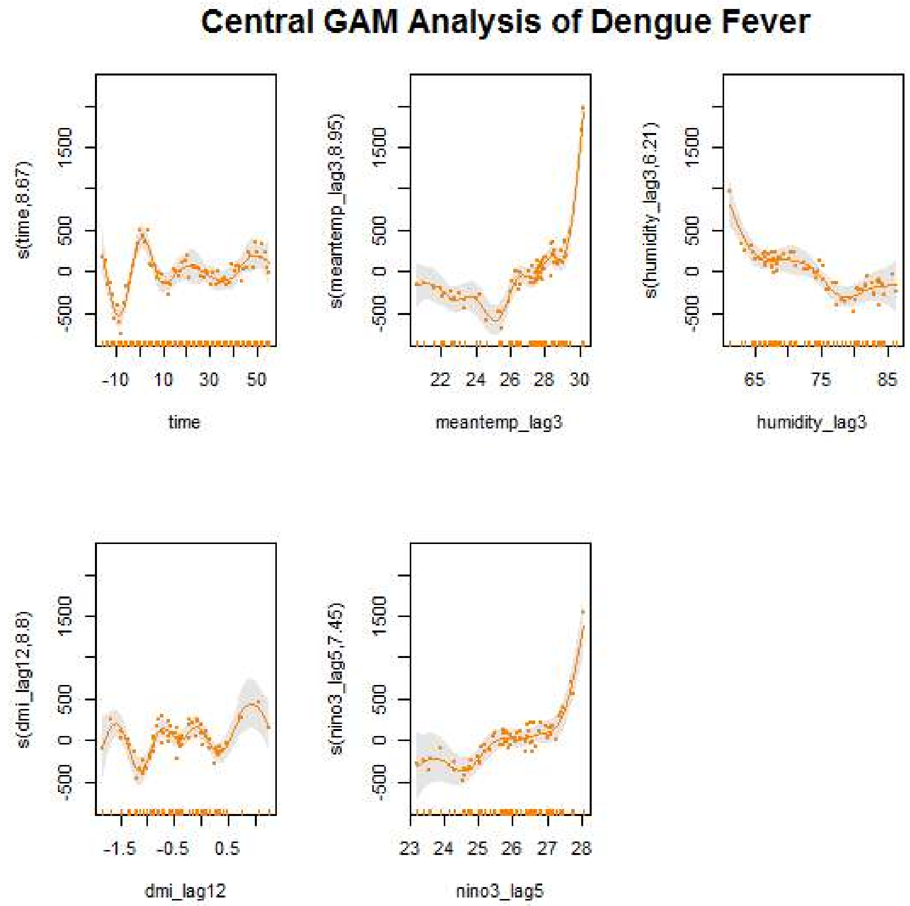

Fig.5. The estimate of the smooth models for dengue fever in Central region.

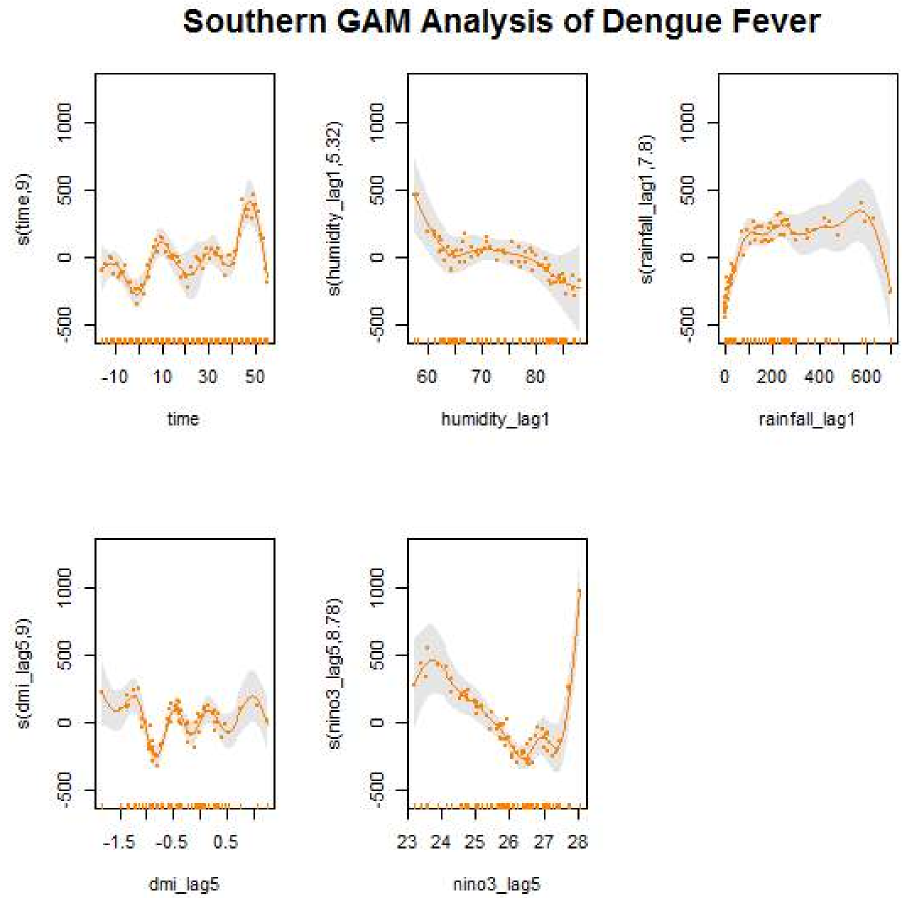

Fig. 6. The estimate of the smooth models for dengue fever in Southern region.

3-2. Typhoid fever

Table 5 showed Pearson correlation between typhoid fever and local weather variables (mean temperature, relative humidity, and rainfall) for all regions. Table 6 showed Pearson correlation between typhoid fever and global weather variables (DMI and NINO3) for all regions. In Northern and Central regions, we can see correlation between typhoid incidence and local weather variables, but the correlation could not be seen in Southern region. For global weather variables, DMI and NINO3 showed correlation with typhoid fever with a faster effect from DMI than NINO3 in Northern and Central regions. But in Southern region, DMI showed no correlation with dengue fever, but NINO3 showed a significant correlation with lagged (4 - 7 months).

Table 5 and table 6 showed the significantly correlation between typhoid fever and weather variables (p-value < 0.05). Lag models were used to examine the lag structure of the weather effects, using GAM Analysis. Each region has different demographic characteristic and weather condition, so the analysis will be conducted partly. Model that have the best fit for describing association between typhoid fever and weather variables are,

$$f(typhoid\_fever)_{north} = \beta_0 + s(time, df) + s(meantemp_0, df) + \beta_1 humid_0 + s(rain_0, df) + s(dmi_0, df) + s(nino3_{-8}, df)$$

for northern region,

$$f(typhoid\_fever)_{central} = \beta_0 + s(time, df) + s(meantemp_{-2}, df) + s(humid_{-2}, df) + s(rain_{-2}, df) + s(dmi_0, df) + s(nino3_{-2}, df)$$

for central region, and

$$f(typhoid\_fever)_{south} = \beta_0 + s(time, df) + s(meantemp_{-3}, df) + \beta_1 dmi_{-12} + s(nino3_{-5}, df)$$

for southern region.

Here some of the models are Mixed Generalized Additive Model, with linear correlation seen in some variables. In northern region, mean temperature, rainfall, Dipole Mode Index (DMI) and ENSO index (NINO3) lag 8 months have non-linear correlation, while relative humidity has positive linear correlation with typhoid fever. In central region, all variables have non-linear correlation with typhoid fever, with mean temperature lag 2 months, relative humidity lag 2 months, rainfall lag 2 months, Dipole Mode Index (DMI), and ENSO index (NINO3) lag 2 months. In southern region, mean temperature lag 3 months and ENSO index (NINO3) lag 5 months have non-linear correlation with typhoid fever, while Dipole Mode Index (DMI) lag 12 months has negative linear correlation with typhoid fever. The comparison between the model and the observed (the count of incidence) for typhoid fever in three regions were presented in Fig. 25 (see appendix).

In northern region, mean temperature showed an increase of cases for mean temperature until 25°C but then showed decreasing. Dipole Mode Index (DMI) showed a decrease of cases of typhoid fever as the value increased. Rainfall and ENSO index (NINO3) lag 8 months showed a significant correlation (p-value < 0.05) with typhoid fever but Fig. 7 showed that there is no clear correlation between both variable and the incidence of typhoid fever, but rainfall showed a slightly negative association. In central region, Dipole Mode Index (DMI) also showed a decrease of cases of typhoid fever as the value increase. Relative humidity lag 2 months and rainfall lag 2 months showed a significant correlation with typhoid fever but Fig. 8 showed that there is no clear correlation between both variable and the incidence of typhoid fever. Mean temperature lag 2 months did not show correlation for temperature below 29°C but then a rapid increase was occurred. A similar pattern could be seen in ENSO index (NINO3) lag 2 months, where the higher value associates to a slight increase of dengue fever incidence until 27°C, but then a rapid increase could be observed.

In southern region, mean temperature lag 3 months and ENSO index (NINO3) lag 5 months showed a significant correlation (p-value < 0.05) with typhoid fever but Fig. 20 showed that there is no clear correlation between both variable and the incidence of typhoid fever. In three regions, Dipole Mode Index (DMI) showed a strong negative correlation with typhoid fever. It means lower Dipole Mode Index (DMI) resulted in higher number of cases of typhoid fever. Lower DMI affect for warmer temperature and heavy rainfall in Lao PDR.

Typhoid fever is a disease that related to clean water and sanitation (Bhan, 2005), so it explained the increased of typhoid incidence with the heavy rain as in less developed country like Lao PDR, the sanitation is poor. Flooding also increase the risk of typhoid fever (Vollaard, 2004), as the water condition is poor in that condition. It explained the increased in incidence of typhoid in Southern region after the flood event in 2009.

Table 5. Pearson correlation between typhoid fever and local weather variables (without and with lag)

time-lag (months)	Northern			Central			Southern	
	Mean temperature	Relative humidity	Rainfall	Mean temperature	Relative humidity	Rainfall	Mean temperature	Relative humidity
0	0.331*	0.483*	0.335*	0.325*	0.384*	0.294*	0.106	−0.012
1	0.454*	0.434*	0.407*	0.347*	0.253*	0.236*	0.111	0.005
2	0.487*	0.265*	0.434*	0.310*	0.037	0.096	0.109	−0.015
3	0.436*	0.045	0.330*	0.266*	−0.165	−0.049	0.122	0.013
4	0.281*	−0.219	0.082	0.116	−0.271*	−0.156	0.155	−0.024
5	0.012	−0.375*	−0.094	−0.073	−0.284*	−0.251*	0.110	−0.020
6	−0.221	−0.435*	−0.217	−0.254*	−0.314*	−0.273*	0.061	−0.042

* Statistically significant

Table 6. Pearson correlation between typhoid fever and global weather variables (without and with lag)

time-lag (months)	Northern		Central		Southern	
	DMI	NINO3	DMI	NINO3	DMI	NINO3
0	-0.380*	-0.285*	-0.372*	-0.015	-0.166	-0.003
1	-0.294*	-0.110	-0.216	0.169	-0.160	0.037
2	-0.138	0.091	-0.020	0.312*	-0.110	0.127
3	-0.027	0.291*	0.013	0.362*	-0.073	0.197
4	0.059	0.400*	-0.014	0.334*	-0.007	0.258*
5	0.117	0.406*	0.035	0.243*	0.017	0.292*
6	0.100	0.310*	0.007	0.135	0.039	0.282*
7	0.120	0.156	-0.055	0.025	0.090	0.260*
8	0.100	-0.016	-0.100	-0.053	0.133	0.194
9	0.134	-0.150	-0.091	-0.085	0.113	0.142
10	0.010	-0.216	-0.111	-0.035	0.050	0.076
11	-0.078	-0.206	-0.203	0.062	-0.009	0.043
12	-0.107	-0.103	-0.186	0.182	-0.054	0.048

* Statistically significant

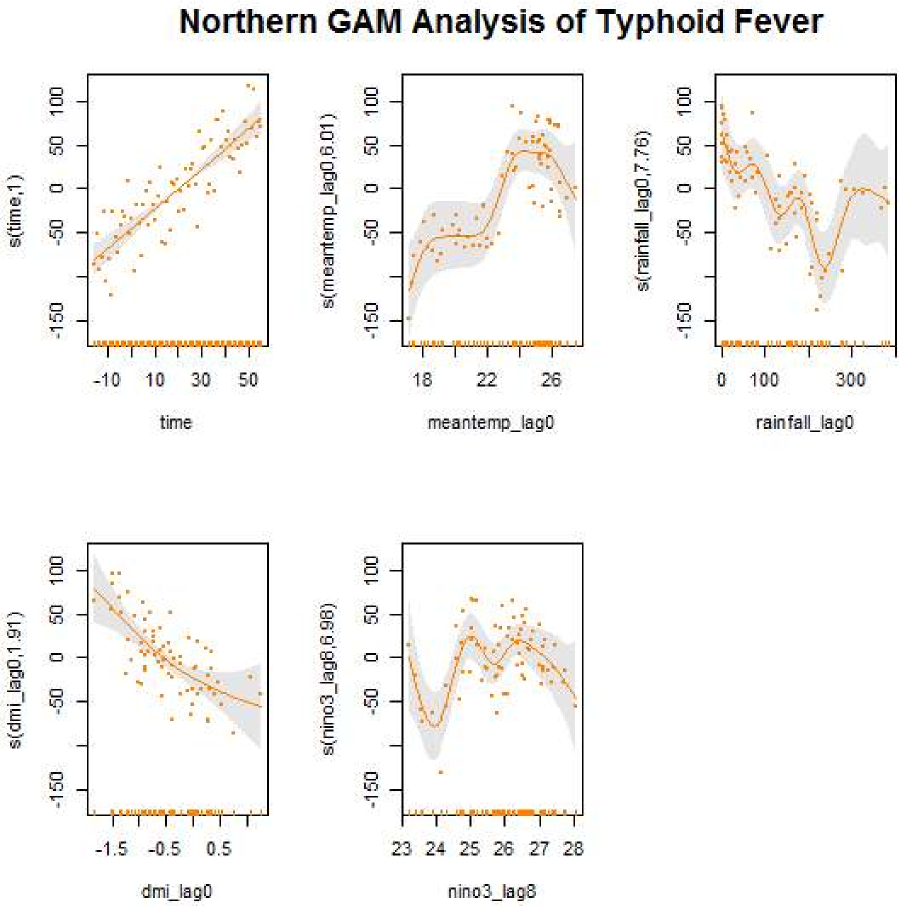

Fig. 7. The estimate of the smooth models for typhoid fever in Northern region.

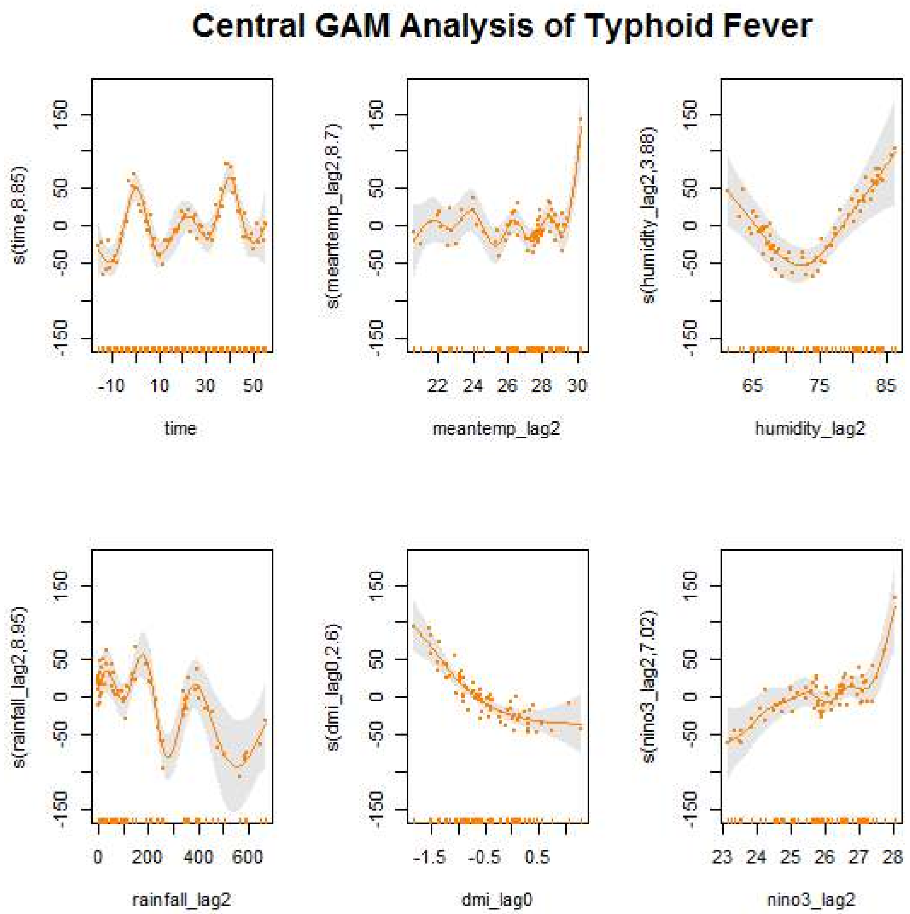

Fig. 8. The estimate of the smooth models for typhoid fever in Central region.

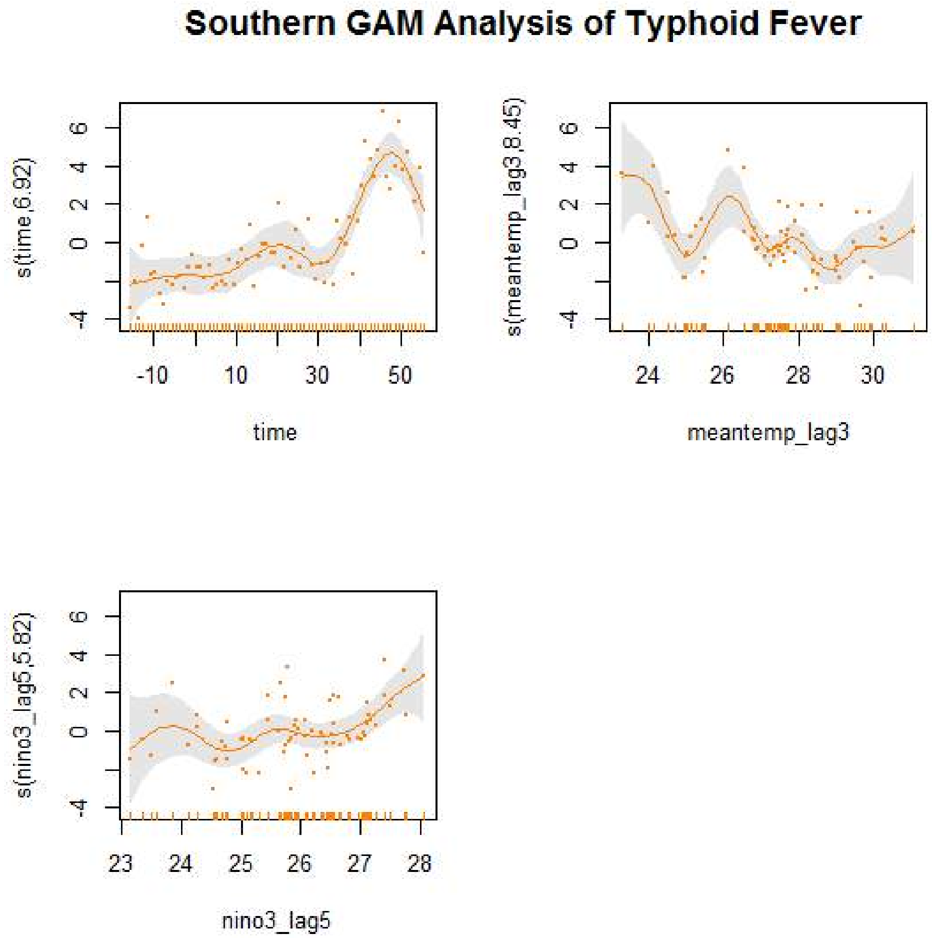

Fig. 9. The estimate of the smooth models for typhoid fever in Southern region.

3-3. Total hepatitis

Table 7 showed Pearson correlation between total hepatitis and local weather variables (mean temperature, relative humidity, and rainfall) for all regions. Table 8 showed Pearson correlation between total hepatitis and global weather variables (DMI and NINO3) for all regions. The result showed that local weather variables have correlation with incidence of hepatitis in Northern region. Central and Southern regions did not show the correlation. For global weather variables, NINO3 showed correlation (lag 9 to 12 months) in Northern region and Central region (lag 11 to 12 months). In Southern region DMI showed correlation with incidence of hepatitis.

Table 7 and table 8 showed the significantly correlation between total hepatitis and weather variables (p-value < 0.05). Lag models were used to examine the lag structure of the weather effects, using GAM Analysis. Each region has different demographic characteristic and weather condition. Model that have the best fit for describing association between total hepatitis and weather variables are,

$$f(tot\_hep)_{north} = \beta_0 + \beta_1 humid_{-1} + s(rain_{-1}, df) + \beta_2 nino3_{-9}$$

for northern region,

$$f(tot\_hep)_{central} = \beta_0 + s(meantemp_0, df) + s(nino3_{-9}, df)$$

for central region, and

$$f(tot\_hep)_{south} = \beta_0 + s(time, df) + \beta_1 humid_0 + s(rain_0, df) + s(dmi_{-3}, df) + s(nino3_{-1}, df)$$

for southern region.

Table 7. Pearson correlation between total hepatitis and local weather variables (without and with lag)

time-lag (months)	Northern			Central			Southern	
	Mean temperature	Relative humidity	Rainfall	Mean temperature	Relative humidity	Rainfall	Mean temperature	Relative humidity
0	0.108	0.354*	0.240*	−0.060	−0.005	−0.029	−0.041	0.064
1	0.283*	0.406*	0.279*	0.102	0.063	0.001	0.072	0.009
2	0.356*	0.256*	0.354*	0.096	0.115	0.114	0.151	0.035
3	0.264*	0.250*	0.415*	0.053	0.138	0.093	−0.038	0.028
4	0.171	0.003	0.193	0.023	0.139	0.224	−0.031	0.064
5	−0.012	−0.077	0.006	−0.003	0.148	0.227	−0.083	0.092
6	−0.156	−0.183	−0.089	−0.006	0.048	0.044	−0.014	0.075

* Statistically significant

Table 8. Pearson correlation between total hepatitis and global weather variables (without and with lag)

time-lag (months)	Northern		Central		Southern	
	DMI	NINO3	DMI	NINO3	DMI	NINO3
0	−0.084	−0.157	−0.015	−0.086	0.070	−0.201
1	−0.062	−0.078	0.064	−0.063	0.251*	−0.156
2	−0.004	0.026	0.035	−0.026	0.312*	−0.097
3	−0.034	0.108	−0.001	0.024	0.128	−0.106
4	−0.062	0.143	−0.026	0.057	−0.032	−0.077
5	−0.088	0.099	0.010	0.091	0.055	0.008
6	0.019	0.060	0.129	0.144	0.302*	0.111
7	0.108	−0.028	0.131	0.135	0.426*	0.179
8	0.092	−0.192	0.103	0.046	0.407*	0.182
9	0.038	−0.360*	−0.036	−0.119	0.206	0.132
10	0.015	−0.418*	−0.074	−0.213	−0.045	0.096
11	−0.054	−0.398*	−0.069	−0.266*	0.001	0.089
12	−0.004	−0.307*	0.051	−0.297*	0.184	0.129

* Statistically significant

Here some of the models are Mixed Generalized Additive Model, with linear correlation for some variables. In northern region, rainfall lag 1 month have non-linear correlation, while relative humidity lag 1 month and ENSO index (NINO3) lag 9 months have linear correlation with total hepatitis. In central region, mean temperature and ENSO index (NINO3) lag 9 months have non-linear correlation with total hepatitis. In southern region, rainfall, Dipole Mode Index (DMI) lag 3 months, and ENSO index (NINO3) lag 1 month have non-linear correlation, while relative humidity has linear correlation with total hepatitis. The comparison between the model and the observed (the count of incidence) for total hepatitis in three regions were presented in Fig. 26 (see appendix).

In northern region (Fig. 10), humidity lag 1 month showed an increase of cases of total hepatitis. Rainfall lag 1 month and ENSO index (NINO3) lag 9 months showed a negative correlation (lower rainfall and NINO3 resulted in higher number of cases of total hepatitis). In central region, mean temperature and ENSO index (NINO3) lag 9 months showed a significant correlation with total hepatitis but Fig. 11 showed that there is no clear correlation between both variable and the incidence of total hepatitis. In southern region, humidity showed an increase of cases of total hepatitis. Dipole Mode Index (DMI) lag 3 months showed a slight increase. Rainfall showed a slightly decrease and ENSO index (NINO3) lag 1 month showed a significant correlation with total hepatitis but Fig. 12 showed that there is no clear correlation between the variable and the incidence of total hepatitis.

