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SARS-CoV-2 effective breeding number estimation in Vitória de Santo Antão/PE, Brazil

Estimativa do número efetivo de reprodução de SARS-CoV-2 em Vitória de Santo Antão/PE, Brasil

Estimación del número efectivo de reproducción de SARS-CoV-2 en Vitória de Santo Antão/PE, Brasil

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Abstract

COVID-19 is an acute respiratory disease with the SARS-CoV-2 virus as etiological agent, triggering a worldwide pandemic of severe acute respiratory syndrome (SARS) from the year 2019. Effective reproduction number expresses the viral spread potential, being favourable in determining the epidemiological outbreak behaviour; and in obtaining crucial information to identify the disease intensity and which interventions should be conducted. The study objective was to analyze COVID-19 transmissibility, in *Vitória de Santo Antão/PE*, municipality, Brazil. Therefore, R_0 and $R_{(t)}$, indicators were estimated, which reflect the effective number of SARS-CoV-2 infection reproduction among the *Vitória de Santo Antão/PE* population, within 107 days from the first confirmed case (covering the disease history to date). Results showed that, to date, measures have been sufficient to effectively reduce the epidemic transmissivity. However, even with slower epidemic growth, the population must remain alert and maintain social distance in order to flatten the curve. In addition, estimates can be understood correctly and therefore enable decisions to be made to help more efficiently control pandemic expansion.

Keywords: Coronavirus; Infectious diseases; Pandemic; Transmissibility; Zoonosis; Parameters.

Resumo

COVID-19 é uma doença respiratória aguda que tem por agente etiológico o vírus SARS-CoV-2, desencadeando uma pandemia mundial de síndrome respiratória aguda grave (SARS) a partir do ano 2019. O número efetivo de reprodução expressa o potencial de disseminação viral, sendo favorável na determinação do comportamento de um surto epidemiológico; e na obtenção de informações cruciais para identificar a intensidade da doença e quais intervenções a serem conduzidas. O objetivo do estudo foi analisar a transmissibilidade de COVID-19 no município de Vitória de Santo Antão/PE, Brasil. Sendo assim, foram estimados os indicadores R_0 e $R_{(t)}$, que refletem o número efetivo de reprodução da infecção por SARS-CoV-2, em meio a população de Vitória de Santo Antão/PE, no período de 107 dias a partir do primeiro caso confirmado (cobrindo o histórico da doença até o momento). Os resultados comprovam que, até a data analisada, as medidas foram suficientes para reduzir de forma eficaz a transmissibilidade da epidemia. Porém, mesmo apresentando crescimento desacelerado da epidemia, a população deve ficar em alerta e manter o distanciamento social a fim de provocar o achatamento da curva. No mais, as estimativas podem ser entendidas em conformidade e, portanto, permitir as tomadas de decisões para ajudar, prevenir e controlar a expansão da pandemia de modo mais eficiente, eficaz, gerando efetividade.

Palavras-chave: Coronavírus; Doenças infecciosas; Pandemia; Transmissibilidade; Zoonose; Estimadores.

Resumen

COVID-19 es una enfermedad respiratoria aguda que tiene para agente etiológico es el virus SARS-CoV-2, desencadenando una pandemia mundial del síndrome respiratorio agudo severo (SARS) a partir del año 2019. El número efectivo de reproducción expresa el potencial de propagación viral, siendo favorables en la determinación el comportamiento de un brote epidemiológico; y en la obtención de información crucial para identificar la intensidad de la enfermedad y cuales intervenciones para ser conducidos. El objetivo del estudio fue analizar la transmisibilidad de COVID-19 en el municipio de Vitória de Santo Antão/PE, Brasil. Siendo así, los indicadores fueron estimados R_0 e $R_{(t)}$, qué reflejan el número efectivo de reproducción de la infección por SARS-CoV-2, en medio de la población de la población de Vitória de Santo Antão/PE, en el período de 107 dias a partir do primeiro caso confirmado (cubriendo la histórico de la enfermedad hasta momento). Los resultados demuestran que, hasta la fecha analizada, las medidas fueron suficientes para reducir efectivamente la transmisibilidad de la epidemia. Sin embargo, mismo presentó crecimiento desacelerado de la epidemia, la población debe permanecer alerta y mantener la distancia social para hacer que la curva se aplana. Además, estas estimaciones pueden entenderse en conformidad y, por lo tanto, permitir las tomar de las decisiones para ayudar, prevenir y controlar la expansión de la pandemia de una forma más eficiente, eficaz, generando efectividad.

