International Journal of Biological and Pharmaceutical Sciences Archive

ISSN: 0799-6616 (Online)
Journal homepage: https://ijbpsa.com/

(RESEARCH ARTICLE)

Modeling of Dengue cases in pediatric age using the objective regression regressive methodology in Villa Clara, Cuba

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International Journal of Biological and Pharmaceutical Sciences Archive, 2023, 05(02), 089–098

Publication history: Received on 21 April 2023; revised on 01 June 2023; accepted on 04 June 2023

Article DOI: https://doi.org/10.53771/ijbpsa.2023.5.2.0048

Abstract

Dengue continues to be the main arbovirosis, with endemic characteristics, in at least 100 countries, affecting an average of 50 million patients per year, and with a high incidence in pediatric ages. To mathematically model the cases of Dengue in pediatric age through the methodology of the Objective Regression Regressive, during the period 2016-2021 in the province of Villa Clara, Cuba. A descriptive, retrospective, analytical-statistical (Objective Regression Regressive methodology) and prospective longitudinal study was carried out. The study area corresponded to Villa Clara province, which is located in the center of Cuba, where the population under study was the 13 municipalities that make up the province. The total number of cases of Dengue fever during the six years covered by the study was 2 013. A database was created for confirmed cases of Dengue in Villa Clara during the years 2016 to 2021, specifically for children under 18 years of age, where the data were entered in files and processed using the SPSS version 22 statistical package, which made it possible to carry out a mathematical modeling of Dengue cases, in the short and long term. The plotting of confirmed cases of Dengue fever showed that the highest incidence of cases was in the months from July to November, with an average of 28 cases studied. The short-term model depends on the cases returned in 1, 2, 7 and 14 months, which indicates a strong dependence on the previous month, so that all monitoring, surveillance, management, control and sanitation actions carried out in advance will have a positive impact on the following month, while the long-term model depended on the cases returned in 12 months, and the trend turned out to be positive and significant. It was possible to model the cases of Dengue, where the trend was to a non-significant decrease in the short term, while in the long term, this trend was to a significant increase, and for which, the cases depended on 1, 2, 7 and 14 months ago, so the best model was the long term, being able to predict the behavior of this infectious entity one year in advance, as well as the extension to longer dates in years.

Keywords: Dengue; Pediatric age; ROR methodology; mathematical modeling; Villa Clara

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1. Introduction

At present, arbovirosis of veterinary-medical relevance continues to be a serious problem for several health programs, since the vector species involved have a marked worldwide dispersion as a consequence of anthropic activity [1,2].

Among the determinant factors that favor the current dispersion of some species of the genus *Aedes*, we can mention the wide range of containers used for breeding as a result of inadequate environmental sanitation, the intensive and extensive use of chemicals that indirectly affects several culicid species, the increase in tourist travel by sea, land and air [3-5], as well as changing climatic conditions, where increases in temperatures and alterations in the rainfall regime have allowed the introduction, establishment and reproduction in places where, a priori, they were not expected [5,6].

One of the arbovirosis with great impact on health systems is Dengue, a febrile disease caused by a Flavivirus of which four serotypes have been described (DEN-1, DEN-2, DEN-3 and DEN-4), which is transmitted to humans through the bite of mosquitoes belonging to the genus *Aedes* [7]. This disease has become a growing public health problem, with emphasis on the Caribbean and Latin America, with the pediatric age group accounting for the largest number of cases [8-12], and was designated by the World Health Organization as one of the ten most important health threats in the world [13].

Dengue is present with endemic characteristics in at least 100 countries, affecting 50 million sick people per year on average [14]. In this regard, it has been described that in the Caribbean region the countries with the highest number of cases in the last decade are Cuba, Puerto Rico, and the Dominican Republic [15,16]. This epidemiological situation has stimulated the execution of research in several countries and regions, in order to know the behavior of Dengue episodes in symptomatic periods, as well as to be able to make comparisons between countries and regions according to age groups, assessing, for example, the affectations in pediatric age [17-20]. Among these studies, we can point out those conducted in Asia [21,22] and Latin America, in which it was observed that the burden of the disease in the age range between 9 and 12 years is higher in Asia compared to Latin America [23].