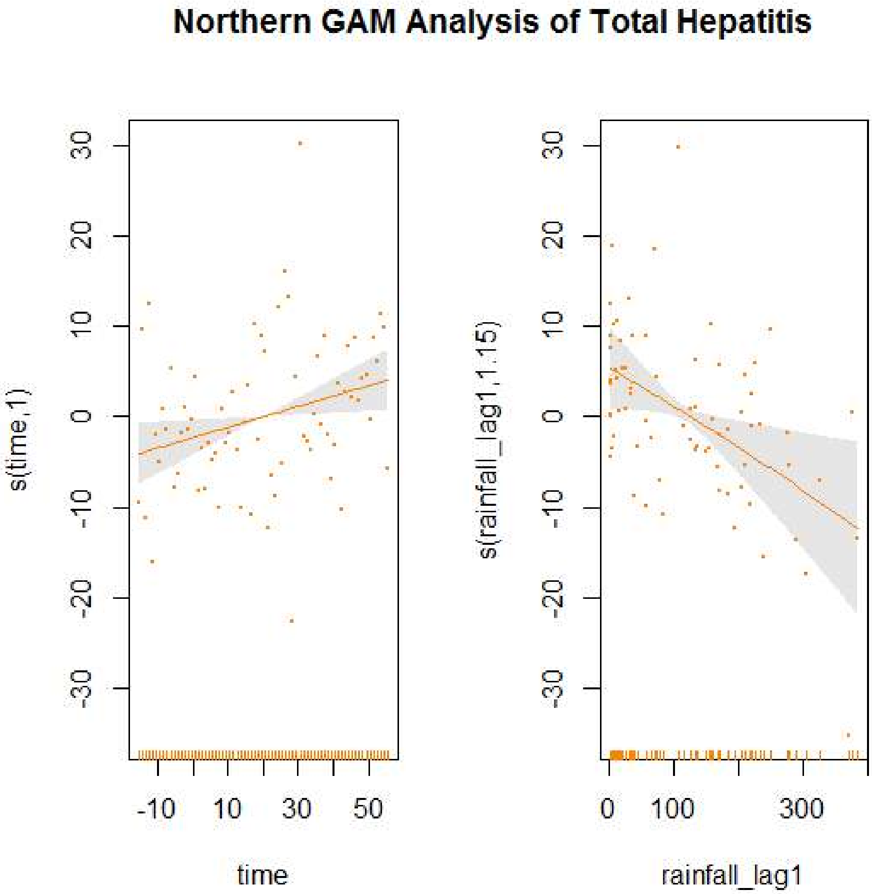

Fig. 10. The estimate of the smooth models for total hepatitis in Northern region.

In central region, there is no clear association between weather variables and total hepatitis. For Northern and Southern region, rainfall and relative humidity has association with total hepatitis. Relative humidity has positive correlation (higher relative resulted in higher number of cases of total hepatitis) while rainfall has negative correlation (higher rainfall resulted in lower number of cases of total hepatitis).

Only hepatitis type A and type E has a seasonal pattern. Limitation in this analysis is the data was not separated by types, but total hepatitis incidence. This could lead to different result than expected. It was showed in Brazil (Villar, 2002) that incidence of hepatitis A is increased in rainy season, but this analysis showed the reversed result. Also for hepatitis E, there was an increase of incidence in late winter and spring in Hongkong (Department of Health, Hongkong, 2011).

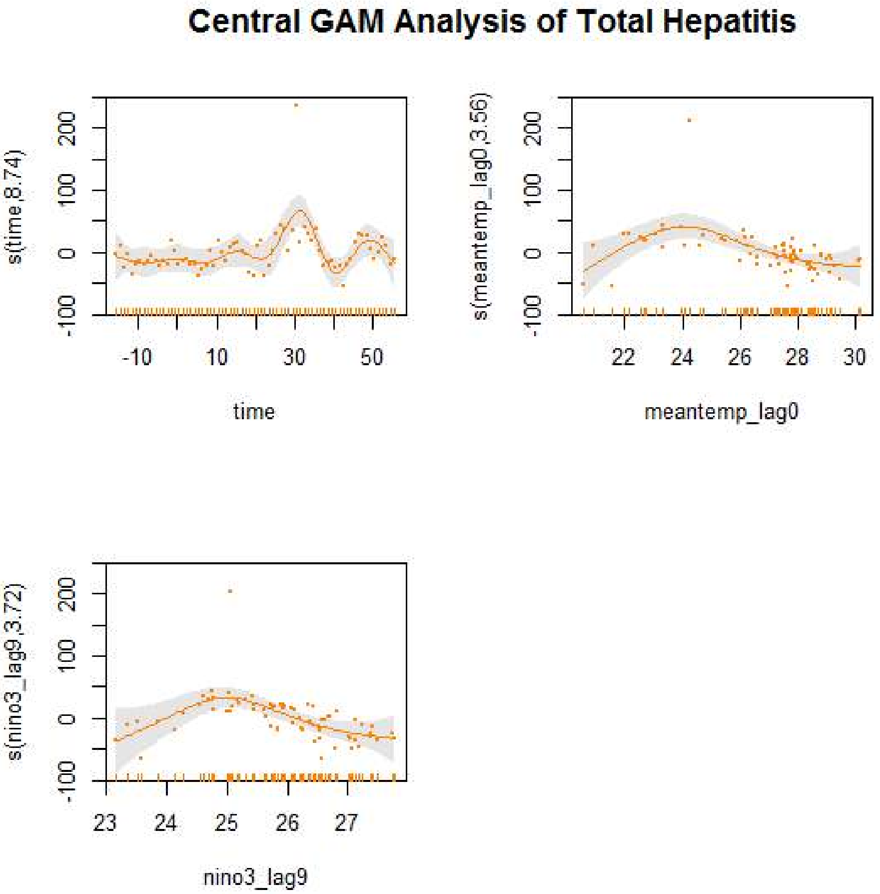

Fig. 11. The estimate of the smooth models for total hepatitis in Central region.

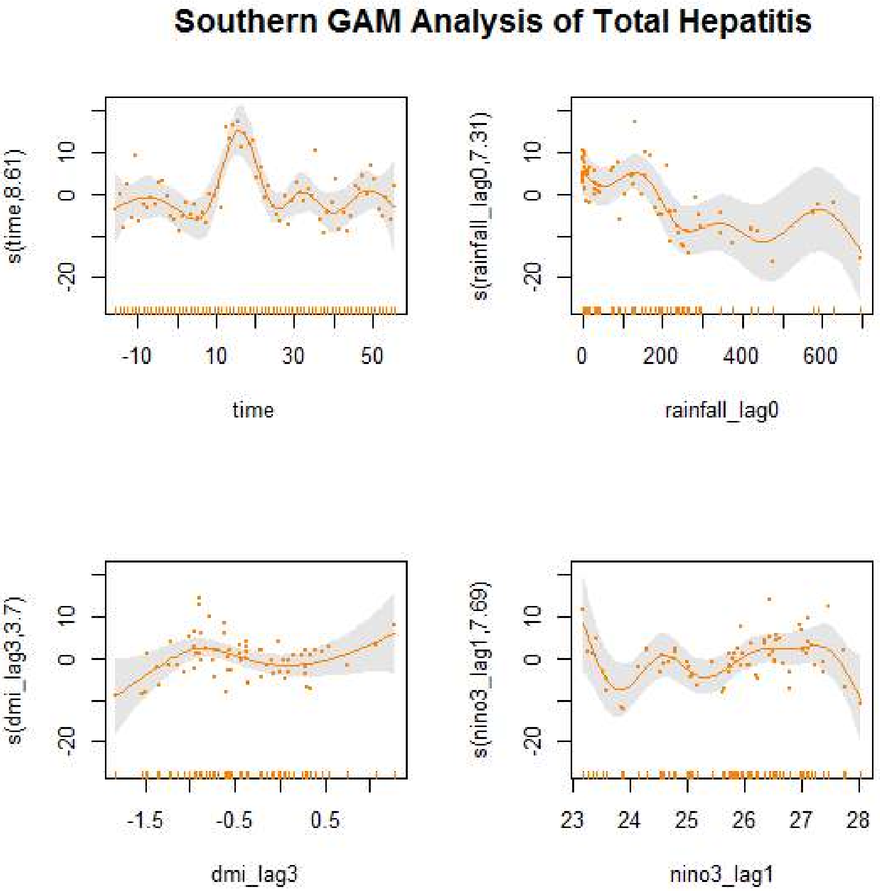

Fig. 12. The estimate of the smooth models for total hepatitis in Southern region.

3-4 Sensitivity analysis

Sensitivity Analysis was used to show the sensitivity of the model over small changes into the model. We conducted the sensitivity analysis by omitting a variable from the model and by changing the lag of variables, by comparing the Standard Error (SE) values. The sensitivity analysis showed that the models were not very sensitive for a small change. The values of SE showed some differences (see tables in appendix), but as the data used are monthly basis, the differences are understandable (as the weather can change enormously over months).

Chapter 4. Discussion

Study in Taiwan (Chen et al. 2012) showed association between infectious diseases and weather variable. Study in Taiwan showed that dengue fever has a strong association with precipitation (rainfall) whereas in this study dengue fever has a strong association with mean temperature and relative humidity, but association with rainfall was not clear. As for Hepatitis A in Taiwan study, the association with precipitation (rainfall) showed statistically insignificant, but this study showed otherwise. These differences might be the consequence of differences in climate and weather condition between two countries.

Study in Puerto Rico (Johansson et al. 2009) also showed a strong and consistent association between temperature, precipitation, and dengue. Moreover they also stated that these associations depend on local characteristics and have a biological interpretation.

Study in Columbia (Poveda et al. 2000) showed a strong association between dengue fever and El Niño, where the outbreak in dengue fever occurred during El Niño event. This study also showed a strong association between dengue fever and El Niño event, where the outbreak of dengue fever occurred during high value of ENSO index (NINO3), which is means the occurring El Niño with lag 5 months.

A study in Dhaka (Dewan et al. 1998) showed that the risk of typhoid fever is high during monsoon. But this study did not show a strong association between rainfall and typhoid fever. This study showed association between typhoid fever and DMI index, where the incidence increase in the negative IOD, which means warmer and heavy rainfall.

Study in association between weather variable and hepatitis A showed that the increase of incidence during hot temperature with heavy rainfall (Villar, 2002). There is also association between hepatitis E and rainfall, where the outbreak was occurred following monsoon rain (Previsani, 2001). This study showed association between rainfall and humidity and total hepatitis, but showed a reversed result. It might be caused by the incidence of other types of hepatitis.

Chapter 5. Conclusion

This study demonstrates that there is association between the incidences of infectious disease and weather variables, local and/or global weather variable. Among three diseases that have been analyzed, dengue fever had the strongest association with weather variables, mean temperature, relative humidity, and ENSO index (NINO3). The association occurred in all three regions. The result also showed that global weather variable (NINO3) effects on the incidence of dengue fever slower than local weather variable (mean temperature and relative humidity).

There is association between typhoid fever and mean temperature, relative humidity, rainfall, and ENSO index (NINO3) but the strongest association occurred between Dipole Mode Index (DMI) and typhoid fever. The association occurred in all three regions. For Total Hepatitis, the association between relative humidity and the disease occurred in northern and southern region, but show no association in central region.

From the result, we conclude that the association between infectious diseases and weather variables in Lao People's Democratic Republic varied in different diseases. For dengue fever, both local and global weather variables showed a strong association, where the effect of global weather variable (NINO3) to the incidence of dengue fever slower than local weather variable (mean temperature and relative humidity). For typhoid fever, global weather variable (DMI) showed the strongest association with the disease. For total hepatitis, local weather variable (relative humidity) showed the strongest association with the disease, but not in all regions.

The difference association between diseases is cause by the biological factors for each disease. *Aedes aegepty* mosquito preferred high temperature and humidity, effect on the outbreak of dengue fever during high temperature. Typhoid fever is a disease caused by food and water contamination that showed an outbreak during rainy season. Hepatitis is also related to heavy rainfall. As shown in some previous studies, the association of infectious disease and weather are differed between diseases.

This variation in association also differed between regions. For dengue fever, as the *Aedes aegepty* prefer high temperature and humidity, the increase of disease incidence occurred in a region with higher temperature. This explains the incidence of dengue fever in central region and southern region are higher than southern region.

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Appendix

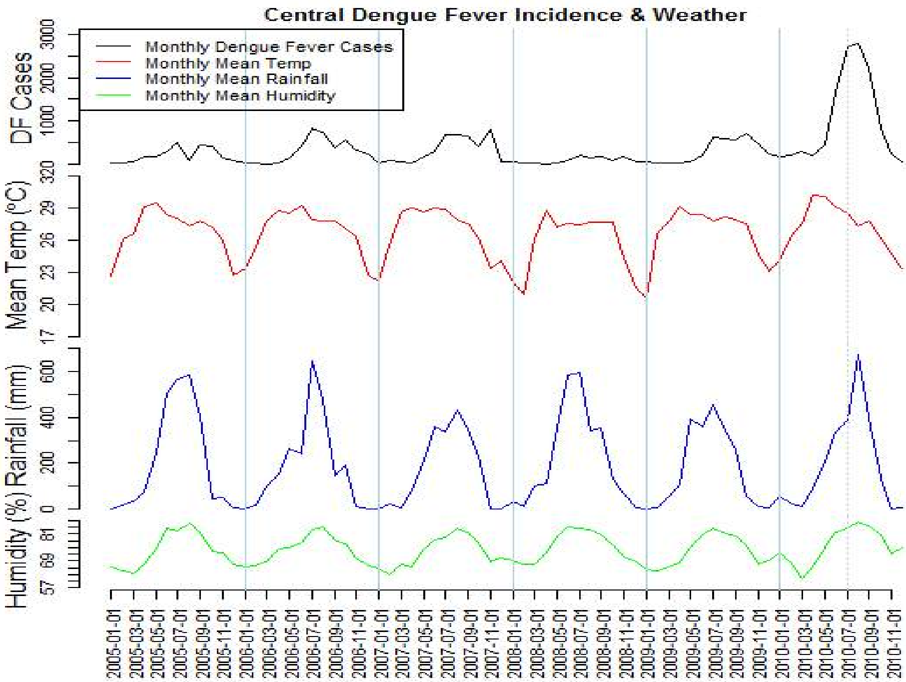

Fig. 13. Time series trend of dengue fever cases, mean temperature (°C), mean rainfall (mm), and mean relative humidity (%) for Central region from 2005 to 2010.

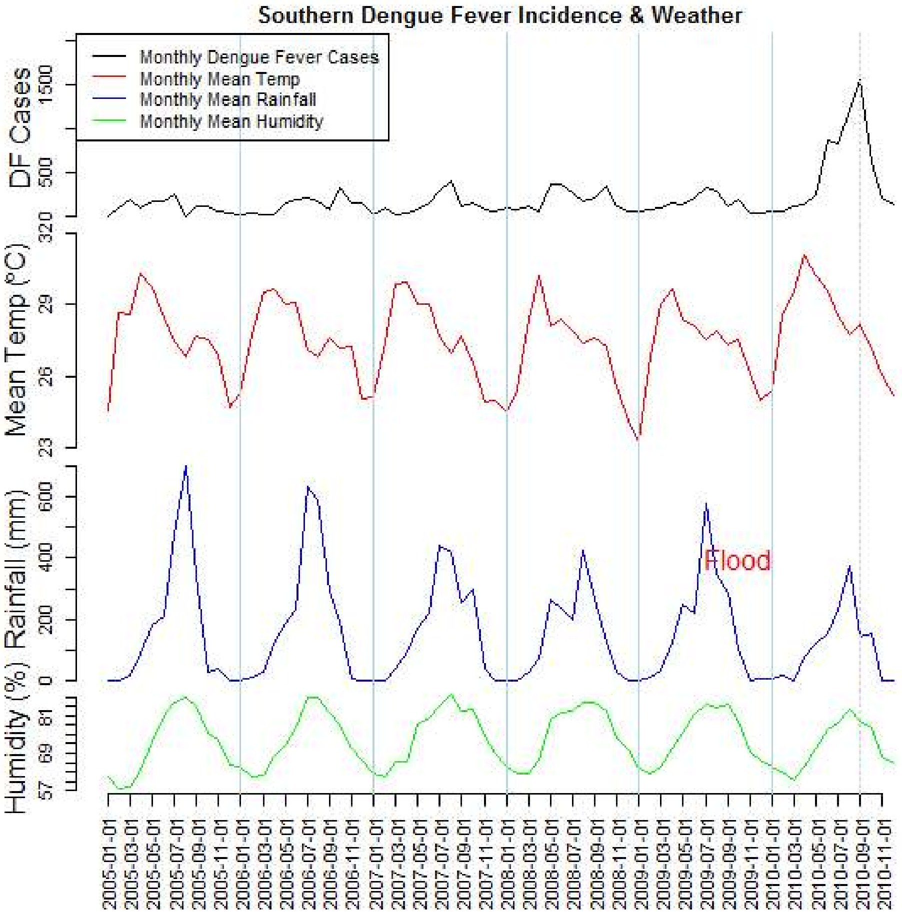

Fig. 14. Time series trend of dengue fever cases, mean temperature (°C), mean rainfall (mm), and mean relative humidity (%) for Southern region from 2005 to 2010.

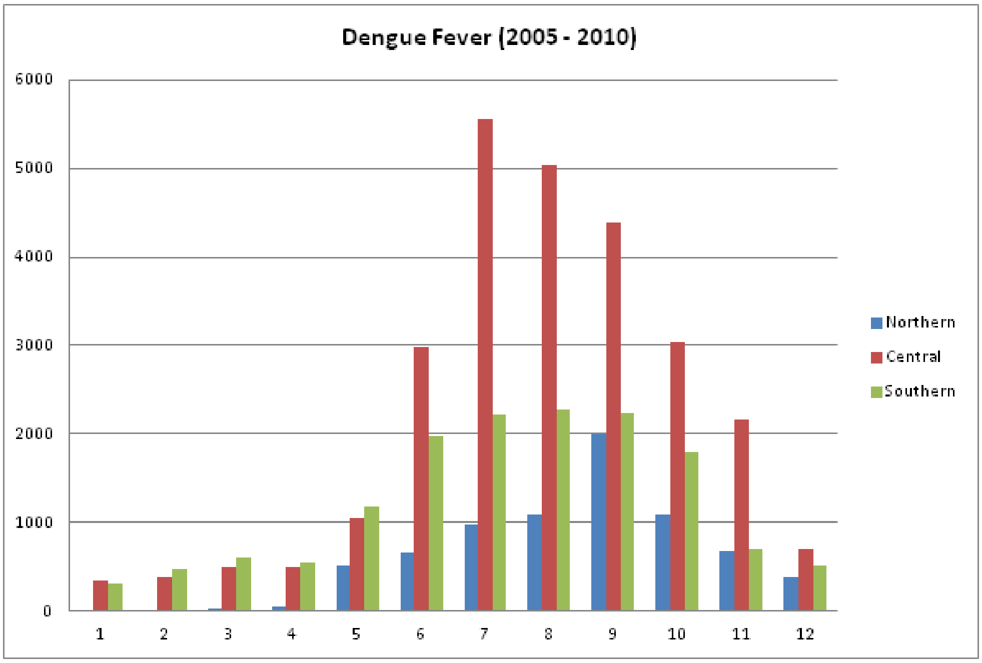

Fig. 15. Monthly trend of dengue fever cases from 2005 to 2010.

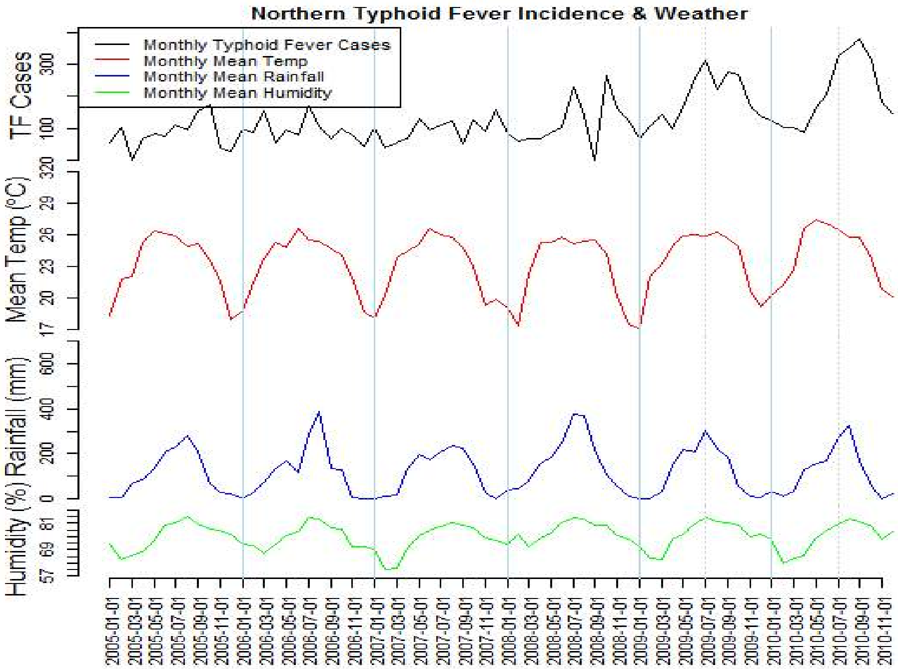

Fig. 16. Time series trend of typhoid fever cases, mean temperature (°C), mean rainfall (mm), and mean relative humidity (%) for Northern region from 2005 to 2010.

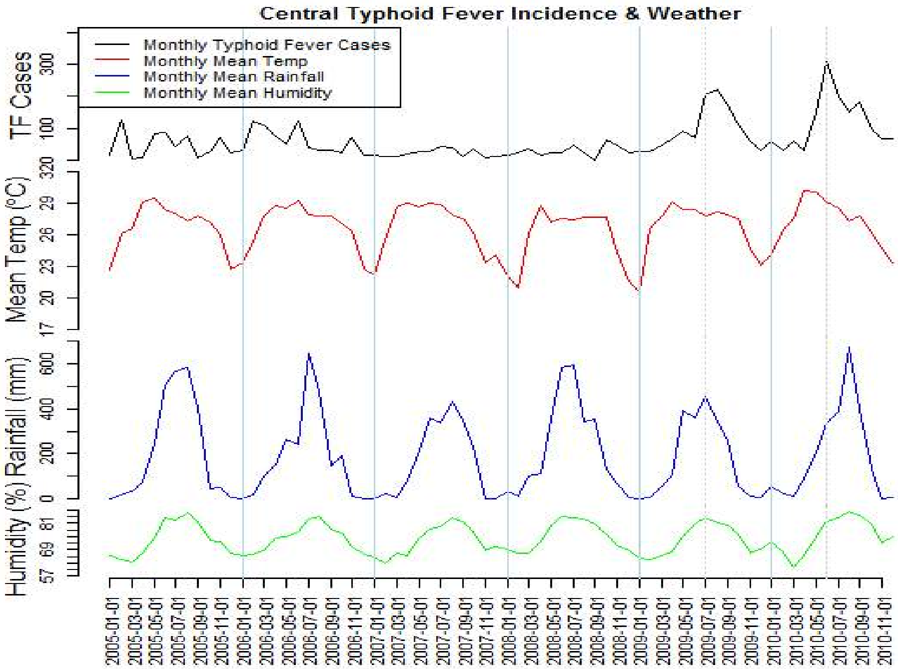

Fig. 17. Time series trend of typhoid fever cases, mean temperature (°C), mean rainfall (mm), and mean relative humidity (%) for Central region from 2005 to 2010.

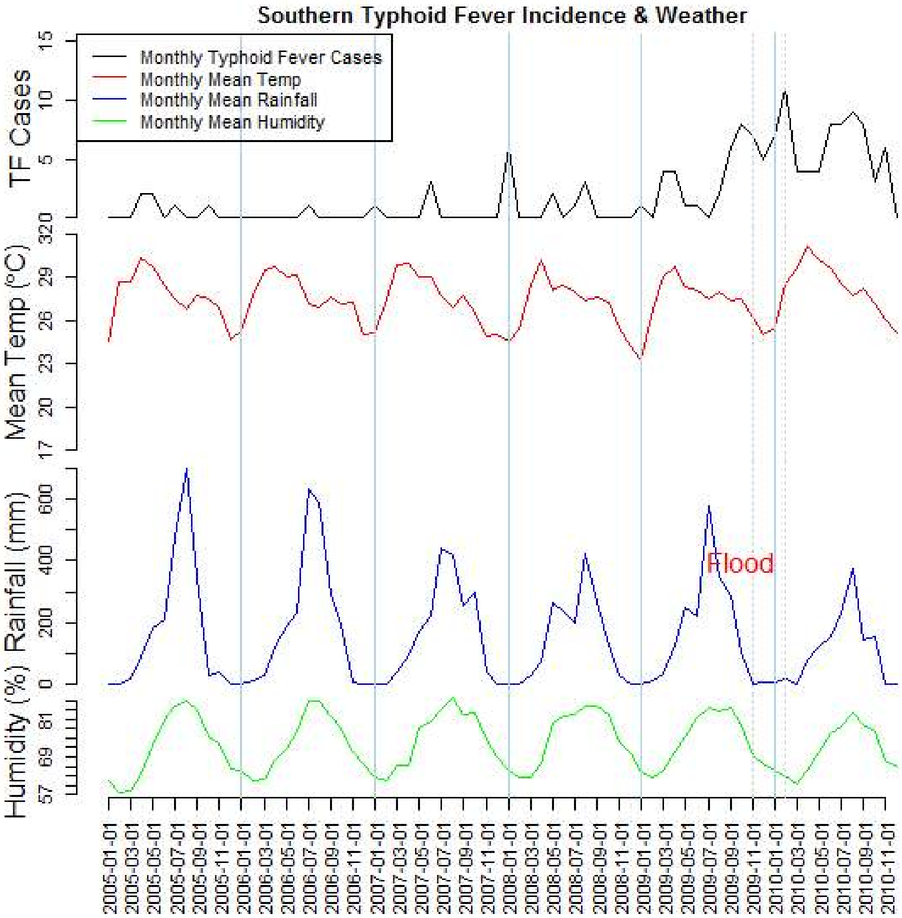

Fig. 18. Time series trend of typhoid fever cases, mean temperature (℃), mean rainfall (mm), and mean relative humidity (%) for Southern region from 2005 to 2010.