Palabras clave: Coronavirus; Enfermedades infecciosas; Pandemia; Transmisibilidad; Zoonosis; Estimadores.

1. Introduction

Since the first disease epicenter in Wuhan (Hubei Province, China) in December 2019, approximately 23.311.719 COVID-19 global cases, including 806.410 deaths, have been confirmed through the epidemiological bulletin of August 24, 2020, becoming a pandemic situation (WHO, 2020b).

From a symptomatic patient's bronchoalveolar lavage fluid sample, RNA metagenomic sequencing detected SARS-CoV-2 as a new strain of Coronaviridae family RNA virus, denominated as 'WH-Human 1' Coronavirus (Wu et al., 2020). The viral genome phylogenetic analysis (29.903 nucleotides) showed that the new virus had greater compatibility (approximately 89.1% nucleotide similarity) with a SARS Coronavirus category (genus *Betacoronavirus*, subgenus *Sarbecovirus*), previously identified in bats in China (Wu et al., 2020).

Coronaviridae family viruses that cause respiratory infections, which can result in Severe Acute Respiratory Syndrome (SRAG), in humans are described as: SARS-CoV-2, appointed as etiological agent of the disease caused by Coronavirus (COVID-19); MERS-CoV, observed in 2012 as a cause of Middle East Respiratory Syndrome (MERS, genus *Betacoronavirus*, subgenus *Merbecovirus*); and SARS-CoV, detected in 2002 as an outbreak cause of Severe Acute Respiratory Syndrome (SARS) (Biscayart et al., 2020; Cespedes & Souza, 2020). Emerging pathogens that make it possible for humans to infect from an animal host, have proven to cause some of the most lethal diseases ever observed (Ahmad et al., 2020). The epidemiological outbreak involving SARS-CoV-2 demonstrates the potential for animal viral contamination as a factor for serious diseases development in humans, with COVID-19 being classified as zoonosis (Wu et al., 2020).

COVID-19 affects individuals in different ways, manifesting asymptomatically or with mild symptoms, and the clinical picture may evolve to severe pneumonia (Kannan et al., 2020). According to World Health Organization, to facilitate early recognition and screening of COVID-19 patients, symptoms can be distinguished into: common such as dry cough, tiredness and fever; less common symptoms such as body pain, headache, skin rash, sore throat, conjunctivitis, diarrhea, loss of taste and/or smell, fingers and/or toes discoloration; and severe symptoms characterized by difficulty breathing or shortness of breath, loss of movement or speech capability, and chest pain or pressure (WHO, 2020a).

In addition, SARS-CoV-2 infection has the potential to contribute to innate or adaptive immune responses activation; nonetheless, uncontrolled innate inflammatory responses and disable adaptive immune responses can cause local or systematic tissue damage (Cao, 2020). Since protective immunity (that is, immunity against reinfection, constituting the mechanism by which vaccines work) is absent in humans; and due to virus's high capacity to resist innate immune responses, greater knowledge of immune response in individuals is necessary for future obtaining of biomarkers, as well as antiviral and immunomodulatory medicines (Felsenstein et al., 2020).

In Brazil, 3.622.861 confirmed cases, and 115.309 deaths due to COVID-19 are estimated. Among this database, 119.357 cases were detected in Pernambuco state (PE), with the death of approximately 7.399 people (BRASIL, 2020). Therefore, it becomes necessary to intensify disease behavior monitoring, and possible changes in epidemiological outbreak, in addition to promoting effective public health strategies, taking into account the isolation and population testing in the fight against COVID-19 (Heymann & Shindo, 2020).

Therefore, study aims to analyze the COVID-19 infectivity rate, in Vitória de Santo Antão/PE municipality, through the novel Coronavirus effective reproductive number. Furthermore, it seeks to verify whether the possible people exodus towards the interior cities affects the disease stabilization in Pernambuco state.

2. Methodology

The analysis was performed using COVID-19 incidence database, using the R software and *EpiEstim* package, presented by Cori (2019). Data were daily collected from the first confirmed case, for a period of 107 days, made available by epidemiological bulletins published by Vitória de Santo Antão/PE Health Department. The bulletins contain the following data: number of confirmed cases, people in isolation, recovered, deaths, tests carried out by municipal network, discarded cases, home monitoring and COVID-19 treatment unit.

