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Research Article

Mathematical Modeling and Climate: Incidence, Repercussion and Impact on Communicable Entities and Vector Organisms

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Abstract: Humanity has suffered throughout history the scourge of potentially fatal diseases, and where climate has a marked and decisive influence. The objective of the study consisted in demonstrating the existing relationship between the transmissible infectious entities Dengue and Malaria with climate by means of mathematical modeling in Villa Clara province, Cuba. The research covered two fundamental aspects: the influence exerted by some meteorological variables on the larval populations of culicidae, and on the Dengue entity. The mathematical model used was the Objective Regressive Regression (ORR) model, where the response variables were defined, as well as the explanatory variables. The general and specific larval densities showed a cyclical and seasonal behavior. Temperature, relative humidity, mean wind speed and atmospheric pressure proved to be excellent predictors of the population dynamics of entomoepidemiological important culicidae. A significant correlation of the infectious entity Dengue with minimum temperature (R=0.332; p=0.023) and water vapor tension (R=0.298; p=0.042) was obtained, as well as an inverse relationship with atmospheric pressure (R=-0.317; p=0.030). It is concluded that there is a close relationship between the infectious entities analyzed and the species of vector organisms with climate, which was corroborated by the mathematical modeling ROR, so it is possible to model and predict, in the short, medium and long term, both the population dynamics of culicidae with entomoepidemiological importance and the incidence of cases of Dengue.

Keywords: climate, Dengue, entomoepidemiological, Objective Regressive Regression (ORR) methodology, mathematical modeling, Villa Clara.

INTRODUCTION:

Humanity has suffered throughout history from the scourge of potentially fatal viral and parasitic diseases, including: Yellow Fever, Dengue, Zika, Chikungunya, Malaria, Chagas, Leishmaniosis, Onchocercosis, Angiostrongylosis, Fasciolosis, among many others, and most of them often involve a vector organism as a common factor (Guzmán & Kourí 2002, WHO, 2019). These diseases are widespread in the tropics, with local variations in risk, so they are highly dependent on rainfall, temperature and rapid unplanned urbanization, among others (Troyo *et al*., 2008; Gould *et al*., 2017; Benavides *et al*., 2021).

To these problems, we can now add global warming and the intensification of extreme meteorological disturbances, which has brought about changes in the behavior of diseases and their transmissions, with the establishment of vector species in places never recorded before (Gore, 2007; Fajardo *et al*., 2016; Real, 2017). Climate change is considered one of the main environmental problems, and its effects undoubtedly have a negative impact on human health (Gore, 2007; Ehelepola *et al*., 2015; Sharmin *et al*., 2015; Márquez *et al*., 2019). There are several studies that relate climatic variables with the increase of infectious diseases, where arbovirosis has been one of the most studied, and it has been shown that there is a positive relationship between climate variation and the incidence of these infectious entities (García *et al*., 2012; Osés *et al*., 2017a; Sánchez *et al*., 2017; Osés *et al*., 2018a; Fimia *et al*., 2020a).

The relationship between the incidence of Dengue and climatological variables is mainly given in the characteristics of the vector, its life cycle and the conditions that favor the proliferation of the vector (Brenda *et al*., 2000; Marquetti, 2006; Fimia *et al*., 2015, Wilke *et al*., 2016). Among the most influential climatic variables, elevated temperature, humidity and precipitation volume are reported (Osés *et al*., 2016, Osés *et al*., 2018b, Machado, 2019; Fimia *et al*., 2020b).

All vector-borne diseases in the world have very high incidence rates; for example, it is estimated that between 50-100 million cases of Dengue fever occur each year (Ortega, 2001; Guzmán *et al*., 2013; Gould *et al*., 2017). This viral entity has been considered for many years as a public health problem in the world, especially in tropical countries where the influences of environmental variables favor the increase of cases each year (Service, 1992; Guzmán *et al*., 2013; Gould *et al*., 2017).

However, the main health problem in terms of vectors continues to be Malaria, with 500 million reported cases and three million deaths each year, of which one million are children under five years of age (Service, 1992; Das & Amalraj, 1997; Dia *et al*., 2003); this entity causes the death of one person every 60 seconds (Dia *et al*., 2003; Póvoa *et al*., 2003; Beck-Johnson *et al*., 2013; Fimia *et al*., 2017a). Cuba, due to its geographic location and climatological characteristics, has a wide fauna of culicidae with proven vectorial capacity, making them of great interest for human and other animal health (Marquetti, 2006; Fimia *et al*., 2017a).

Efforts to control vector-borne diseases have been hampered in part by the development of drug-resistant etiologic agents, insecticide-resistant mosquitoes, environmental contamination, residual effect of chemicals, high prices of insecticides in the market and operational failures (Das & Amalraj, 1997; Guzmán *et al*., 1999; Ayala *et al*., 2008; Ngoagouni *et al*., 2015; Fimia *et al*., 2016; Alarcón *et al*., 2017).

