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Early Warning Impact of Temperature and Rainfall Anomalies onto West Nile Virus Human Cases †

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Abstract: West Nile Virus (WNV) is transmitted among amplifying hosts and transferred through the bites of mosquitoes; humans and other mammals may become infected. The overwintering of infected mosquitoes is important for next season's circulation of the virus. In this study, we combined the available climatic and entomological data at the municipality level to identify the impact of the wintertime climatic anomalies on the survival ability of diapausing mosquitoes in Central Macedonia, a region with great epidemiological interest in Greece. The analysis indicated a strong dependence of the mosquito abundances with spring temperature and winter precipitation, depending on the land use type and the geomorphology of the municipalities.

Keywords: climatic anomalies; West Nile Fever human cases; vectors; diapausing; climate change impact; data analysis; municipality level

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1. Introduction

West Nile Virus (WNV) is a neurotropic mosquito-borne virus that belongs to the flavivirus genus [1]. The virus is maintained in an enzootic cycle between mosquitoes and amplifying hosts, primarily birds [2]. The virus is transmitted to humans by infected mosquitoes, especially *Culex pipiens* [3,4]. Still, there are no vaccines for humans [5,6]. The impacts of climatic parameters such as temperature, relative humidity and total precipitation are significant factors for WNV transmission in Europe [7,8]. Due to the possibility of WNV to persist in mosquitoes throughout the winter season in Europe [9], the overwintering of infected mosquitoes is determinant for the circulation of WNV in the next season.

The aim of this work is to investigate the association between *Culex* abundances and temperature and total precipitation anomalies of the previous months. Climate data were acquired from ERA5 (European Centre for Medium-Range Weather Forecasts), and *Culex* abundance data were obtained through the mosquito surveillance network of ECODEVELOPMENT S.A. (ECODEV), a mosquito control company. The investigation area was the Region of Central Macedonia in Northern Greece, while the study was conducted at the municipality level. This research provides a potential early warning signal for the early increase in mosquito abundances and for a potential outbreak of West Nile Fever (WNF) human cases.

2. Materials and Methods

2.1. Investigation Area and Data

The study area was the region of Central Macedonia in Northern Greece, an area of great epidemiological interest for the study of WNV due to repeated outbreaks of WNV human cases. Air temperature and total precipitation data were considered as critical climate factors in WNV transmission dynamics. Data for Central Macedonia were acquired from the European Centre for Medium-Range Weather Forecast (ECMWF) and referred to the period from 1980 to 2022. Concerning the *Culex* abundance data, entomological dataset for more than 10 years (2011–2022) was provided by ECODEV, which maintains the largest mosquito surveillance network in Greece. Every 15 days, the mosquito specialists collected and determined the genus, the total number of species and that of infected mosquitoes using CO_2/light traps.

2.2. Methodology

The period from 1980 to 2009 was used to construct the mean state ("climate"), while the period of 2010–2022 was used to identify anomalies. Anomaly is a measure of the variation (increase or decrease) in the specific climatic parameter in year *y* in relation to the average prevailing climatic conditions during the period from 1980 to 2009. Effects of temperature and total precipitation on mosquito population were investigated for diapausing *Culex pipiens*. Specifically, the effect of temperature anomaly or total precipitation anomaly was investigated based on the following formula:

$$\text{ratio} = (\text{Measure of } \textit{Culex} \text{ population level})_y / (\text{Last measurement of } \textit{Culex}_{(y-1)}).$$

The last measurement of *Culex* mosquito abundance equals to the average value of the measured mosquitoes of the last two months of measurement (September–October), while the Measure of *Culex* population level is defined as the average value of mosquito abundance in the month in which the maximum abundance occurred, one month before and one month after the peak. Index y refers to the research year, $y - 1$ to the previous year and $2012 \leq y \leq 2022$. Correlations between the ratio and monthly anomalies from November to May were examined at the 95% CI.