The effective reproduction number represents the new infections average number that an infected individual cause. If this measure is greater than 1, the number of new cases from infected individuals is expected to increase. Therefore, if this measure is less than 1, it is expected that the number of new cases of infected individuals will decrease. The threshold value of 1 is called the epidemic threshold. This number allows us to estimate how many secondary infections are likely to occur from a single infection in an area (Kucharski et al., 2020). Therefore, this value was used to analyze the epidemic's spread dynamics.

2.1. Basic Reproduction Number R_0

R_0, defined as basic reproduction number, represents the average number of new infections caused by an infected individual in the epidemic initial phase population. This value, called by Lotka (1939) "reproducibility" or "infectivity", is calculated according to following equation:

$$R_0 = \frac{a}{c} = \left(1 + \frac{\lambda}{b}\right)\left(1 + \frac{\lambda}{c}\right) \tag{1}$$

where *a* represents the effective contact rate, *b* corresponds to the rate in which infected people become infectious, *c* the rate in which infectious people are isolated and λ the growth rate.

2.2. Effective reproduction number $R_{(t)}$

According to Cori (2013), individuals have an infectivity pattern given by a probability distribution $w_{(s)}$, dependent on the time since the infection of the case, *s*, but independent of time *t*. The higher the $w_{(s)}$ at a time *s*, the more infectious an individual is. This distribution depends on intrinsic individual biological factors.

The effective reproduction number $R_{(t)}$ can be estimated by the ratio of new infections number generated at time *t*, given by $I_{(t)}$, and the infection incidence sum up to time *t-1*, weighted by distribution $w_{(s)}$. $R_{(t)}$ is the secondary infections average that an infected individual can generate assuming that same conditions at time t are maintained. From this, we can simulate the $R_{(t)}$ through the relation:

$$R_{(t)} = \frac{I_{(t)}}{\Sigma_{s=1}^{t} I(t-s)\, w_{(s)}} \tag{2}$$

2.3. Model

The model was developed by Wallinga & Teunis (2004) to analyze SARS cases reproduction number, being expanded to state space models by Durbin & Koopman (2012). Cori (2019) developed the *EpiEstim* package for the R software, used in estimation and analysis of $R_{(t)}$ reproduction numbers of epidemic curves.

Some package applications are found in studies by Munoz, Montoya and Loaiza (2016), analyzing Dengue in a Colombia region between 2012 and 2013; Thompson et al. (2019), analyzing Influenza H1N1 in United States in 2019, Middle-East Respiratory Syndrome (MERS) in Saudi Arabia between 2014 and 2015, and Ebola in West Africa between 2013 and 2016. The model was also used to analyze COVID-19 in several countries: Najafi (2020) uses it to map the infection in Iran; Moirano, Schmid and Barone-Adesi (2020) uses the estimated $R_{(t)}$ to analyze the mitigation measures used in northern Italy; Moon et al. (2020) analyze quarantine efficiency in Seoul, South Korea, between January and March 2020; and Senel (2020) carried out an analysis for Turkey.

Estimate biggest challenge was to parametrize mean and standard deviation consistently, and for that, some simulations with literature parameters were evaluated (Ainslie et al., 2020; Nishiura, Linton, & Akhmetzhanov, 2020; Gupta et al., 2020). For greater precision, uncertain parameterization was performed, with minimums and maximums established in the previous parameters.

The most obvious limitation is the data underreporting. The strategy of testing only severe cases makes the number of tests precarious. In addition, most tests were performed in private laboratories. Of those that were performed in public institutions, there are rapid tests whose accuracy is weak. Not enough information is found, including presence of rapid tests among those in private networks. The information about testing, present in the database, only started to be released from the forty-first day after the first case.

2.4. Shapiro-Wilk Test

The Shapiro-Wilk (SW) test (1965) was developed to test whether a random sample of size n follows Normal Distribution. The SW test depends on the correlation between the data provided and their corresponding normal scores, whose hypotheses are defined by:

H_0 : The sample comes from a Normal population;

H_1 : The sample does not come from a Normal population.