There is the possibility of making forecasts of high quality, precision and certainty using several methodologies, among which stands out, the methodology of Regressive Objective Regression (ROR), which due to its simplicity and accuracy can open an important window to know the future of climate variables or daily data, years in advance (Osés *et al*., 2017b; Osés *et al*., 2018a, b); this cycle can be extended to the 11 years of the solar cycle, or to higher cycles, which are known in nature; the population dynamics of mollusks and insects, such as culicidae and their interactions with certain environmental variables, can also be modeled, with the aim of establishing prophylactic and timely control measures in epidemiological surveillance programs (Fimia *et al*., 2017b; González *et al*., 2017; Machado *et al*., 2018). Consequently, there is a growing need to develop and implement other strategies for the control of infectious entities and their vectors, which can complement existing methods in a more effective and efficient way.

The objective of the research was to demonstrate the relationship between the transmissible infectious entities Dengue and Malaria with climate through mathematical modeling in Villa Clara province, Cuba.

MATERIALS AND METHODS

Study area

The research was carried out in Villa Clara province, Cuba, whose provincial capital is Santa Clara municipality and covered the 13 municipalities that comprise it (Figure 1). Villa Clara province is located in the central region of the island of Cuba (Latitude: 22º 29'40" N, Longitude: 79º28'30" W), and has the following geographical limits; to the west, with Matanzas province, to the east, with Sancti Spíritus province and to the south, with Cienfuegos province (Figure 1).

Figure 1. Political-administrative map of Cuba with the 13 municipalities of Villa Clara province

Period of study and data collection

The research covered the period from 2008 to 2020. Retrospective data on the main species of culicidae identified in the 304 permanent breeding sites and 218 temporary breeding sites in the province were collected from the existing control sheets/records kept in the Statistical Department of the Provincial Unit of Surveillance and Antivectorial Control (UPVLA) of Villa Clara province. The method used to collect mosquito larvae was the ladle method (WHO, 1982). Likewise, the mosquito species to which the larvae belonged were identified by means of the MSB-9 stereo microscope, using specialized keys (Pérez-Vigueras, 1956; Méndez *et al*., 2005; González, 2006) and taking into account all recent changes in the systematics and taxonomy of Culicidae (Reinert, 2000, 2001 and 2004).

In the case of Dengue, a cross-sectional descriptive research was conducted in the province of Villa Clara, Cuba, from January 2017 to December 2020. The universe consisted of all patients who contracted Dengue fever during that period. The selected sample coincided with the total population under study. Monthly data corresponding to the number of Dengue cases in the province were used, and for the same period, a climatic database was created, which included variables from the Yabú meteorological station, located in Santa Clara municipality, capital of Villa Clara province. Both qualitative and quantitative variables were taken into account:

N of monthly cases
Incidence by municipality
Incidence rates by municipality
Average temperature (T. media)
Maximum temperature (T. max)
Minimum Temperature (T. min)
Average Humidity (Med. R.H. Med)
Maximum Relative Humidity (RHx)
Minimum Relative Humidity (RHn)
Precipitation (Prec)
Wind speed (Vmed)
Station Atmospheric Pressure (Patm)
Cloudiness (Nub)
Saturation Deficit (Dsat)
Water Vapor Tension (Tva)

The technique for obtaining and collecting data was based on the use of the "Panorama of Diseases" register, which is obligatory, as well as the Provincial Meteorological Center's record of observations during the study period. The information obtained from these records was entered into a database, which was processed in the SPSS software, version 25. The Pearson coefficient was calculated and the Chi-square test was applied; in addition, the cases of Dengue were modeled in the short and long term using the methodology of the Regressive Objective Regression (ROR), with climatic variables (minimum temperature and precipitation).

Determination of time series and trends

In addition to collecting data on the main species of culicidae identified in the province, data were collected on larval densities, both general and specific (Anopheline) in each of the 13 municipalities of the province during the aforementioned study period. These data were organized in the Windows Excel application by years and months; that is, three columns were placed: the first with the years, the second with the 12 months that make up each year and the third with the values of the General Larval Density (GLD) and Specific Larval Density (SLD). This procedure was done for each municipality in the province. After organizing the data, we proceeded to obtain the time series and trend for each of the aforementioned variables, which was reflected in the line figures prepared for all the municipalities.

Development of Predictive Models for Culicidae Population Dynamics

Objective Regressive Regression (ORR) modeling was used to develop the predictive model. The following were defined as response variables: General Larval Density (GLD) and Specific Larval Density (SLD), and as explanatory variables: meteorological variables: Maximum Relative Humidity (RHX), Mean Relative Humidity (MRH), Minimum Relative Humidity (MRH), Maximum Temperatures (TX), Mean Temperatures (MT), Minimum Temperatures (MT), Provincial Precipitation (Prec.), Cloudiness (Nub.), Average Wind Speed (VMV), Atmospheric Pressure (PA). Data for both response and explanatory variables are from the same time period (2008-2015). The data of the meteorological variables were requested to the Provincial Meteorological Center of Villa Clara and they come from the four Meteorological stations of Villa Clara province, located in the municipalities of Santa Clara, Manicaragua, Caibarién and Sagua La Grande. The data obtained were processed by means of Pearson correlations and Student's t-test, as a statistical significance test. The statistical package SPSS ver. 13.

