Acta Tropica 182 (2018) 190–197

Contents lists available at ScienceDirect

Acta Tropica

journal homepage: www.elsevier.com/locate/actatropica

Time series analysis of dengue surveillance data in two Brazilian cities

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ARTICLE INFO

Keywords:
Dengue
Time series analysis
Arima
Brazil
Forecasting
America region

ABSTRACT

The aim of the study was to evaluate the temporal patterns of dengue incidence from 2001 to 2014 and forecast for 2015 in two Brazilian cities. We analysed dengue surveillance data (SINAN) from Recife, 1.6 million population, and Goiania, 1.4 million population. We used Auto-Regressive Integrated Moving Average (ARIMA) modelling of monthly notified dengue incidence (2001–2014). Forecasting models (95% prediction interval) were developed to predict numbers of dengue cases for 2015. During the study period, 73,479 dengue cases were reported in Recife varying from 11 cases/100,000 inhab (2004) to 2418 cases/100,000 inhab (2002). In Goiania, 253,008 dengue cases were reported and the yearly incidence varied from 293 cases/100,000 inhab (2004) to 3927 cases/100,000 inhab (2013). Trend was the most important component for Recife, while seasonality was the most important one in Goiania. For Recife, the best fitted model was ARIMA $(1,1,3)^{12}$ and for Goiania Seasonal ARIMA $(1,0,2)\ (1,1,2)^{12}$. The model predicted 4254 dengue cases for Recife in 2015; SINAN registered 35,724 cases. For Goiania the model predicted 33,757 cases for 2015; the reported number of cases by SINAN was 74,095, within the 95% prediction interval. The difference between notified and forecasted dengue cases in Recife can be explained by the co-circulation of dengue and Zika virus in 2015. In this year, all cases with rash were notified as "dengue-like" illness. The ARIMA models may be considered a baseline for the time series analysis of dengue incidence before the Zika epidemic.

1. Introduction

Dengue is an important vector-borne disease, transmitted by urban adapted *Aedes* mosquitoes and a major global public health threat. Four distinct serotypes (DENV-1 to DENV-4) cause both asymptomatic infections and a wide spectrum of clinical forms, ranging from mild to severe (Guzman and Harris, 2015; Messina et al., 2014; The Trung and Wills, 2014). The epidemiology of dengue is modulated by the susceptible population of humans, mosquito density, the profile of circulating serotypes, and environmental conditions (Brady et al., 2015, 2012; Stanaway et al., 2016). There is no specific antiviral treatment for dengue. Control relies mainly on surveillance and integrated vector interventions in urban areas (Guzman and Harris, 2015; Wilder-Smith et al., 2016). A dengue vaccine (CYD-TDF) was recently tested and licensed in six countries (Asian and Latin America) (Ferguson et al., 2016) but not yet recommended by World Health Organization (WHO) (WHO, 2016a). Another new dengue vaccine (TetraVax-DV) is being evaluated in several Brazilian settings (ClinicalTrials.gov, 2016).

Worldwide, dengue cases increased from 2.2 million in 2010–3.2 million in 2015, with transmission detected in new areas and large outbreaks in 2015. Approximately half a million severe dengue cases are estimated to require hospitalization each year, with 2.5% resulting in death (WHO, 2016b). Other estimates indicated an even higher magnitude of dengue infection and disease worldwide, ranging from 60 million (Stanaway et al., 2016) to 96 million of symptomatic cases in 2010 (Bhatt et al., 2013). The Americas accounted for 2.35 million cases (~73.4%) of dengue; with more than 10 thousand severe cases and 1181 deaths being estimated (WHO, 2016b). Brazil and Mexico had

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https://doi.org/10.1016/j.actatropica.2018.03.006
Received 22 September 2017; Received in revised form 9 March 2018; Accepted 10 March 2018
Available online 12 March 2018
0001-706X/

the bulk of cases in the Americas (Bhatt et al., 2013). Reducing mortality and morbidity are among the goals of WHO global strategy for dengue prevention and control for the period 2012–2020 (WHO, 2012). In 2013, the global burden of dengue was estimated as 1.14 million disability-adjusted life-years, based on both fatal and non-fatal outcomes (Stanaway et al., 2016). A multicentre study conducted in 2012–2013 in Brazil showed a high economic impact of dengue at societal level during epidemic and endemic periods (Martelli et al., 2015).