Multiple linear regression was used to estimate the influence of temperature anomaly and total precipitation anomaly of the month the year before the year of observation and the ratio (Measure of *Culex* population level in a given year/last measurement of *Culex* the year before). Specifically, in $Y = b_0 + b_1 * X_1 + b_2 * X_2$,
Y = Ratio,
X_1 = Temperature anomaly of month,
X_2 = Total precipitation anomaly of month,
b_0, b_1, b_2: Regression coefficients, month; from $\text{November}_{(y-1)}$ to May_y,
y: The research year, $y - 1$: the previous year and $2012 \leq y \leq 2022$.

3. Results

Figure 1 shows the municipalities of the region of Central Macedonia and the municipalities in which the same temperature anomaly and total precipitation anomaly had a statistically significant effect on the ratio for the period of 2011–2022 (colored). When the coefficient of determination (R^2) value exceeded 0.5, the overall and the individual *p*-values were lower than the significance level of 0.05, and a significant linear regression relationship existed between the ratio and the predictor variables (a couple of temperature and precipitation anomalies). There were five clusters (11 municipalities) in this region for which the temperature and total precipitation anomalies combined with the last mosquito measurement of the previous year were able to statistically significantly predict the order of magnitude of this year's mosquito abundance. Specifically, in two out of five clusters (Clusters 1, 4), the April temperature anomaly combined with the February total precipitation anomaly was found to be statistically significant, while in two out of five clusters (Clusters 2, 5), anomalies in the total precipitation of the winter months combined with anomalies in temperature 3 months later were characterized as statistically significant variables. In addition, there were two municipalities (Cluster 3) in which the November temperature anomaly combined with the December precipitation anomaly emerged as statistically significant. The multiannual variability of annual predicted and observed ratio in 11 municipalities where the variation in the ratio could be predicted by temperature and total precipitation anomalies is provided in Figure 2, as well as measured (blue) and predicted (red) annual ratio in 11 municipalities where R^2 between temperature anomaly and total precipitation anomaly versus ratio was found to be significant. Values of regression coefficients, R^2 and *p*-value in each cluster are presented in Table 1, as well as the clusters of municipalities emerged according to the coefficient of model determination (R^2) between temperature anomaly and total precipitation anomaly versus the ratio.

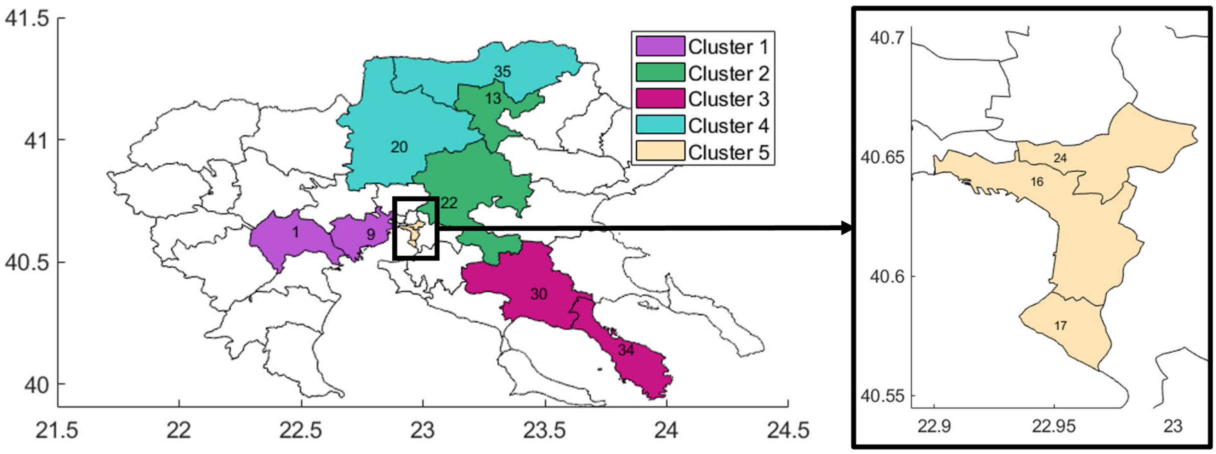

Figure 1. Map of municipalities of the Central Macedonia region. Municipalities in which the associations of overwintering ratio with Temperature and Total precipitation Anomalies were statistically significant for the period of 2011–2022 are colored.