Objective Regressive Regression methodology (ORR)

In this methodology, the dichotomous variables DS, DI and NoC must be created first, where: NoC: Number of cases of the base (its coefficient in the model represents the trend of the series). DS = 1, if NoC is odd; DI = 0, if NoC is even, and vice versa. DS represents a sawtooth function and DI this same function, but in inverted form, so that the variable to be modeled is trapped between these parameters and a large amount of variance is explained.

Subsequently, the module corresponding to the Regression analysis of the statistical package SPSS version 19.0 (IBM Company) is executed, specifically the ENTER method where the predicted variable and the ERROR are obtained. Then, the autocorrelograms of the ERROR variable are obtained, paying attention to the maximum of the significant partial autocorrelations (PACF), and then the new variables are calculated, taking into account the significant Lag of the PACF. Finally, these variables are included in the new regression, regressed in a process of successive approximations until a white noise in the regression errors is obtained. In the case of atmospheric pressure, the lags of one year in advance were used.

RESULTS AND DISCUSSION

To date, 43 species of mosquitoes distributed in 15 genera have been identified in Villa Clara province, being the best represented and distributed species *Anopheles albimanus* (Wiedemann, 1821), *Culex quinquefasciatus* (Say, 1823), *Cx. nigripalpus* (Theobald, 1901), *Gymnometopa mediovittata* (Coquillett, 1906), *Psorophora confinnis* (Lynch Arribálzaga,1891), *Aedes aegypti* (Linnaeus, 1762) and *Ae. albopictus* (Skuse, 1894) (present in all 13 municipalities of this province), followed by *Culex corniger* (Theobald, 1903), *Ochlerotatus scapularis* (Rondan, 1848) and *Psorophora ciliata* (Fabricius, 1794) (in 12 of the 13 existing municipalities), all of which are shown in table 1.

Table 1. Distribution of mosquito species identified by municipality

Species of mosquitoes		Municipios	Total
Aedeomyia squamipennis	(Lynch Arribálzaga,1878)	9, 12	**2**
Anopheles albimanus	(Wiedemann, 1821)	1, 2, 3, 4, 5, 6, 7, 8,9,10,11,12,13	**13**
An. atropos	(Dyar y Knab, 1906)	5,6	**2**
An. grabhamii	(Theobald, 1901)	5,6,11	**3**
An. vestitipennis	(Dyar y Knab, 1906)	3,5,6,7,8,9,11	**7**
An. crucians	(Wiedemann, 1828)	5,8,12	**3**
Aedes aegypti	**(Linnaeus, 1762)**	**1, 2, 3, 4, 5, 6, 7, 8,9,10,11,12,13**	**13**
Ae. albopictus	(Skuse, 1894)	1, 2, 3, 4, 5, 6, 7, 8,9,10,11,12,13	**13**
Howardina walkeri	(Theobald, 1901)	2, 6,11,12	**4**
Coquillettidia nigricans	(Coquillett, 1904)	9,11	**2**
Culex atratus	(Theobald,1901)	4,5,6,8,9,10	**6**
Cx. bahamensis	(Dyar y Knab, 1906)	6,8	**2**
Cx. cancer	(Theobald, 1901)	1,5,6	**3**
Cx. chidesteri	(Dyar, 1921)	1,2,6,8,9,11,12	**7**
Cx. corniger	(Theobald, 1903)	1, 2, 3, 4, 5, 6, 7, 8,9,10,12,13	**12**
Cx. erraticus	(Dyar y Knab, 1906)	4, 5, 6, 7, 8,9,10,12,13	**9**
Cx. iolambdis	(Dyar, 1918)	8,9	**2**
Cx. nigripalpus	(Theobald, 1901)	1, 2, 3, 4, 5, 6, 7, 8,9,10,11,12,13	**13**
Cx. pilosus	(Dyar y Knab, 1906)	1,3,4,5,6,8,13	**7**
Cx. quinquefasciatus	(Say, 1823)	1, 2, 3, 4, 5, 6, 7, 8,9,10,11,12,13	**13**
Cx. sphinx	(Howard, 1915)	6	**1**
Cx. secutor	(Theobald, 1901)	8,13	**2**
Cx. americanus	(Neveu-Lemaire, 1902)	6,9	**2**
Gymnometopa mediovittata	(Coquillett, 1906)	1, 2, 3, 4, 5, 6, 7, 8,9,10,11,12,13	**13**
Mansonia titillans	(Walker, 1848)	3,6,8,9,10,11,12	**7**
Limatus durhamii	(Theobald, 1901)	9,12	**2**
Ochlerotatus scapularis	(Rondan, 1848)	1, 2, 3, 4, 5, 6, 7, 8,9,10,11,12	**12**
Oc. sollicitans	(Walker, 1856)	1,3,4,5,6,7,10,11	**8**
Oc. taeniorhynchus	(Wiedemann, 1821)	1, 2, 3, 4, 5, 6, 7, 10,11	**9**
Oc. tortilis	(Theobald, 1903)	3,4,5,7,9	**5**
Orthopodomyia signifera	(Coquillett, 1896)	8,12	**2**
Psorophora ciliata	(Fabricius, 1794)	1, 2, 3, 4, 6, 7, 8,9,10,11,12,13	**12**
Ps. confinnis	(Lynch Arribálzaga,1891)	1, 2, 3, 4, 5, 6, 7, 8,9,10,11,12,13	**13**
Ps. howardii	(Coquillett, 1901)	6,7,8,9,10,12,13	**7**
Ps. johnstonii	(Grabham, 1905)	6	**1**
Ps. pygmaea	(Theobald, 1903)	1,4,5,6,7,9,10,13	**8**
Ps. santamarinai	(González Broche, 2000)	6	**1**
Ps. insularia	(Dyar y Knab, 1906)	6	**1**
Ps. infinis	(Dyar y Knab, 1906)	8	**1**
Toxorhynchites portoricensis	(von Röder, 1885)	5,6	**2**
Uranotaenia sapphirina	(Osten-Sacken, 1868)	3,4,5,6,7,8,9,11,12	**9**
Wyeomyia vanduzeei	(Dyar y Knab, 1906)	9	**1**
Wy. mitchelli	(Theobald, 1905)	8,9	**2**