Surveillance of infectious disease is defined as the systematic reporting, monitoring and data analysis of cases, aimed at public health prevention and control (Porta, 2014). Brazil reported a dramatic increase in dengue incidence in 2015, with over 1.5 million cases, approximately three times higher than the previous year (Brasil, 2016; WHO, 2016b). Brazil has one of the most comprehensive dengue surveillance systems (Brady et al., 2015), which has been widely used to describe the epidemiology of dengue (Coelho et al., 2016; Ruberto et al., 2015; Siqueira et al., 2005; Teixeira et al., 2013), define outbreaks (Brady et al., 2015; Runge-Ranzinger et al., 2008) and dynamics of dengue infection in different urban areas of the country (Amaku et al., 2016, 2015). Mathematical and statistical models are frequently used to describe dynamics of dengue transmission (Amaku et al., 2016, 2015; Chen et al., 2015; Silawan et al., 2008). Time series models can evaluate trend and seasonality patterns of dengue incidence and are useful for forecasting. Several time series analysis of dengue described patterns of dengue in Brazilian cities, such as: Rio de Janeiro (Luz et al., 2008), Campinas and Ribeirao Preto (Martinez et al., 2011; Martinez and Da Silva, 2011). The performance of infectious diseases forecasts was recently evaluated for Mexico showing that climate data did not significantly improve the seasonal autoregressive model (Johansson et al., 2016).

Recently, cocirculation of other arboviruses, in particular chikungunya (2014) and Zika (2015), was detected in Brazil. These vector-borne diseases have similar epidemiology and symptoms which might lead to misclassification of dengue cases and a possible overestimation of dengue notification (Faria et al., 2016; Musso and Gubler, 2016; Silva et al., 2016; Wilder-Smith et al., 2016). Cocirculation of dengue, Zika and/or chikungunya viruses might occur in areas infested with *Aedes aegypti* mosquitoes since this competent vector has a widespread distribution in Brazil (Musso and Gubler, 2016). Zika cases were not a notifiable disease before 2016, therefore cases were registered as "dengue-like" disease in the previous year in Brazil (Brito et al., 2016; Pessôa et al., 2016).

Our study aimed to evaluate the temporal patterns of dengue incidence from 2001 to 2014 in Recife in the Northeast region and Goiania in the Midwest region using Autoregressive Integrated Moving Average (ARIMA) models. We constructed time series models for dengue and forecasted the dengue incidence for 2015. This analysis is invaluable to evaluate temporal trend of dengue incidence before the introduction of these other arboviruses and any dengue vaccine.

2. Material and methods

2.1. Study areas

We analysed dengue surveillance data from two Brazilian cities: Recife, capital of Pernambuco State, and Goiania, capital of Goias State. Recife is located in the Northeast region, on the Atlantic coast (08° 03′ South latitude and 34° 52′ West longitude), with annual average temperature of 25.8 °C and 1804 mm precipitation. The estimated 2015 population was approximately 1.6 million inhabitants, with a population density 7040 inhabitants/km^2 (Instituto Brasileiro de Geografia e Estatistica, 2015). Goiania, located in the Midwest region (16° 41′ South latitude 49° 15′ West longitude) at an altitude of 749 m, has annual average temperature of 23.1 °C and 1414 mm precipitation. Its estimated 2015 population was approximately 1.4 million inhabitants, with a population density of 1777 inhabitants/km^2 (Instituto Brasileiro de Geografia e Estatistica, 2015). These cities are located in two distinct regions of Brazil and have distinct pattern of dengue disease. Although both cities present high dengue incidence, the DENV-1 serotype was introduced to Recife seven years before Goiania (1987 and 1994 respectively) (Amaku et al., 2016; Barcellos and Lowe, 2014; Siqueira et al., 2005; Teixeira et al., 2013). These distinct epidemiological characteristics offer opportunity to assess the generalizability of modelling techniques.

2.2. Data collection

We used the dengue data extracted from the Brazilian National Notifiable Diseases Information System (SINAN) for Recife and Goiania, from 2001 to 2015. All suspected outpatient and inpatients dengue cases from public and private health services are included in the SINAN database (Teixeira et al., 2013). This electronic data is transmitted from municipal to state and national levels. The surveillance report include data on: demographic, days since onset of symptoms, clinical findings, serologic tests (IgM antibodies, NS1 detection), virus isolation, RT-PCR, DENV serotype, histopathology and imunohistochemistry, case classification according to disease severity and outcome. In this dataset, the laboratory results were rarely available since it is not a required data for dengue notification. According to the Brazilian Ministry of Health (MoH) and WHO, dengue case is defined as fever (2–7 days) and two of the following criteria: nausea/vomiting, rash, aches and pains, positive tourniquet test, leukopenia and any warning sign. Laboratory confirmation is done by virological, molecular and/or serological methods. (Brasil, 2013, 2009). During the period 2001–2013, cases were classified as: dengue fever, dengue with complications, dengue haemorrhagic fever or dengue shock syndrome. Since 2014, Brazilian MoH adopted the revised 2009 WHO classification: dengue fever, dengue with warning signs and severe dengue (Brasil, 2013, 2009; WHO, 2009). We included all dengue cases confirmed by clinical/epidemiological and/or laboratorial, registered in Recife and Goiania.

