Original Article

Prediction of visceral leishmaniasis incidence using the Seasonal Autoregressive Integrated Moving Average model (SARIMA) in the state of Maranhão, Brazil

Previsão da incidência da leishmaniose visceral usando o modelo de média móvel integrado autorregressivo sazonal (SARIMA) no Maranhão, Brasil

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Abstract

Visceral leishmaniasis (VL) is an infectious disease predominant in countries located in the tropics. The prediction of occurrence of infectious diseases through epidemiologic modeling has revealed to be an important tool in the understanding of its occurrence dynamic. The objective of this study was to develop a forecasting model for the incidence of VL in Maranhão using the Seasonal Autoregressive Integrated Moving Average model (SARIMA). We collected monthly data regarding VL cases from the National Disease Notification System (SINAN) corresponding to the period between 2001 and 2018. The Box-Jenkins method was applied in order to adjust a SARIMA prediction model for VL general incidence and by sex (male or female) for the period between January 2019 and December 2013. For 216 months of this time series, 10,431 cases of VL were notified in Maranhão, with an average of 579 cases per year. With regard to age range, there was a higher incidence among the pediatric public (0 to 14 years of age). There was a predominance in male cases, 6437 (61.71%). The Box-Pierce test figures for overall, male and female genders supported by the results of the Ljung-Box test suggest that the autocorrelations of residual values act as white noise. Regarding monthly occurrences in general and by gender, the SARIMA models (2,0,0) (2,0,0), (0,1,1) (0,1,1) and (0,1,1) (2, 0, 0) were the ones that mostly adjusted to the data respectively. The model SARIMA has proven to be an adequate tool for predicting and analyzing the trends in VL incidence in Maranhão. The time variation determination and its prediction are decisive in providing guidance in health measure intervention.

Keywords: visceral leishmaniasis, time series studies, prediction models.

Resumo

A leishmaniose visceral (LV) é uma doença de natureza infecciosa, predominante em países de zonas tropicais. A predição de ocorrência de doenças infecciosas através da modelagem epidemiológica tem se revelado uma importante ferramenta no entendimento de sua dinâmica de ocorrência. O objetivo deste estudo foi desenvolver um modelo de previsão da incidência da LV no Maranhão usando o modelo de Média Móvel Integrada Autocorrelacionada Sazonal (SARIMA). Foram coletados os dados mensais de casos de LV através do Sistema de Informação de Agravos de Notificação (SINAN) correspondentes ao período de 2001 a 2018. O método de Box-Jenkins foi aplicado para ajustar um modelo de predição SARIMA para incidência geral e por sexo (masculino e feminino) de LV para o período de janeiro de 2019 a dezembro de 2023. Durante o período de 216 meses dessa série temporal, foram registrados 10.431 casos de LV no Maranhão, com uma média de 579 casos por ano. Em relação à faixa etária, houve maior registro no público pediátrico (0 a 14 anos). Houve predominância do sexo masculino, com 6437 casos (61,71%). Os valores do teste de Box-Pierce para incidência geral, sexo masculino e feminino reforçados pelos resultados do teste Ljung-Box sugerem que as autocorrelações de resíduos apresentam um comportamento de ruído branco. Para incidência mensal geral e por sexo masculino e feminino, os modelos SARIMA (2,0,0) (2,0,0), (0,1,1) (0,1,1) e (0,1,1) (2, 0, 0) foram os que mais se ajustaram aos dados, respectivamente. O modelo SARIMA se mostrou uma ferramenta adequada de previsão e análise da tendência de incidência da LV no Maranhão. A determinação da variação temporal e sua predição são determinantes no norteamento de medidas de intervenção em saúde.

Palavras-chave: leishmaniose visceral, estudos de séries temporais, modelos de predição.

1. Introduction

Visceral Leishmaniasis (VL) is a neglected disease, infectious by nature, predominant in tropical countries, caused by obligate intracellular protozoa of the genus Leishmania, and the family Trypanosomatidae (McCall et al., 2013; Bispo et al., 2020).

In Brazil, the geographical limits of the area this disease covers have suffered a significant expansion from the rural area into the urban centers in the last decades (Cavalcante et al., 2020). Urban development is an important factor that helped VL expansion. However, other risk factors discovered contribute to the occurrence of this disease (Freire et al., 2019): malnutrition (Lima et al., 2018), uneven income distribution (Nunes et al., 2019), inadequate sewage disposal, among others (Sevá et al., 2017).