The test statistic W is calculated according the following equation:

$$W = \frac{\left(\sum_{i=1}^{n} a_i x_{(i)}\right)^2}{\sum_{i=1}^{n} (x_i - \bar{x})^2} \tag{3}$$

where $x_{(i)s}$ are the ranked sample values, a_i are the mean generated constants, $\bar{x}$ is the sample mean and n is the observations number (Shapiro & Wilk, 1965).

Under H_0, if $W > W_{(\alpha,n)}$ or $P\left(W > W_{(\alpha,n)} \middle| H_0\right) > \alpha$, H_0 cannot be rejected. Consequently, the sample comes from Normal distribution with a 5% significance level, where $W_{(\alpha,n)}$ is the tabular value used to compare with the W statistic value.

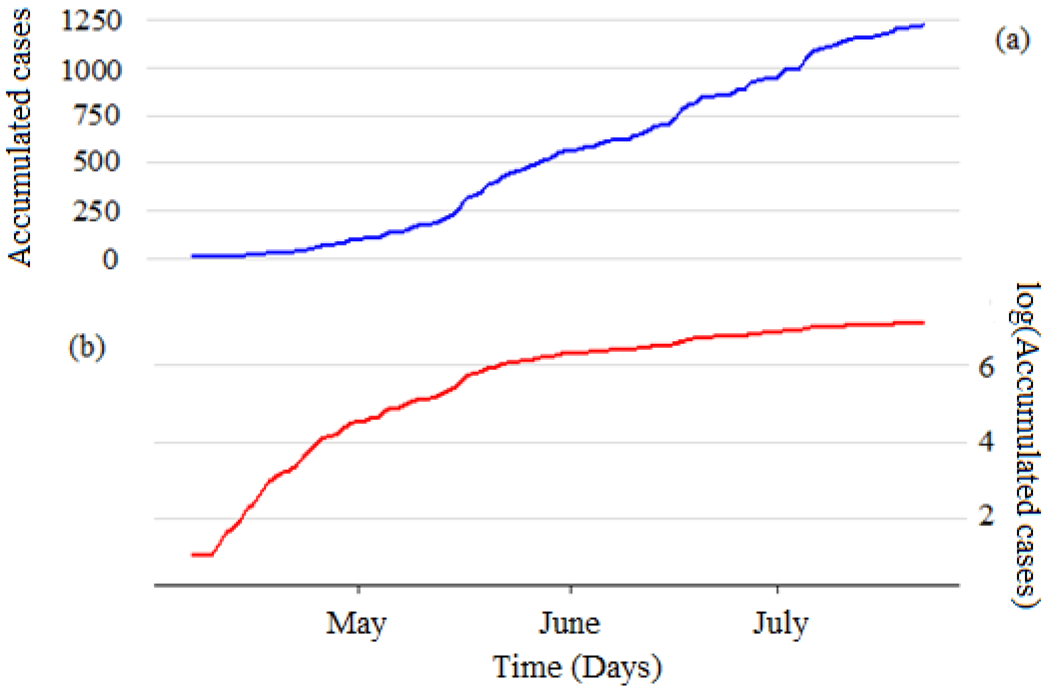
3. Results and Discussion

In Figure 1a, checks the cumulative number of COVID-19 confirmed cases in Vitória de Santo Antão/PE municipality, between April 7, 2020 and July 22, 2020. Between these two dates, accumulated cases number increased from 1 to 1222. The observed growth has characteristics of an exponential distribution, with parameter $\lambda = 0.087$, which implies a doubling time in cases number in $\ln(2) / \lambda = 7.96$ days.

When analyzing the last 53 days, λ corresponded to 0.102, which implies a doubling time in cases number of 6.79 days. Therefore, the increase in λ value, implies a growth rate deceleration.

Examining Figure 1b, confirmed coronavirus cases in Vitória de Santo Antão/PE municipality, with a logarithmic scale, it is possible to identify a slowdown in virus spread. Consequently, this result demonstrates that the municipality accumulated cases reached the plateau.

Figure 1. (a) Accumulated number of cases detected in Vitória de Santo Antão/PE, between 07/04 to 07/22/2020; (b) Natural logarithm of cumulative cases number.



