GSC Biological and Pharmaceutical Sciences

eISSN: 2581-3250 CODEN (USA): GBPSC2

Cross Ref DOI: 10.30574/gscbps

Journal homepage: https://gsconlinepress.com/journals/gscbps/

(Research Article)

Modeling and prediction of dengue cases in the short and long term in Villa Clara, Cuba using climatic variables and objective regressive regression

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GSC Biological and Pharmaceutical Sciences, 2022, 18(03), 035–045

Publication history: Received on 23 January 2022; revised on 01 March 2022; accepted on 03 March 2022

Article DOI: https://doi.org/10.30574/gscbps.2022.18.3.0090

Abstract

Climate has an important influence on infectious diseases and their different modes of transmission. Dengue is among the most relevant for Cuban public health. Due to the pronounced effect that environmental changes can have on the biology of *Aedes aegypti*, it is very likely that the epidemiology of this arbovirosis will be profoundly influenced by future climate change. The aim of the study was to analyze the possible relationship between meteorological variables and the incidence of Dengue in Villa Clara province, Cuba during the years 2017-2020, and to perform a predictive model of the behavior of the disease during 2021. Retrospective research was carried out in which the possible effects of diversifications of temperature, precipitation, humidity, water vapor tension, atmospheric pressure, wind speed, cloudiness and saturation deficit on the deviations in the epidemiological curves of Dengue infection in Villa Clara (2017-2020) were analyzed to predict the future behavior of the referred entity during the current year. A correlation of the infectious entity 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 a predictive model was obtained for 2021 with high reliability, in which a decrease in the incidence of Dengue is predicted in the month of March until July, but after August to December the values will increase greatly.

Keywords: Climate change; Dengue; Infectious diseases; Objective Regressive Regression; Climatic variables

1. Introduction

Dengue is an infectious disease transmitted mainly by the bite of the *Aedes aegypti* mosquito (Linnaeus, 1762) [1-3], although transmission has been reported from other species, such as *Ae. albopictus* (Skuse, 1894) [3-5]. It is a viral infection that does not have a well-defined treatment, and although there are many studies, it has not yet been possible to determine an effective vaccine to prevent the high incidence rates, especially in tropical regions [1, 3, 5, 7, 9, 10].

The origin of the term Dengue is not entirely clear. Although perhaps the Swahili word "dinga" or "dyenga" homonym of Swahili "Ki denga pepo" (meaning sudden attack brought on by an "evil spirit") The first potential record of a case of dengue, comes from a Chinese medical encyclopedia of the Jin Dynasty from 265 to 420 but the first definitive case report dates from 1789, and is attributed to Benjamin Rush, who coined the term "break bone fever", because of the

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associated symptoms of myalgias and arthralgias [1-3]. According to a historical account of the presence of dengue fever in the Americas, the disease may have first appeared in 1635 in Martinique and Guadeloupe, but the disease was identified and named as such in 1779 [3, 5, 7, 11, 12, 13].

Dengue fever is currently considered a public health problem in the world, especially in tropical countries where the influences of environmental variables favor the increase of cases every year [2, 3, 5, 9].

Climate change is considered one of the main environmental problems and its effects undoubtedly have a negative impact on human health [14-19]. 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 [16-19].

The relationship between the incidence of dengue and climatological variables is given mainly in the characteristics of the vector, its life cycle and the conditions that favor the proliferation of the vector [1, 3, 17, 20, 21, 23]. Among the most influential climatic variables are reported the elevation of temperature, humidity and volume of precipitation [17-23].

The indicators of dengue in Cuba have been varying over the years, showing sudden outbreaks, given by the incorporation of species and the virus itself in the national territory, but no epidemic outbreak has been reported in relation to changes in meteorological variables, even so, the study of the correlations between these variables and the emergence of new cases helps in the realization of predictive models of the behavior of the incidence of the disease in the near future, as well as in the management of outbreaks of this disease [24-27].

The objective of the research consisted of analyzing the possible relationship between meteorological variables and the incidence of Dengue in Villa Clara, Cuba during the years 2017-2020 by means of a predictive model of the behavior of the disease during 2021.

2. Material and methods

Cross-sectional descriptive research was conducted in Villa Clara province, 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 Villa Clara province were used.

2.1. Data collection and compilation

Data collection and compilation was carried out by means of a documentary review of the records and statistical files at the Provincial Unit of Surveillance and Antivectorial Fight (UPVLA) and at the Provincial Department of Health Statistics of Villa Clara, where the entire entomological history of the work cycles conceived in the 13 municipalities of the province is compiled, which is periodically reported in statistical tables established for such purposes by the National Direction of Surveillance and Antivectorial Control (DNVLA) and the Department of Health Statistics of the Ministry of Public Health (MINSAP). The "Panorama of Diseases" register, of obligatory declaration, was also used, as well as the control register of observations of the Provincial Meteorological Center of Villa Clara during the study period.