Legend: List of municipalities of Villa Clara province: 1 Corralillo, 2 Quemado de Güines, 3 Sagua la Grande, 4 Encrucijada, 5 Camajuaní, 6 Caibarién, 7 Remedios, 8 Placetas, 9 Santa Clara, 10 Cifuentes, 11 Santo Domingo, 12 Ranchuelo and 13 Manicaragua.

Of the 69 species of mosquitoes registered for Cuba (González, 2013), in Villa Clara, the number of identified species is 43/62.31 %, so that species was collected in all the fluvial ecosystems sampled, which evidenced the great ecological plasticity of the entomofauna of culicidae existing in our country, in spite of being an archipelago, which corroborates the results obtained by García (1977) and González (1985).

The genera best represented and with a marked presence in the municipalities studied were *Anopheles*, *Culex* and *Psorophora*, while the species best represented and distributed in this province were *An. albimanus*, *Cx. quinquefasciatus*, *Cx. nigripalpus*, *Gy. mediovittata*, *Ps. confinnis*, *Ae. aegypti* and *Ae. albopictus* (present in all 13 municipalities of this province), followed by *Culex corniger*, *Ochlerotatus scapularis* and *Psorophora ciliata* (in 12 of the 13 existing municipalities), being the most common and best represented species in this investigation: *An. albimanus*, *An. crucians*, *Cx. atratus*, *Cx. quinquefasciatus*, *Cx. Nigripalpus* and *Ps. confinnis*, because they were distributed in almost all the ecosystems sampled, where they appeared in relatively high abundance, a fact that agrees with the results obtained by Marquetti (2006), specifically for *Cx. quinquefasciatus* in the urban ecosystem; this result also confirms the criteria of Mattingly (1962), Scorza (1972) and Cruz & Cabrera (2006) in relation to the extraordinary adaptive capacity and high ecological plasticity of *Cx. quinquefasciatus* in the most diverse and possible habitats provided by man.

The fact that *Ae. aegypti* and *Ae. albopictus* are gaining ground and space in Villa Clara province is notorious and relevant. These species are of high entomoepidemiological risk because of their involvement in several infectious entities (Komar, 2003; Mackenzie *et al*., 2005; Pupo *et al*., 2011; Guzmán *et al*., 2013), among which Dengue, Yellow Fever, West Nile virus, Chikungunya and Zika virus stand out; but reality has shown us, that at present, these two species are practically present throughout the length and breadth of the national geography, expanding increasingly, colonizing an important number of breeding sites generated by human activity together with environmental variables (Bangs *et al*., 2006), thus showing their high ecological plasticity and high capacity to adapt to the most dissimilar ecological niches (Marquetti, 2006; Fimia *et al*., 2015).

When mathematically modeling the influence of the meteorological variables under study on the Specific Larval Density (*An. albimanus*) in the hatcheries (Table 2), it was observed that the correlations between anopheline larval density and temperatures were positive and highly significant for minimum and mean temperatures, which indicates that as temperatures increase, specific larval densities also increase, results that coincide with those reached by García *et al*. (2012) and Beck-Johnson *et al*. (2013), who state that temperatures rather than rainfall play an important role in increasing anopheline larval density and malaria transmission. Both maximum and minimum temperatures have a positive association with anopheline larval densities and could be used as a predictor of the rate of *Anopheles* spp. infestation (Zhang *et al*., 2010).

Table 2. Modeling of temperature on Specific Larval Density (SLD)

Modeling variables	Mean temperature	Maxime temperature	Minimum temperature
Anopheline Larval Density (ALD)	0.09 (**)	0.08 (*)	0.10 (**)

** Pearson's correlation significant at the 0.01 level (bilateral)

* Pearson's correlation significant at the 0.05 level (bilateral)

Source: Statistical records of the Institute of Meteorology of Villa Clara.