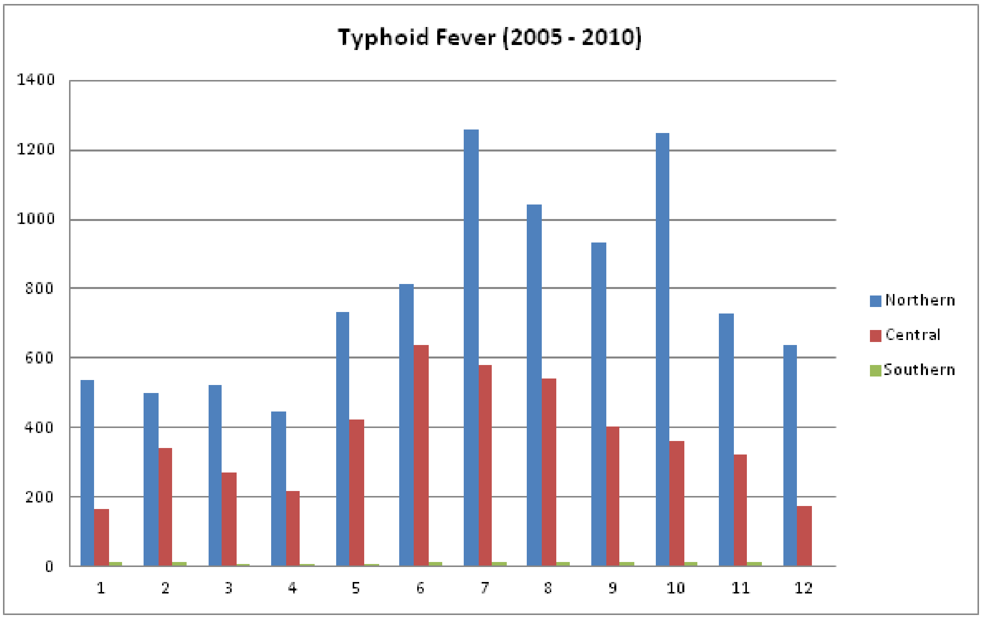

Fig. 19. Monthly trend of typhoid fever cases from 2005 to 2010.

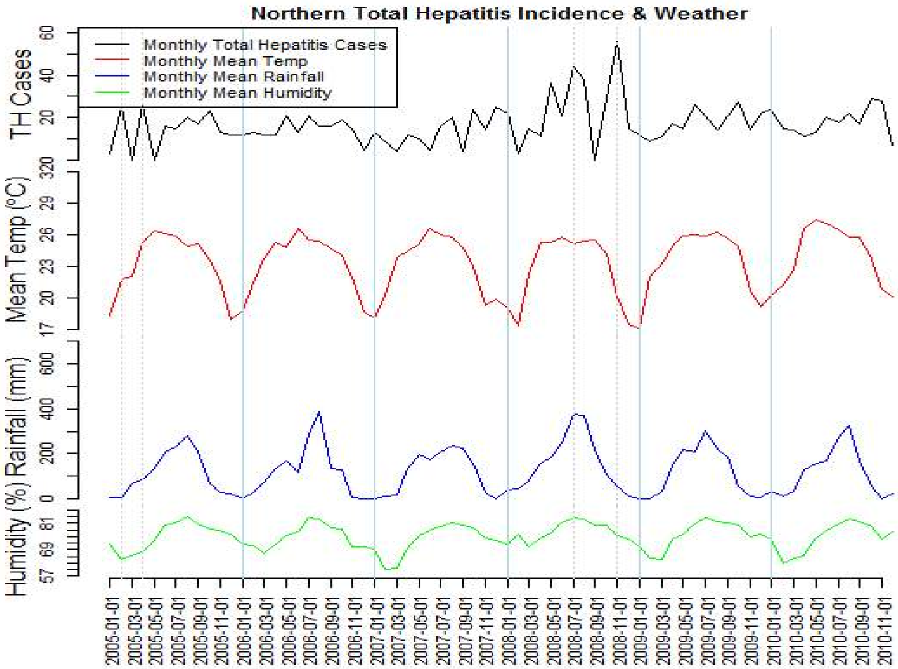

Fig. 20. Time series trend of total hepatitis cases, mean temperature (°C), mean rainfall (mm), and mean relative humidity (%) for Northern region from 2005 to 2010.

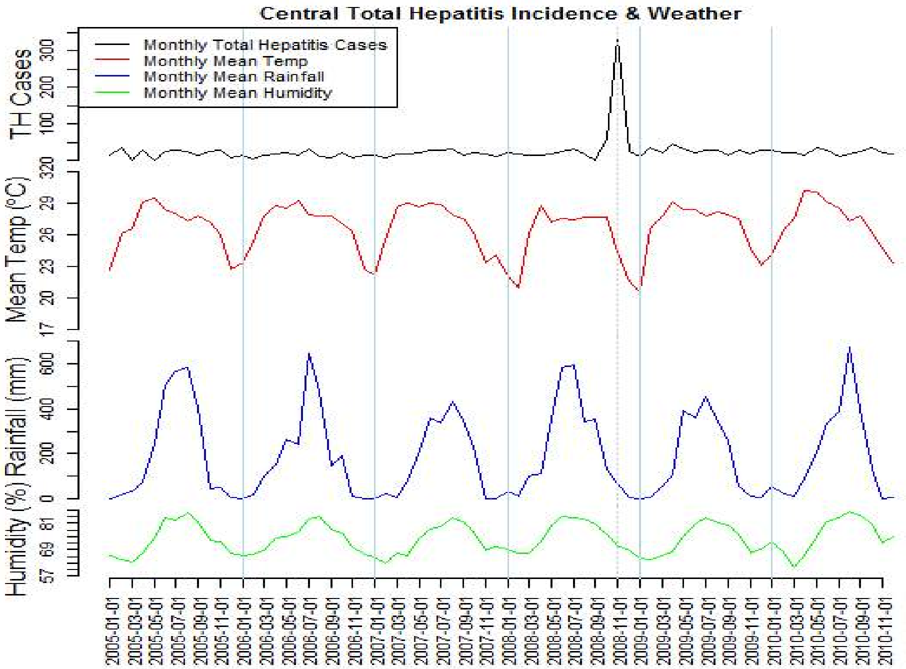

Fig. 21. Time series trend of total hepatitis cases, mean temperature (°C), mean rainfall (mm), and mean relative humidity (%) for Central region from 2005 to 2010.

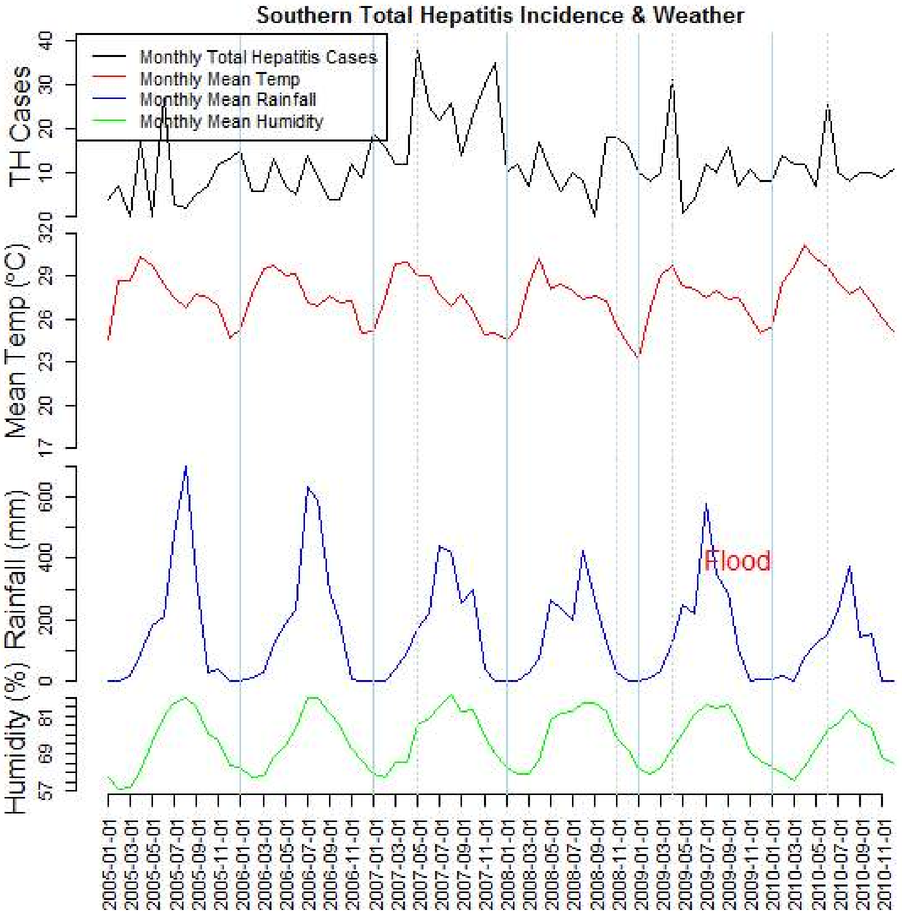

Fig. 22. Time series trend of total hepatitis cases, mean temperature (°C), mean rainfall (mm), and mean relative humidity (%) for Southern region from 2005 to 2010.

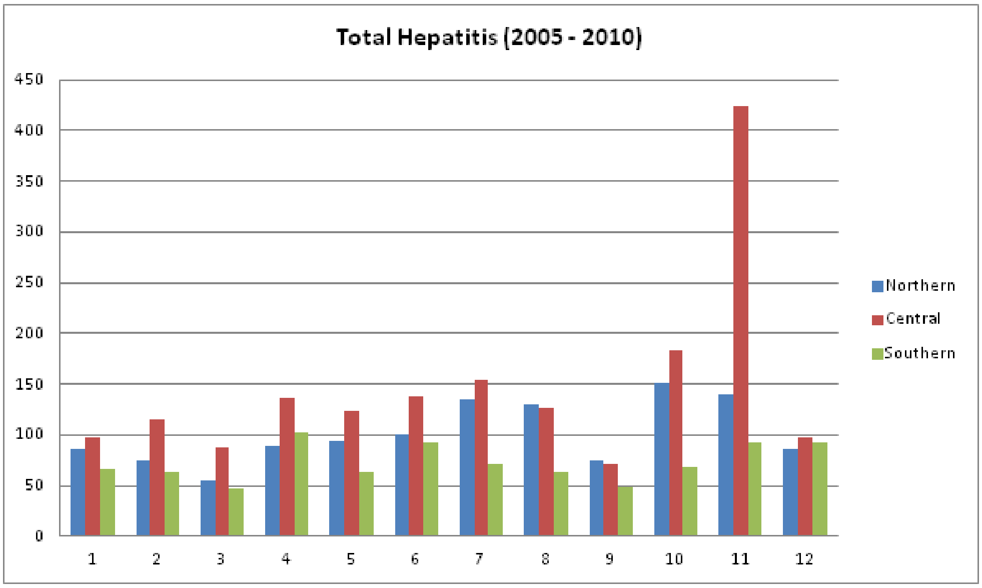

Fig. 23. Monthly trend of total hepatitis cases from 2005 to 2010.

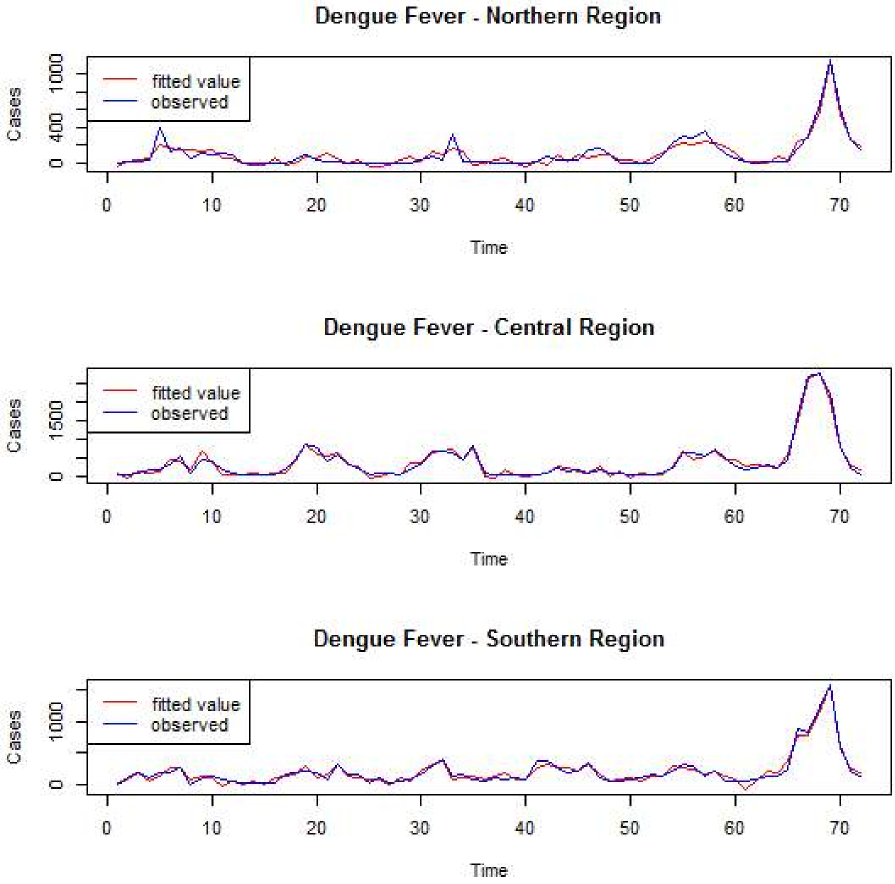

Fig. 24. The comparison between fitted model and the observed of dengue fever incidence in the northern, central, and southern region.

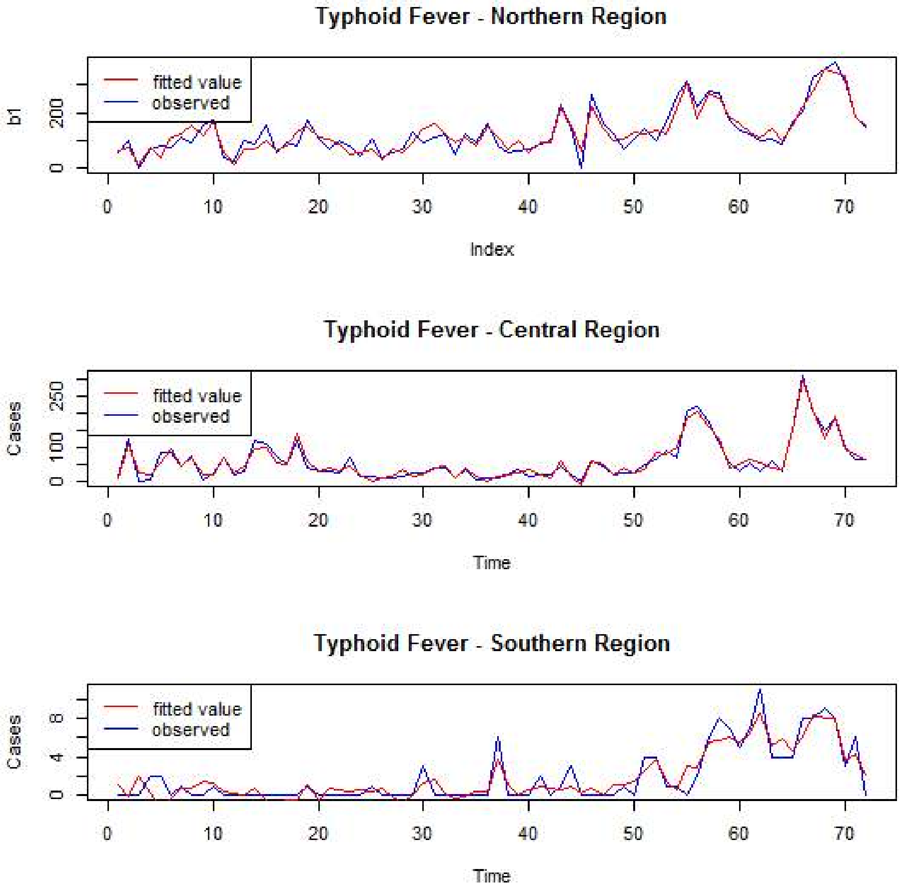

Fig. 25. The comparison between fitted model and the observed of typhoid fever incidence in the northern, central, and southern region.

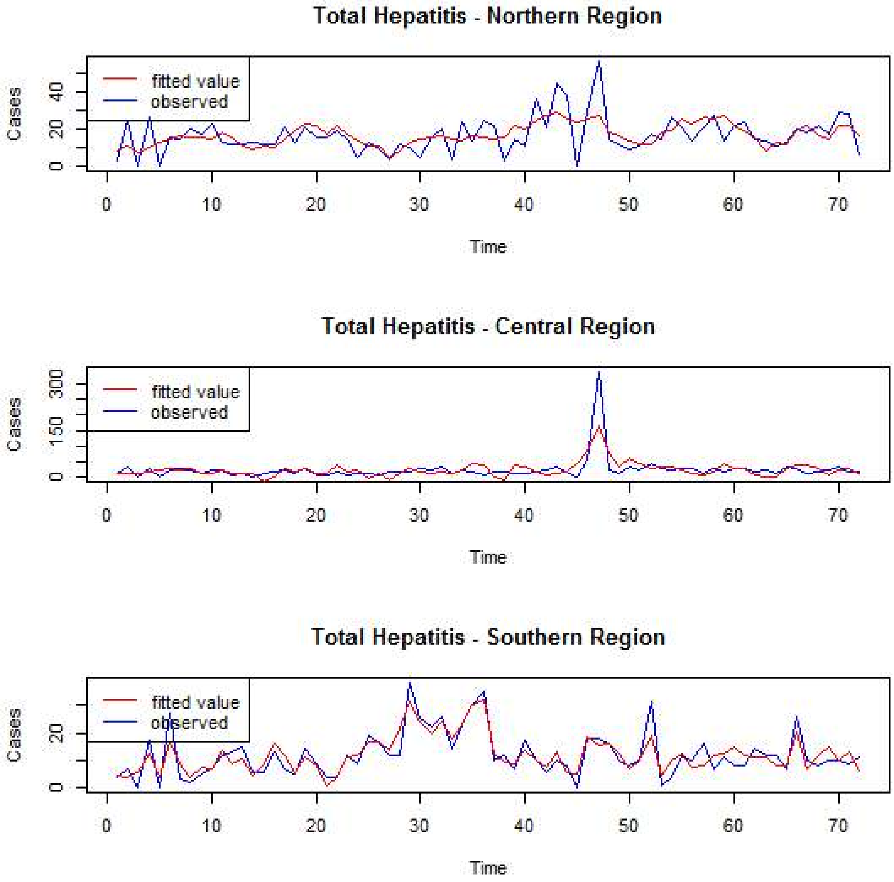

Fig. 26. The comparison between fitted model and the observed of total hepatitis incidence in the northern, central, and southern region.

Table 9. Comparison of SE values of omitted variables from the fitted model for dengue fever - Northern region.

	Mean Temp	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE	SE
FULL MODEL	10.058	4.652	0.312	28.879	20.792
Mean temp omitted	-	4.656	0.267	28.894	18.608
Humidity omitted	10.400	-	0.251	28.698	19.222
Rainfall omitted	8.548	3.592	-	28.037	20.379
DMI omitted	10.615	4.720	0.322	-	21.325
NINO3 omitted	9.065	4.193	0.310	28.279	-

Table 10. Comparison of SE values of omitted variables from the fitted model for dengue fever - Central region.

	Mean Temp	Humidity	DMI	NINO3
	SE	SE	SE	SE
FULL MODEL	30.898	8.439	91.414	54.726
Mean temp omitted	-	7.948	81.914	49.361
Humidity omitted	30.042	-	91.542	58.001
DMI omitted	26.496	7.834	-	54.225
NINO3 omitted	29.459	9.158	100.047	-

Table 11. Comparison of SE values of omitted variables from the fitted model for dengue fever - Southern region.

	Mean Temp	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE	SE
FULL MODEL	22.936	6.965	0.322	49.767	33.709
Mean temp omitted	-	6.765	0.331	50.975	32.342
Humidity omitted	21.750	-	0.207	46.810	32.970
Rainfall omitted	22.962	4.464	-	45.138	33.745
DMI omitted	22.653	6.471	0.289	-	32.097
NINO3 omitted	21.415	6.791	0.322	47.824	-

Table 12. Comparison of SE values of changing lag structure from the fitted model for dengue fever - Northern region. Number represents the lag structure for the variables respectively.

	Mean Temp	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE	SE
FULL MODEL* (4-4-4-2-5)	10.058	4.652	0.312	28.879	20.792
2-2-2-2-2	9.964	5.240	0.340	30.246	19.269
2-2-2-2-5	10.118	4.414	0.341	29.955	21.734
2-2-2-5-5	12.412	5.079	0.413	39.353	24.571
4-4-4-2-2	9.171	4.627	0.315	30.187	20.360
4-4-4-5-5	10.726	4.813	0.333	33.348	23.102
6-6-6-2-2	10.303	4.065	0.280	32.019	21.503
6-6-6-2-5	9.226	4.783	0.265	31.396	19.506
6-6-6-5-5	8.495	4.723	0.273	30.169	20.253
6-6-6-6-6	9.269	4.593	0.271	30.004	20.466
6-6-6-12-12	8.817	4.075	0.293	31.348	18.755

*Number: (Mean temp-Humidity-Rainfall-DMI-NINO3)

Table 13. Comparison of SE values of changing lag structure from the fitted model for dengue fever - Central region. Number represents the lag structure for the variables respectively.

	Mean Temp	Humidity	DMI	NINO3
	SE	SE	SE	SE
FULL MODEL* (3-3-12-5)	30.898	8.439	91.414	54.726
3-3-5-5	29.736	7.907	91.629	63.633
3-3-5-6	26.200	8.941	82.757	61.562
3-3-6-5	29.708	7.904	89.013	61.054
3-3-6-6	27.775	9.038	90.001	66.124
3-3-12-12	28.526	11.367	103.115	68.913
6-6-5-5	27.760	11.041	88.601	57.977
6-6-5-6	32.729	10.637	90.227	59.935
6-6-6-5	28.760	11.431	91.984	57.458
6-6-6-6	32.770	10.689	93.259	59.136
6-6-12-5	30.904	11.463	95.272	60.842

*Number: (Mean temp-Humidity-DMI-NINO3)

Table 14. Comparison of SE values of changing lag structure from the fitted model for dengue fever - Southern region. Number represents the lag structure for the variables respectively.

	Mean Temp	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE	SE
FULL MODEL* (4-1-1-5-5)	22.936	6.965	0.322	49.767	33.709
1-1-1-1-1	18.141	6.333	0.316	45.101	29.115
1-1-1-1-5	15.670	5.936	0.297	43.470	29.390
1-1-1-5-1	18.866	6.741	0.338	47.347	28.956
1-1-1-5-5	15.483	6.703	0.330	49.588	31.761
1-1-1-6-6	16.817	6.321	0.301	48.391	28.761
1-1-1-12-12	17.180	7.040	0.298	41.920	37.030
4-1-1-1-1	26.398	7.853	0.341	56.027	26.314
4-1-1-1-5	27.898	7.145	0.307	52.431	32.495
4-1-1-5-1	22.614	7.177	0.348	48.449	24.868
4-1-1-6-6	25.665	6.773	0.296	50.382	31.489
4-1-1-12-12	24.260	7.343	0.296	49.240	31.610
4-4-4-1-1	16.810	5.241	0.249	46.854	29.026
4-4-4-5-5	17.851	5.175	0.287	46.538	31.259
4-4-4-6-6	17.814	4.649	0.248	44.035	32.105
4-4-4-12-12	17.390	4.878	0.245	44.790	30.590

*Number: (Mean temp-Humidity-Rainfall-DMI-NINO3)

Table 15. Comparison of SE values of omitted variables from the fitted model for typhoid fever - Northern region.

	Mean Temp	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE	SE
FULL MODEL	3.491	1.580	0.132	10.649	8.626
Mean temp omitted	-	1.661	0.120	11.188	8.919
Humidity omitted	3.651	-	0.109	11.103	8.980
Rainfall omitted	3.003	1.239	-	10.428	7.666
DMI omitted	3.764	1.700	0.141	-	9.078
NINO3 omitted	3.405	1.560	0.117	10.300	-

Table 16. Comparison of SE values of omitted variables from the fitted model for typhoid fever - Central region.

	Mean Temp	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE	SE
FULL MODEL	3.486	2.368	0.076	9.114	6.630
Mean temp omitted	-	2.243	0.076	9.137	5.478
Humidity omitted	3.289	-	0.037	9.128	5.422
Rainfall omitted	3.480	1.144	-	9.098	6.159
DMI omitted	3.759	2.560	0.082	-	7.174
NINO3 omitted	2.876	1.941	0.071	9.156	-

Table 17. Comparison of SE values of omitted variables from the fitted model for typhoid fever - Southern region.