2.3. Data standardization

During the study period, the dataset for the years 2001–2006, 2007–2013 and 2014 had differences regarding number and variables names, requiring harmonization. After checking and cleaning the dataset was standardized for the entire period to perform time series analysis for Recife and Goiania. Duplicated and missing records were identified and deleted by SINAN automated routine (Coelho et al., 2016). We excluded dengue cases coded as discarded, i.e. an initial dengue diagnosis having superseded, using the dengue classification variable.

2.4. Data management and statistical analysis

We explored the temporal patterns of dengue cases for each city by plotting monthly incidence for the study period. We evaluated the overall features of the data using this graphical approach: trends (increase, decrease), seasonality, outliers, smooth changes in structure (Chatfield, 2000).

We performed Seasonal Decomposition of Time Series by Loess (STL). Time series were decomposed into three components: trend, seasonal and remainder (residual). STL decomposition data were graphed on four panels: data (monthly dengue incidence), seasonal (variation in the data within a year), trend (variation in the data in the long-term period) and remainder (variation that remains after removing seasonal and trend components) (Cleveland et al., 1990; Silawan et al., 2008).

When seasonality was an important component we applied exploratory data analysis to display the variation of the monthly dengue incidence (2001–2014). The seasonal box-plot allows to show the incidence of dengue distribution, including median values, the first and

third quartile ranges, expected minimum and maximum values, outliers and extreme values (Tukey, 1977).

2.5. The ARIMA models

Estimating parameters

We used the Box-Jenkins approach to fit Auto-Regressive Integrated Moving Average (ARIMA) models, which are defined by three terms (*p, d, q*) and used for non-seasonal time series. The first step of the model identification was to evaluate the trend component (*d*). We explored the monthly incidence of dengue cases with 12 months periodicity ($S = 12$ observations per year). We transformed the series by differencing the scores (months) to make it stationary, if appropriate. The number of differencing operations is the *d* parameter. Logarithmic transformation (logarithm natural, ln) was applied to stabilize the variance in one city (Goiania). As a second step, we identified the auto-regressive (AR) component (value of *p*). As a third step, we identified the moving average (MA) component, value of *q* (Box and Jenkins, 1976; Hyndman and Khandakar, 2008; Nobre et al., 2001).

We included the seasonal component using Seasonal Auto-Regressive Integrated Moving Average (SARIMA) model if the previous analysis indicated evidence of seasonality. This component has three more parameters denoted *P, D* and *Q* (Hyndman and Athanasopoulos, 2013; Nobre et al., 2001). These parameters are similar to *p, d* and *q* but operate on the scale of the periodicity (12 months). For example, $P = 1$ means an autoregressive term of order 1 on the annual scale, i.e. the value in any month depends, in part, on the value in the same month of the previous year.

Analysis of the shape of the autocorrelation functions (ACF) and partial autocorrelation functions (PACF) allowed estimation of the AR and MA parameters and therefore identification of plausible models (Hamilton and Watts, 1978).

In order to identify the best model, we fitted several ARIMA models and carried out diagnostic validation considering the distribution of standardized residuals. We applied diagnosis checks (Ljung-Box test) to the residuals for each estimated model; residuals must be equivalent to white noise (Box and Pierce, 1970; Ljung and Box, 1978). We compared the models by the corrected Akaike Information Criterion (AICc) and selected the one with the lowest AICc value (Akaike, 1974). We used the final ARIMA models to predict monthly dengue cases for the year of 2015 (12 months), with 95% prediction interval (95% PI). We compared these predictions with the observed data (SINAN).

The statistical analysis for STL decomposition, estimation of ARIMA models and figures were performed using the package *stats*, software R version 3.3.3 (The R Foundation for Statistical Computing, Vienna, Austria; http://www.r-project.org).