The association between temperature and population dynamics of culicidae has been investigated in many studies, particularly in tropical and sub-tropical areas. The results of this study are consistent with previous studies in other regions of the world (Zhou *et al*., 2004; Zhang *et al*., 2015).

The correlations between specific larval density with Relative Humidity were also positive and highly significant. Indicating, that as relative humidity increases, larval density increases (Table 3). We agree with Farajzadeh *et al*. (2015), who define relative humidity as a vital meteorological variable in the survival of mosquitoes of the genus Anopheles. These researchers further found relative humidity and temperature to be strong predictors of *Anopheles* mosquito abundance. Wilke *et al*. (2016) found associations between mosquito abundance and meteorological variables. In addition, they consider that predictive models based on meteorological variables can provide important information on the population dynamics of culicidae. Average relative humidity is a suitable predictor of anopheline larval density, and thus malaria transmission (Aduh-Prah & Kofi-Tetteh, 2015; Alkhaldy, 2017).

Table 3. Modeling of Relative Humidity on Larval Specific Density

Modeling variables	Mean relative humidity	Maximum relative humidity	Minimum relative humidity
Anopheline Larval Density (ALD)	0.07 (*)	0.09 (**)	0.10 (**)

* Pearson's correlation significant at the 0.05 level (bilateral)
** Pearson's correlation significant at the 0.01 level (bilateral).
Source: Statistical records of the Institute of Meteorology of Villa Clara.

In Table 4, when correlating the climatological variables (precipitation, cloudiness and average wind speed), no correlation was observed between anopheline larval density with precipitation and cloudiness. Mean wind speed had a negative and highly significant correlation, indicating that as mean wind speed decreases, larval density increases. These findings are in agreement with those found by Bezerra *et al*. (2016), who did not find a positive association between *Anopheles* spp. larval density and rainfall. The highest larval densities determined by them were found in the months of the rainy period. This can be explained by the fact that, in the rainy season, the frequently high levels of rainfall could modify the life cycle of the culicidae, since an excessive increase in water levels in the breeding sites could contribute to the immature forms of the mosquito escaping or dying, and not being able to complete their life cycle. In addition, we agree with Aduh-Prah & Kofi-Tetteh (2015) who, despite finding that there was no significant association between rainfall and larval densities, consider that there is evidence that rainfall is an important predictor of larval density.

Table 4. Modeling of rainfall, cloud cover and mean wind speed on anopheline larval density

Modeling variables	Precipitations	Cloudiness	Mean wind speed
Anopheline Larval Density (ALD)	0.02	0.05	0.09 (**)

** Correlation significant at the 0.01 level (bilateral).
Source: Statistical records of the Institute of Meteorology of Villa Clara.

Table 5 shows that atmospheric pressure is a good predictor of culicidae larval densities, since a positive and significant association was found between both variables. As well as the influence exerted by the North Atlantic anticyclone, which dictates the behavior of atmospheric pressure in Cuba.

Table 5. Modeling of atmospheric pressure on General Larval Density (GLD) in the municipality of Corralillo

	Unstandardized coefficients		Standardized coefficients		
Modeling Variable	**B**	**Standard error**	**Beta**	**t**	**Sig.**
Atmospheric Pressure	.002	.001	3.744	3.123	.003

This finding can be explained by the fact that oxygen taken under partial or total gas pressures is only regulated by changes in spiracle movements. At reduced oxygen tensions, both the opening and the time the spiracles remain open increases. At low atmospheric pressures, the spiracles remain permanently open, so that dehydration may be the main cause of mortality at low atmospheric pressures (Galun & Fraenkel, 1961).

This finding constitutes a really novel result of the present work, since atmospheric pressure is a meteorological variable scarcely studied in terms of the influence that it can exert on the larval densities of culicidae of entomoepidemiological importance, since most of the investigations reviewed at national and international level address in their models the following meteorological variables: temperature, relative humidity and precipitation; however, atmospheric pressure has remained a scarcely studied variable, perhaps because of the very narrow range in which its values fluctuate over time. In fact, we were forced to find a biological explanation for the influence of atmospheric pressure on the General Larval Density (GLD) of culicidae, and we found the article by Galun & Fraenkel (1961) who investigated the influence of atmospheric pressure on mosquito larval densities artificially, since they had to create a team to achieve this purpose.

Effects of some meteorological variables on Dengue fever in Villa Clara province

In relation to the calculation of Pearson's correlation coefficient and its statistical significance, between the incidence of Dengue cases and the climatological variables, it should be noted that there was a significant correlation (r=0.332; p=0.023) between this variable and the Minimum Temperature, as this increases, the cases of Dengue increase, and in the case of Atmospheric Pressure it was also significant (r=-0.317; p=0.030), since as this increases, the cases of Dengue decrease. Water Vapor Tension was significant (r=-0.298; p=0.042), as it increases, cases of Dengue also increase. The other variables were not significant (Table 6).