Table 1. Clustering municipalities of the region according to the coefficient of model determination (R^2) between temperature anomaly and total precipitation anomaly versus ratio.

Cluster	Municipalities		Estimated Coefficients				RMSE	R^2	*p*-Value
			Estimate	Standard Error	Test Statistic	*p*-Value			
1	1, 9	Intercept	3.88	0.56	6.98	0.000	1.99	0.52	0.001
		X_1 = T Anomaly April$_y$	−1.00	0.39	−2.58	0.018			
		X_2 = TP Anomaly February$_y$	0.29	0.06	4.51	0.000			
2	13, 22	Intercept	−9.16	3.69	−2.48	0.042	2.61	0.79	0.004
		X_1 = T Anomaly February$_y$	6.90	1.94	3.56	0.009			
		X_2 = TP Anomaly November$_{y-1}$	0.31	0.12	2.59	0.036			
3	30, 34	Intercept	−0.19	1.11	−0.17	0.870	1.58	0.56	0.026
		X_1 = T Anomaly November$_{y-1}$	1.16	0.42	2.77	0.022			
		X_2 = TP Anomaly December$_{y-1}$	0.16	0.06	2.69	0.025			
4	20, 35	Intercept	4.10	0.87	4.69	0.000	2.85	0.62	0.002
		X_1 = T Anomaly April$_y$	−0.95	0.45	−2.12	0.044			
		X_2 = TP Anomaly February$_y$	0.38	0.08	4.54	0.001			
5	16, 17, 24	Intercept	3.03	0.29	10.64	0.000	0.841	0.79	0.001
		X_1 = T Anomaly April$_y$	1.49	0.49	3.06	0.014			
		X_2 = TP Anomaly January$_y$	−0.16	0.03	−4.83	0.001			

Some characteristics of the municipalities could cause similar *Culex* population developments, and thus the clustering of these municipalities is possibly related to land use, geomorphology and human activities. Regarding the reasons why municipalities might belong to the same cluster, two municipalities (IDs = 1 and 9, Cluster 1) have rice fields with particularly favorable conditions for mosquito proliferation. In fact, the municipalities belonging to Clusters 2 and 4 have similar land and geomorphology, respectively. Municipalities with IDs = 30 and 34 are characterized by mountainous regions on the one hand and touristic areas on the other hand. The abundances of *Culex* mosquitoes in both municipalities are relatively low, which might be related to lower productivity in mountainous areas and intensive mosquito control in tourist areas. Examining the results of studying the reasons that could lead municipalities to form a cluster, it can be determined that there are three urban municipalities (IDs = 16, 17 and 24). Urban areas are characterized by higher temperatures (due to the urban heat island effect) and *Culex* abundances are related to human activities and a plentitude of breeding sites such as rain water catch basins, which are often highly productive in *Culex*.