	Mean Temp	DMI	NINO3
	SE	SE	SE
FULL MODEL	0.192	0.467	0.259
Mean temp omitted	-	0.411	0.223
DMI omitted	0.173	-	0.267
NINO3 omitted	0.171	0.484	-

Table 18. Comparison of SE values of changing lag structure from the fitted model for typhoid fever - Northern region. Number represents the lag structure for the variables respectively.

	Mean Temp	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE	SE
FULL MODEL* (0-0-0-0-8)	3.491	1.580	0.132	10.649	8.626
0-0-0-0-0	3.568	1.864	0.120	10.633	6.600
0-0-0-0-4	3.514	1.572	0.117	10.353	6.638
0-0-0-4-4	4.169	2.151	0.160	14.884	7.883
0-0-0-4-8	3.917	1.989	0.168	13.415	8.977
0-0-0-8-8	3.762	1.733	0.137	12.250	8.998
0-0-0-0-12	3.752	1.733	0.118	10.513	7.023
0-0-0-4-12	4.070	2.259	0.161	14.261	7.870
0-0-0-8-12	4.164	1.960	0.129	12.626	7.650
0-0-0-12-12	3.924	1.802	0.128	11.469	7.567
6-6-6-0-4	3.123	1.535	0.099	10.312	7.217
6-6-6-4-4	3.416	1.699	0.111	12.059	8.297
6-6-6-4-8	3.946	1.556	0.113	11.860	8.898
6-6-6-0-8	3.907	1.388	0.101	11.400	8.698
6-6-6-8-8	4.285	1.491	0.109	13.159	9.559
6-6-6-0-12	3.129	1.546	0.110	10.374	6.861
6-6-6-4-12	3.458	1.736	0.124	11.740	7.634
6-6-6-8-12	3.464	1.706	0.123	12.092	7.613
6-6-6-12-12	3.533	1.633	0.117	12.561	7.515

*Number: (Mean temp-Humidity-Rainfall-DMI-NINO3)

Table 19. Comparison of SE values of changing lag structure from the fitted model for typhoid fever - Central region. Number represents the lag structure for the variables respectively.

	Mean Temp	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE	SE
FULL MODEL* (2-2-2-0-2)	3.486	2.368	0.076	9.114	6.630
2-2-2-0-0	2.867	2.273	0.072	9.913	6.856
2-2-2-2-2	3.847	2.553	0.086	11.610	7.282
2-2-2-4-4	3.900	2.152	0.081	12.013	8.504
2-2-2-6-6	3.171	2.286	0.080	11.097	7.282
2-2-2-12-12	2.938	2.138	0.071	10.165	7.405
4-4-4-0-2	3.292	1.998	0.064	10.476	6.293
4-4-4-2-2	2.958	2.126	0.067	10.300	7.201
4-4-4-4-4	3.695	2.169	0.073	11.208	6.951
4-4-4-6-6	3.797	1.920	0.071	11.656	8.476
4-4-4-12-12	3.294	1.767	0.066	10.865	7.435
6-6-6-0-2	3.753	1.474	0.056	9.614	7.107
6-6-6-2-2	4.121	1.631	0.062	11.960	7.866
6-6-6-4-4	3.102	1.827	0.059	10.874	7.520
6-6-6-6-6	3.998	1.904	0.062	11.500	7.495
6-6-6-12-12	3.270	1.601	0.060	11.170	6.156

*Number: (Mean temp-Humidity-Rainfall-DMI-NINO3)

Table 20. Comparison of SE values of changing lag structure from the fitted model for typhoid fever - Southern region. Number represents the lag structure for the variables respectively.

	Mean Temp	DMI	NINO3
	SE	SE	SE
FULL MODEL (3-12-5)	0.192	0.467	0.259
3-3-3	0.177	0.424	0.268
3-5-5	0.186	0.468	0.293
3-5-6	0.164	0.439	0.253
3-6-6	0.166	0.456	0.262
3-6-12	0.161	0.439	0.254
3-12-12	0.173	0.482	0.247
6-5-5	0.157	0.434	0.247
6-5-6	0.191	0.429	0.295
6-6-6	0.189	0.434	0.293
6-6-12	0.168	0.453	0.260
6-12-5	0.173	0.462	0.252
6-12-12	0.171	0.473	0.265

*Number: (Mean temp-DMI-NINO3)

Table 21. Comparison of SE values of omitted variables from the fitted model for total hepatitis - Northern region.

	Humidity	Rainfall	NINO3
	SE	SE	SE
FULL MODEL	0.247	0.018	1.285
Humidity omitted	-	0.014	1.345
Rainfall omitted	0.184	-	0.994
NINO3 omitted	0.258	0.014	-

Table 22. Comparison of SE values of omitted variables from the fitted model for total hepatitis - Central region.

	Mean Temp	NINO3
	SE	SE
FULL MODEL	2.268	4.830

Table 23. Comparison of SE values of omitted variables from the fitted model for total hepatitis - Southern region.

	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE
FULL MODEL	0.215	0.011	1.589	0.794
Humidity omitted	-	0.006	1.587	0.800
Rainfall omitted	0.108	-	1.560	0.791
DMI omitted	0.214	0.011	-	0.805
NINO3 omitted	0.211	0.011	1.573	-

Table 24. Comparison of SE values of changing lag structure from the fitted model for total hepatitis - Northern region. Number represents the lag structure for the variables respectively.

	Humidity	Rainfall	NINO3
	SE	SE	SE
FULL MODEL* **(1-1-9)**	0.247	0.018	1.285
1-1-1	0.318	0.016	1.045
1-1-3	0.275	0.018	1.131
1-1-6	0.276	0.014	1.042
1-1-12	0.315	0.015	1.259
3-3-3	0.309	0.016	1.079
3-3-6	0.244	0.016	1.171
3-3-9	0.275	0.015	1.045
3-3-12	0.265	0.016	1.417
6-6-3	0.247	0.016	1.225
6-6-6	0.290	0.016	1.211
6-6-9	0.231	0.014	1.174
6-6-12	0.260	0.015	1.151

*Number: (Humidity-Rainfall-NINO3)

Table 25. Comparison of SE values of changing lag structure from the fitted model for total hepatitis - Central region. Number represents the lag structure for the variables respectively.

	Mean Temp	NINO3
	SE	SE
FULL MODEL* (0-9)	2.268	4.830
0-0	2.149	3.993
0-3	2.448	4.875
0-6	1.965	4.178
0-12	2.046	4.461
3-0	2.430	4.530
3-3	2.111	4.217
3-6	2.382	5.081
3-9	1.962	4.192
3-12	2.170	4.746
6-0	2.055	3.842
6-3	2.466	4.941
6-6	2.127	4.550
6-9	2.384	5.110
6-12	1.887	4.140

*Number: (Mean temp-NINO3)

Table 26. Comparison of SE values of changing lag structure from the fitted model for total hepatitis - Southern region. Number represents the lag structure for the variables respectively.

	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE
FULL MODEL* (0-0-3-1)	0.215	0.011	1.589	0.794
0-0-1-1	0.229	0.013	1.845	0.928
0-0-3-3	0.213	0.011	1.629	1.065
0-0-6-1	0.233	0.012	1.715	0.797
0-0-6-6	0.243	0.012	1.717	0.941
0-0-9-1	0.212	0.011	1.647	0.834
0-0-9-9	0.233	0.010	1.713	1.301
0-0-12-1	0.215	0.011	1.622	0.804
0-0-12-12	0.234	0.012	1.682	1.017
3-3-1-1	0.249	0.010	1.585	1.170
3-3-3-1	0.274	0.011	1.637	1.179
3-3-3-3	0.249	0.012	1.778	1.030
3-3-6-1	0.271	0.012	1.675	1.110
3-3-6-6	0.218	0.011	1.714	1.133
3-3-9-1	0.276	0.012	1.763	1.148
3-3-9-9	0.249	0.012	1.769	0.973
3-3-12-1	0.267	0.011	1.585	1.149
3-3-12-12	0.243	0.011	1.791	1.419
6-6-1-1	0.164	0.009	1.597	0.824
6-6-3-1	0.168	0.009	1.614	0.838
6-6-3-3	0.189	0.009	1.830	1.258
6-6-6-1	0.162	0.009	1.578	0.775
6-6-6-6	0.180	0.009	1.641	0.970
6-6-9-1	0.171	0.009	1.712	0.812
6-6-9-9	0.183	0.009	1.728	1.169
6-6-12-1	0.182	0.010	1.726	0.818
6-6-12-12	0.190	0.010	1.715	0.993

*Number: (Humidity-Rainfall-DMI-NINO3)

요약(국문초록)

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배경: 감염성 질환과 기후변화/날씨변수가 감염성 질환 발생에 미치는 영향에 대해 조사하기 위한 모델링과 연구가 있었었다. 특히 대부분의 개발도상국이 위치하고 있는 열대 및 아열대 지방에서 감염성질환의 발생 빈도는 여전히 높으며, 이는 국가의 경제발전을 저해하며 중요 해결 과제이다. 본 연구의 목표는 감염성 질환이 건강문제로 남아있는 라오스에서 기상변수와 감염성질환의 관계를 규명하고자 한다.

방법: 감염성질환과 기상변수 사이의 관계를 알아보기 위하여 일반화 부가모형 (Generalized Additive Model, GAM)을 이용하여 분석하였다. 라오스의 각 지역(북부, 중부, 남부지역)의 뎅기열(Dengue Fever), 장티푸스(Typhoid fever), 간염(Total Hepatitis) 발생 데이터와 각 지역의 온도, 상대 습도, 강우량을 이용하여 질병발생과 기상변수의 관계를 확인하였으며 글로벌변수(Global index) 로서 DMI와NINO3를 분석모형에 이용하였다.

결론: 뎅기열 질환과 기상변수는 가장 강한 연관성을 가지고 있었으며 그 다음으로는 장티푸스와 간염이 기상변수의 영향을 받는 것을 확인하였다. 각 지역변수(Local variables) 중에서는 평균온도와 상대습도, 글로벌 기상변수 중에서는 NINO3 가 뎅기열과 강한 연관성을 갖는 것을 확인 할 수 있었다. 장티푸스의 경우 DMI 변수가 가장 큰 영향을 미쳤다. 총 간염 발생의 경우 각 지방의 상대습도가 가장 높은 연관성을 주는 것을 확인할 수 있었으나 라오스 중앙지역에서는 그 관련성을 확인 할 수 없었다.

주요어: DMI, NINO3, 감염성질환, 간염, 강수량, 뎅기열, 라오스, 습도, 온도, 일반화부가모형, 장티푸스

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Association between Infectious Diseases and Weather Variables in Lao People′s Democratic Republic

국내 만성질환자에서의 독감예방접종과 관련 특성

2014년 2월

서울대학교 보건대학원

보건학과 통계전공

Prima Lydia

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지도교수 김 호

이 논문을 보건학 석사 학위논문으로 제출함
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Prima Lydia의 석사학위논문을 인준함
2014 년 2 월

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Abstract

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Background: Existing studies and models of the effect of climate condition on the incidence of infectious diseases have been conducted to examine the association between infectious diseases and weather variables. Infectious diseases incidences are still high in tropical and subtropical zones, which most of them are developing countries, and remain as major health problems due to economically challenged situations. Our aim is to investigate the association between infectious diseases and weather variable (local and global) in Lao People's Democratic Republic, a tropical and developing country, where infectious diseases are still the major health problem.

Method: We analyzed the incidence of three diseases data (dengue fever, typhoid fever, and total hepatitis) and five weather variables (mean temperature, relative humidity, rainfall, DMI, and NINO3) using Generalized Additive Models (GAMs) analysis, to conduct a fitted model that shows the association between infectious diseases and weather variables.

Conclusion: The association is the strongest in dengue fever, followed by typhoid fever, and total hepatitis. For Lao People's Democratic Republic, both local and global weather variables (mean temperature, relative humidity, and NINO3) showed strong association with dengue fever. For typhoid fever, global weather variable (DMI) showed the strongest association. For total hepatitis, local weather variable (relative humidity) showed the strongest association in Northern and Southern regions but showed no association in Central region.

Key words: Dengue fever, DMI, Generalized Additive Models, Infectious diseases, Lao, NINO3, Rainfall, Relative humidity, Temperature, Total hepatitis, Typhoid fever

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Chapter 1. Introduction

The effect of climate and the environment on infectious diseases has been a subject of debate, speculation, and serious study for centuries (Shape, 1991). Infectious diseases may be classified into two categories based on the mode of transmission: from person to person (through direct contact or droplet exposure) and those spread indirectly through an intervening vector organism (mosquito or tick) or a non-biological physical vehicle (soil or water). Infectious diseases also may be classified by their natural reservoir as anthroponoses (human reservoir) or zoonoses (animal reservoir) (Patz et al. 2003).

Many infectious diseases of humans are restricted to, or more prevalent in, tropical and subtropical zones (Ostfeld, 2009). Infectious diseases incidences are still high in tropical and subtropical zones, which most of them are developing countries, and remain as major health problems due to economically challenged situations.

Dengue fever is a viral illness caused by infection of the dengue virus that spread by the bite of an infected dengue mosquito (usually the *Aedes aegypti* species), and occurs in tropical and sub-tropical areas of the world (CDC). The outbreak of dengue can occur anytime as long as the mosquitos are active, however high temperature and humidity are the conditions that favor the survival of mosquito (WHO). *Aedes aegypti* prefer to lay its eggs in human-made container around homes that collected rainwater. *Aedes aegypti* females will often feed on several persons during a single blood meal and may transmit dengue virus to multiple persons in a short time, so it is common that several members in a household become ill with dengue fever (Gubler, 1998).

Typhoid fever is an infectious disease that is caused by the bacteria *Salmonella enterica* serotype typhi (*S. typhi*) (Bhan, 2005) that spread by eating or drinking contaminated food (Sharma, 2009) and water (Mermin, 1999). Typhoid fever's risk factor are also including poor sanitation (Karkey, 2010) and flooding (Vollaard, 2004). The incidence of typhoid fever has decline in Europe and America as clean water and good sewage system are developed. However, the incidence remains high in developing countries as sanitation and water in those countries are still in poor condition. *S typhi* is restricted to human beings (Bhan, 2005).

Hepatitis is an inflammation of liver, commonly caused by viral infection, with five main hepatitis viruses, type A, B, C, D, and E. Hepatitis A and E typically caused ingestion of contaminated food or water, whereas hepatitis B, C and D usually occur as a result of parenteral contact with infected body fluids, such as receipting of contaminated blood or blood products, invasive medical procedures using contaminated equipment and for hepatitis B transmission from mother to baby at birth, from family member to child, and also by sexual contact (WHO).

The DMI index is an indicator that represent the difference in SST anomaly between the tropical western Indian Ocean (50°E - 70°E, 10°S - 10°N) and the tropical south-eastern Indian Ocean (90°E - 110°E, 10°S - Equator) (Saji, 1999). A positive IOD period is characterized by cooler than normal water in the tropical eastern Indian Ocean and warmer than normal water in the tropical western Indian Ocean and a negative IOD period is characterized by warmer than normal water in the tropical eastern Indian Ocean and cooler than normal water in the tropical western Indian Ocean.

The Nino3 SST anomaly index is an indicator of eastern tropical Pacific El Nino conditions, calculated with SSTs in the box 150°W -

90°W, 5°S – 5°N (NOAA). During El Nino phase, there is a warming in the eastern equator Pacific and during La Nina phase, there is a cooling in the eastern equator Pacific (Lipp, 2002).

Some studies have been conducted to examine the association between infectious diseases and weather variables. A study in China shows that temperature has correlation with changes of spatial and temporal distribution of dengue fever (Bai et al. 2013). A study in Taiwan shows that extreme precipitation events were associated with the occurrence of 8 infectious diseases (including hepatitis A and dengue fever) with lags of 0–70 days (Chen et al. 2012). Study in 14 island nations of the South Pacific shows that there were positive correlations between global climate variable (SOI index) and dengue fever in 10 countries (Hales et al. 1999). A study in Dhaka (Dewan et al. 1998) did not show a strong association between rainfall and typhoid fever however it showed that the risk of the disease is high during monsoon.

Chapter 2. Methods

2-1. Study design and setting

Lao People's Democratic Republic is a landlocked country located in the Indochina Peninsular (Mekong Region). Lao PDR belongs to WHO's Western Pacific region (Kimball, 2008), bordered to the northwest by Myanmar and China, to the east by Vietnam, to the south by Cambodia, and to the west by Thailand. Lao PDR has a tropical monsoon climate which causes significant rainfall and high humidity, with a pronounced rainy season from May through October, a cool dry season from November through February, and a hot dry season in March and April (Savada, 1994). The average annual rainfall in the country is about 1,300 - 3,000 mm and average temperature is 26.5°C.

Fig. 1. Geographical location of Lao People's Democratic Republic
(Source: http://en.wikipedia.org/wiki/Provinces_of_Laos)

Lao People's Democratic Republic can be considered to consist of three geographical regions: northern, central, and southern. This study will cover all three regions in Lao. Geographical location of Lao People's Democratic Republic is shown in Fig. 1, and the list of provinces based on regions is shown in Table 1.

Table 1. Provinces in Lao People's Democratic Republic

Region	Province
Northern	Phôngsali
	Luang Namtha
	Oudômxai
	Bokèo
	Louangphabang
	Houaphan
	Xaignabouli
	Xiangkhouang
Central	Vientiane(CAPITAL)
	Vientiane Province
	Bolikhamxai
	Khammouan
	Savannakhét
Southern	Salavan
	Xékong
	Champasak
	Attapu

2-2. Data collection and processing

All cases of diseases reported from January 2005 to December 2010 were obtained from the Center for Laboratory and Epidemiology Department of Hygiene and Prevention. The cases of diseases were monthly reported by all health post and center, also region hospital to Center for Laboratory and Epidemiology Department of Hygiene and Prevention, Ministry of Health of Lao PDR (Kim, 2011). From 21 diseases available, 3 infectious diseases were selected to this study based on potential association with climate change. The 3 diseases selected are dengue fever (ICD-10, A90), typhoid fever (ICD-10, A01.0), and total hepatitis (ICD-10, B15–B19, K75.9).

All meteorological data were obtain from Department of Meteorology and Hydrology, Ministry of Natural Resources and Environment (Lao PDR). All the data were provided in daily basis and we use the variables as follows: Mean Temperature (°C), Humidity (Mean Humidity of air in %), and Total Daily Rainfall (mm) for each province. Daily weather data was converted into monthly basis. For the analysis data was grouped according to the regions (Northern, Central, and Southern) of Lao PDR.

Daily basis data of DMI and NINO3 was publicly accessible from the National Oceanic and Atmospheric Administration (NOAA), United State Department of Commerce (http://www.noaa.gov/). DMI and NINO3 data was converted into monthly basis data for the purpose of analysis.

2-3. Statistical Analysis

Descriptive analysis and monthly time series approach were calculated for all diseases and weather variables to investigate the distribution of the data and the association between all infectious diseases with weather variables. Pearson correlation and p-value were calculated to examine the significance of the association between diseases and weather variables. Monthly mean incidences were calculated to examine the quality of correlation.

Generalized Additive Models (GAMs) for time series (Wood. 2006) were used to model the simultaneously non-linear structure in the association between monthly diseases data and weather variables. Lag models were used to examine the lag structure of the weather effects with lag up to 6 months for local variables (Mean Temperature (°C), Humidity (%), and Rainfall (mm)). For global weather variables (DMI (Dipole Mode Index in °C) and NINO3 (ENSO index in °C)) lag up to 12 months were used.

Sensitivity Analysis was used to show the sensitivity of the model over small changes into the model. We conducted the sensitivity analysis by omitting a variable from the model and by changing the lag of variables.

The Microsoft Excel and R statistical software was used for the analysis the contributed package MGCV used to fit the GAMs. The MGCV package uses generalized cross-validation to select the degree of freedom for each smooth (non-linear) term (Wood. 2006). The lag models were fit using MGCV and DLNM package.

2-3. Limitation

There was limitation in the data available, especially in disease and meteorological data. The diseases reported just the number of cases and lack more detail clinical information. The quality of the data was not very good especially in the Total Hepatitis cases data. Total hepatitis was used in the analysis because the possibility of association with seasonal variable, especially Hepatitis A (Villar, 2002) and Hepatitis E (Previsani, WHO, 2001). Even though the data available for Hepatitis was not specified by the types, but this analysis was expected to see an association with seasonality.

Another limitation occurred in the meteorological data, where there were substantial missing values. There were some problems in some provinces, especially in the Southern region (et. some values above 100% for Humidity). The limitation in the data made the whole data unstable and not very reliable, but it expected that it could reflect the association.

Chapter 3. Results

Descriptive statistics for all variables are shown in Table. 2. The average numbers of monthly cases of dengue fever from 2005 to 2010 were 104.33, 369.93, and 206.03 for Northern, Central, and Southern region, respectively. These result showed that the cases of dengue fever was the highest in Central region, followed by Southern region, and Northern region has the lowest incidence. For typhoid fever, the average numbers of monthly cases from 2005 to 2010 were 130.51, 61.71, and 1.86 for Northern, Central, and Southern region, respectively. These result showed that the cases of typhoid fever was the highest in Northern region, followed by Central region and the lowest in Southern region. For total hepatitis, the average numbers of monthly cases from 2005 to 2010 were 16.92, 24.43, and 12.08 for Northern, Central, and Southern region, respectively. These result showed that the cases of total hepatitis was the highest in Central region, followed by Northern region and Southern region was the least among all regions.

Average of mean temperatures for Northern, Central, and Southern region from 2005 to 2010 were 23.30°C, 26.64°C, and 27.52°C, respectively. Averages of mean humidity were 75.18%, 74.13%, and 73.26% for Northern, Central, and Southern region from 2005 to 2010, respectively. Average of mean rainfall for Northern, Central, and Southern region from 2005 to 2010 were 23.30mm, 26.64mm, and 27.52mm, respectively. Average of Dipole Mode Index (DMI) and ENSO index (NINO3) from 2005 to 2010 were -0.45°C and 25.74°C, respectively.

Table 2. Descriptive statistics for the study regions from 2005 - 2010

Variable	Northern				Central				Southern			
	Min	Mean	Max	SD	Min	Mean	Max	SD	Min	Mean	Max	SD
Diseases												
Dengue Fever	0.00	104.33	1160.00	184.74	5.00	369.93	2788.00	547.38	0.00	206.03	1567.00	258.91
Typhoid Fever	0.00	130.51	380.00	82.30	0.00	61.71	308.00	59.68	0.00	1.86	11.00	2.83
Total Hepatitis	0.00	16.92	56.00	9.74	0.00	24.43	336.00	38.55	0.00	12.08	38.00	8.07
Weather Variables												
Mean Temp (°C)	17.09	23.30	27.46	2.89	20.57	26.64	30.19	2.36	23.31	27.52	31.09	1.72
Mean RH (%)	59.82	75.18	84.30	6.00	61.19	74.13	86.30	6.96	57.51	73.26	87.83	8.87
Mean Rainfall (mm)	0.31	123.31	386.00	106.98	0.00	193.22	672.62	197.13	0.00	157.06	697.83	173.45
DMI	−1.82	−0.45	1.27	0.64	−1.82	−0.45	1.27	0.64	−1.82	−0.45	1.27	0.64
NINO3	23.17	25.74	28.05	1.28	23.17	25.74	28.05	1.28	23.17	25.74	28.05	1.28

Time series trends were used to examine the trend of all variables (diseases and weather variables). Fig. 2, Fig. 13, and Fig. 14 showed there was increasing of dengue fever cases in three regions in 2010 (Fig. 13 and Fig. 14 were presented in the Appendix). The trend of increasing in mean temperatures was also seen for the last 3 years. Mean rainfall decreased in northern and southern region, but showed an increasing on 2010 in central region. This trend also could be seen in relative humidity trend. There is a slightly decrease in northern and southern region, but showed a slightly increase on 2010 in central region. Fig. 15 (see appendix) showed monthly trend of dengue fever cases from 2005 to 2010. This figure showed that there is an increase in dengue fever cases on rainy season, and showed a decrease on dry season. This figure showed a high quality of correlation between dengue fever and seasonal variables.

Fig. 16, Fig. 17, and Fig 18 (see appendix) showed there was increasing of typhoid cases in all three regions for the last 3 years, which also could be seen in mean temperature trends. In the southern region, Fig. 18 showed an increase in the incidence of typhoid fever after the flooding event in 2009, as flooding is one of the risk factor of the disease (Vollaard, 2004). Fig. 19 (see appendix) showed monthly trend of typhoid fever cases from 2005 to 2010. This figure showed that there is an increase in dengue fever cases on rainy season, and showed a decrease on cool dry season. Typhoid fever showed the least cases on hot dry season. This figure also shows a high quality of correlation between typhoid fever and seasonal variables.

Fig. 20 and Fig. 21 (see appendix) showed an outbreak of total hepatitis cases in 2008 in northern and central region, but in southern region from Fig. 22 (see appendix), the outbreak could be seen in

2007 and there is a slightly increase in the beginning of 2009 and the midyear of 2010. Fig. 23 (see appendix) showed monthly trend of total hepatitis cases from 2005 to 2010. This figure showed that there is no significant increase in monthly total hepatitis cases, but an outbreak of total hepatitis case was shown on November in central region caused by the disease outbreak in November 2008. This figure showed a low quality of correlation between total hepatitis and seasonal variables.