Table 6. Correlation of climatological variables with the incidence of Dengue cases. Villa Clara 2017-2020

Climatological Variables	Pearson correlation	Sig. (bilateral)
Mean temperature	0.268	0.069
Maximum temperature	0.194	0.192
Minimum temperature	0.332	0.023
Maximum relative humidity	-0.23	0.412
Minimum relative humidity	0.155	0.299
Mean relative humidity	0.127	0.396
Saturation density	0.002	0.991
Atmospheric pressure	-0.317	0.030
Cloudiness	0.079	0.596
Average wind speed	-0.013	0.933
Precipitations	-0.120	0.423
Water Vapor Tension	0.298	0.042

Source: Provincial Meteorological Center and Overview of notifiable diseases. Villa Clara 2017-2020.

Regarding the relationship of climatological variables with the incidence of Dengue. It was observed that the distributions of confirmed cases increased in the summer months and decreased considerably in the winter months. The intervals in which the considerable increase in cases was observed also coincided with the cyclonic season in Cuba, so it is inferred that there is a relationship in terms of the meteorological determinants that determine this period in the national territory and the incidence of Dengue, which is consistent with results obtained by other researchers, both in Villa Clara province and in other locations in Cuba (Rodríguez *et al*., 2006; Fimia *et al*., 2012; Diéguez *et al*., 2015; Fimia *et al*., 2016; Machado *et al*., 2018).

In relation to the geographical distribution, a higher incidence was identified in the municipality of Santa Clara, which corresponds to an urban area with a higher population density, so it should be considered that the urbanization factor has a positive influence on the number of reported cases, which is consistent with results obtained by other authors, both in Cuba and in countries of the American continent (Diéguez *et al*., 2015; Fajardo *et al*., 2016; González *et al*., 2019; Ayala *et al*., 2021; Rydzanicz *et al*., 2021).

Dengue cases were modeled in the short term using the ROR methodology (Table 7) with the climatic variables (Tmin and Prec), the latter variable was used even though no significant relationship was found in the study, because it is widely used in the studies consulted, due to its demonstrated incidence in the vector's life cycle. This model explains 95.4% of the variance, with an error of 135 cases, the Durbin Watson statistic is close to 2, so we are in the presence of a valid model; there is no more information on the errors.

Table 7. Summary of the model using the ROR methodology

Model summary [c, d]

Model	R	R squared[b]	R squared adjusted	Standard error of estimation	Durbin-Watson
1	.954[a]	.911	.866	134.963	2.182

a. Predictors: Lag17Prec, Lag8Total, Lag14Total, DS, Lag2Total, Lag10Total, DI, Lag1Total, NoC, Lag1Tmin.
b. For regression through the origin (the model without intercept), R-squared measures the proportion of the variability in the dependent variable over the origin explained by the regression. This CANNOT be compared to R-squared for models that include intercept.
c. Dependent variable: Total
d. Linear regression through the origin

In relation to the analysis of climatological variables, there was concordance between the results of the study and others reviewed, in which temperature and relative humidity are variables with high correlation with the incidence of Dengue (Osés *et al*., 2018a, b; Fimia *et al*., 2019; Machado, 2019; Fimia *et al*., 2020a, b).

Temperature, humidity and wind directly influence the occurrence of Dengue outbreaks; high temperature with average humidity and low winds create conditions conducive to an increase in the intensity of disease transmission (Garcia *et al*., 2012; Osés *et al*., 2018a, b; Fimia *et al*., 2019; Fimia *et al*., 2020b). The influence of environmental temperature on the *Aedes* spp mosquito and the transmission of the Dengue virus, has postulated that, due to the action of climate change, the mosquito has appeared and adapted in places where it was not frequent, allowing the viruses to spread uncontrolled in different regions, potentiated by climatic variables (precipitation and humidity), which influence the infestation of areas in tropical and subtropical regions, related to a greater availability of breeding sites, and a higher frequency of feeding under conditions of water stress, which is a modulating factor in the emergence of epidemics and increase virus transmission (Diéguez *et al*., 2015; Osés *et al*., 2018a, b; Fimia *et al*., 2019; Fimia *et al*., 2020b).

The model was significant at 100 % (Table 8), with a Fisher's F of 20, significant at 100 %.

Table 8. Analysis of Variance of the model for short-term Dengue

ANOVA[a,b]

Model		Sum of squares	gl	Quadratic mean	F	Sig.
1	Regression	3727352.201	10	372735.220	20.463	.000[c]
	Residue	364301.799	20	18215.090		
	Total	4091654.000[d]	30			

a. Dependent variable: Total
b. Linear regression through the origin
c. Predictors: Lag17Prec, Lag8Total, Lag14Total, DS, Lag2Total, Lag10Total, DI, Lag1Total, NoC, Lag1Tmin.
d. This total sum of squares is not corrected for the constant because the constant is zero for regression through the origin.