3. Results

In the city of Recife the yearly incidence of dengue varied from 139 cases in 2004–35,044 cases in 2002, during the study period (2001–2014). The higher incidences were registered in the years: 2002 (n = 35,044) considered epidemic year, 2010 (n = 9900) and 2012 (n = 10,146). During the study period, 73,479 dengue cases were reported in Recife. We pointed out the only peak of cases in 2002 with around 98% of cases between January and May followed by several years with lower occurence of dengue cases. (Fig. 1A)

In the city of Goiania the yearly incidence of dengue varied from 3462 in 2004–54,724 in 2013. The epidemic years were: 2002 (n = 15,437), 2008 (n = 22,088), 2009 (n = 23,992), 2010 (n = 43,360), 2013 (n = 54,724) and 2014 (n = 26,547). During the study period, 253,008 dengue cases were reported in Goiania (Fig. 1B).

Fig. 2 presents the monthly cases (ln data for Goiania), trend, seasonal and residual (remainder) components derived from seasonal-trend decomposition for Recife (A) and Goiania (B). The STL decomposition based on loess showed that trend is the most important component for the city of Recife (Fig. 2A), while seasonality is the most important one in Goiania (Fig. 2B).

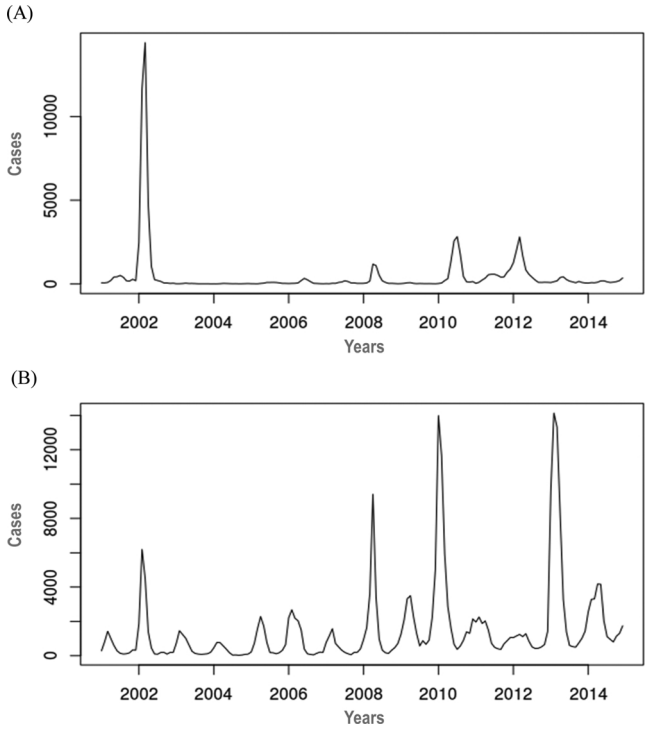

Fig. 1. Reported monthly dengue case data in Recife (A) and Goiania (B), Brazil (2001–2014).

Considering that seasonality was an important component for the city of Goiania we performed exploratory analysis of dengue incidence (ln data) for the period 2001–2014. The analysis showed that highest incidence was registered from December to May with one outlier of 13,985 dengue cases registered in January 2010; lowest incidence from July to September, and cases increased from October (Fig. 3).

Legend. The box encompasses 50% of the distribution, line within the box represents median values, border lines represent the first and the third quartile and dot represents outliers.

We tested several models for the city of Recife; however, none was adequate according to the model diagnosis. We opted to exclude the peak year of 2002 due to its outlier value. This epidemiological pattern was also reported by Amaku et al., indicating different intensity of transmission after 2002 (Amaku et al., 2016). After the exclusion of 2002 and the previous year (2001), it was possible to build-up an adjusted model for the period 2003–2014 and forecasting for 2015. For Recife, the autocorrelation functions (ACFs) and partial autocorrelation functions (PACFs) suggested that the best fit model was ARIMA $(1,1,3)^{12}$. Surveillance data registered 35,467 dengue cases between 2003 and 2014; our model fitted 33,372 cases for the same period. After fitting the model for the period 2003–2014 we used the model to the forecast monthly dengue number of cases for the year 2015. (Fig. 4A and Table 1)

For the city of Goiania, we used the natural logarithm of dengue incidence for 2001–2014. Four ARIMA models were tested; three were excluded by model diagnosis. Analysis of ACFs and PACFs suggested that the best fit model was SARIMA $(1,0,2)\ (1,1,2)^{12}$. In this time series, there was a strong seasonal component (1,1,2) together with the aseasonal component (1,0,2), considered mixed model. This final SARIMA model was auto-fitted with drift by R software. Between 2001 and 2014 SINAN registered 253,008 dengue cases; our model estimated 235,080 cases for this period. (Fig. 4B and Table 1)

Blue line represents the observed monthly dengue cases; Red dotted line represents fitted monthly dengue cases; Black line and shaded area