2.2. Meteorological variables

A climatic database was prepared, which included variables from the seven meteorological stations in Villa Clara province. Both qualitative and quantitative variables were taken into account, operationalized as follows:

- 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)

2.3. Data analysis and processing

The information obtained from these records was entered into a database, which was organized by years and months using the Windows Excel application. For data processing, the SPSS version 25 software was used; in addition, the Pearson coefficient was calculated and the Chi-square test was applied, and the short- and long-term Dengue cases were modeled using the Objective Regressive Regression methodology (ORR), with climatic variables.

2.4. Objective Regressive Regression Methodology (ORR)

For the modeling and prediction of Dengue cases in the short and long term, as well as climatic variables, it was carried out using the Objective Regressive Regression methodology (ORR) (28, 29), for which, in a first step, dichotomous variables DS, DI and NoC are created, where:

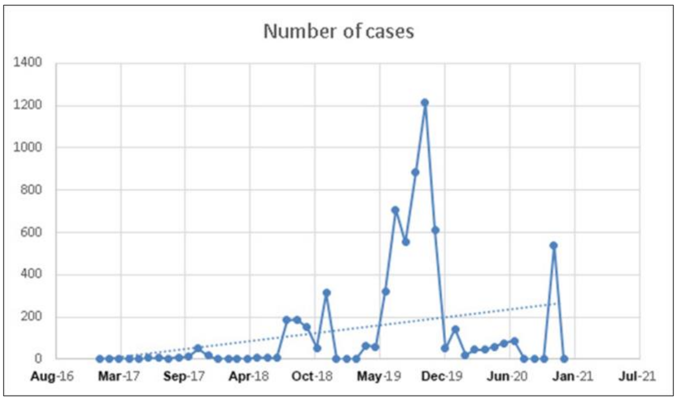
NoC: Number of cases in the base,
DS = 1, if NoC is odd; DI = 0, if NoC is even, when DI=1, DS=0 and vice versa.

Subsequently, the module corresponding to the Regression analysis of the statistical package SPSS version 19.0 (IBM Company) will be executed, specifically the ENTER method where the predicted variable and the ERROR are obtained.

Then the autocorrelograms of the variable ERROR will be obtained, paying attention to the maximums of the significant partial autocorrelations PACF. The new variables were then calculated taking into account the significant Lag of the PACF. Finally, these regressed variables were included in the new regression in a process of successive approximations until a white noise in the regression errors was obtained. In the case of atmospheric pressure, lags of 1 year in advance can be used, as other authors have done for the climatic indexes, although it is unlikely that 11 years in advance will yield results, since we only have data for 11 years in the base, nevertheless, in the monthly data we will try to use the results for the atmospheric pressure meteorological variable.

3. Results

The distribution of confirmed cases of dengue fever in Villa Clara province during the period from January 2019 to December 2020 is shown below. It is observed that there is an increasing trend from May to October (Figure 1).



Source: Overview of notifiable diseases. Villa Clara 2017-2020.

Figure 1 Distribution of confirmed cases of Dengue according to month of confirmation. Villa Clara 2017-2020

Table 1 Distribution of confirmed cases according to municipality of residence. Villa Clara 2017-2020

Municipalities of residence	**Number of cases by years**					**% of total cases of the municipality**
	2017	**2018**	**2019**	**2020**	**Total**	
Santa Clara	60	331	4072	869	5332	81.90
Remedios	1	8	13	5	27	0.41
Placetas	2	39	41	23	105	1.61
Caibarién	3	6	12	14	35	0.54
Camajuaní	1	10	67	25	103	1.58
Encrucijada	2	4	18	1	25	0.38
Sagua la Grande	16	162	22	8	208	3.20
Quemado de Güines	2	7	13	0	22	0.34
Santo Domingo	10	128	32	15	185	2.84
Ranchuelo	3	6	38	17	64	0.999
Corralillo	1	23	11	0	35	0.54
Manicaragua	11	58	104	30	203	3.12
Cifuentes	1	129	26	10	166	2.55
Total	113	911	4 469	1 017	6 510	100

Source: Overview of notifiable diseases. Villa Clara 2017-2020.

Table 2 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	-0.123	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 Panorama of notifiable diseases. Villa Clara 2017-2020.

Table 1 shows the distribution of confirmed cases according to area of residence (January 2017 to December 2020), being 2019 the year with the highest number of cases, with 4 469 and the municipality of Santa Clara, with the highest number of cases during the entire period studied, with 5 332, representing 81.90 % of the total number of cases, followed by the municipality of Manicaragua, with 203/3.12 % and then the municipality of Sagua la Grande (208/3.20 %), while the rest of the municipalities presented a lower number of cases.

Table 2 shows 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 is 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 is 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, Dengue cases increase. The other variables were not significant.

Table 3 Summary of the model using ROR

Model summary[c, d]					
Model	**R**	**R square[b]**	**Adjusted R-squared**	**Standard error of the estimate**	**Durbin-Watson**
1	0.954[a]	0.911	0.866	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.

Table 4 Analysis of Variance of the model for Dengue in the short term

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: Lag17 Prec, Lag8 Total, Lag14 Total, DS, Lag2 Total, Lag10 Total, DI, Lag1 Total, NoC, Lag1 Tmin; d. This total sum of squares is not corrected for the constant because the constant is zero for regression through the origin.