The ROR model in question (Table 9) consists of the following variables: DS (sawtooth) and DI (inverted sawtooth), which are dichotomous variables and the number of Dengue cases in backward steps in 1, 2, 8, 8, 10 and 14 months (Lag1Total, Lag2Total, Lag8 Total,Lag10 Total, lag14 Total), also depends, on the Tmin regressed on 1 month (Lag1Tmin), and the Prec regressed on 17 months (Lag17Prec), as this increases, the cases of Dengue increase, for example, when the precipitation is 100 mm, the number of cases of Dengue increases by 131 cases in the month, the trend was significant to increase in 41 cases. All variables were significant.

Table 9. ROR modeling for Dengue cases regressed over time with some climatic variables

Coefficients [a,b]

Model		Unstandardized coefficients		Standardized coefficients	t	Sig.
		B	Standard error	Beta		
1	DS	-3105.190	439.709	-5.945	-7.062	.000
	DI	-2974.767	431.547	-5.696	-6.893	.000
	Tendency	41.202	7.518	3.752	5.480	.000
	Lag1Total	.321	.141	.321	2.285	.033
	Lag2Total	-.447	.143	-.430	-3.132	.005
	Lag8Total	-.458	.142	-.440	-3.212	.004
	Lag10Total	-.577	.137	-.555	-4.229	.000
	Lag14Total	-1.526	.239	-1.038	-6.397	.000
	Lag1Tmin	103.065	16.538	5.845	6.232	.000
	Lag17Prec	1.312	.283	.606	4.637	.000

a. Dependent variable: Total
b. Linear regression through the origin

Variations in the water temperature in which mosquito larvae develop influence their survival. Thus, the development of *Ae. aegypti* is reduced when the water temperature decreases or increases due to the physiological optimum range, which oscillates between 16 and 35 °C (Sharmin *et al*., 2015; Benítez, 2018; Márquez *et al*., 2019; Fimia *et al*., 2019). The effect of climate change has been evaluated on different aspects of Ae. aegypti biology, where precipitation and temperature have been reported as factors that influence not only the population dynamics of this species, but also its ability to transmit different types of viruses (Fimia *et al*., 2015; Sharmin *et al*., 2015; Osés *et al*., 2016; Wilke *et al*., 2016; Benítez, 2018; Márquez *et al*., 2019).

Moreover, precipitation plays an important role as a predisposing factor for Dengue, because while temperature influences virus replication, precipitation is related to mosquito habitat (Garcia *et al*., 2012; Xu *et al*., 2014; Sharmin *et al*., 2015; Wilke *et al*., 2016; Márquez *et al*., 2019). Although the increase in temperatures generates that humans store more water, so that the vector can spread more easily to urban areas; when the La Niña phenomenon occurs, soil moisture and naturally accumulated water residues are conducive to the vector's reproductive cycle (Troyo *et al*., 2008; Diéguez *et al*., 2015; Bezerra *et al*., 2016; Fajardo *et al*., 2016; Machado *et al*., 2018).

The inverse relationship between the incidence of Dengue and atmospheric pressure could be due to the fact that the higher the atmospheric pressure, the lower the probability of rainfall. On the other hand, the direct relationship of dependence between cloudiness and temperature with the increase of Dengue cases is due to the fact that the higher the temperature, the higher the cloudiness, and with it, also increases the probability of rainfall, creating favorable conditions for the proliferation of the vector (Fimia *et al*., 2015; Osés *et al*., 2016; Fimia *et al*., 2019; Machado *et al*., 2019).

A long-term model was performed, that is, with a lag of 12 months (1 year) to search in advance in the forecast, obtaining a model that explains 82.9 %, with an error of 306 cases, where Fisher's F was 3.6, significant at 95 % (Table 10).

Table 10. Long-term modeling on a 12-month basis

ANOVA[a,b]

Model		**Sum of squared**	**gl**	**Quadratic mean**	**F**	**Sig.**
1	Regression	2679044.400	8	334880.550	3.569	.021[c]
	Residue	1219818.600	13	93832.200		
	Total	3898863.000[d]	21			

a. Dependent variable: Total

b. Linear regression through the origin

c. Predictors: Lag14Patm, Lag26Total, Lag20Total, DI, Lag14Total, Lag13Total, NoC, Lag13Tmin.

d. This total sum of squares is not corrected for the constant because the constant is zero for regression through the origin.

Below are the results of the long-term model. In red the predicted value for the year 2021, where an increase is expected in the month of February to decrease from March to July, then from August to December, the values will increase greatly (Table 11).