The objective of the research consisted of mathematically modeling by means of the ROR methodology, the cases of Dengue in pediatric age during the period 2016-2021 in the province of Villa Clara, Cuba.

2. Material and methods

2.1. Study area

The research was carried out in Villa Clara province (Latitude: 22º 29'40'' N, Longitude: 79º28'30'' W), Cuba, whose provincial capital is the Santa Clara municipality and covered the 13 municipalities that comprise it. It has geographical limits to the north with the Atlantic Ocean, to the east with the provinces of Sancti Spiritus and Ciego de Avila, to the south with Sancti Spiritus and to the west with the provinces of Matanzas and Cienfuegos. With a territorial extension of 8,412 km^2, including 719 keys, it is the fifth largest of the 16 provinces of the national territory; its extension represents 7.8% of the total area of the country.

2.2. Population

The 13 municipalities that make up Villa Clara province.

2.3. Total cases diagnosed by year

2016 (111), 2017 (92), 2018 (1 125), 2019 (372), 2020 (18) and 2021 (295), for a total of 2 013 cases during the six years covered by the study.

2.4. Methods and techniques for gathering information

The documentary review of the records and statistical files existing in the Provincial Pediatric Hospital "José Luis Miranda", located in the head municipality, as well as the files of the Provincial Department of Health Statistics of Villa Clara, where all the health history of the 13 municipalities of the province is compiled, which is periodically reported in statistical tables established for such purposes by the Department of National Health Statistics of the Ministry of Public Health (MINSAP) of Cuba. All this made it possible to make a database for confirmed cases of Dengue in Villa Clara during the years 2016 to 2021, specifically for children under 18 years of age, where the data were entered in files and processed using the SPSS version 22 statistical package, which made it possible to carry out a mathematical modeling, in the short and long term for these cases.

2.5. The methodology of Objective Regressive Regression (ORR)

The prognosis was performed with the use of the Regression Objective Regression (ROR) methodology that has been implemented in different variables such as viruses and bacteria circulating in Villa Clara province [24-27].

The modeling (ROR), is based on a combination of Dummy variables with ARIMA modeling, where only two Dummy variables are created and the trend of the series is obtained, it requires few cases to be used and allows using also, exogenous variables that make it possible to model and forecast in the long term, depending on the exogenous variable, it has given better results than ARIMA in some variables, such as HIV modeling, entities of viral etiology/arbovirosis and parasitic entities [28-34].

In the ROR methodology, dichotomous variables DS, DI and NoC are created in a first step, 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) 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 maximums of the significant partial autocorrelations PACF. The new variables are then calculated according to the significant Lag of the PACF. Finally, these regressed variables are included in the new regression in a process of successive approximations until a white noise in the regression errors is obtained.

2.6. Ethical aspects

The research was subject to ethical standards, where all the information collected and provided was used only for the stated purpose. It did not involve physical or psychological affectations, in order to generate new knowledge without violating the ethical principles established for these cases. On the other hand, all authors involved in the research, publication and dissemination of the results are responsible for the reliability and accuracy of the results shown [35].

3. Results

Figures 1 and 2 show the plotting of confirmed cases, where the highest incidence of cases was in the months of July to November, and the mean number of cases studied was close to 28 cases.