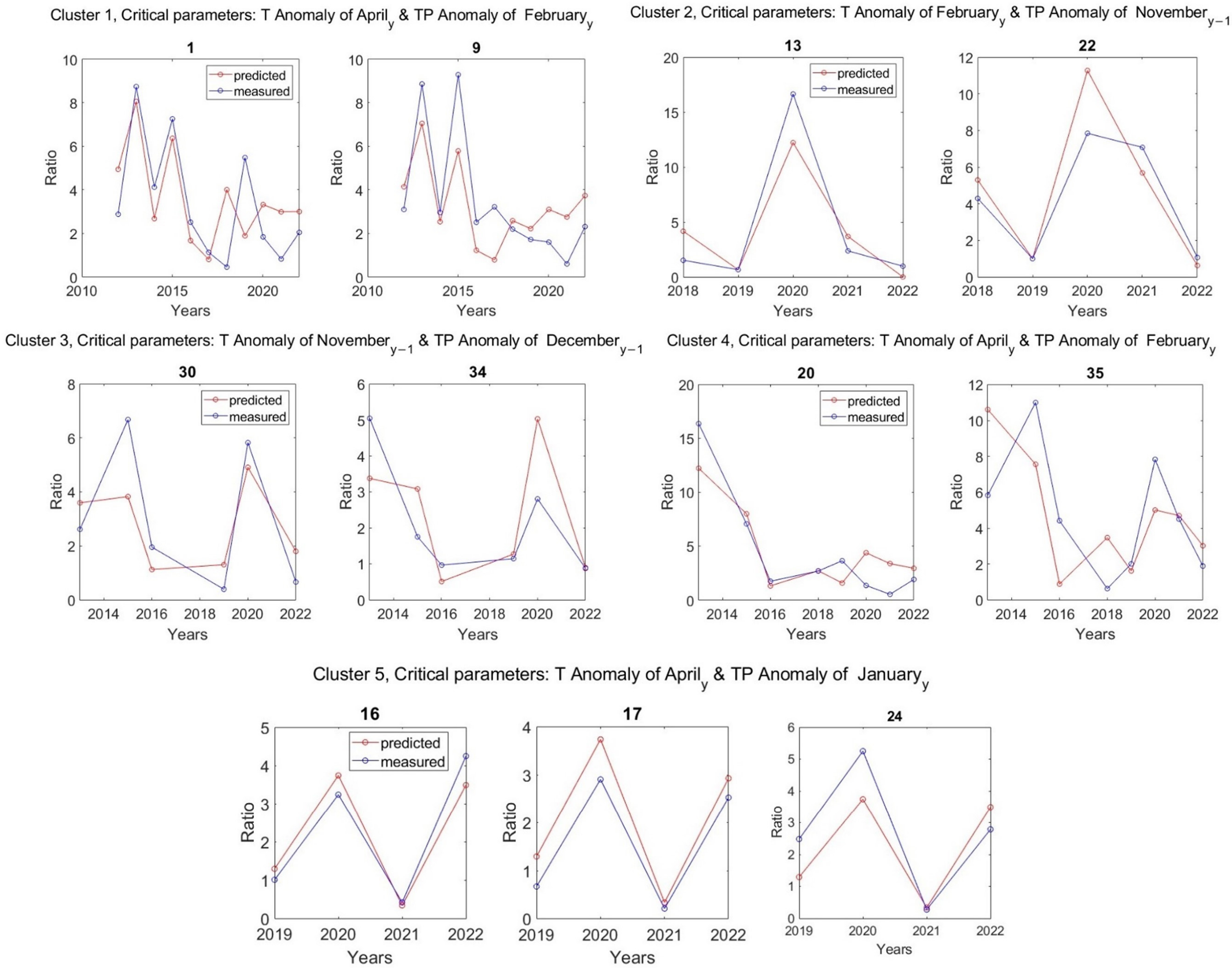

Figure 2. Measured (blue) and predicted (red) annual ratio in 11 municipalities where R^2 between temperature anomaly and total precipitation anomaly versus ratio was found to be significant.

4. Discussion

The aim of this study was to identify climatic and entomological patterns and characteristics that contributed to the variability in the mosquito populations in the region of Central Macedonia in northern Greece. The specific region is an area of epidemiological interest due to repetitive human outbreaks. Therefore, employing the available entomological and climatic data of the period of 2010–2022, we investigated the correlation of temperature and total precipitation anomalies with *Culex* abundance. Five clusters of municipalities emerged in which the correlation was found to be statistically significant. In most municipalities, a strong dependence of the mosquito abundances with February–April temperature and previous November–February total precipitation anomalies was found to be determinant for the successful forecasting of the order of magnitude of mosquito abundance in the current year. The classification of municipalities into clusters is justified by land use type, geomorphology and human activities.

WNV transmission poses a threat for public health. The prediction of WNV spread is challenging because it spreads via the complicated interaction of the enzootic transmission cycle between birds and mosquitoes with humans as dead-end hosts and the climatic sensitivity of the mosquito and the pathogen. It was found that projected climatic anomalies for winter–spring combined with the last recorded mosquito population (autumn of previous year) can provide generally accurate estimates of the foreseen peak mosquito populations in the coming season. The role played by the initial population of *Culex* in the enzootic cycle for the amplification of the pathogen requires further research.

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Conflicts of Interest: The authors declare no conflict of interest.

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