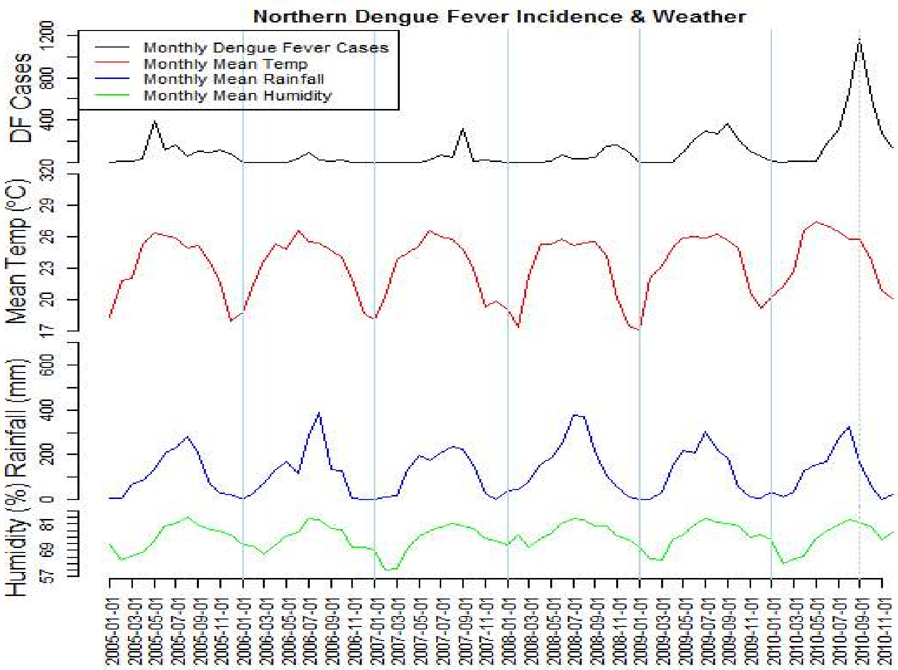

Fig. 2. Time series trend of dengue fever cases, mean temperature (°C), mean rainfall (mm), and mean relative humidity (%) for Northern region from 2005 to 2010.

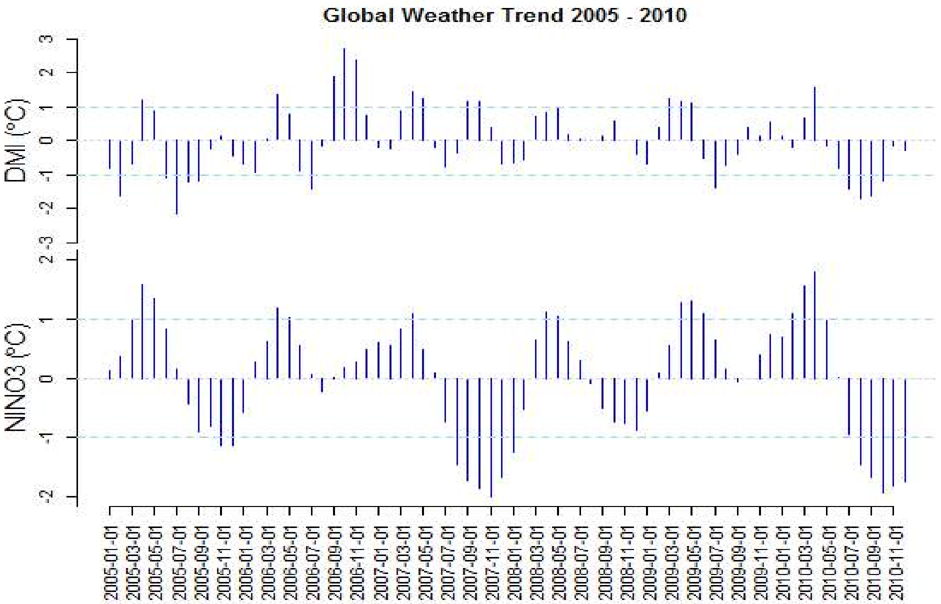

Fig. 3. Standardization-Time series trend of Dipole Mode Index (DMI) and ENSO Index (NINO3), 2005 - 2010

Fig. 3 showed time series trend of Dipole Mode Index (DMI) and ENSO Index (NINO3) from 2005 to 2010. Dipole Mode Index (DMI) showed negative value, characterized by warmer than normal water in the tropical eastern Indian Ocean and cooler than normal water in the tropical western Indian Ocean. In reverse, Dipole Mode Index (DMI) showed positive value, characterized by cooler than normal water in the tropical eastern Indian Ocean and warmer than normal water in the tropical western Indian Ocean. As for Lao PDR, negative phase means warmer weather and heavy rainfall, in contrast positive phase means colder weather and can lead to dry season (low rainfall). ENSO Index (NINO3) showed that there are some El Niño conditions (positive value, warmer) and La Niña (negative value, cooler).

3-1. Dengue fever

Table 3 showed Pearson correlation between dengue fever and local weather variables (mean temperature, relative humidity, and rainfall) for all regions. Table 4 showed Pearson correlation between dengue fever and global weather variables (DMI and NINO3) for all regions. The tables showed that for all local weather variables, maximum lags are up to 4 months, but for global weather variables, DMI and NINO3 showed different pattern. DMI has correlation at up to 2 months as NINO3 up to 7 months. This result showed that DMI has faster effect on dengue fever that NINO3.

Table 3 and table 4 showed the significantly correlation between dengue fever and weather variables (p-value < 0.05). Lag models were used to examine the lag structure of the weather effects, using GAM (Generalized Additive Model) analysis. For local weather variables lagged up to 6 months data were used, and up to 12 months (a year) for global weather variables. Each region has different demographic characteristic and weather condition, so the analysis will be conducted partly. Model that have the best fit for describing association between dengue fever and weather variables are,

$$\begin{aligned} f(dengue\_fever)_{north} &= \beta_0 + s(time, df) + s(meantemp_{-4}, df) + s(humid_{-4}, df) + s(rain_{-4}, df) + s(dmi_{-2}, df) \\ &+ s(nino3_{-5}, df) \end{aligned}$$

for northern region,

$$
\begin{aligned}
f(dengue\_fever)_{central} & \\
&= \beta_0 + s(time, df) + s(meantemp_{-3}, df) + s(humid_{-3}, df) + s(dmi_{-12}, df) \\
&+ s(nino3_{-5}, df)
\end{aligned}
$$

for central region, and

$$
\begin{aligned}
f(dengue\_fever)_{south} & \\
&= \beta_0 + s(time, df) + \beta_1 meantemp_{-4} + s(humid_{-1}, df) + s(rain_{-1}, df) + s(dmi_{-5}, df) \\
&+ s(nino3_{-5}, df)
\end{aligned}
$$

for southern region.

Here some of the models are Mixed Generalized Additive Model, with linear correlation for some variables. In northern region, all variables have non-linear correlation with dengue fever incidence, with mean temperature lag 4 months, relative humidity lag 4 months, rainfall lag 4 months, DMI lag 2 months, and NINO3 lag 5 months. In central region, all significant variables have non-linear correlation with dengue fever, with mean temperature lag 3 months, relative humidity lag 3 months, Dipole Mode Index (DMI) lag 12 months, and ENSO index (NINO3) lag 5 months as variables. Rainfall showed no significant association with dengue fever in central region. In southern region, relative humidity lag 1 month, rainfall lag 1 month, Dipole Mode Index (DMI) lag 5 months and ENSO index (NINO3) lag 5 months have non-linear correlation, while mean temperature lag 4 months has linear correlation with dengue fever. The comparison between the model and the observed (the count of incidence) for dengue fever in three regions were presented in Fig. 24 (see appendix).

Table 3. Pearson correlation between dengue fever and local weather variables (without and with lag)

	Northern			Central			Southern		
time-lag (months)	Mean temperature	Relative humidity	Rainfall	Mean temperature	Relative humidity	Rainfall	Mean temperature	Relative humidity	Rainfall
0	0.281*	0.425*	0.249*	0.240*	0.532*	0.464*	0.171	0.380*	0.259*
1	0.416*	0.402*	0.414*	0.402*	0.517*	0.472*	0.317*	0.292*	0.256*
2	0.453*	0.273*	0.429*	0.497*	0.327*	0.326*	0.416*	0.106	0.130
3	0.437*	0.062	0.281*	0.495*	0.056	0.135	0.452*	−0.104	−0.027
4	0.299*	−0.165	0.124	0.385*	−0.223	−0.075	0.407*	−0.306*	−0.190
5	0.094	−0.405*	−0.072	0.146	−0.395*	−0.228	0.221	−0.432*	−0.288*
6	−0.144	−0.523*	−0.279*	−0.172	−0.455*	−0.352*	−0.029	−0.461*	−0.362*

* Statistically significant

Table 4. Pearson correlation between dengue fever and global weather variables (without and with lag)

	Northern		Central		Southern	
time-lag (months)	DMI	NINO3	DMI	NINO3	DMI	NINO3
0	-0.380*	-0.285*	-0.372*	-0.015	-0.166	-0.003
1	-0.294*	-0.110	-0.216	0.169	-0.160	0.037
2	-0.138	0.091	-0.020	0.312*	-0.110	0.127
3	-0.027	0.291*	0.013	0.362*	-0.073	0.197
4	0.059	0.400*	-0.014	0.334*	-0.007	0.258*
5	0.117	0.406*	0.035	0.243*	0.017	0.292*
6	0.100	0.310*	0.007	0.135	0.039	0.282*
7	0.120	0.156	-0.055	0.025	0.090	0.260*
8	0.100	-0.016	-0.100	-0.053	0.133	0.194
9	0.134	-0.150	-0.091	-0.085	0.113	0.142
10	0.010	-0.216	-0.111	-0.035	0.050	0.076
11	-0.078	-0.206	-0.203	0.062	-0.009	0.043
12	-0.107	-0.103	-0.186	0.182	-0.054	0.048

* Statistically significant

In northern region, mean temperature showed a rapid increase of cases for mean temperature (lag4) above 26°C. The same pattern also could be seen in ENSO index (NINO3) (lag5), which showed an increase of cases above 26°C. Fig. 4 also showed that higher number of cases associated to lower relative humidity and higher rainfall.

In central region, mean temperature showed a rapid increase of cases for mean temperature (lag3) above 27°C. The same pattern also could be seen in ENSO index (NINO3) (lag5), which showed a rapid increase of cases above 27°C. Relative humidity showed a negative correlation with dengue fever, where lower relative humidity (lag3) related to higher cases of dengue fever. In southern region, ENSO index (NINO3) (lag5) showed a rapid increase of cases for mean temperature (lag3) above 27°C. Relative humidity (lag1) showed a negative correlation with dengue fever, where lower relative humidity related to higher cases of dengue fever.

In central region, dipole mode index (DMI) (lag12) showed a significant correlation (p-value < 0.05), but smooth model that shown in Fig. 5 showed that there is no clear correlation between Dipole Mode Index (DMI) with dengue fever. The same result also could be seen in southern region. Rainfall showed a significant correlation (p-value < 0.05), but then model in Fig. 6 showed that there is no clear correlation between rainfall with dengue fever. In southern region, mean temperature showed a positive linear correlation with the incidence of dengue fever.

In three regions, mean temperature, relative humidity, and ENSO Index (NINO3) showed a strong correlation with dengue fever. Mean temperature and NINO3 showed a positive correlation (higher mean temperature and higher value of NINO3 resulted in higher number of incidence of dengue fever) and relative humidity showed negative correlation (lower relative humidity resulted in higher number of incidence of dengue fever). Since the survival of dengue mosquito prefers a high temperature (WHO), it is expected to see that higher temperature showed a high incidence of dengue. It explained why the incidence of cases was higher in higher temperature. Relative humidity decreased as the temperature increased (Valsson, 2011) explain the increase of incidence of dengue fever as the humidity lower.

The lag structure showed that local weather variables (mean temperature and relative humidity) have faster effect for the incidence of dengue fever than global variable (NINO3), except for DMI affect in northern region, where lag 2 months of DMI have a significant association with incidence of dengue fever, while all three local variables showed significant affect with lag 4 months.

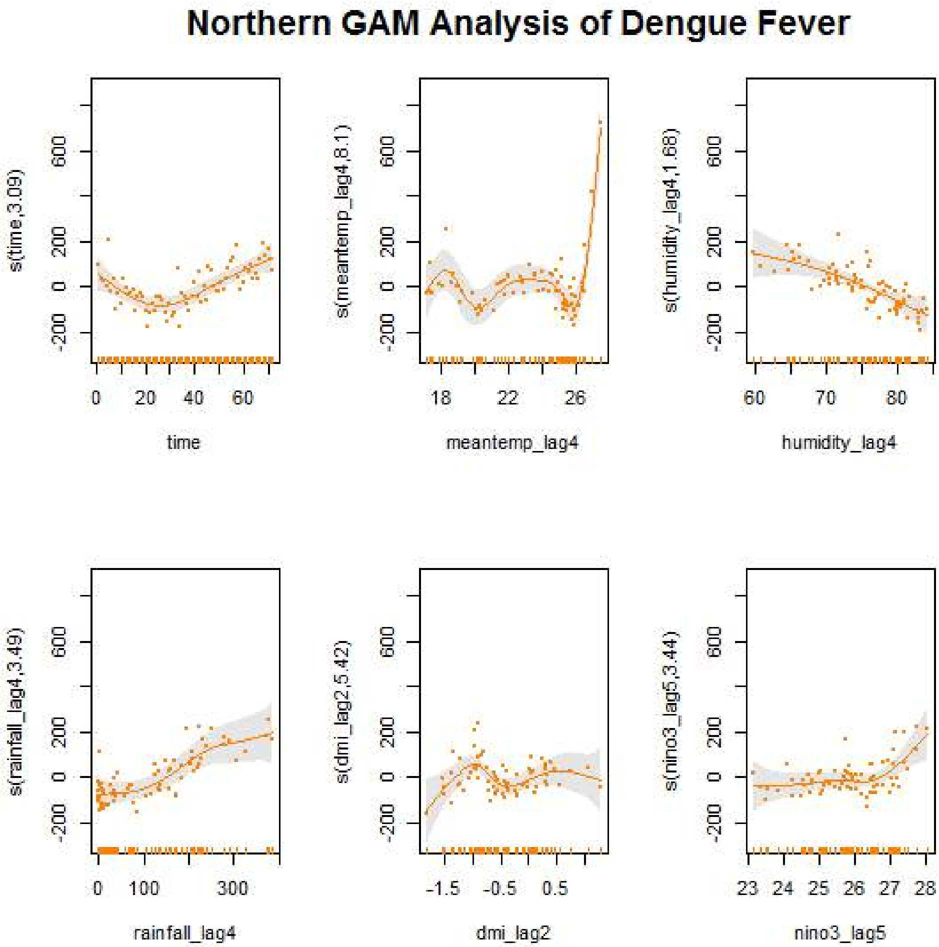

Fig. 4. The estimate of the smooth models for dengue fever in Northern region.

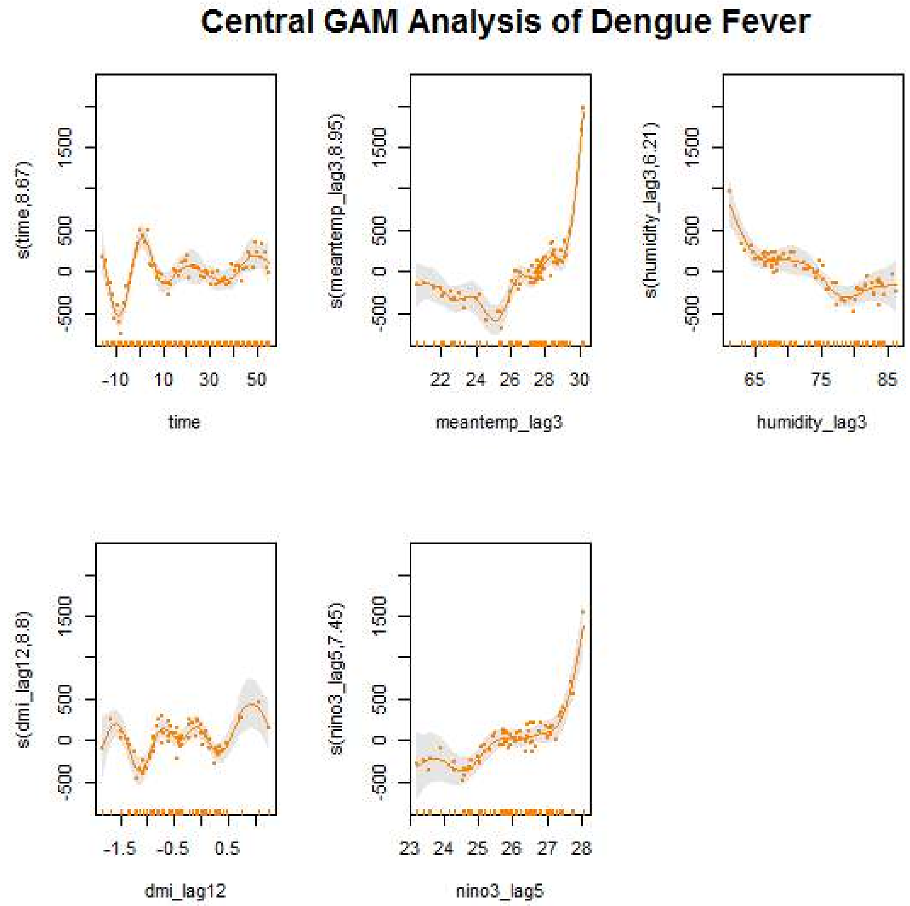

Fig.5. The estimate of the smooth models for dengue fever in Central region.

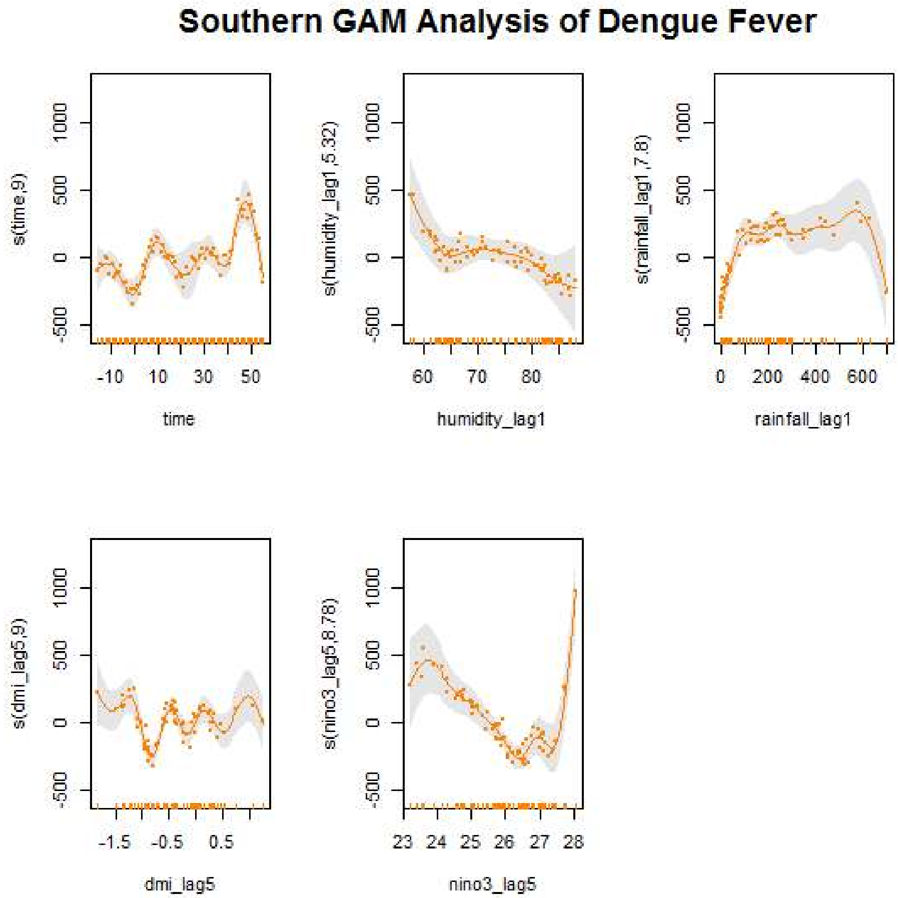

Fig. 6. The estimate of the smooth models for dengue fever in Southern region.

3-2. Typhoid fever

Table 5 showed Pearson correlation between typhoid fever and local weather variables (mean temperature, relative humidity, and rainfall) for all regions. Table 6 showed Pearson correlation between typhoid fever and global weather variables (DMI and NINO3) for all regions. In Northern and Central regions, we can see correlation between typhoid incidence and local weather variables, but the correlation could not be seen in Southern region. For global weather variables, DMI and NINO3 showed correlation with typhoid fever with a faster effect from DMI than NINO3 in Northern and Central regions. But in Southern region, DMI showed no correlation with dengue fever, but NINO3 showed a significant correlation with lagged (4 - 7 months).

Table 5 and table 6 showed the significantly correlation between typhoid fever and weather variables (p-value < 0.05). Lag models were used to examine the lag structure of the weather effects, using GAM Analysis. Each region has different demographic characteristic and weather condition, so the analysis will be conducted partly. Model that have the best fit for describing association between typhoid fever and weather variables are,

$$f(typhoid\_fever)_{north} = \beta_0 + s(time, df) + s(meantemp_0, df) + \beta_1 humid_0 + s(rain_0, df) + s(dmi_0, df) + s(nino3_{-8}, df)$$

for northern region,

$$f(typhoid\_fever)_{central} = \beta_0 + s(time, df) + s(meantemp_{-2}, df) + s(humid_{-2}, df) + s(rain_{-2}, df) + s(dmi_0, df) + s(nino3_{-2}, df)$$

for central region, and

$$f(typhoid\_fever)_{south} = \beta_0 + s(time, df) + s(meantemp_{-3}, df) + \beta_1 dmi_{-12} + s(nino3_{-5}, df)$$

for southern region.

Here some of the models are Mixed Generalized Additive Model, with linear correlation seen in some variables. In northern region, mean temperature, rainfall, Dipole Mode Index (DMI) and ENSO index (NINO3) lag 8 months have non-linear correlation, while relative humidity has positive linear correlation with typhoid fever. In central region, all variables have non-linear correlation with typhoid fever, with mean temperature lag 2 months, relative humidity lag 2 months, rainfall lag 2 months, Dipole Mode Index (DMI), and ENSO index (NINO3) lag 2 months. In southern region, mean temperature lag 3 months and ENSO index (NINO3) lag 5 months have non-linear correlation with typhoid fever, while Dipole Mode Index (DMI) lag 12 months has negative linear correlation with typhoid fever. The comparison between the model and the observed (the count of incidence) for typhoid fever in three regions were presented in Fig. 25 (see appendix).

In northern region, mean temperature showed an increase of cases for mean temperature until 25°C but then showed decreasing. Dipole Mode Index (DMI) showed a decrease of cases of typhoid fever as the value increased. Rainfall and ENSO index (NINO3) lag 8 months showed a significant correlation (p-value $<$ 0.05) with typhoid fever but Fig. 7 showed that there is no clear correlation between both variable and the incidence of typhoid fever, but rainfall showed a slightly negative association. In central region, Dipole Mode Index (DMI) also showed a decrease of cases of typhoid fever as the value increase. Relative humidity lag 2 months and rainfall lag 2 months showed a significant correlation with typhoid fever but Fig. 8 showed that there is no clear correlation between both variable and the incidence of typhoid fever. Mean temperature lag 2 months did not show correlation for temperature below 29°C but then a rapid increase was occurred. A similar pattern could be seen in ENSO index (NINO3) lag 2 months, where the higher value associates to a slight increase of dengue fever incidence until 27°C, but then a rapid increase could be observed.

In southern region, mean temperature lag 3 months and ENSO index (NINO3) lag 5 months showed a significant correlation (p-value $<$ 0.05) with typhoid fever but Fig. 20 showed that there is no clear correlation between both variable and the incidence of typhoid fever. In three regions, Dipole Mode Index (DMI) showed a strong negative correlation with typhoid fever. It means lower Dipole Mode Index (DMI) resulted in higher number of cases of typhoid fever. Lower DMI affect for warmer temperature and heavy rainfall in Lao PDR.

Typhoid fever is a disease that related to clean water and sanitation (Bhan, 2005), so it explained the increased of typhoid incidence with the heavy rain as in less developed country like Lao PDR, the sanitation is poor. Flooding also increase the risk of typhoid fever (Vollaard, 2004), as the water condition is poor in that condition. It explained the increased in incidence of typhoid in Southern region after the flood event in 2009.