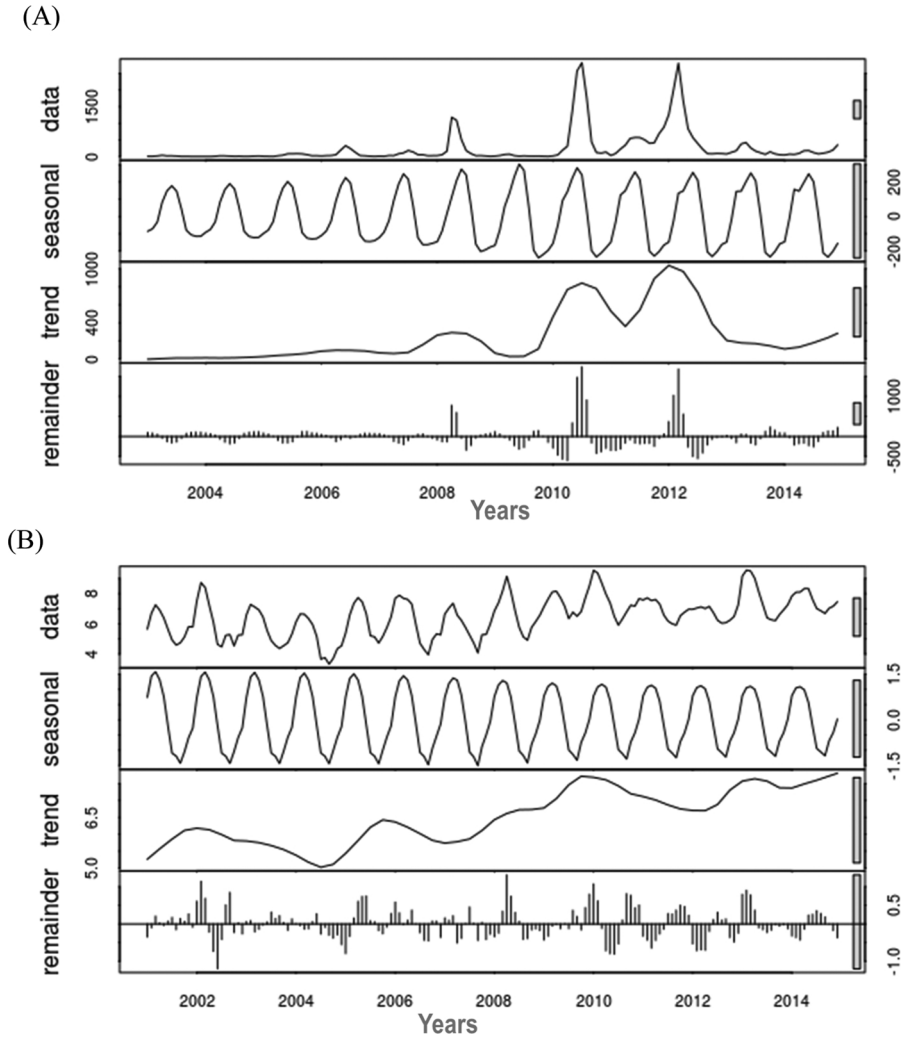

Fig. 2. Trend, seasonal and residual (remainder) components derived from STL decomposition of monthly dengue cases for the city of Recife (A) and Goiania (B) (ln data), during 2001–2014.

show forecast for 2015 with 95% prediction interval.

AR: autoregressive; MA: moving average; SAR: seasonal autoregressive; SMA: seasonal moving average; AICc: corrected Akaike Information Criterion

Table 2 shows the monthly forecast of dengue cases according to the model in 2015 with 95% prediction interval (95% PI) for both cities. For Recife, the model predicted total number of dengue cases for 2015 was 4254 varying from 440 in January to 325 cases in December. In 2015, the maximum predicted number of dengue cases was 15,543. The surveillance system (SINAN) registered a total of 35,724 dengue cases and/or "dengue-like" illness for the city of Recife; the peak months were March (5426 cases) and April (6138 cases), June-September 2015 has the lowest incidence recorded, from 1302 to 1948 cases. For Goiania, the forecasting model varied from 5874 dengue cases in March