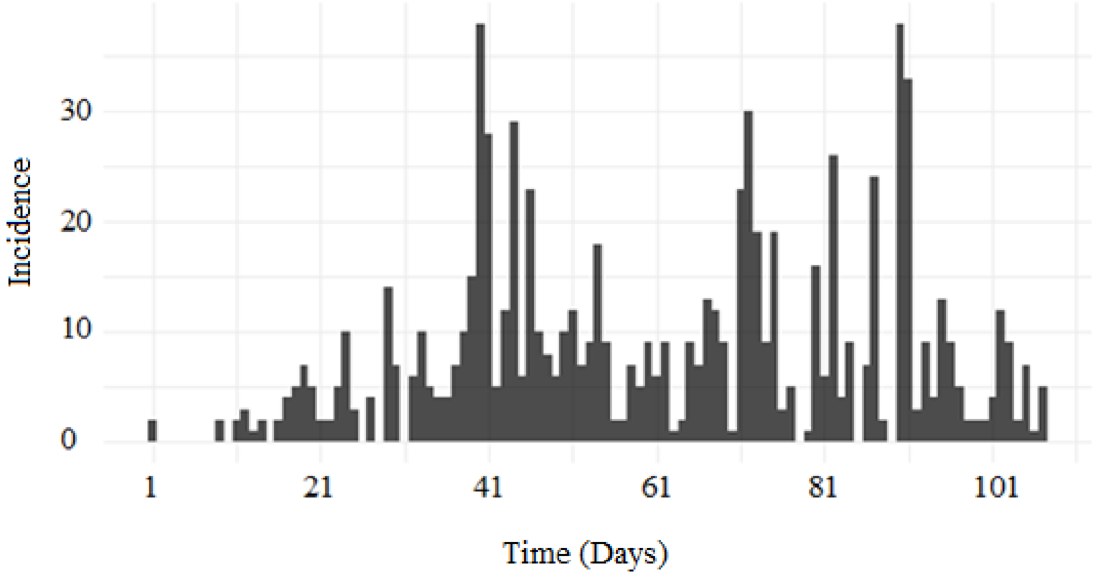
Source: Authors (2020).

Figure 2 features new cases incidence rate in Vitória de Santo Antão/PE municipality. On April 7, 2020, the municipality registered its first three COVID-19 infection cases, whose incidence rate was approximately 2.16% (labeled as day 1); up to 1220 confirmed cases, on July 22, 2020 (day 107) with an 5.76% incidence.

It is observed that incidence rates fluctuate with days passing by. However, while the big trends are obvious, caution is needed when it comes to smaller trends, which may come to be considered as just random variations in daily counts.

The highest incidences coincided with the days 16/05/2020 and 05/07/2020, presenting 31.19%, demonstrating that pandemic reveal random behavior. Therefore, containment measures are essential, eliminating to the maximum the community broadcasts to cushion the disease spread (Schuchmann et al., 2020). Moreover, when applying Shapiro-Wilk test, was checked non-normality in incidence rates (p-valor < 0.05).

Figure 2. COVID-19 daily incidence in Vitória de Santo Antão/PE municipality, Brazil.



Source: Authors (2020).