Table 5. Pearson correlation between typhoid fever and local weather variables (without and with lag)

time-lag (months)	Northern			Central			Southern	
	Mean temperature	Relative humidity	Rainfall	Mean temperature	Relative humidity	Rainfall	Mean temperature	Relative humidity
0	0.331*	0.483*	0.335*	0.325*	0.384*	0.294*	0.106	−0.012
1	0.454*	0.434*	0.407*	0.347*	0.253*	0.236*	0.111	0.005
2	0.487*	0.265*	0.434*	0.310*	0.037	0.096	0.109	−0.015
3	0.436*	0.045	0.330*	0.266*	−0.165	−0.049	0.122	0.013
4	0.281*	−0.219	0.082	0.116	−0.271*	−0.156	0.155	−0.024
5	0.012	−0.375*	−0.094	−0.073	−0.284*	−0.251*	0.110	−0.020
6	−0.221	−0.435*	−0.217	−0.254*	−0.314*	−0.273*	0.061	−0.042

* Statistically significant

Table 6. Pearson correlation between typhoid fever and global weather variables (without and with lag)

time-lag (months)	Northern		Central		Southern	
	DMI	NINO3	DMI	NINO3	DMI	NINO3
0	−0.380*	−0.285*	−0.372*	−0.015	−0.166	−0.003
1	−0.294*	−0.110	−0.216	0.169	−0.160	0.037
2	−0.138	0.091	−0.020	0.312*	−0.110	0.127
3	−0.027	0.291*	0.013	0.362*	−0.073	0.197
4	0.059	0.400*	−0.014	0.334*	−0.007	0.258*
5	0.117	0.406*	0.035	0.243*	0.017	0.292*
6	0.100	0.310*	0.007	0.135	0.039	0.282*
7	0.120	0.156	−0.055	0.025	0.090	0.260*
8	0.100	−0.016	−0.100	−0.053	0.133	0.194
9	0.134	−0.150	−0.091	−0.085	0.113	0.142
10	0.010	−0.216	−0.111	−0.035	0.050	0.076
11	−0.078	−0.206	−0.203	0.062	−0.009	0.043
12	−0.107	−0.103	−0.186	0.182	−0.054	0.048

* Statistically significant

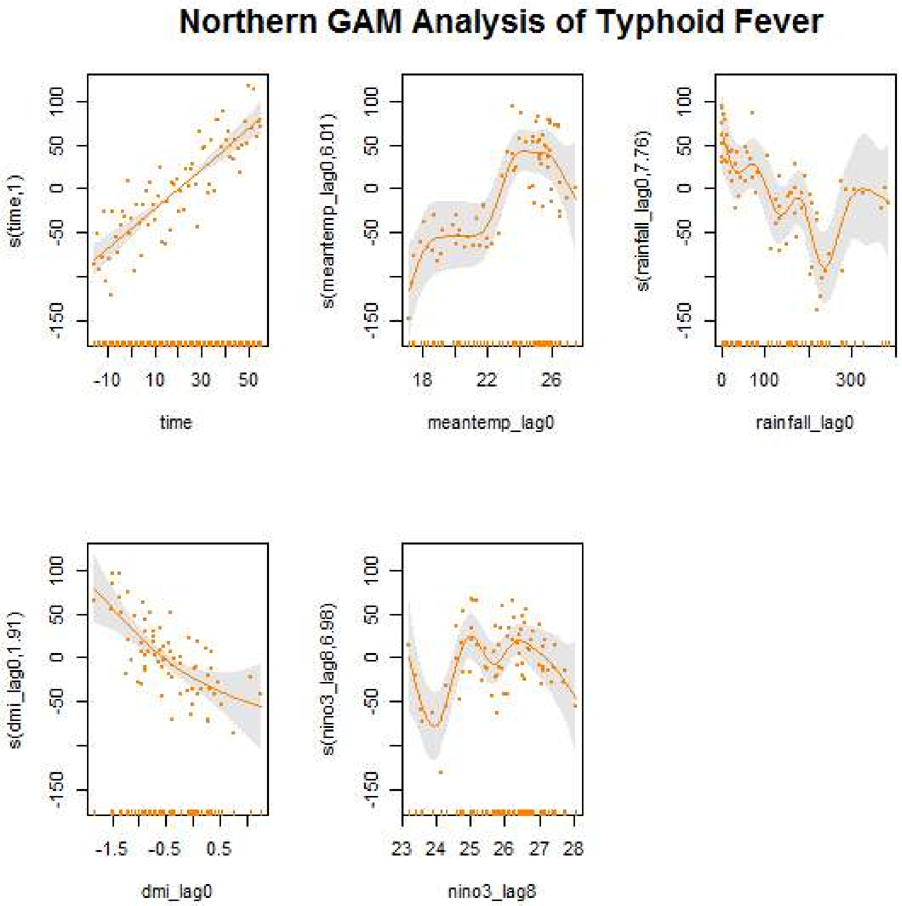

Fig. 7. The estimate of the smooth models for typhoid fever in Northern region.

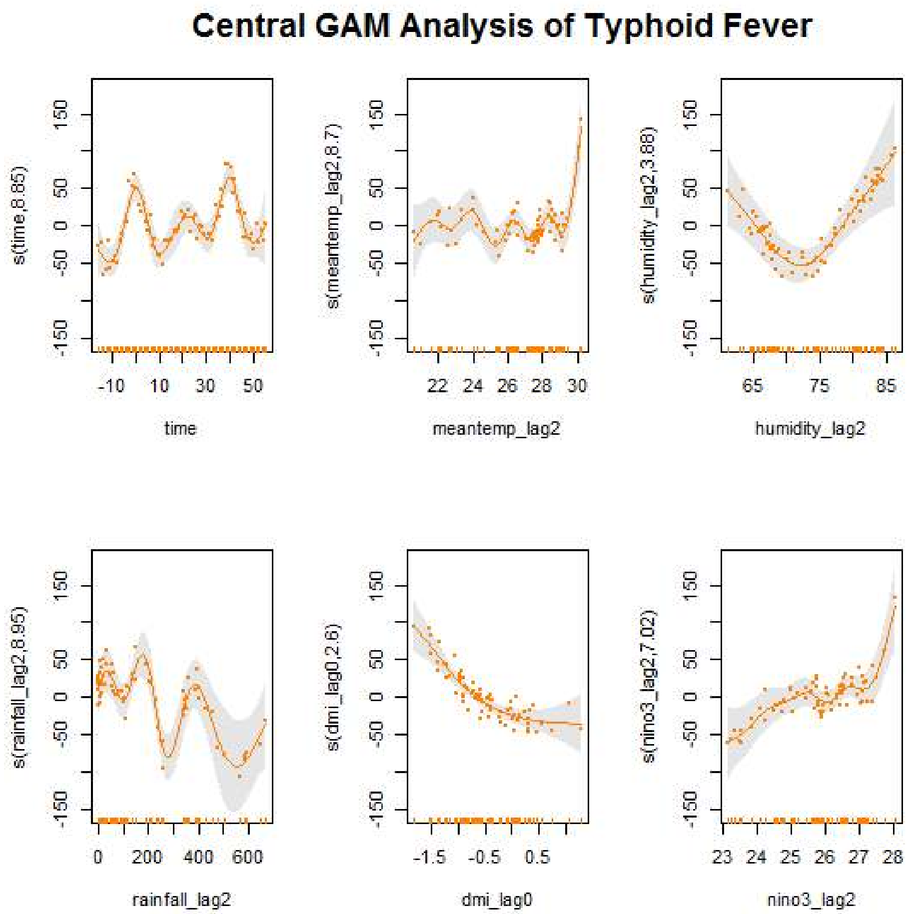

Fig. 8. The estimate of the smooth models for typhoid fever in Central region.

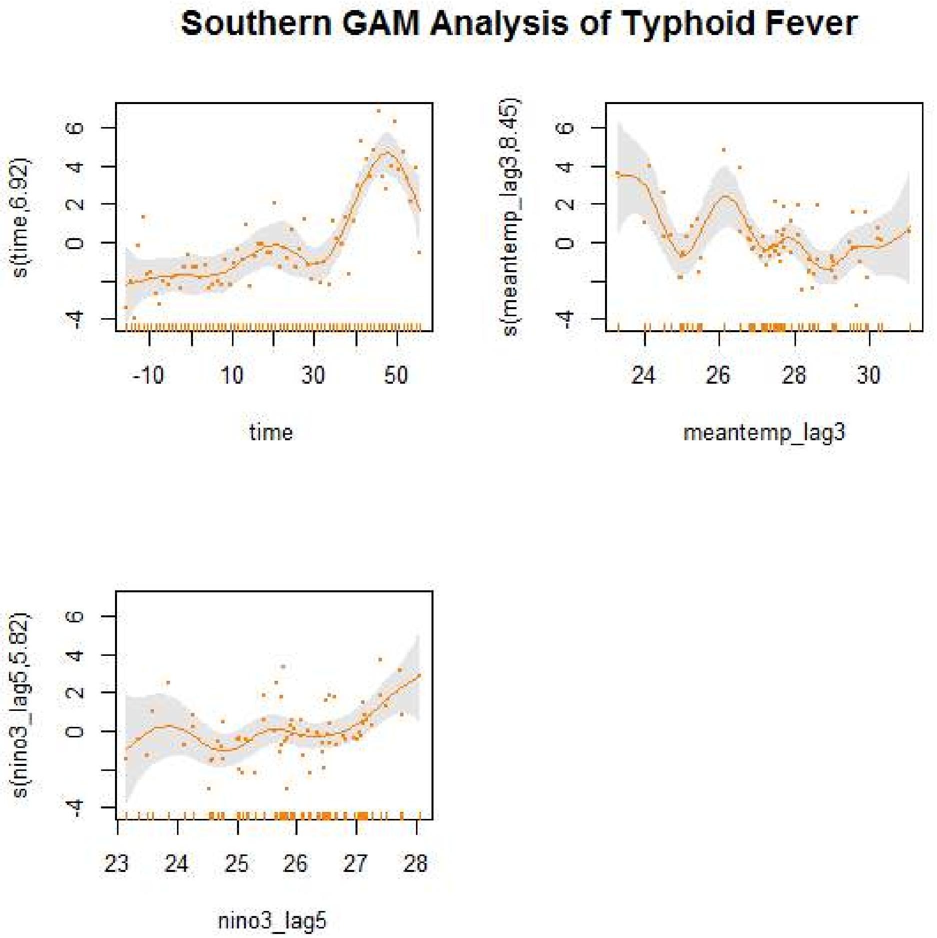

Fig. 9. The estimate of the smooth models for typhoid fever in Southern region.

3-3. Total hepatitis

Table 7 showed Pearson correlation between total hepatitis and local weather variables (mean temperature, relative humidity, and rainfall) for all regions. Table 8 showed Pearson correlation between total hepatitis and global weather variables (DMI and NINO3) for all regions. The result showed that local weather variables have correlation with incidence of hepatitis in Northern region. Central and Southern regions did not show the correlation. For global weather variables, NINO3 showed correlation (lag 9 to 12 months) in Northern region and Central region (lag 11 to 12 months). In Southern region DMI showed correlation with incidence of hepatitis.

Table 7 and table 8 showed the significantly correlation between total hepatitis and weather variables (p-value < 0.05). Lag models were used to examine the lag structure of the weather effects, using GAM Analysis. Each region has different demographic characteristic and weather condition. Model that have the best fit for describing association between total hepatitis and weather variables are,

$$f(tot\_hep)_{north} = \beta_0 + \beta_1 humid_{-1} + s(rain_{-1}, df) + \beta_2 nino3_{-9}$$

for northern region,

$$f(tot\_hep)_{central} = \beta_0 + s(meantemp_0, df) + s(nino3_{-9}, df)$$

for central region, and

$$f(tot\_hep)_{south} = \beta_0 + s(time, df) + \beta_1 humid_0 + s(rain_0, df) + s(dmi_{-3}, df) + s(nino3_{-1}, df)$$

for southern region.

Table 7. Pearson correlation between total hepatitis and local weather variables (without and with lag)

time-lag (months)	Northern			Central			Southern	
	Mean temperature	Relative humidity	Rainfall	Mean temperature	Relative humidity	Rainfall	Mean temperature	Relative humidity
0	0.108	0.354*	0.240*	−0.060	−0.005	−0.029	−0.041	0.064
1	0.283*	0.406*	0.279*	0.102	0.063	0.001	0.072	0.009
2	0.356*	0.256*	0.354*	0.096	0.115	0.114	0.151	0.035
3	0.264*	0.250*	0.415*	0.053	0.138	0.093	−0.038	0.028
4	0.171	0.003	0.193	0.023	0.139	0.224	−0.031	0.064
5	−0.012	−0.077	0.006	−0.003	0.148	0.227	−0.083	0.092
6	−0.156	−0.183	−0.089	−0.006	0.048	0.044	−0.014	0.075

* Statistically significant

Table 8. Pearson correlation between total hepatitis and global weather variables (without and with lag)

time-lag (months)	Northern		Central		Southern	
	DMI	NINO3	DMI	NINO3	DMI	NINO3
0	−0.084	−0.157	−0.015	−0.086	0.070	−0.201
1	−0.062	−0.078	0.064	−0.063	0.251*	−0.156
2	−0.004	0.026	0.035	−0.026	0.312*	−0.097
3	−0.034	0.108	−0.001	0.024	0.128	−0.106
4	−0.062	0.143	−0.026	0.057	−0.032	−0.077
5	−0.088	0.099	0.010	0.091	0.055	0.008
6	0.019	0.060	0.129	0.144	0.302*	0.111
7	0.108	−0.028	0.131	0.135	0.426*	0.179
8	0.092	−0.192	0.103	0.046	0.407*	0.182
9	0.038	−0.360*	−0.036	−0.119	0.206	0.132
10	0.015	−0.418*	−0.074	−0.213	−0.045	0.096
11	−0.054	−0.398*	−0.069	−0.266*	0.001	0.089
12	−0.004	−0.307*	0.051	−0.297*	0.184	0.129

* Statistically significant

Here some of the models are Mixed Generalized Additive Model, with linear correlation for some variables. In northern region, rainfall lag 1 month have non-linear correlation, while relative humidity lag 1 month and ENSO index (NINO3) lag 9 months have linear correlation with total hepatitis. In central region, mean temperature and ENSO index (NINO3) lag 9 months have non-linear correlation with total hepatitis. In southern region, rainfall, Dipole Mode Index (DMI) lag 3 months, and ENSO index (NINO3) lag 1 month have non-linear correlation, while relative humidity has linear correlation with total hepatitis. The comparison between the model and the observed (the count of incidence) for total hepatitis in three regions were presented in Fig. 26 (see appendix).

In northern region (Fig. 10), humidity lag 1 month showed an increase of cases of total hepatitis. Rainfall lag 1 month and ENSO index (NINO3) lag 9 months showed a negative correlation (lower rainfall and NINO3 resulted in higher number of cases of total hepatitis). In central region, mean temperature and ENSO index (NINO3) lag 9 months showed a significant correlation with total hepatitis but Fig. 11 showed that there is no clear correlation between both variable and the incidence of total hepatitis. In southern region, humidity showed an increase of cases of total hepatitis. Dipole Mode Index (DMI) lag 3 months showed a slight increase. Rainfall showed a slightly decrease and ENSO index (NINO3) lag 1 month showed a significant correlation with total hepatitis but Fig. 12 showed that there is no clear correlation between the variable and the incidence of total hepatitis.

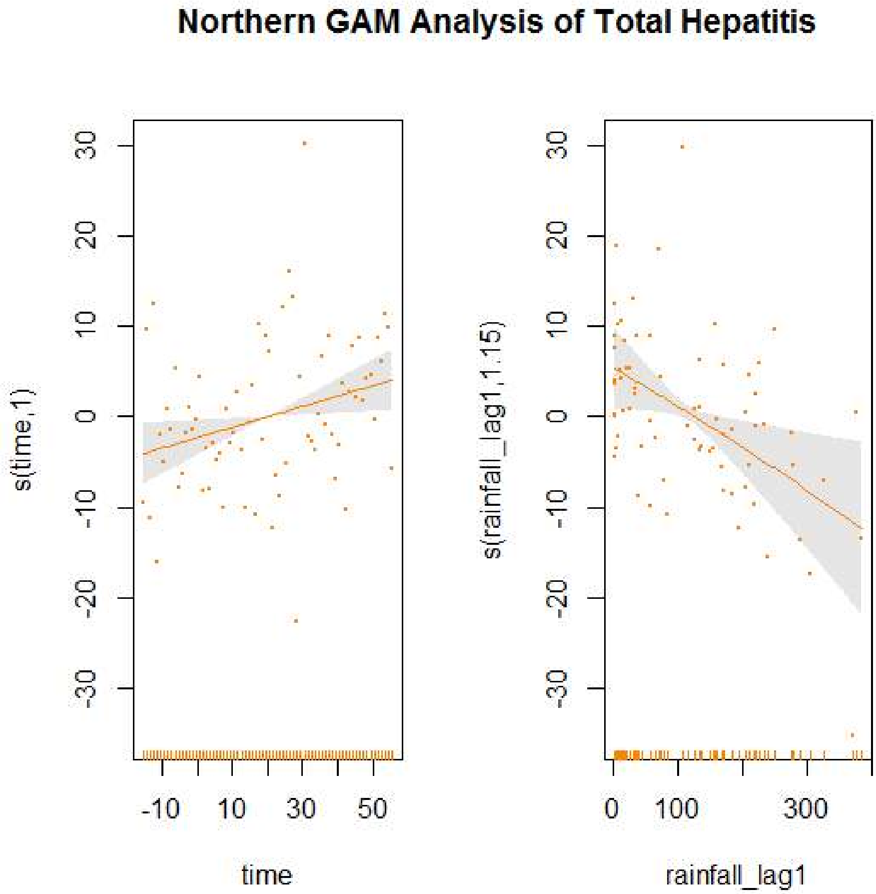

Fig. 10. The estimate of the smooth models for total hepatitis in Northern region.

In central region, there is no clear association between weather variables and total hepatitis. For Northern and Southern region, rainfall and relative humidity has association with total hepatitis. Relative humidity has positive correlation (higher relative resulted in higher number of cases of total hepatitis) while rainfall has negative correlation (higher rainfall resulted in lower number of cases of total hepatitis).

Only hepatitis type A and type E has a seasonal pattern. Limitation in this analysis is the data was not separated by types, but total hepatitis incidence. This could lead to different result than expected. It was showed in Brazil (Villar, 2002) that incidence of hepatitis A is increased in rainy season, but this analysis showed the reversed result. Also for hepatitis E, there was an increase of incidence in late winter and spring in Hongkong (Department of Health, Hongkong, 2011).

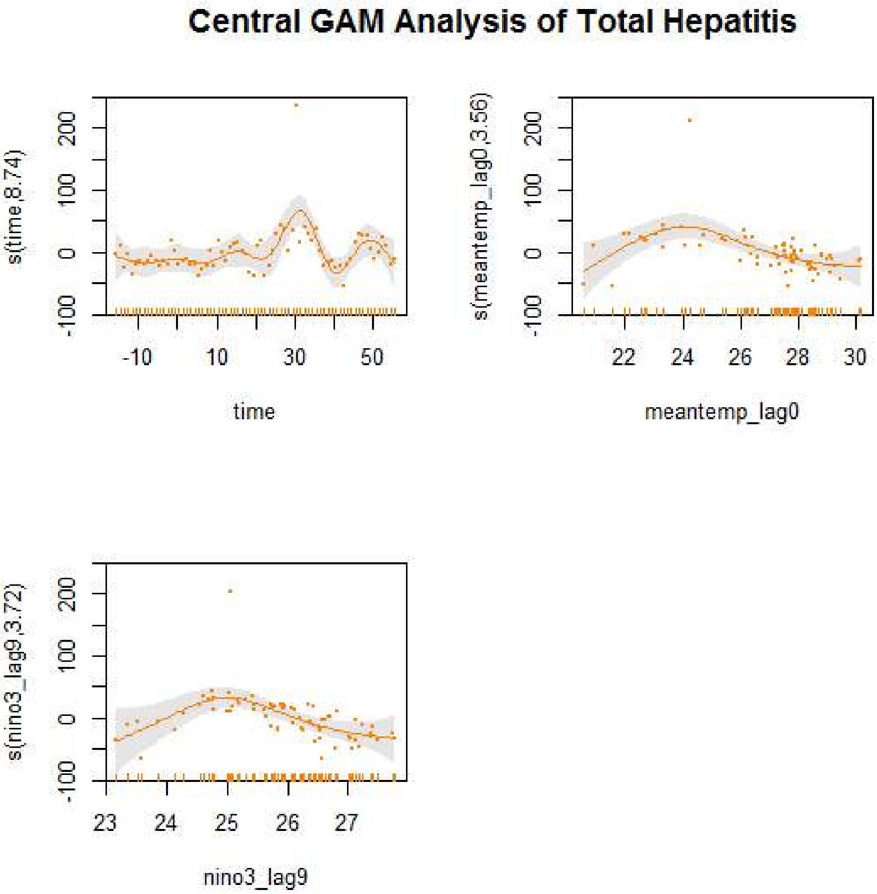

Fig. 11. The estimate of the smooth models for total hepatitis in Central region.

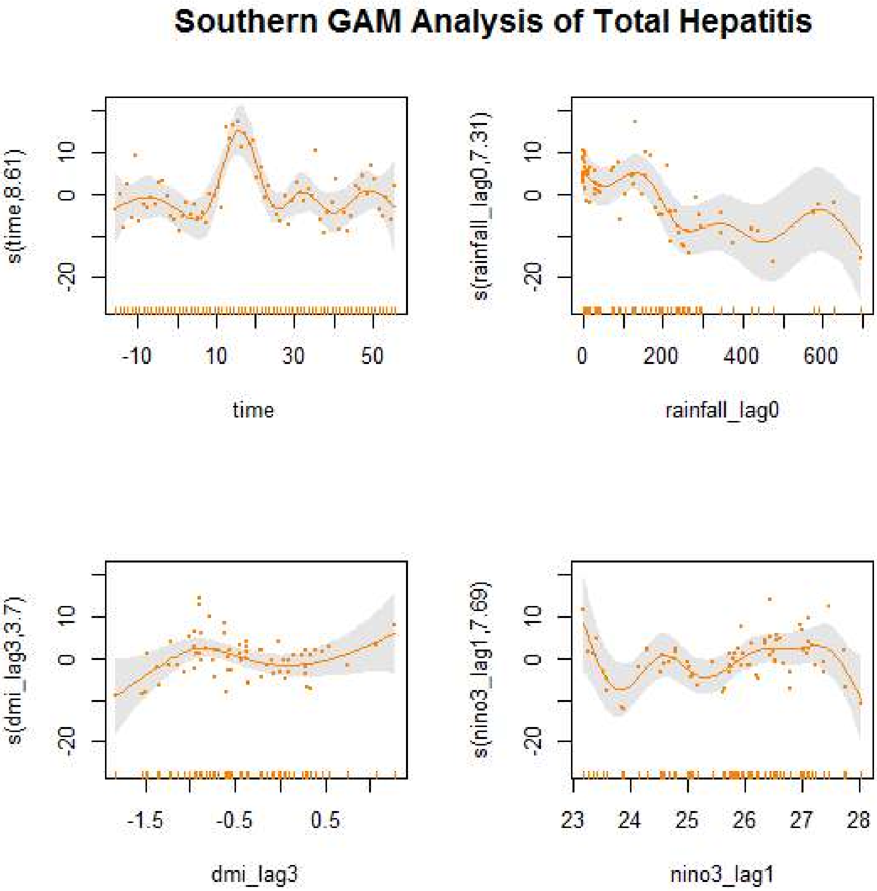

Fig. 12. The estimate of the smooth models for total hepatitis in Southern region.

3-4 Sensitivity analysis

Sensitivity Analysis was used to show the sensitivity of the model over small changes into the model. We conducted the sensitivity analysis by omitting a variable from the model and by changing the lag of variables, by comparing the Standard Error (SE) values. The sensitivity analysis showed that the models were not very sensitive for a small change. The values of SE showed some differences (see tables in appendix), but as the data used are monthly basis, the differences are understandable (as the weather can change enormously over months).

Chapter 4. Discussion

Study in Taiwan (Chen et al. 2012) showed association between infectious diseases and weather variable. Study in Taiwan showed that dengue fever has a strong association with precipitation (rainfall) whereas in this study dengue fever has a strong association with mean temperature and relative humidity, but association with rainfall was not clear. As for Hepatitis A in Taiwan study, the association with precipitation (rainfall) showed statistically insignificant, but this study showed otherwise. These differences might be the consequence of differences in climate and weather condition between two countries.

Study in Puerto Rico (Johansson et al. 2009) also showed a strong and consistent association between temperature, precipitation, and dengue. Moreover they also stated that these associations depend on local characteristics and have a biological interpretation.

Study in Columbia (Poveda et al. 2000) showed a strong association between dengue fever and El Niño, where the outbreak in dengue fever occurred during El Niño event. This study also showed a strong association between dengue fever and El Niño event, where the outbreak of dengue fever occurred during high value of ENSO index (NINO3), which is means the occurring El Niño with lag 5 months.

A study in Dhaka (Dewan et al. 1998) showed that the risk of typhoid fever is high during monsoon. But this study did not show a strong association between rainfall and typhoid fever. This study showed association between typhoid fever and DMI index, where the incidence increase in the negative IOD, which means warmer and heavy rainfall.

Study in association between weather variable and hepatitis A showed that the increase of incidence during hot temperature with heavy rainfall (Villar, 2002). There is also association between hepatitis E and rainfall, where the outbreak was occurred following monsoon rain (Previsani, 2001). This study showed association between rainfall and humidity and total hepatitis, but showed a reversed result. It might be caused by the incidence of other types of hepatitis.

Chapter 5. Conclusion

This study demonstrates that there is association between the incidences of infectious disease and weather variables, local and/or global weather variable. Among three diseases that have been analyzed, dengue fever had the strongest association with weather variables, mean temperature, relative humidity, and ENSO index (NINO3). The association occurred in all three regions. The result also showed that global weather variable (NINO3) effects on the incidence of dengue fever slower than local weather variable (mean temperature and relative humidity).