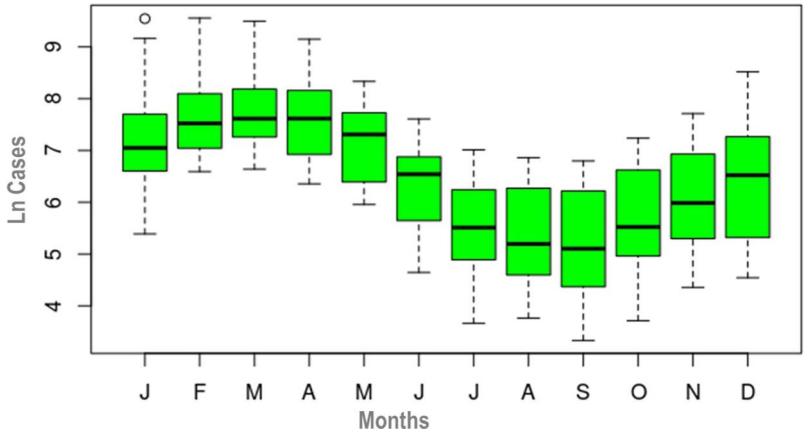

Fig. 3. Seasonal box-plot distribution of monthly dengue cases (ln data) in Goiania, Brazil (2001–2014).

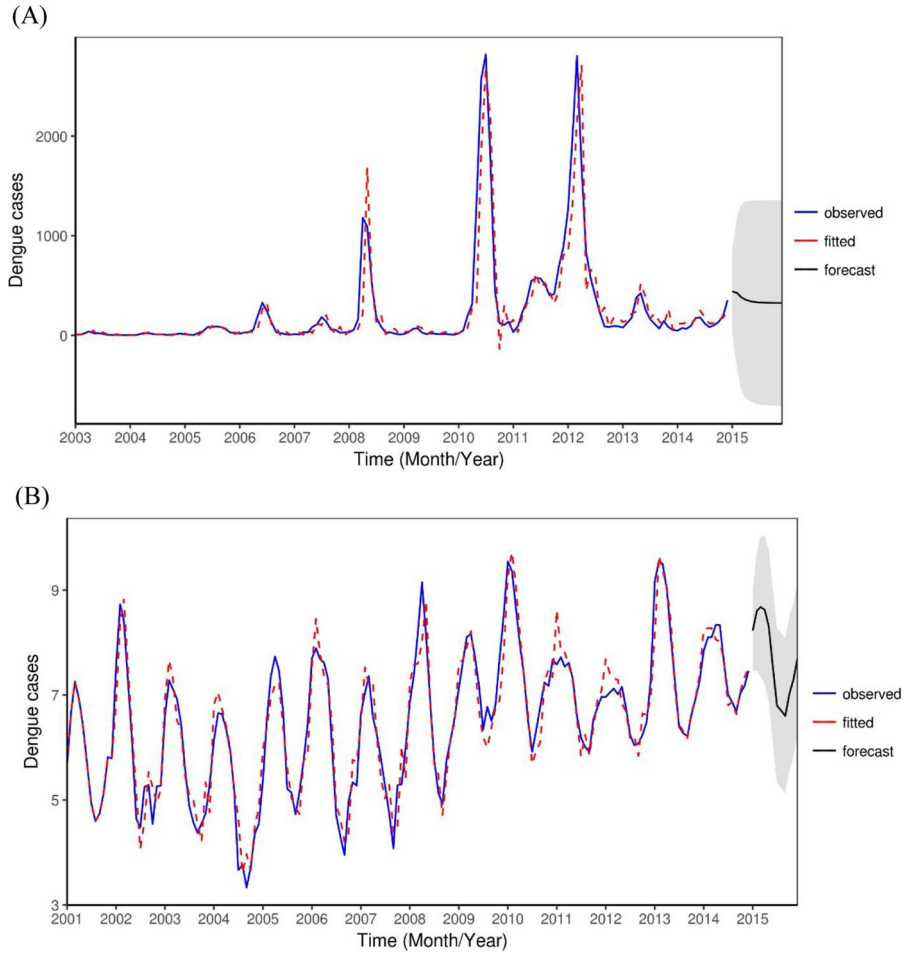

Fig. 4. Monthly time series 2003–2014 for Recife for observed and fitted dengue cases, and forecast dengue cases for 2015 (A); Monthly time series 2001–2014 for Goiania for observed and fitted dengue cases (ln data), and forecast monthly dengue cases for 2015 (B).

2015–737 cases in September 2015. For the entire year of 2015, the forecasted was 33,757 dengue cases, with a maximum of 127,191 cases. In 2015, a total of 74,095 dengue cases and/or "dengue-like" illness were registered by SINAN in Goiania.