Table 5 Summary of the confirmation of the ROR model and its relationship with some climate 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	0.000
	DI	-2974.767	431.547	-5.696	-6.893	0.000
	Tendencia	41.202	7.518	3.752	5.480	0.000
	Lag1Total	.321	0.141	0.321	2.285	0.033
	Lag2Total	-.447	0.143	-0.430	-3.132	0.005
	Lag8Total	-.458	0.142	-0.440	-3.212	0.004
	Lag10Total	-.577	0.137	-0.555	-4.229	0.000
	Lag14Total	-1.526	0.239	-1.038	-6.397	0.000
	Lag1Tmin	103.065	16.538	5.845	6.232	0.000
	Lag17Prec	1.312	.283	.606	4.637	0.000

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

Dengue cases were modeled in the short term using the ROR methodology (Table 3) 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 proven 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. The ROR model in question (Table 5) 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), depends also, 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.

The model was significant at 100 % (Table 4), with a Fisher's F of 20, significant at 100 %.

A long-term model was performed, that is, with a delay of 12 months (1 year) to search in advance in the prognosis, obtaining a model that explains 82.9 %, with an error of 306 cases, where Fisher's F was 3.6, significant at 95 % (Table 6).

Tabla 6 Long term modeling with lag

ANOVA[a, b]						
Model		**Sum of squares**	**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: Lag14 Patm, Lag26 Total, Lag20 Total, DI, Lag14 Total, Lag13 Total, NoC, Lag13T min.; 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 current year, in this 2021 an increase is foreseen in the month of February to decrease from March to July, then from August to December the values will increase greatly (Table 7).

Table 7 Long-term model for the predicted value in 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.

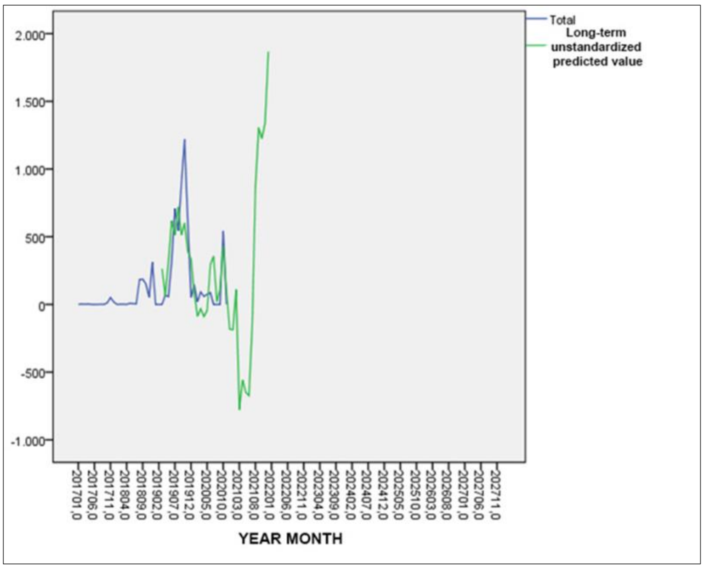


Figure 2 Long-term forecast of Dengue cases in Villa Clara, Cuba

4. Discussion

In the present investigation, climatological variables were related to the incidence of dengue. It was observed that the distributions of confirmed dengue 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 agrees with results obtained by other researchers, both in Villa Clara province and in other localities in Cuba [21, 29, 30, 31, 32, 38].

Regarding the geographical distribution, a higher incidence was identified in Santa Clara municipality, 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 cases reported, which is consistent with results obtained by other authors, both in Cuba and in countries of the American continent [33-40].

Regarding the analysis of climatological variables, there is concordance between the results of this study and others reviewed, in which temperature and relative humidity are variables with a high correlation with the incidence of Dengue [17, 19, 24, 26, 41, 42].

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 [18, 25, 27, 41, 42]. 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 virus to spread uncontrollably 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 in conditions of water stress, which is a modulating factor in the emergence of epidemics and increase the transmission of viruses [14, 16, 18, 22, 25, 27]. Variations in the temperature of the water 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 [14, 16, 42, 43, 45]. The effect of climate change has been evaluated in different aspects of the biology of *Ae. aegypti*, 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 [14, 16, 20, 22, 24, 25, 45].

Moreover, precipitation plays an important role as a predisposing factor for Dengue, because while temperature influences virus replication, precipitation is related to the mosquito's habitat [14, 16, 18, 22, 39, 44]. Although the increase in temperature causes humans to 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 [2, 8, 10, 21, 31, 39, 47, 48].

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, the probability of rainfall increases, creating favorable conditions for the proliferation of the vector [17, 19, 20, 24, 25, 26, 46].

5. Conclusion

The ROR methodology allowed obtaining good results for Dengue cases in the short and long term and even made possible the modeling and prediction of cases for this infectious entity in a prophylactic manner, making it an excellent predictive tool for entities not only of viral etiology.

Compliance with ethical standards

Acknowledgments

The author would like to thank all those who have helped the author in this research, but especially to Prof. David del Valle Laveaga, for his advice and financial contribution to defray the costs of processing the article.

Disclosure of conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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