The occurrence prediction of infectious diseases through epidemiological modeling has proven to be an important tool in understanding its occurrence dynamic. This directed approach guarantees an efficient manner in which to distribute and allocate resources by exploring VL's occurrence dynamic (Nightingale et al., 2020).

Visceral Leishmaniasis has been reported in all regions of Brazil. In the last years, there has been confirmation of an increase in the number of cities that report cases in the South and Southeast. Nevertheless, the Northeast stands out as the region with the largest number of registered cases, particularly in Bahia, Ceará, Piauí and Maranhão States (Costa et al., 2020; Machado et al., 2020).

The reports of VL in Maranhão date back to 1982 in São Luís Island (Silva et al., 2008). Later surveys revealed the expansion from there into other cities mainly due to urban development, great migratory flow and tax incentives for industrial district implementation (Mendes et al., 2002).

Epidemiologic data show that Maranhão has one of the biggest areas of VL incidence in Brazil (Furtado et al., 2015). Therefore, there is agreement that investigating mechanisms capable of predicting the incidence of VL in this State is an opportunity. The objective of this study was to develop a VL incidence prediction model using data between January 2001 and December 2018 in order to provide financial support for preventive and control measures against this disease, based on management and hinged on evidence.

2. Material and Methods

2.1. Study area

Maranhão State is located in the extreme northeastern area of the Northeast Region in Brazil, it borders three other states: Piauí (to the east), Tocantins (to the south and southwest) and Pará (to the west), in addition to the Atlantic Ocean (to the north). Its territory is 331,937.450 km^2 and it is divided into 217 cities. In 2018, the estimated number of inhabitants was 7,035,055 (IBGE, 2010).

2.2. Study design and sources of information

This is a descriptive epidemiological study of time series type with data obtained from the Brazilian National Disease Notification System (SINAN). The population data was collected from the Brazilian Institute of Geography and Statistics (IBGE), based on information in the state's census (2000 and 2010) and population estimates for the intercensal years (from 2001 to 2018).

2.3. Data analysis

For the time-series analysis, we used data corresponding to the incidence of VL between January 2001 and December 2018. The ratio between the number of monthly cases and the population residing in Maranhão for the respective period was used to calculate the monthly incidence of VL, based on the annual population estimates produced by the IBGE. The rate of occurrence was calculated by 100,000 inhabitants using *Microsoft Office® Excel* 2013 (Washington, USA).

Afterwards, the monthly average incidence rate was calculated in order to find a mathematical model that could adjust to the data and predict the general incidence and incidence by gender. The seasonal SARIMA model $(p,d,q)(P,D,Q)_s$ allows a description of the variability of the processes related to time, linear, stationary (d = D = 0), or non-stationary written in the following form (Equation 1):

$$\Delta\left(B^s\right)\Phi(B)(1-B)^d\left(1-B^s\right)^D T\left(X_t\right) = \Psi\left(B^s\right)\Theta(B)Z_t \quad (1)$$

where,

$$\Phi(B)=1-\varnothing_1 B-\varnothing_2 B^2 -...-\varnothing_p B^p, \Theta(B)=1-\theta_1 B-\theta_2 B^2 -...-\theta_q B^q$$

respectively, the mean autoregressive and mobile polynomials of the non-seasonal

$$\Delta\left(B^s\right)=1-\Phi_1 B-\Phi_2 B^2 -...-\Phi_P B^P e \Psi\left(B^s\right)=1-\Theta_1 B-\Theta_2 B^2 -...-\Theta_Q B^Q,$$

respectively, autoregressive polynomials and moving average polynomials of the seasonal part of the S. T period is the transformation to stabilize, if needed, the variance (generally called Box Cox transformation), while Z_t represents the process of white noise (uncorrected process, zero mean and constant variance). The letters p and q represent, respectively, the number of parameters of autoregressive pieces and moving average parts, with seasonal period S. The letters P and Q are the equivalent numbers to these parameters between seasonal periods. Letters d and D, respectively, represent degrees of simple differentiation and the seasonal differentiation needed to transform a non-stationary series into a stationary one (Nobre et al., 2001; Lin et al., 2015; Dabral and Murry, 2017).