4. Discussion

In our study the time series analysis of dengue incidence (2001–2014) suggested that large variation of transmission patterns in two Brazilian cities. For Recife, Northeast region, the data showed one large peak in the year 2002 with more than 35 thousand cases, followed by two small peaks in 2010 and 2012. For Goiania, Midwest region, there was an increase in the incidence of dengue with several epidemic peaks years reaching more than 54 thousand cases in 2013. While the best fitted model for the city of Recife was non seasonal ARIMA $(1,1,3)^{12}$; for the city of Goiania the seasonal component was strong and the best fitted model was SARIMA $(1,0,2)(1,1,2)^{12}$. During the study period, December to May were the months with higher dengue incidence in Goiania, coinciding with the rainy season regionally. In contrast, the city of Recife has fairly constant climate values of high

Table 2
Forecasted monthly dengue cases (95% prediction interval) for the cities of Recife and Goiania, 2015.

2015	Recife			Goiania		
	Predicted cases	Lower 95% PI	Higher 95% PI	Predicted cases	Lower 95% PI	Higher 95% PI
January	440	29	851	3744	1732	8095
February	429	–	1184	5452	1746	17,026
March	384	–	1312	5874	1543	22,360
April	358		1343	5549	1347	22,855
May	344	–	1352	4030	946	17,168
June	336	–	1354	1837	425	7940
July	331	–	1355	896	206	3897
August	328	–	1356	814	187	3551
September	327	–	1357	737	169	3218
October	326	–	1358	1115	255	4874
November	326	–	1360	1479	338	6466
December	325	–	1361	2229	510	9741
Total	**4254**		15,543	**33,757**	9404	127,191

Table 1
ARIMA models, coefficients and corrected Akaike Information Criterion for Recife and Goiania, Brazil.

	ARIMA (p,d,q) $(P,D,Q)^S$	AR1	MA1	MA2	MA3	SAR1	SMA1	SMA2	Drift	AICc
Recife	ARIMA $(1,1,3)^{12}$	0.566	−0.024	−0.535	−0.380					1,943.03
Goiania	SARIMA $(1,0,2)$ $(1,1,2)^{12}$	0.666	0.422	0.184		−0.692	−0.080	−0.653	0.014	176.84

humidity and precipitation throughout the year (Siqueira et al., 2005; Teixeira et al., 2013). Therefore, the time series analysis allowed to describe different patterns of dengue distribution in two Brazilian settings.

How to interpret such distinct patterns of dengue distribution during the same time period in two Brazilian cities? Brazil is a continental country and dengue virus was introduced in the late 80′s in Recife (Atlantic coast) and in the 90′s, seven years later, DENV-1 was the first serotype to be detected in Goiania (Midwest). Interestingly, a previous study of the diffusion of dengue in Brazil used dengue incidence extracted from the surveillance data (SINAN), using the capital of Recife and Goiania as examples, as in our study. The authors described differences in the time period of achieving high intensity of dengue transmission when taking into account the threshold over 300 cases per 100,000 inhabitants for intense dengue transmission (Barcellos and Lowe, 2014). In Recife, a high intensity of dengue transmission was detected earlier – before 2002 – while in Goiania this threshold was reached later: between 2002 and 2005. In general, differences in the incidence of dengue reflect the time period of the intensity of dengue virus circulation in different urban areas, the vector density and the remaining susceptible population (Amaku et al., 2016; Barcellos and Lowe, 2014; Morato et al., 2015).

In Rio de Janeiro, the time series analysis of dengue incidence from 1997 to 2004 using seasonal ARIMA was considered adequate to predict dengue incidence for the year 2005, suggesting that this model could be expanded to other geographical areas and to monitoring dengue and other infectious diseases (Luz et al., 2008). In concordance with the previous study, the results from time series analysis in two Brazilian cities (Campinas and Ribeirao Preto) in Sao Paulo State, considered that seasonal ARIMA models were reliable for prediction of the dengue incidence one year ahead. However, the authors pointed out that sometimes forecasting dengue incidence in epidemic years could be more complex due to the possibility of the introduction or reintroduction of dengue serotypes and the lack of immunity of population (Martinez et al., 2011; Martinez and Da Silva, 2011). Amaku et al. (2016) analysed the dynamics of dengue transmission using Ross-Macdonald model for the city of Recife in order to predict outbreaks of dengue fever, using surveillance data for the last decade (Amaku et al., 2016). The authors also described the 2001–2002 outbreak followed by years with marginal dengue transmission. They explained this epidemiological context by the reduced number of susceptible individuals due to herd immunity since DENV serotypes (DENV1 to DENV4) circulated in the last the three decades in Recife (Amaku et al., 2016, 2015; Cordeiro et al., 2007). Seroprevalence studies for dengue antibodies assessment conducted in Recife in 2005–2006 showed that almost 90% of Recife population had immunity to one or more serotypes (Braga et al., 2010; Castanha et al., 2013).