There is association between typhoid fever and mean temperature, relative humidity, rainfall, and ENSO index (NINO3) but the strongest association occurred between Dipole Mode Index (DMI) and typhoid fever. The association occurred in all three regions. For Total Hepatitis, the association between relative humidity and the disease occurred in northern and southern region, but show no association in central region.

From the result, we conclude that the association between infectious diseases and weather variables in Lao People's Democratic Republic varied in different diseases. For dengue fever, both local and global weather variables showed a strong association, where the effect of global weather variable (NINO3) to the incidence of dengue fever slower than local weather variable (mean temperature and relative humidity). For typhoid fever, global weather variable (DMI) showed the strongest association with the disease. For total hepatitis, local weather variable (relative humidity) showed the strongest association with the disease, but not in all regions.

The difference association between diseases is cause by the biological factors for each disease. *Aedes aegepty* mosquito preferred high temperature and humidity, effect on the outbreak of dengue fever during high temperature. Typhoid fever is a disease caused by food and water contamination that showed an outbreak during rainy season. Hepatitis is also related to heavy rainfall. As shown in some previous studies, the association of infectious disease and weather are differed between diseases.

This variation in association also differed between regions. For dengue fever, as the *Aedes aegepty* prefer high temperature and humidity, the increase of disease incidence occurred in a region with higher temperature. This explains the incidence of dengue fever in central region and southern region are higher than southern region.

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Appendix

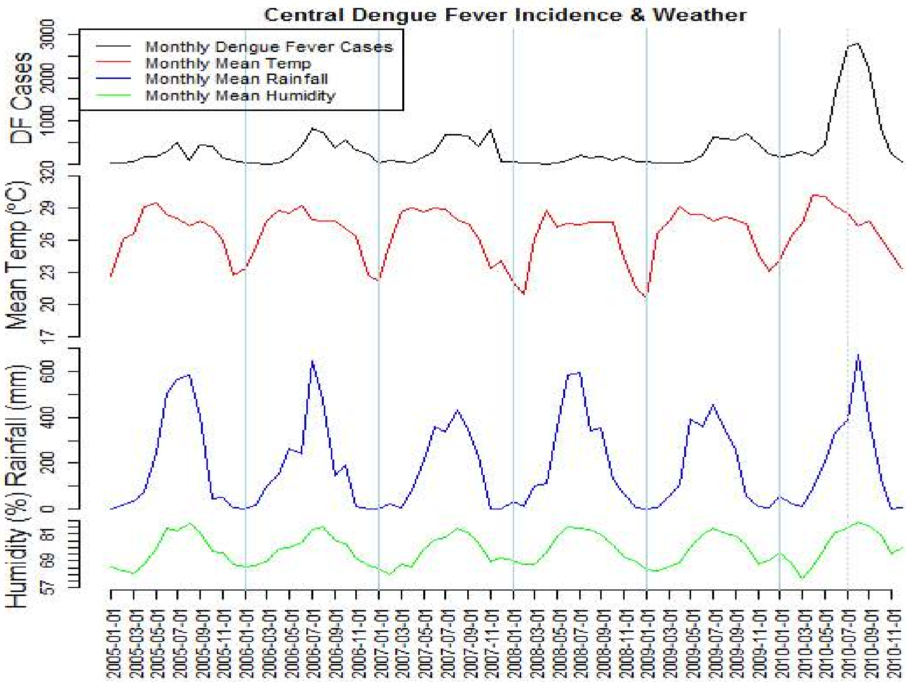

Fig. 13. Time series trend of dengue fever cases, mean temperature (°C), mean rainfall (mm), and mean relative humidity (%) for Central region from 2005 to 2010.

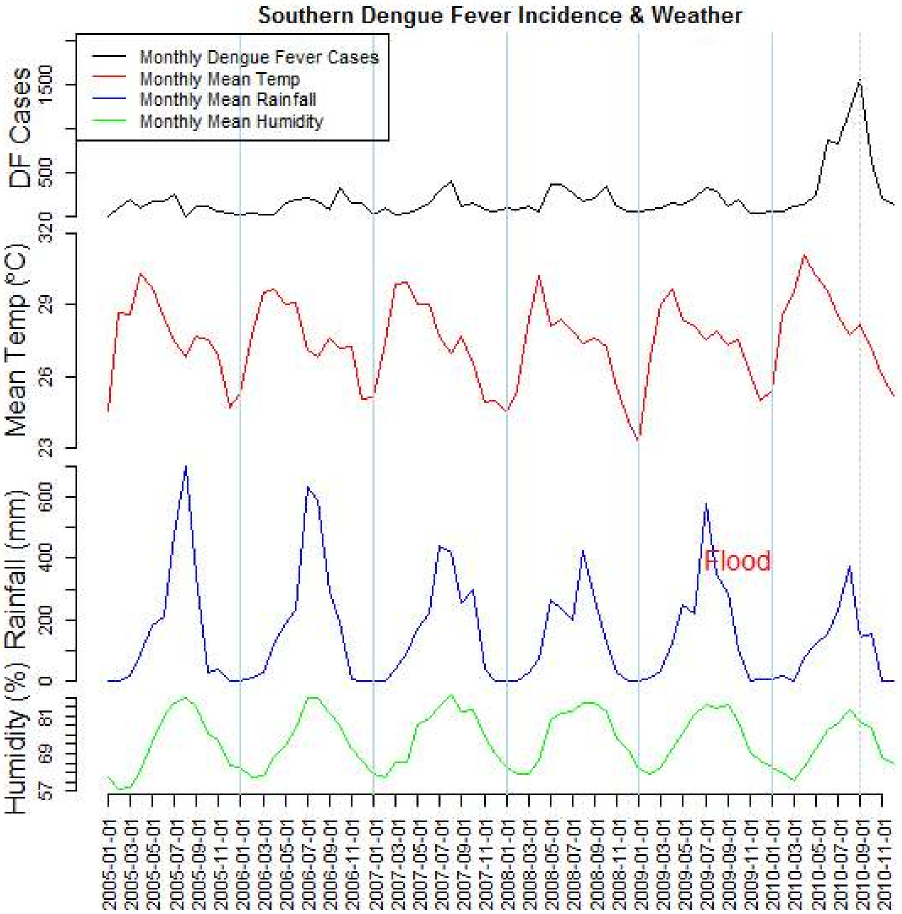

Fig. 14. Time series trend of dengue fever cases, mean temperature (°C), mean rainfall (mm), and mean relative humidity (%) for Southern region from 2005 to 2010.

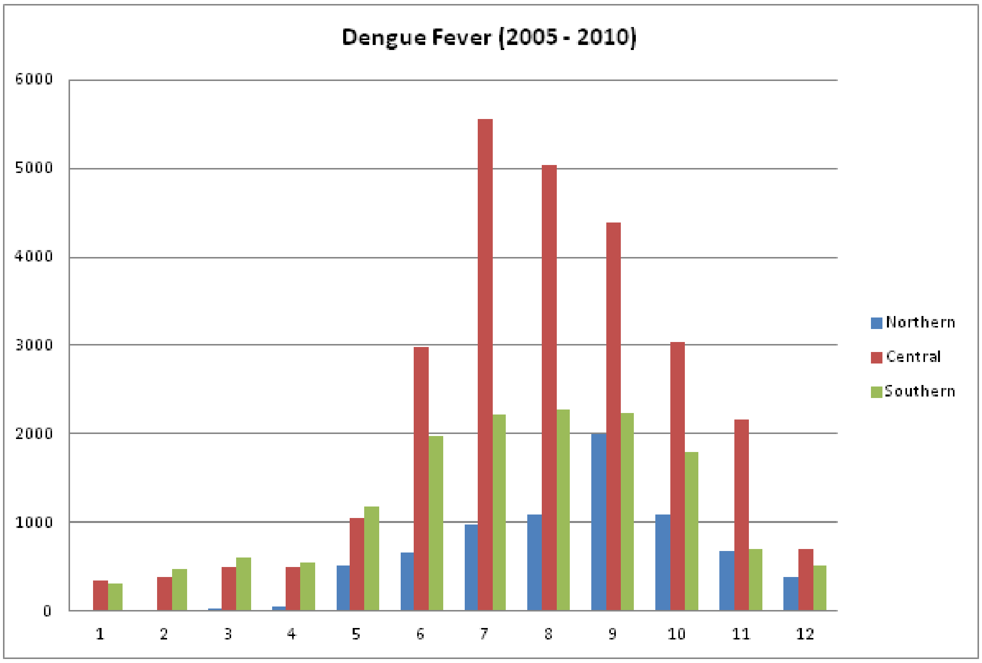

Fig. 15. Monthly trend of dengue fever cases from 2005 to 2010.

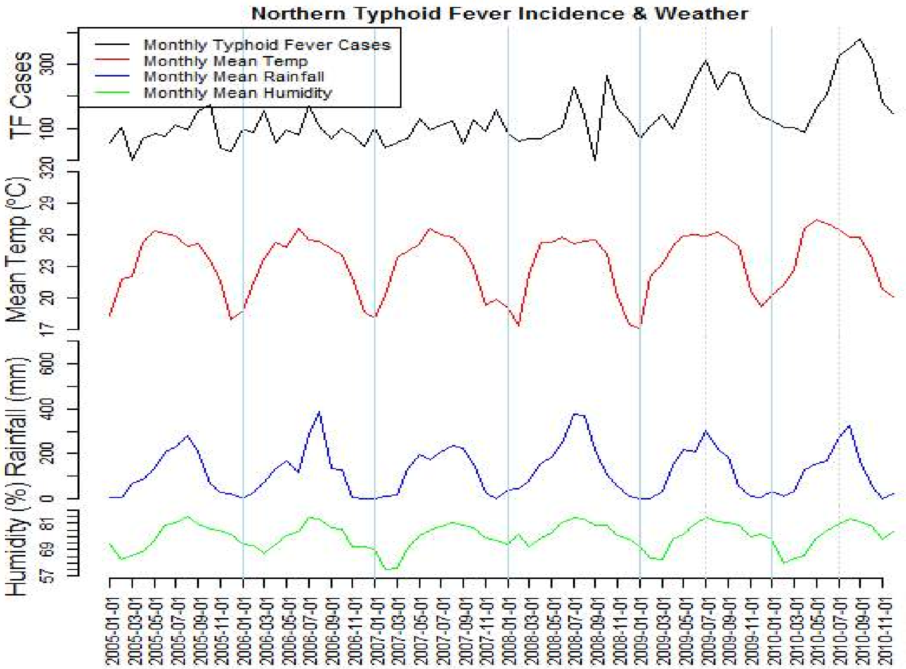

Fig. 16. Time series trend of typhoid fever cases, mean temperature (°C), mean rainfall (mm), and mean relative humidity (%) for Northern region from 2005 to 2010.

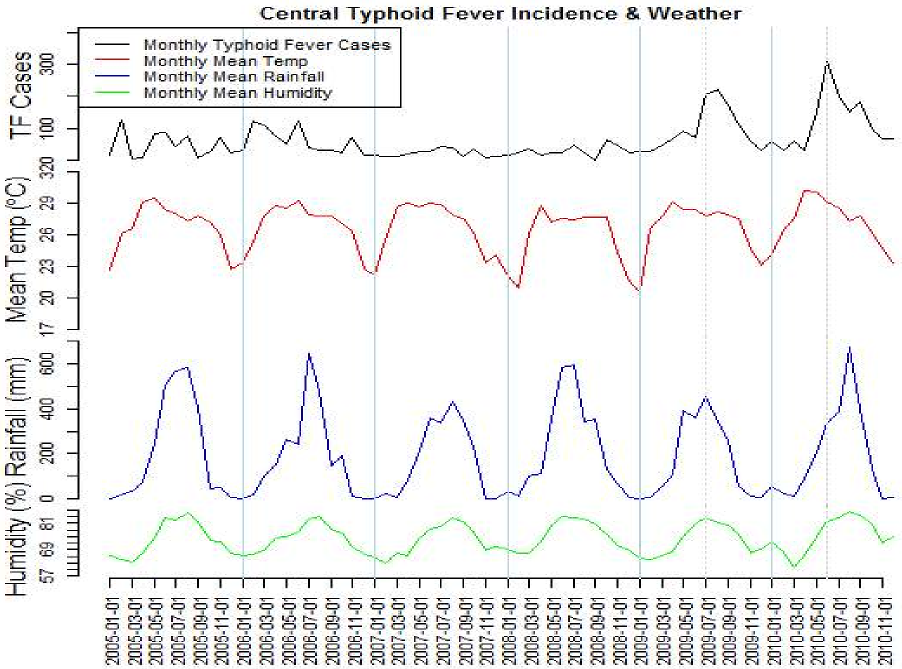

Fig. 17. Time series trend of typhoid fever cases, mean temperature (°C), mean rainfall (mm), and mean relative humidity (%) for Central region from 2005 to 2010.

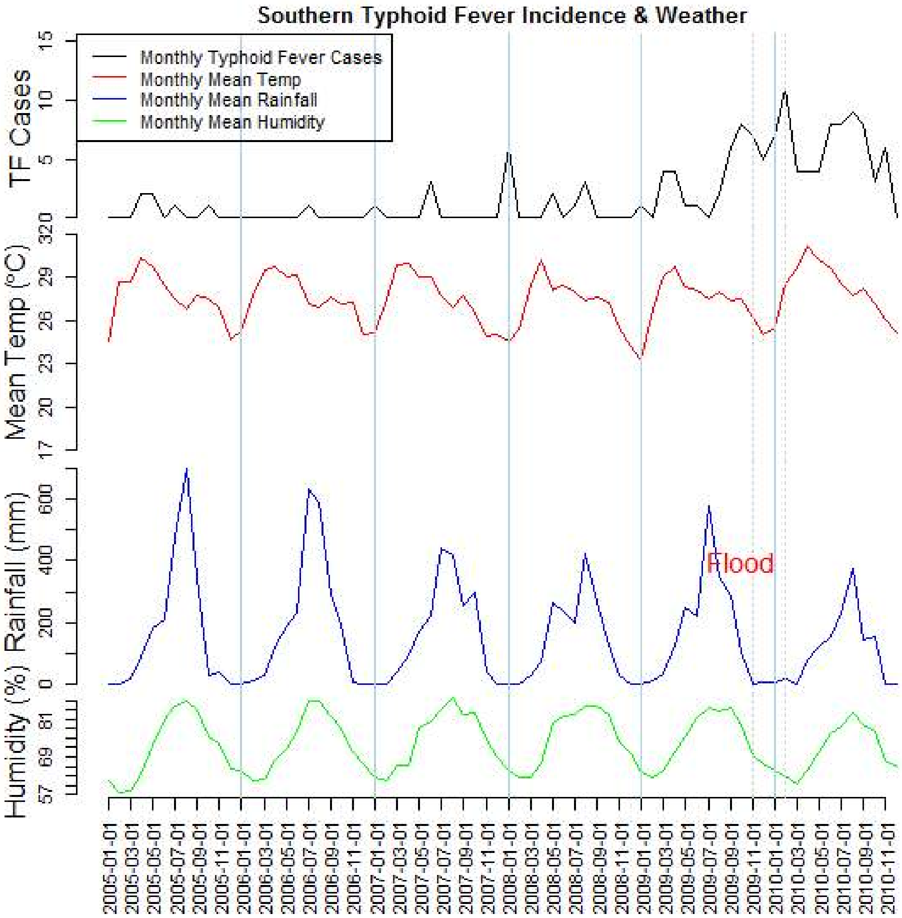

Fig. 18. Time series trend of typhoid fever cases, mean temperature (℃), mean rainfall (mm), and mean relative humidity (%) for Southern region from 2005 to 2010.

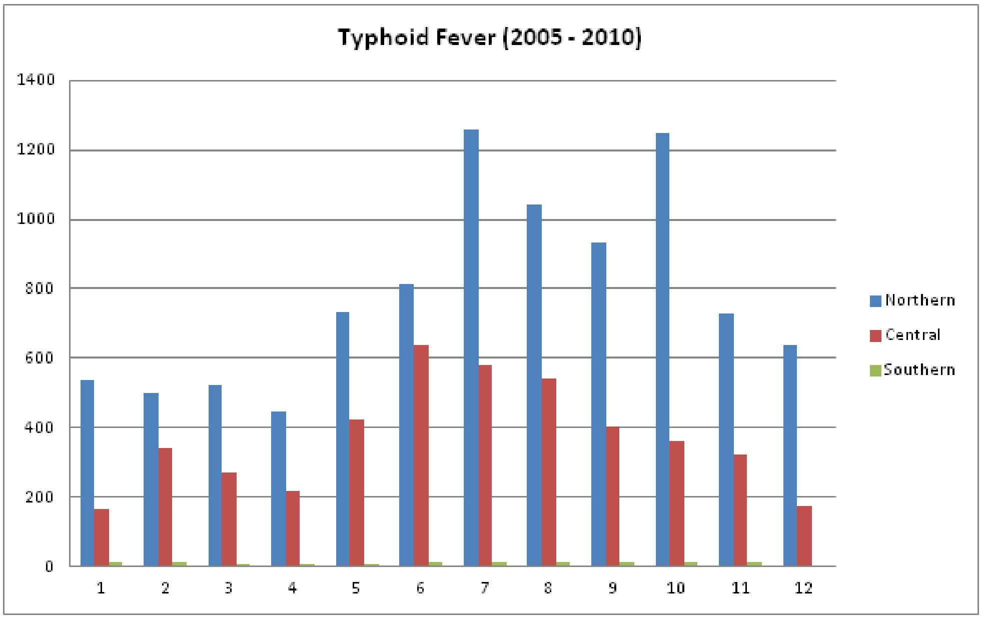

Fig. 19. Monthly trend of typhoid fever cases from 2005 to 2010.

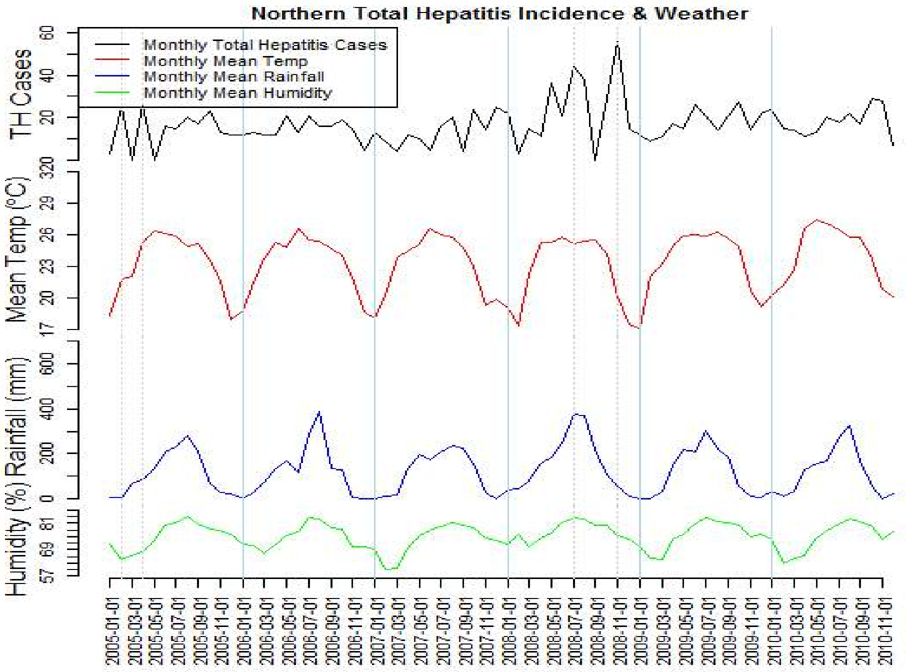

Fig. 20. Time series trend of total hepatitis cases, mean temperature (°C), mean rainfall (mm), and mean relative humidity (%) for Northern region from 2005 to 2010.

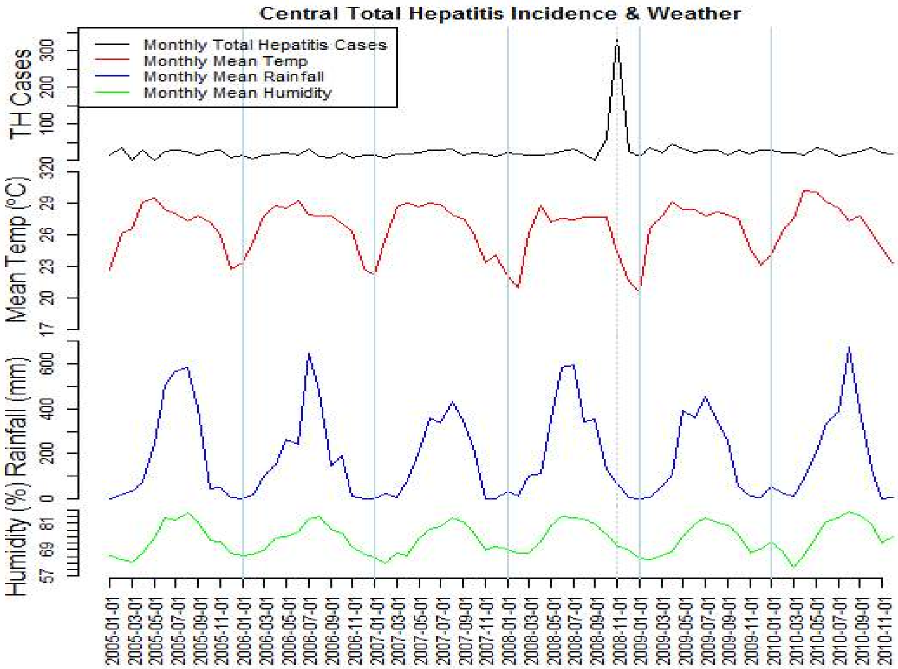

Fig. 21. Time series trend of total hepatitis cases, mean temperature (°C), mean rainfall (mm), and mean relative humidity (%) for Central region from 2005 to 2010.

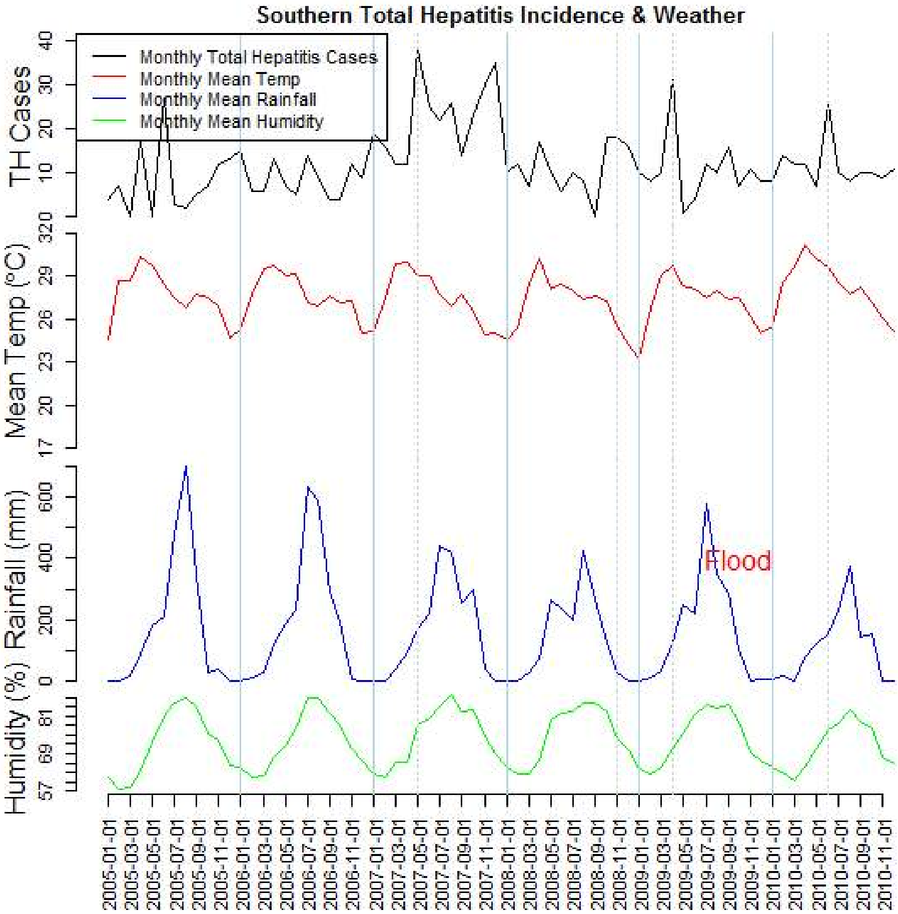

Fig. 22. Time series trend of total hepatitis cases, mean temperature (°C), mean rainfall (mm), and mean relative humidity (%) for Southern region from 2005 to 2010.