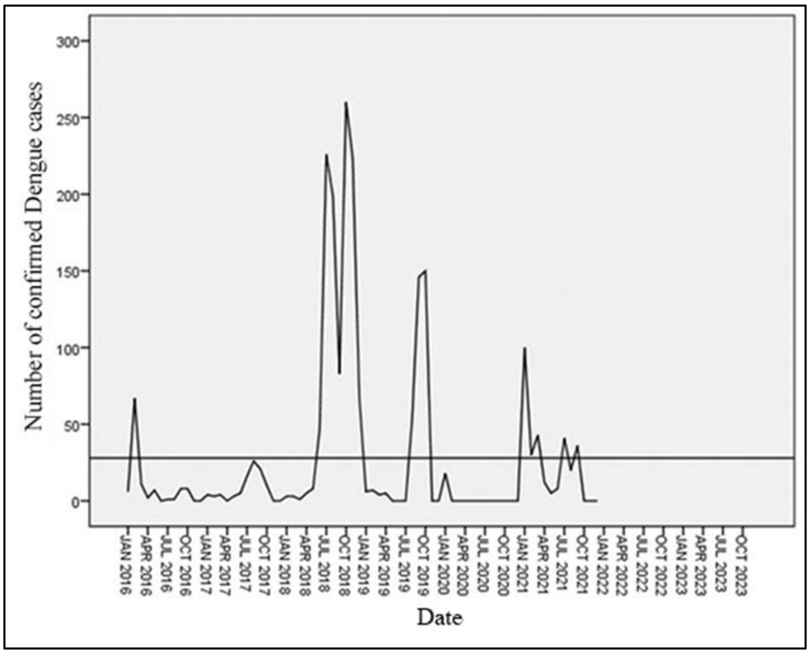

Figure 1 Plotting of Dengue cases, 2016-2021 by month for Villa Clara province

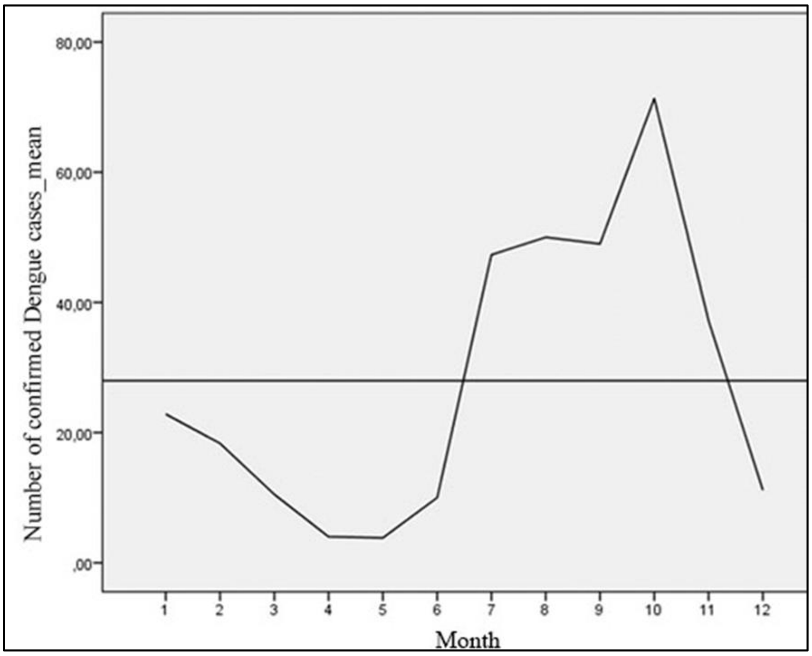

Figure 2 Behavior of the average number of cases of Dengue fever by month

The highest value occurred in the month of October 2018 with 260 cases, and a large standard deviation (57.573 cases), while in the short-term model 98.7 % of the variability was explained with an error of only 13.4 cases (Table 1). Fisher's F was significant at 100 %, with a value of 97.361, and a sum of square of 286765.000d, result of the ANOVA test (a. Dependent variable: number of confirmed with Dengue; b. Linear regression through the origin; c. Predictors: Step44, Step62, Step33, Step36, Step61, Step47, Step45, Step34, Step31, LAG7Cases, LAG14Cases, DS, DI, LAG1Cases, LAG2Cases, NoC and d. This total sum of squares is not corrected for the constant because the constant is zero for regression through the origin).