In our study it was not possible to link the dengue outbreaks with the predominant serotype due to the paucity of serotype data in the surveillance system for the studied period (data not shown). A review of the epidemiological trend of dengue disease in Brazil 2000–2010 indicated that DENV-1 was the predominant serotype at the beginning of the decade; DENV-3 from 2003 and DENV-2 from 2007 (Teixeira et al., 2013).

The estimated ARIMA model for Goiania fitted adequately to the observed dengue incidence data for the 2001–2014 and the exclusion of the years 2001–2002 was necessary for model build for Recife. For Recife, the model predicted ~15.5 thousand dengue cases as the higher prediction interval in 2015. This forecasting indicated at least 20,000 cases less than the total of 35,729 cases registered by SINAN. In fact, during the year 2015, a MoH recommendation led to all cases of exanthematic disease being notified as “dengue-like”, hence overestimating dengue incidence. This disparity between observed and predicted cases may now be explained by the introduction of Zika virus in the city in 2015 (Brasil, 2016). Assuming that the model prediction is a reasonable reflection of dengue incidence, approximately 20 thousand of Zika cases could have been misdiagnosed as dengue virus infection during the first wave of Zika virus in Recife. A cross-sectional study, conducted a during the peak of 2015 outbreak in Recife showed that 86% of 1046 suspected cases of arbovirus could be classified as Zika cases (Brito et al., 2016). Our results showed that the 2015 estimated dengue cases from the ARIMA model could be from 44% to 88% smaller than the registered cases by SINAN. The cocirculation of Zika, chikungunya, and DENV-1 was also described in this study area in 2015 (Pessôa et al., 2016). Recent surveillance-based analysis (2015–2016) showed that approximately 80% initially suspected dengue cases have been discarded after investigation and considered as possible Zika virus cases (de Oliveira et al., 2017).

The present study has the inherent limitation of using secondary data from dengue surveillance. Such data are prone to underreporting or over-reporting during endemic or epidemic years, or bias to health units capacity in reporting dengue cases (Barcellos and Lowe, 2014; Morato et al., 2015; Runge-Ranzinger et al., 2008). Another drawback of dengue surveillance is the scarce data on serotypes, hampering the identification of the main serotypes causing outbreaks (Barcellos and Lowe, 2014). We tested several models for the city of Recife but the ARIMA model was considered appropriate only when we excluded the year 2002, the largest outbreak, and consequently 2001 from the time series. As noted in our study the introduction of Zika virus and/or other urban vector-borne diseases like chikungunya might distort the dengue notification as occurred in the last three years in Brazil (Brasil, 2016; Pessôa et al., 2016). Climate variables, vector density and spatial distribution of cases were out of the scope of the analysis; however, the seasonality patterns presented in Goiania may be due to climate variation. Including climate variables in the model could give a better fit but this has been a controversial issue in the literature, some studies indicated an improvement while others did not find significant change in the adjusted model (Johansson et al., 2016).

5. Conclusions

Our findings showed evidence of the heterogeneity of dengue temporal patterns in two settings in Brazil during 2001–2014. The ARIMA models fitted adequately for the time series of dengue incidence for Recife and Goiania, the later with a seasonal component. The adequacy of prediction might be hampered due to the co-circulation of other arbovirus in the year of prediction. Differences between the models may be explained by the introduction of dengue virus in the late 80′s in Recife and in the 90′s in Goiania and important differences in the intensity of transmission. The time series models may be considered as a baseline for the time series analysis of dengue incidence before the Zika epidemic (2015), chikungunya virus introduction (2014) and before DENV vaccine implementation in Brazil. It was also an opportunity to estimate the number of Zika cases in 2015 previous to the implementation of the Zika notification. The time series analysis could be applied to other settings in order to provide early warning of the increase in arbovirus diseases.

Conflicts of interest

None.

Ethics statement

Ethical approval for the study was obtained from the Ethical Committee of the Faculty of Medical Sciences – University of Pernambuco (CAAE: 56731716.7.0000.5192). We obtained the dataset from the Brazilian dengue surveillance system without identification variables.

Acknowledgements

FC received CAPES scholar for MSc. Brazilian Ministry of Education. Partial support from the National Council for Scientific and Technological Development (Conselho Nacional de Desenvolvimento Cientifico e Tecnologico [CNPq]; scholarship 306708/2014-0 to CMTM, 308818/2013-0 to RAAX, and 306222/2013-2 to WVS).

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