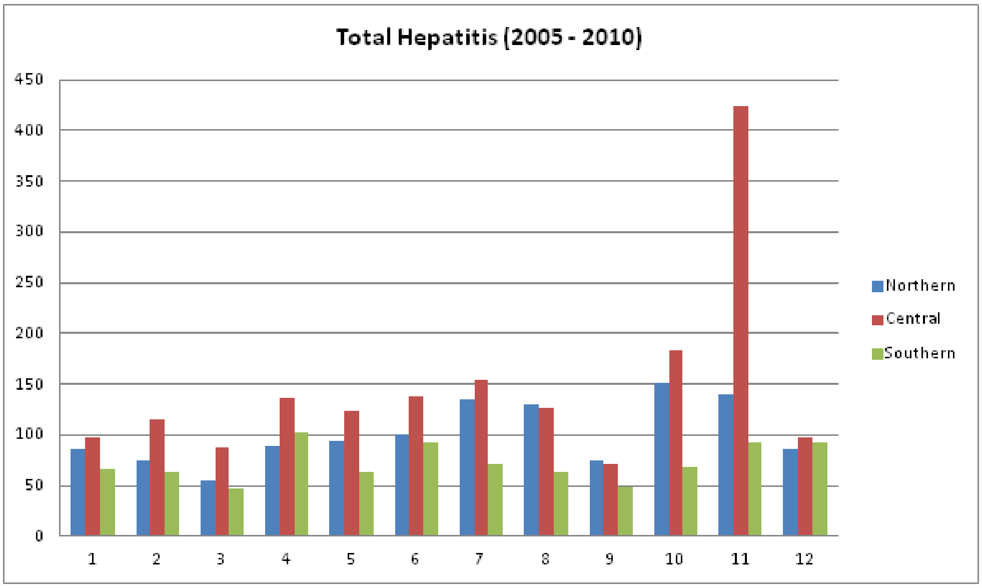

Fig. 23. Monthly trend of total hepatitis cases from 2005 to 2010.

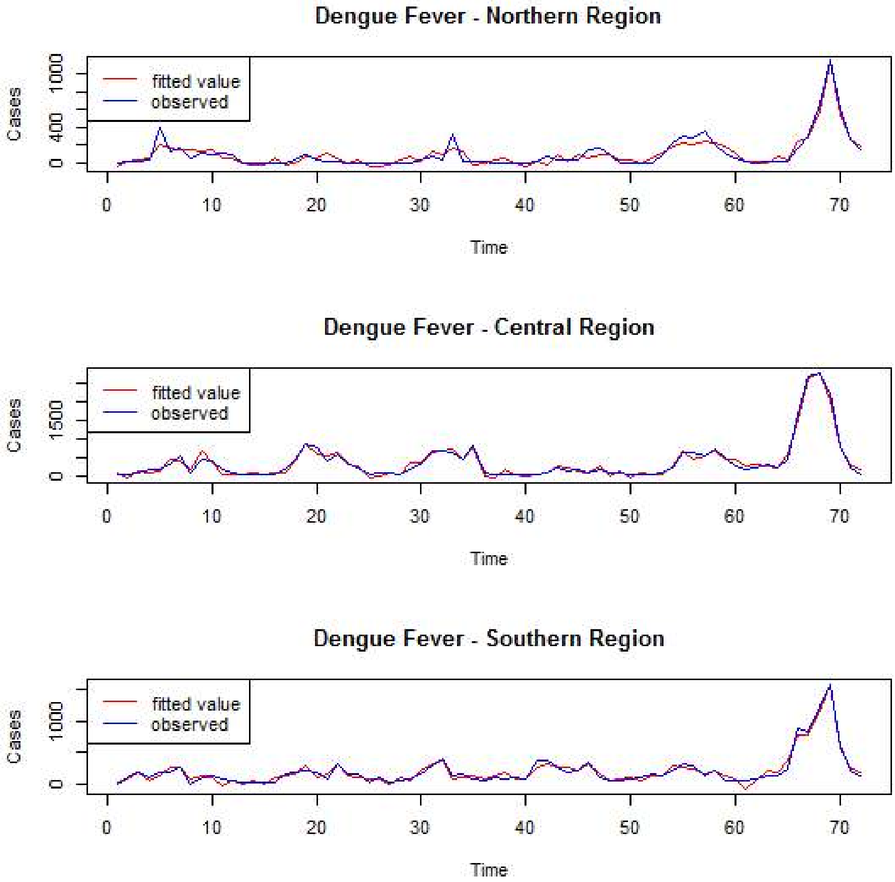

Fig. 24. The comparison between fitted model and the observed of dengue fever incidence in the northern, central, and southern region.

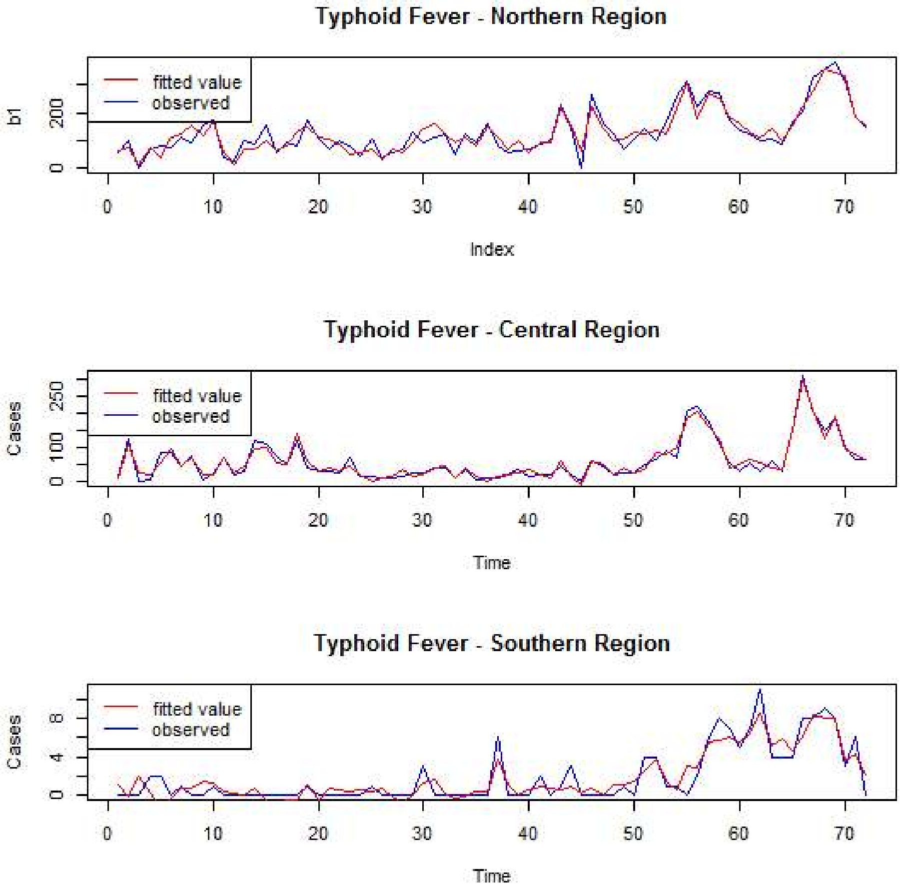

Fig. 25. The comparison between fitted model and the observed of typhoid fever incidence in the northern, central, and southern region.

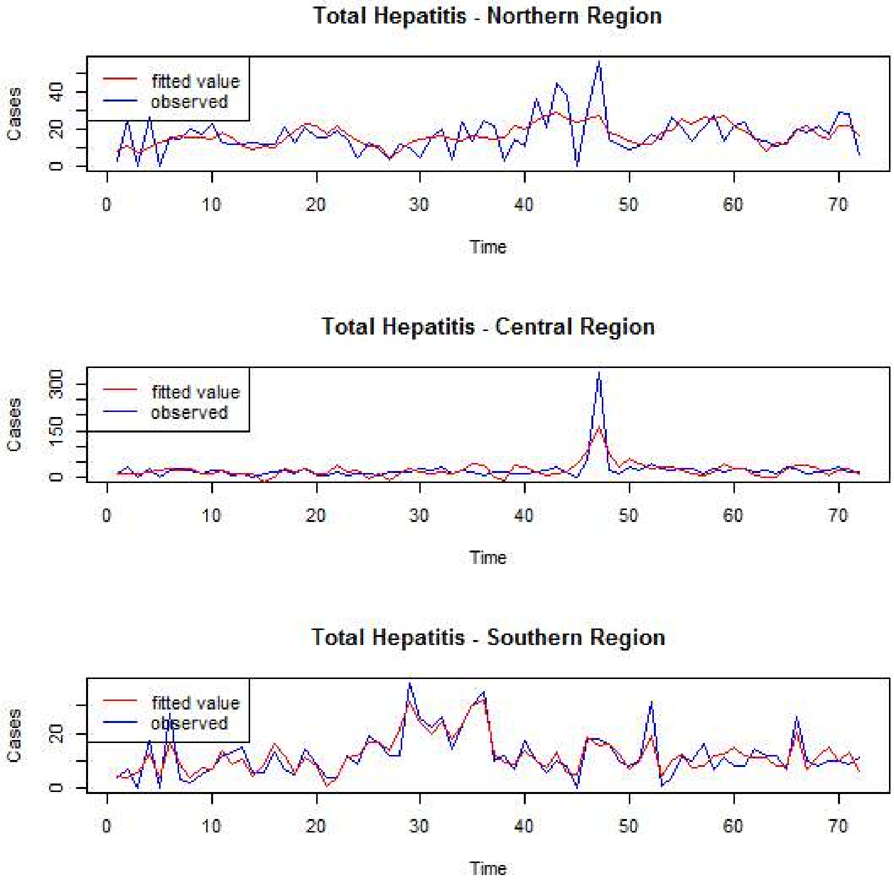

Fig. 26. The comparison between fitted model and the observed of total hepatitis incidence in the northern, central, and southern region.

Table 9. Comparison of SE values of omitted variables from the fitted model for dengue fever - Northern region.

	Mean Temp	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE	SE
FULL MODEL	10.058	4.652	0.312	28.879	20.792
Mean temp omitted	-	4.656	0.267	28.894	18.608
Humidity omitted	10.400	-	0.251	28.698	19.222
Rainfall omitted	8.548	3.592	-	28.037	20.379
DMI omitted	10.615	4.720	0.322	-	21.325
NINO3 omitted	9.065	4.193	0.310	28.279	-

Table 10. Comparison of SE values of omitted variables from the fitted model for dengue fever - Central region.

	Mean Temp	Humidity	DMI	NINO3
	SE	SE	SE	SE
FULL MODEL	30.898	8.439	91.414	54.726
Mean temp omitted	-	7.948	81.914	49.361
Humidity omitted	30.042	-	91.542	58.001
DMI omitted	26.496	7.834	-	54.225
NINO3 omitted	29.459	9.158	100.047	-

Table 11. Comparison of SE values of omitted variables from the fitted model for dengue fever - Southern region.

	Mean Temp	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE	SE
FULL MODEL	22.936	6.965	0.322	49.767	33.709
Mean temp omitted	-	6.765	0.331	50.975	32.342
Humidity omitted	21.750	-	0.207	46.810	32.970
Rainfall omitted	22.962	4.464	-	45.138	33.745
DMI omitted	22.653	6.471	0.289	-	32.097
NINO3 omitted	21.415	6.791	0.322	47.824	-

Table 12. Comparison of SE values of changing lag structure from the fitted model for dengue fever - Northern region. Number represents the lag structure for the variables respectively.

	Mean Temp	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE	SE
FULL MODEL* (4-4-4-2-5)	10.058	4.652	0.312	28.879	20.792
2-2-2-2-2	9.964	5.240	0.340	30.246	19.269
2-2-2-2-5	10.118	4.414	0.341	29.955	21.734
2-2-2-5-5	12.412	5.079	0.413	39.353	24.571
4-4-4-2-2	9.171	4.627	0.315	30.187	20.360
4-4-4-5-5	10.726	4.813	0.333	33.348	23.102
6-6-6-2-2	10.303	4.065	0.280	32.019	21.503
6-6-6-2-5	9.226	4.783	0.265	31.396	19.506
6-6-6-5-5	8.495	4.723	0.273	30.169	20.253
6-6-6-6-6	9.269	4.593	0.271	30.004	20.466
6-6-6-12-12	8.817	4.075	0.293	31.348	18.755

*Number: (Mean temp-Humidity-Rainfall-DMI-NINO3)

Table 13. Comparison of SE values of changing lag structure from the fitted model for dengue fever - Central region. Number represents the lag structure for the variables respectively.

	Mean Temp	Humidity	DMI	NINO3
	SE	SE	SE	SE
FULL MODEL* (3-3-12-5)	30.898	8.439	91.414	54.726
3-3-5-5	29.736	7.907	91.629	63.633
3-3-5-6	26.200	8.941	82.757	61.562
3-3-6-5	29.708	7.904	89.013	61.054
3-3-6-6	27.775	9.038	90.001	66.124
3-3-12-12	28.526	11.367	103.115	68.913
6-6-5-5	27.760	11.041	88.601	57.977
6-6-5-6	32.729	10.637	90.227	59.935
6-6-6-5	28.760	11.431	91.984	57.458
6-6-6-6	32.770	10.689	93.259	59.136
6-6-12-5	30.904	11.463	95.272	60.842

*Number: (Mean temp-Humidity-DMI-NINO3)

Table 14. Comparison of SE values of changing lag structure from the fitted model for dengue fever - Southern region. Number represents the lag structure for the variables respectively.

	Mean Temp	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE	SE
FULL MODEL* (4-1-1-5-5)	22.936	6.965	0.322	49.767	33.709
1-1-1-1-1	18.141	6.333	0.316	45.101	29.115
1-1-1-1-5	15.670	5.936	0.297	43.470	29.390
1-1-1-5-1	18.866	6.741	0.338	47.347	28.956
1-1-1-5-5	15.483	6.703	0.330	49.588	31.761
1-1-1-6-6	16.817	6.321	0.301	48.391	28.761
1-1-1-12-12	17.180	7.040	0.298	41.920	37.030
4-1-1-1-1	26.398	7.853	0.341	56.027	26.314
4-1-1-1-5	27.898	7.145	0.307	52.431	32.495
4-1-1-5-1	22.614	7.177	0.348	48.449	24.868
4-1-1-6-6	25.665	6.773	0.296	50.382	31.489
4-1-1-12-12	24.260	7.343	0.296	49.240	31.610
4-4-4-1-1	16.810	5.241	0.249	46.854	29.026
4-4-4-5-5	17.851	5.175	0.287	46.538	31.259
4-4-4-6-6	17.814	4.649	0.248	44.035	32.105
4-4-4-12-12	17.390	4.878	0.245	44.790	30.590

*Number: (Mean temp-Humidity-Rainfall-DMI-NINO3)

Table 15. Comparison of SE values of omitted variables from the fitted model for typhoid fever - Northern region.

	Mean Temp	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE	SE
FULL MODEL	3.491	1.580	0.132	10.649	8.626
Mean temp omitted	-	1.661	0.120	11.188	8.919
Humidity omitted	3.651	-	0.109	11.103	8.980
Rainfall omitted	3.003	1.239	-	10.428	7.666
DMI omitted	3.764	1.700	0.141	-	9.078
NINO3 omitted	3.405	1.560	0.117	10.300	-

Table 16. Comparison of SE values of omitted variables from the fitted model for typhoid fever - Central region.

	Mean Temp	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE	SE
FULL MODEL	3.486	2.368	0.076	9.114	6.630
Mean temp omitted	-	2.243	0.076	9.137	5.478
Humidity omitted	3.289	-	0.037	9.128	5.422
Rainfall omitted	3.480	1.144	-	9.098	6.159
DMI omitted	3.759	2.560	0.082	-	7.174
NINO3 omitted	2.876	1.941	0.071	9.156	-

Table 17. Comparison of SE values of omitted variables from the fitted model for typhoid fever - Southern region.

	Mean Temp	DMI	NINO3
	SE	SE	SE
FULL MODEL	0.192	0.467	0.259
Mean temp omitted	-	0.411	0.223
DMI omitted	0.173	-	0.267
NINO3 omitted	0.171	0.484	-

Table 18. Comparison of SE values of changing lag structure from the fitted model for typhoid fever - Northern region. Number represents the lag structure for the variables respectively.

	Mean Temp	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE	SE
FULL MODEL* **(0-0-0-0-8)**	3.491	1.580	0.132	10.649	8.626
0-0-0-0-0	3.568	1.864	0.120	10.633	6.600
0-0-0-0-4	3.514	1.572	0.117	10.353	6.638
0-0-0-4-4	4.169	2.151	0.160	14.884	7.883
0-0-0-4-8	3.917	1.989	0.168	13.415	8.977
0-0-0-8-8	3.762	1.733	0.137	12.250	8.998
0-0-0-0-12	3.752	1.733	0.118	10.513	7.023
0-0-0-4-12	4.070	2.259	0.161	14.261	7.870
0-0-0-8-12	4.164	1.960	0.129	12.626	7.650
0-0-0-12-12	3.924	1.802	0.128	11.469	7.567
6-6-6-0-4	3.123	1.535	0.099	10.312	7.217
6-6-6-4-4	3.416	1.699	0.111	12.059	8.297
6-6-6-4-8	3.946	1.556	0.113	11.860	8.898
6-6-6-0-8	3.907	1.388	0.101	11.400	8.698
6-6-6-8-8	4.285	1.491	0.109	13.159	9.559
6-6-6-0-12	3.129	1.546	0.110	10.374	6.861
6-6-6-4-12	3.458	1.736	0.124	11.740	7.634
6-6-6-8-12	3.464	1.706	0.123	12.092	7.613
6-6-6-12-12	3.533	1.633	0.117	12.561	7.515

*Number: (Mean temp-Humidity-Rainfall-DMI-NINO3)

Table 19. Comparison of SE values of changing lag structure from the fitted model for typhoid fever - Central region. Number represents the lag structure for the variables respectively.

	Mean Temp	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE	SE
FULL MODEL* (2-2-2-0-2)	3.486	2.368	0.076	9.114	6.630
2-2-2-0-0	2.867	2.273	0.072	9.913	6.856
2-2-2-2-2	3.847	2.553	0.086	11.610	7.282
2-2-2-4-4	3.900	2.152	0.081	12.013	8.504
2-2-2-6-6	3.171	2.286	0.080	11.097	7.282
2-2-2-12-12	2.938	2.138	0.071	10.165	7.405
4-4-4-0-2	3.292	1.998	0.064	10.476	6.293
4-4-4-2-2	2.958	2.126	0.067	10.300	7.201
4-4-4-4-4	3.695	2.169	0.073	11.208	6.951
4-4-4-6-6	3.797	1.920	0.071	11.656	8.476
4-4-4-12-12	3.294	1.767	0.066	10.865	7.435
6-6-6-0-2	3.753	1.474	0.056	9.614	7.107
6-6-6-2-2	4.121	1.631	0.062	11.960	7.866
6-6-6-4-4	3.102	1.827	0.059	10.874	7.520
6-6-6-6-6	3.998	1.904	0.062	11.500	7.495
6-6-6-12-12	3.270	1.601	0.060	11.170	6.156

*Number: (Mean temp-Humidity-Rainfall-DMI-NINO3)

Table 20. Comparison of SE values of changing lag structure from the fitted model for typhoid fever - Southern region. Number represents the lag structure for the variables respectively.

	Mean Temp	DMI	NINO3
	SE	SE	SE
FULL MODEL (3-12-5)	0.192	0.467	0.259
3-3-3	0.177	0.424	0.268
3-5-5	0.186	0.468	0.293
3-5-6	0.164	0.439	0.253
3-6-6	0.166	0.456	0.262
3-6-12	0.161	0.439	0.254
3-12-12	0.173	0.482	0.247
6-5-5	0.157	0.434	0.247
6-5-6	0.191	0.429	0.295
6-6-6	0.189	0.434	0.293
6-6-12	0.168	0.453	0.260
6-12-5	0.173	0.462	0.252
6-12-12	0.171	0.473	0.265

*Number: (Mean temp-DMI-NINO3)

Table 21. Comparison of SE values of omitted variables from the fitted model for total hepatitis - Northern region.

	Humidity	Rainfall	NINO3
	SE	SE	SE
FULL MODEL	0.247	0.018	1.285
Humidity omitted	-	0.014	1.345
Rainfall omitted	0.184	-	0.994
NINO3 omitted	0.258	0.014	-

Table 22. Comparison of SE values of omitted variables from the fitted model for total hepatitis - Central region.

	Mean Temp	NINO3
	SE	SE
FULL MODEL	2.268	4.830

Table 23. Comparison of SE values of omitted variables from the fitted model for total hepatitis - Southern region.

	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE
FULL MODEL	0.215	0.011	1.589	0.794
Humidity omitted	-	0.006	1.587	0.800
Rainfall omitted	0.108	-	1.560	0.791
DMI omitted	0.214	0.011	-	0.805
NINO3 omitted	0.211	0.011	1.573	-

Table 24. Comparison of SE values of changing lag structure from the fitted model for total hepatitis - Northern region. Number represents the lag structure for the variables respectively.

	Humidity	Rainfall	NINO3
	SE	SE	SE
FULL MODEL* (1-1-9)	0.247	0.018	1.285
1-1-1	0.318	0.016	1.045
1-1-3	0.275	0.018	1.131
1-1-6	0.276	0.014	1.042
1-1-12	0.315	0.015	1.259
3-3-3	0.309	0.016	1.079
3-3-6	0.244	0.016	1.171
3-3-9	0.275	0.015	1.045
3-3-12	0.265	0.016	1.417
6-6-3	0.247	0.016	1.225
6-6-6	0.290	0.016	1.211
6-6-9	0.231	0.014	1.174
6-6-12	0.260	0.015	1.151

*Number: (Humidity-Rainfall-NINO3)

Table 25. Comparison of SE values of changing lag structure from the fitted model for total hepatitis - Central region. Number represents the lag structure for the variables respectively.

	Mean Temp	NINO3
	SE	SE
FULL MODEL* (0-9)	2.268	4.830
0-0	2.149	3.993
0-3	2.448	4.875
0-6	1.965	4.178
0-12	2.046	4.461
3-0	2.430	4.530
3-3	2.111	4.217
3-6	2.382	5.081
3-9	1.962	4.192
3-12	2.170	4.746
6-0	2.055	3.842
6-3	2.466	4.941
6-6	2.127	4.550
6-9	2.384	5.110
6-12	1.887	4.140

*Number: (Mean temp-NINO3)

Table 26. Comparison of SE values of changing lag structure from the fitted model for total hepatitis - Southern region. Number represents the lag structure for the variables respectively.

	Humidity	Rainfall	DMI	NINO3
	SE	SE	SE	SE
FULL MODEL* (0-0-3-1)	0.215	0.011	1.589	0.794
0-0-1-1	0.229	0.013	1.845	0.928
0-0-3-3	0.213	0.011	1.629	1.065
0-0-6-1	0.233	0.012	1.715	0.797
0-0-6-6	0.243	0.012	1.717	0.941
0-0-9-1	0.212	0.011	1.647	0.834
0-0-9-9	0.233	0.010	1.713	1.301
0-0-12-1	0.215	0.011	1.622	0.804
0-0-12-12	0.234	0.012	1.682	1.017
3-3-1-1	0.249	0.010	1.585	1.170
3-3-3-1	0.274	0.011	1.637	1.179
3-3-3-3	0.249	0.012	1.778	1.030
3-3-6-1	0.271	0.012	1.675	1.110
3-3-6-6	0.218	0.011	1.714	1.133
3-3-9-1	0.276	0.012	1.763	1.148
3-3-9-9	0.249	0.012	1.769	0.973
3-3-12-1	0.267	0.011	1.585	1.149
3-3-12-12	0.243	0.011	1.791	1.419
6-6-1-1	0.164	0.009	1.597	0.824
6-6-3-1	0.168	0.009	1.614	0.838
6-6-3-3	0.189	0.009	1.830	1.258
6-6-6-1	0.162	0.009	1.578	0.775
6-6-6-6	0.180	0.009	1.641	0.970
6-6-9-1	0.171	0.009	1.712	0.812
6-6-9-9	0.183	0.009	1.728	1.169
6-6-12-1	0.182	0.010	1.726	0.818
6-6-12-12	0.190	0.010	1.715	0.993

*Number: (Humidity-Rainfall-DMI-NINO3)

요약(국문초록)

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배경: 감염성 질환과 기후변화/날씨변수가 감염성 질환 발생에 미치는 영향에 대해 조사하기 위한 모델링과 연구가 있었다. 특히 대부분의 개발도상국이 위치하고 있는 열대 및 아열대 지방에서 감염성질환의 발생 빈도는 여전히 높으며, 이는 국가의 경제발전을 저해하며 중요 해결 과제이다. 본 연구의 목표는 감염성 질환이 건강문제로 남아있는 라오스에서 기상변수와 감염성질환의 관계를 규명하고자 한다.

방법: 감염성질환과 기상변수 사이의 관계를 알아보기 위하여 일반화 부가모형 (Generalized Additive Model, GAM)을 이용하여 분석하였다. 라오스의 각 지역(북부, 중부, 남부지역)의 뎅기열(Dengue Fever), 장티푸스(Typhoid fever), 간염(Total Hepatitis) 발생 데이터와 각 지역의 온도, 상대 습도, 강우량을 이용하여 질병발생과 기상변수의 관계를 확인하였으며 글로벌변수(Global index) 로서 DMI와NINO3를 분석모형에 이용하였다.

결론: 뎅기열 질환과 기상변수는 가장 강한 연관성을 가지고 있었으며 그 다음으로는 장티푸스와 간염이 기상변수의 영향을 받는 것을 확인하였다. 각 지역변수(Local variables) 중에서는 평균온도와 상대습도, 글로벌 기상변수 중에서는 NINO3 가 뎅기열과 강한 연관성을 갖는 것을 확인 할 수 있었다. 장티푸스의 경우 DMI 변수가 가장 큰 영향을 미쳤다. 총 간염 발생의 경우 각 지방의 상대습도가 가장 높은 연관성을 주는 것을 확인할 수 있었으나 라오스 중앙지역에서는 그 관련성을 확인할 수 없었다.

주요어: DMI, NINO3, 감염성질활, 간염, 강수량, 뎅기열, 라오스, 습도, 온도, 일반화부가모형, 장티푸스

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