While investigating the best model, the VL series (general, male and female) were divided into two parts (practice and validation). The practice part was intended to estimate values for the parameters, and the validation part to verify if the model was excelling at making predictions, in other words, to verify whether the MAPE (mean absolute percentage error) was at its lowest possible and, thus, be able to forecast the value for VL incidence.

In order to define the models, we used AIC (Akaike information criterion) measures, BIC (Bayesiano information criterion) and MAPE. It is worth highlighting that MAPE had the biggest priority in deciding among the models tested, once it indicates the percentage in which the model is producing errors. After the models were

chosen, we checked whether they met the assumptions of independent residues and were distributed in an identical manner (Ljung-Box and Box-Pierce Tests), with normal distribution and average zero (Shapiro Wilk Test), and constant variance (Rank e Turning Test). Finally, the validated models were used to predict the values for the monthly incidence for the period between 2019 and 2023. The software used in the analysis was the R (version 4.0.2).

2.4. Ethical aspects

This study involved free, public, secondary data, without mention to the names of individuals in the cases, ethically respecting what was established in the National Health Council Resolution # 510, dated April 7, 2016, therefore not requiring the approval of the Ethics in Research Committee.

3. Results

During the period between 2001 and 2018, 10,431 cases of VL were reported in Maranhão, with an average of 579 cases per year. The smallest and largest numbers registered occurred in the years 2012, with 342 (3.28%), and in 2017, with 793 (7.60%) cases, respectively. The highest rate of incidence happened in 2003 (13.47/100,000 inhabitants). Regarding age range, there was a higher rate among the pediatric public (0-14 years of age). There was predominance among the male gender, with 6437 cases (61.71%) (Figure 1).
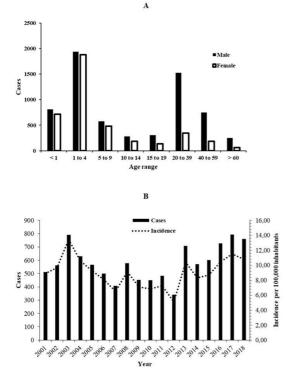

Figure 1. Time distribution of visceral leishmaniasis cases in Maranhão, 2001-2018 (1A); VL case distribution in Maranhão according to age range and gender, from 2001 to 2018 (1B).

In Figure 2, the ACF and PACF graphs describe the time dependence structure of VL monthly incidence. We found that the analysis of the time models' residue was exhibited independently and spread out in an identical manner, with normal distribution, mean zero and constant variance.

The Box-Pierce test values for general incidence (0.145; p= 0.703), male (0.157; p= 0.692), female (0.264; p= 0.607) supported by the Ljung-Box test for general incidence (0.143; p= 0.705), male (0.155; p= 0.694), female (0.260; p= 0.610) suggest that the autocorrelation of residuals act as white noise (Table 1).

In Table 2, shows values AIC, BIC and MAPE for different SARIMA models. Regarding general incidence, (2,0,0)(2,0,0) with AIC -111,141, BIC -91,232 and MAPE of 9,503, turned out to be the most adequate. For the incidence by gender male and female, the models SARIMA (0,1,1)(0,1,1) with AIC 37,756, BIC 47,513, MAPE 16,582 and SARIMA (0,1,1)(2,0,0) with AIC -27,619, BIC -14,366 and MAPE 24,583, were the ones that had the best adjustment to the data, respectively. Such models were used for predicting the occurrence of the disease during the period between January 2019 and December 2023.

In Figure 3, exhibits the behavior of the time series for the real and predicted values. In addition, it shows predictions for general incidence and incidence by gender, according the SARIMA model, for the next 60 months compared to the period analyzed. Altogether, there was a decreasing trend observed for the total incidence. However, for the incidence in women, an increasing trend was verified for the same period.

4. Discussion

Visceral Leishmaniasis is a parasitic disease, usual in many regions of the world. The SARIMA models have proven to be an important tool in strengthening epidemiologic surveillance of this illness (Bhatnagar et al., 2012). In the last years, many studies have used these mathematical models to make predictions about infectious diseases like tuberculosis, mumps, dengue, malaria and, most recently, Covid-19 (Ebhuoma et al., 2018; Mao et al., 2018; Liu et al., 2020; Koyuncu et al., 2021).