Table 1 Summary of the short-term model for the number of Dengue cases

Descriptive statistics					
	N	**Minimum**	**Maximum**	**Media**	**Standard desviation**
Number of cases	72	0	260	27.96	57.573
N valid (per list)	72				
Summary of the model					
Model	R	R squared	R Adjusted squared	Standard error of the estimate	Durbin-Watson
1	0.987[a]	0.974	0.964	13.389	2.499

a. Predictors: Step44, Step62, Step33, Step36, Step61, Step47, Step45, Step34, Step31, LAG7Cases, LAG14Cases, DS, DI, LAG1Cases, LAG2Cases, NoC; 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: Number of confirmed with Dengue; d. Linear regression through the origin

The model in question, in the short term, depends on the cases returned in 1, 2, 7 and 14 months, which indicates a strong dependence on the previous month, so that all monitoring, surveillance, management, control and sanitation actions carried out in advance will have a positive impact on the following month, and in a very decisive and impacting way; It also depends on 2, 7 and 14 months ago, which corresponds to the cycle of approximately six months that divides the rainy and rainy periods that characterize the climate of Cuba, as well as the annual cycle. The Step variables are cases that have an important impact on the series by greatly increasing the cases, some variables were not significant, but they contributed variance to the model, and for this reason they are left in the model. The trend (NoC) is small and negative, but not significant (Table 2).

Table 2 Short-term model results based on coefficients

Coefficients^{a,b}						
Model		**Unstandardized coefficients**		**Standardized coefficients**	**t**	**Sig.**
		B	**Standard error**	**Beta**		
1	DS	5.968	5.610	0.060	1.064	0.294
	DI	2.328	5.730	0.023	.406	0.687
	NoC	-0.039	0.110	-0.026	-.358	0.722
	LAG1Cases	0.890	0.041	0.890	21.772	0.000
	LAG14Cases	0.061	0.034	0.060	1.805	0.078
	LAG7Cases	-0.018	0.030	-0.018	-.620	0.538
	LAG2Cases	-0.153	0.052	-0.153	-2.943	0.005
	Step31	180.452	13.845	0.337	13.034	0.000
	Step34	214.018	16.352	0.400	13.088	0.000
	Step45	80.129	15.578	0.150	5.144	0.000
	Step47	-120.264	15.068	-0.225	-7.982	0.000
	Step61	96.439	13.945	0.180	6.916	0.000
	Step36	-93.112	18.294	-0.174	-5.090	0.000
	Step33	-65.163	17.037	-0.122	-3.825	0.000
	Step62	-58.915	14.375	-0.110	-.098	0.000
	Step44	50.664	13.732	0.095	3.689	0.001

a. Dependent variable: Number of confirmed with Dengue; b. Linear regression through the origin

A long-term forecast was performed, which explains 99.5% of the variance with an error of 9.9 cases; this is a tool to have an idea of how Dengue cases will behave one year in advance, and thus be able to take prophylactic measures that will lead to fewer cases. Fisher's F was 143, higher than in the short-term model, but still significant at 100%. This long-term model depends on the cases regressed over 12 months (Table 3); here the trend was positive and significant.

Table 3 Long-term model results based on coefficients

Coefficients^{a,b}						
Model		**Unstandardized coefficients**		**Standardized coefficients**	**t**	**Sig.**
		B	**Standard error**	**Beta**		
1	DS	-8.082	7.578	-0.073	-1.066	0.296
	DI	-13.798	7.895	-0.124	-1.748	0.092
	NoC	0.0447	0.144	0.291	3.113	0.004
	LAG13Casos	-0.069	0.051	-0.067	-1.334	0.194
	LAG26Casos	-0.079	0.028	-0.078	-2.843	0.009