Table 11. Long-term modeling for the year 2021

Case summaries[a]

	Years/ Months	**Total**	**Unstandardized Predicted Value**	**Unstandardized residual**
27	201903.00	0	263.17511	-263.17511
28	201904.00	67	65.31128	1.68872
29	201905.00	58	320.96671	-262.96671
30	201906.00	321	618.48470	-297.48470
31	201907.00	709	512.88789	196.11211
32	201908.00	544	719.47803	-175.47803
33	201909.00	888	512.70928	375.29072
34	201910.00	1221	602.22787	618.77213
35	201911.00	607	391.42575	215.57425
36	201912.00	51	335.65956	-284.65956
37	202001.00	144	81.85423	62.14577
38	202002.00	19	-87.79324	106.79324
39	202003.00	92	-32.54104	124.54104
40	202004.00	59	-89.12622	148.12622
41	202005.00	75	-45.43644	120.43644
42	202006.00	87	294.02186	-207.02186
43	202007.00	0	356.46147	-356.46147
44	202008.00	0	20.81879	-20.81879
45	202009.00	0	112.73595	-112.73595
46	202010.00	541	430.91737	110.08263
47	202011.00	0	100.10287	-100.10287
48	202012.00	.	-183.01860	.
49	202101.00	.	-186.50764	.
50	202102.00	.	110.59928	.
51	202103.00	.	-777.22693	.
52	202104.00	.	-557.63272	.
53	202105.00	.	-649.93080	.
54	202106.00	.	-673.56864	.
55	202107.00	.	-159.39669	.
56	202108.00	.	873.05625	.
57	202109.00	.	1305.09638	.
58	202110.00	.	1225.58847	.
59	202111.00	.	1342.80937	.
60	202112.00	.	1866.51432	.
Total **N**	**100**	**47**	**34**	**21**

a. Limited to the first 100 cases.

Figure 2 shows the good coincidence of the model, despite the fact that we are in the presence of a model 1 year in advance, a significant increase in Dengue cases in the province is expected for the second half of the year, a matter that should be treated with caution, so taking preventive measures would be very beneficial.

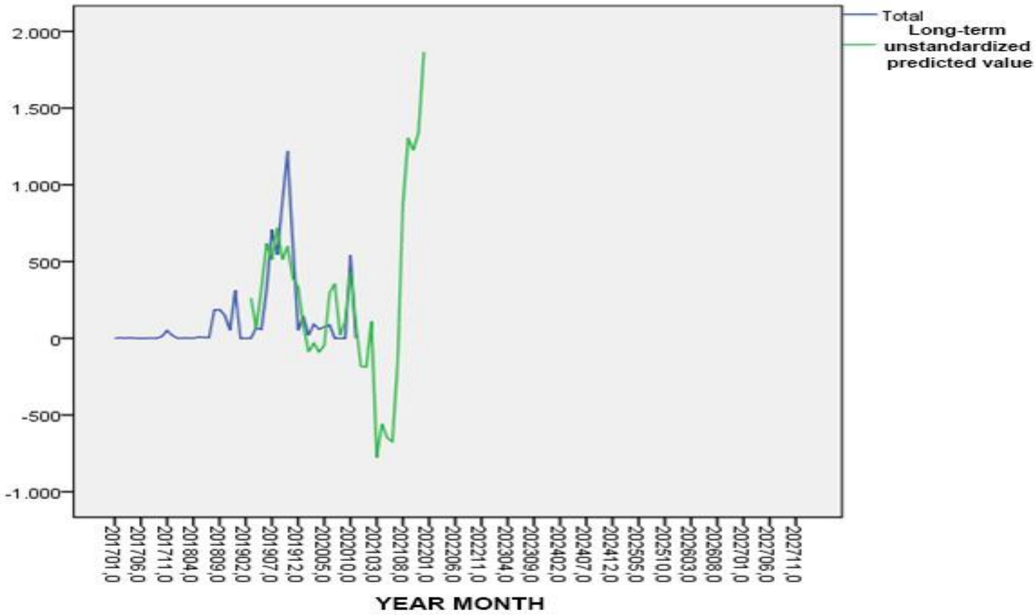

Figure 2. Long-term forecast for Dengue cases in Villa Clara, Cuba

The ROR methodology consists of several steps and allows not only to mathematically model the larval densities of mosquitoes, as well as the population dynamics of mollusks, but goes beyond (possibility of modeling infectious entities of different etiologies, such as HIV/AIDS, Cholera, Influenza, Acute Respiratory Infections (ARI), Acute Bronchial Asthma (CAAB), Fasciolosis, Angiostrongylosis and even, in the estimation of the length and area of the universe, monthly forecasting of precipitation and extreme temperatures, forecasting of meteorological disturbances (hurricanes), prediction of the latitude and longitude of earthquakes, search for information on white noise, modeling of the Equivalent Effective Temperature (TEE) and Atmospheric Pressure (PA) up to the electricity consumption of a municipality, province and/or nation) (Osés & Grau, 2011; Osés *et al*., 2017b; Osés *et al*., 2018c; Osés *et al*., 2019).

CONCLUSIONS

It is concluded that there is a close relationship between the infectious entities analyzed and the species of vector organisms with the climate, demonstrated by means of the predictive model for the specific and general larval densities of culicidae, and the mathematical modeling ROR for the Dengue entity, so that it is possible to model and predict, Thus, it is possible to model and predict, in the short, medium and long term, both the population dynamics of culicidae with entomoepidemiological importance and the incidence of cases of Dengue, with very good results, making the ROR methodology an excellent predictive tool not only for transmissible entities of viral and parasitic etiology.

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