This work is original and important because the occurrence of emerging VL outbreaks in Maranhão is a reality that has brought a significant impact upon public health. This study is the first to apply the SARIMA modeling to forecast the general incidence and incidence by gender from 2019 to 2023. This allowed for the analysis of seasonal distribution, where the SARIMA model (2,0,0) (2,0,0) was the one to adjust the best to the general incidence. In this investigation, the models that presented the best adjustment to reflect the trend for monthly incidence of this disease and incidence in males and females were SARIMA (0,1,1) (0,1,1) and (0,1,1) (2,0,0), respectively.

The SARIMA model has some limitations that make it unpopular when it comes to time-series analysis of infectious diseases. In general, it assumes that the predicted values have a linear correlation to past values, therefore inadequate for non-linear problems of greater complexity (Guo et al., 2019). Moreover, we used secondary data in
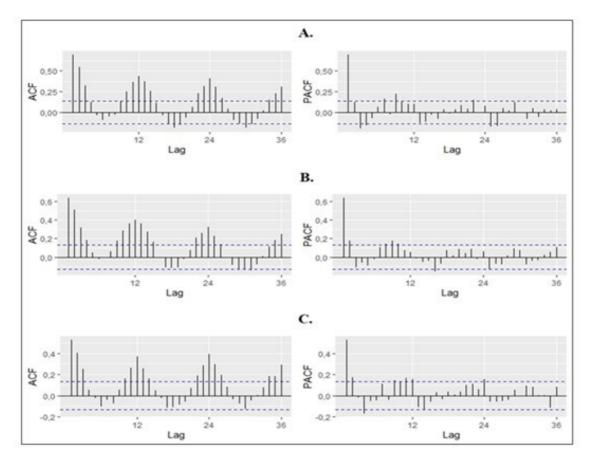
Figure 2. Autocorrelation function values (ACF) and partial autocorrelation function values (PACF) for monthly incidence of VL (A), male (B) and female (C).

Table 1. Residue analysis of time models for general incidence and by gender of visceral leishmaniasis in Maranhão, between 2001 and 2018.

Test	General Incidence		Incidence for males		Incidence for females	
	Statistical test	*p-value	Statistical test	p-value	Statistical test	p-value
Ljung-Box	0.143	0.705	0.155	0.694	0.260	0.610
Box-Pierce	0.145	0.703	0.157	0.692	0.264	0.607
Shapiro Wilk	0.990	0.122	0.989	0.098	0.987	0.060
Rank test	0.646	0.518	-0.409	0.683	0.322	0.747
Turning test	0.054	0.957	1.350	0.177	0.389	0.697

*p-value ≤0.05.

this study, subject to problems related to incomplete or duplicated data, which demands careful evaluation of the information (Rocha and Pinheiro, 2020). It is important to point out that social, economic, and environmental factors can influence the incidence of VL (Valero and Uriarte, 2020). Nevertheless, these factors were not taken into account in this pilot analysis of temporal series.

Similar to what occurs with other vector-borne diseases, the tendency of occurrence of VL is influenced by environmental factors (Rahmanian et al., 2021). The environmental particularities of each geographic location reveal situations of diversified occurrence of VL and may partially explain the maintenance of endemicity in the prediction model proposed in this study (Sharafi et al., 2017).

The continuous surveillance of VL is a key issue for its control, as it allows the evaluation of the past and present in order to reduce the future burden of this important disease (Ferreira et al., 2021). Furthermore, this study reinforces the need for actions that minimize the problem of underreporting. Here, there is an evident need for continuous training of human resources responsible
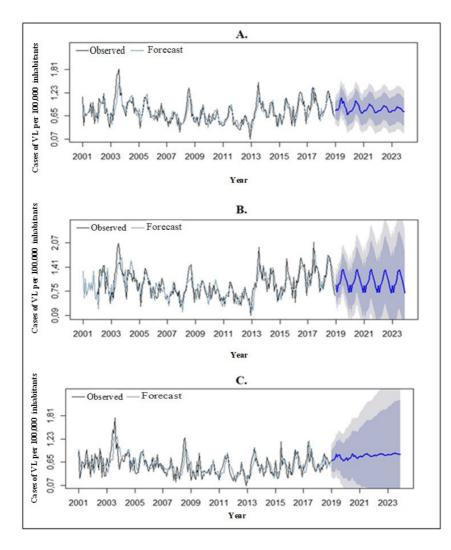
Figure 3. VL Prediction incidence (per 100,000 inhabitants), according to the SARIMA model, Maranhão, Brazil. Black line – Original, blue line – Estimate; the Y-axis represents the incidence in decimals and the X-axis represents years.A) Prediction for general VL incidence according to the SARIMA model (2,0,0)(2,0,0). B) Prediction for VL incidence by gender according to the SARIMA model (0,1,1)(0,1,1).C) Prediction for VL incidence in women according to the SARIMA model (0,1,1)(2,0,0).