	LAG19Casos	-0.055	0.024	-0.054	-2.258	0.033
	LAG14Casos	.043	.040	0.042	1.075	0.292
	Step31	220.991	10.661	0.414	20.730	0.000
	Step34	259.227	10.657	0.485	24.324	0.000
	Step45	139.394	12.079	0.261	11.540	0.000
	Step47	3.303	14.775	0.006	.224	0.825
	Step61	98.467	11.420	0.184	8.622	0.000
	Step36	65.075	10.628	0.122	6.123	0.000
	Step33	77.673	10.577	0.145	7.344	0.000
	Step62	22.620	10.420	0.042	2.171	0.039
	Step44	62.189	14.408	0.116	4.316	0.000
	Step35	215.856	10.529	0.404	20.501	0.000
	Step32	199.596	10.756	0.374	18.557	0.000
	Step46	142.538	11.446	0.267	12.453	0.000
	Step30	47.750	10.844	0.089	4.,403	0.000

a. Dependent variable: Number of confirmed with Dengue; b. Linear regression through the origin.

Figures 3 and 4 show the good behavior of the actual value and its forecast, as well as the errors made, which are small.

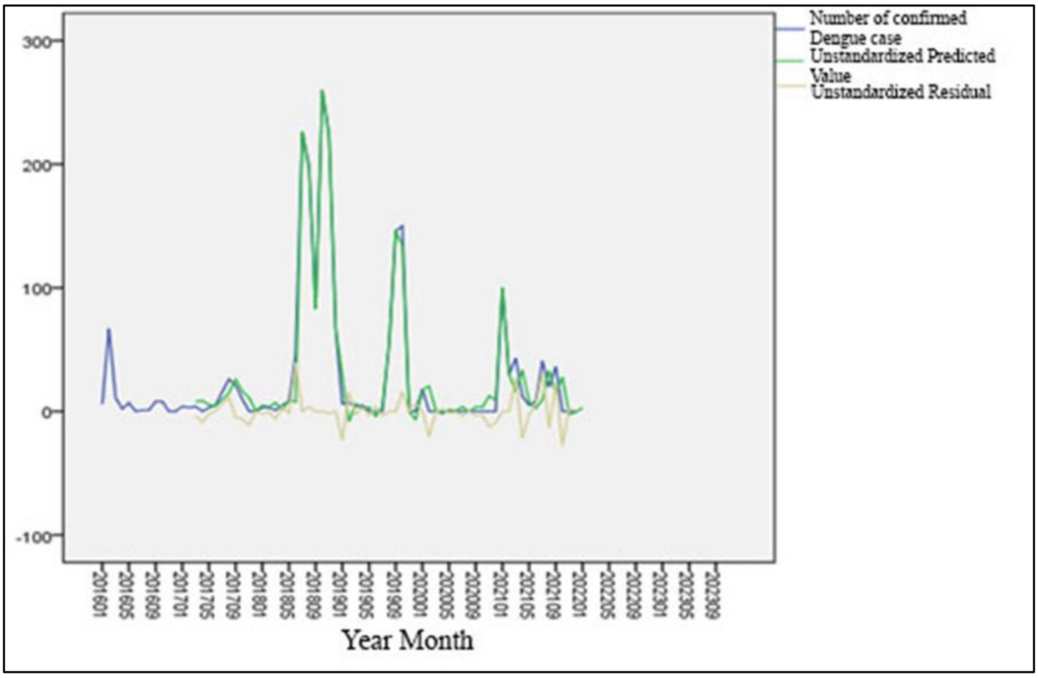

Figure 3 Actual and predicted value in the short term

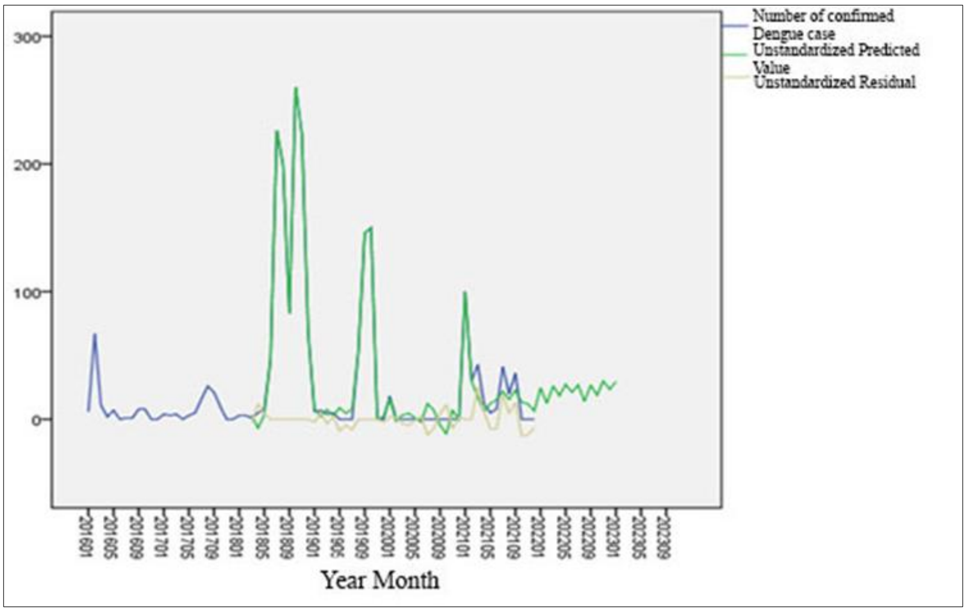

Figure 4 Actual and predicted long-term value

4. Discussion

It was possible to corroborate the existing correlation between the cases of Dengue fever with the months of greater larval focality and even, with the months where the population peaks occur for this mosquito species (July-November), which is not exclusive of Villa Clara province, results that coincide with studies carried out in previous years [2,21,36], being the month of October 2018 where the greatest number of cases (260) was presented, aspect concordant with the rainy period for Cuba, where climatological variables have a favorable incidence on the population densities of culicidae, both in the larval and adult phase, hence these are the months of greatest entomoepidemiological risk for these arboviral infectious entities, which coincides with results obtained in Cuba as in other countries of the region [2,8,39-43].

The short-term model, depended on the cases returned in 1, 2, 7 and 14 months, with a strong dependence on the previous month, also depended on 2, 7 and 14 months ago, which corresponds to the cycle of approximately six months that, divides the rainy and little rainy periods that characterize the climate of Cuba, as well as the annual cycle [2,21,36-38]. Therefore, all monitoring, surveillance, management, control and sanitation actions carried out in advance will have a positive, decisive and impacting repercussion on the following month [25,26,33].