for epidemiological surveillance. The notification of VL should always be reinforced and encouraged to have a real understanding of the impact of prevention measures and timely control of the disease based on official data, which enables the implementation of prediction models with a good representation of the epidemiological behavior of the disease (Cota et al., 2021).

Concerning the age of the notified cases, there was incidence in all ages, although we observed a prevailing incidence in individuals aged between 0 and 14 years old (6,870 cases; 65.88%). Children younger than 1 year of age represented 14.69% of the cases. The predominance in the pediatric public is related to the endemic area, namely the Northeast Region of Brazil, where individuals have low immunity, nutritional deficiency, greater exposure to the presence of phlebotoms in surroundings and/or home due to the presence of sunlight and pets (Rodrigues et al., 2017;

Guerra et al., 2019; Oliveira et al., 2021). Menezes et al. (2016), observed a significant association between living in environments with at least one risk factor and a greater vulnerability to the occurrence of the disease.

In terms of occurrence by gender, the illness was predominant in individuals of the male sex. This information agrees with reports in different states in northeastern Brazil, as Alagoas and Rio Grande do Norte (Barbosa, 2013; Rocha et al., 2018). Some studies suggest that this difference in gender could be associated to behavioral and social aspects of women and men's lives, which influence the degree of exposure to the pathogen. The extent to which there is access to public services seems to influenc this disparity between genders (Cloots et al., 2020; Dahal et al., 2021). Hormonal factors can also contribute to a greater susceptibility to infections and diseases (Reis et al., 2017).

Table 2. Measures of different SARIMA models for VL general incidence and incidence by gender in Maranhão, between 2001 and 2018.

Series	Models	AIC	BIC	MAPE
General	(4,0.3) (2,0,0)	90.635	127.135	13.968
	(1,1,1) (2,0,0)	-93.067	-76.501	8.911
	(9,1,0) (1,0,0)	-85.419	-48.974	12.291
	(3,1,0) (0,0,0)	-47.636	-34.384	43.067
	(0,1,1) (0,0,0)	-48.810	-42.183	37.336
	(1,0,1) (2,0,0)	-108.112	-88.204	9.638
	(2,0,0) (2,0,0)	-111.141	-91.232	9.503
	(0,1,3) (0,0,0)	-56.043	-42.790	20.134
Male	(2,1,2) (1,0,0)	53.637	73.516	27.433
	(1,1,1) (2,0,0)	48.699	65.265	19.571
	(0,1,1) (0,1,2)	37.084	50.093	17.059
	(0,1,2) (0,1,2)	38.664	54.925	16.751
	(0,1,1) (0,1,1)	37.756	47.513	16.582
	(1,0,1) (2,0,0)	38.731	58.640	22.698
	(2,0,0) (2,0,0)	38.063	57.972	23.579
	(2,1,2) (2,0,0)	42.798	65.990	22.736
Female	(2,1,2) (2,0,0)	-57.770	-34.578	41.494
	(1,1,1) (2,0,0)	-60.831	-44.265	23.658
	(2,1,3) (0,0,0)	-9.068	4.184	26.502
	(0,1,4) (0,0,0)	-13.604	-6.978	23.137
	(1,0,1) (2,0,0)	-71.334	-51.425	25.295
	(2,0,0) (2,0,0)	-71.598	-51.689	25.013
	(0,1,1) (2,0,0)	-27.619	-14.366	24.583

AIC: Akaike information criterion; BIC: Bayesiano information criterion; MAPE: mean absolute percentage error.

The proposed SARIMA model has proven to be adequate in predicting and analyzing the time aspects of VL in Maranhão, revealing that this disease will persist as a grave public health problem in the next years, which reinforces the need for preventive measures and control. Furthermore, the prediction of this disease's incidence enables health authorities to make decisions based on evidence, which allows the identification of epidemic peaks in the future.

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