The long-term prognosis explained 99.5% of the variance with an error of 9.9 cases; this model depends on the cases regressed in 12 months, and here the trend was positive and significant, so it is an excellent tool to take into account for the evolution of Dengue cases one year in advance, and thus be able to take prophylactic measures that lead to fewer cases [2,26,34,36-38].

5. Conclusion

It was possible to model the cases of Dengue, observing a trend in the short term to a non-significant decrease, while in the long term, this trend is to a significant increase, where the cases depend on 1, 2, 7 and 14 months ago, so the best model was the long term one. The behavior of this infectious entity can be predicted one year in advance. This is a study that could be extended to a longer date in years to see the impact of the solar cycle, which is approximately 11 years.

Compliance with ethical standards

Acknowledgments

To all the members of the Statistics Department of the Provincial Pediatric Hospital of Villa Clara province, who kindly gave us all the data for the research.

Disclosure of conflict of interest

The authors express that there is no conflict of interest.

Statement of ethical approval

The present research paper does not contain any studies conducted on animals/humans by any of the authors. We worked with a database provided by the colleagues in charge of recording and controlling the database of the Pediatric Provincial Hospital of Villa Clara.

Statement of informed consent

The Declaration of Informed Consent did not apply to this study, since we worked with numerical data obtained from a digital database.

Author's declaration

The authors hereby declare that the work presented in this article is original and that they will bear any liability for claims relating to the content of this article.

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