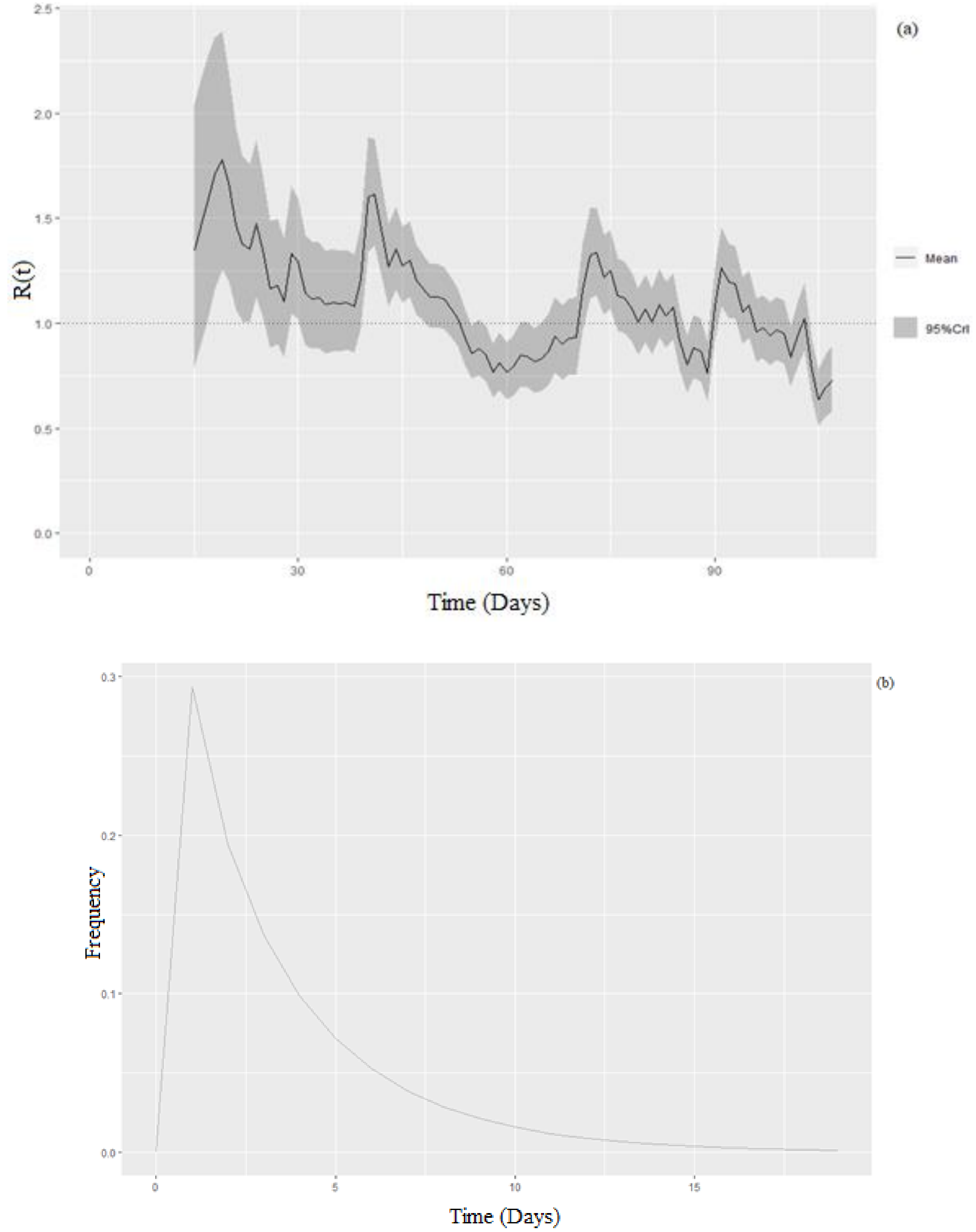
In Figure 3a, it is observed that the slope of effective reproduction number curve showed a decline since the pandemic early stages, strongly suggesting that containment efforts are progressively reducing disease transmission in Vitória de Santo Antão/PE municipality. Similar result was found in Barros et al. (2020), demonstrating a transmissibility stabilization in Garanhuns municipality.

In addition, checks that sliding window estimates of seven days of outbreak (7-14 April 2020) were an average of 1.57, in which at this time the largest of *R* was verified, approaching the peak of 1.78. The adjusted Gamma distribution is shown in Figure 3b, using the mean 2.97 and standard deviation 3.29 in accordance with Prete et al. (2020) study.

Therefore, the methodology consists of visualizing them and estimating some important statistics that are used to evaluate and plan measures that prevent transmission. Monitoring *R* over time provides feedback on interventions effectiveness and the need to intensify control efforts; since the public health policies objective is to reduce the *R* below the threshold of 1 and as close as possible to 0, thus bringing the epidemic to the “under control” state, as noted in Figure 3a. According to the microbiologist Natalia Pasternack, president of *Questão de Ciência* Institute (IQC), it is important that this behavior remains stable for two epidemiological weeks (Vidale & Senechal. 2020).

Extensive study by Ganyani et al. (2020), demonstrate that the COVID-19 transmission process occurs before the onset of symptoms and due to the rapid spread, resulting in serial intervals shorter than expected. However, for Vitória de Santo Antão/PE municipality, this characteristic was not verified at the pandemic beginning. However, after the ninety-fourth day, stabilization occurred, in which interval and mean was below 1.

Figure 3. (a) Estimate of $R_{(t)}$ and (b) distribution with the parameters estimated based on the study: *Serial Interval Distribution of SARS-CoV-2 Infection in Brazil*.



Source: Authors (2020).

It is observed that at pandemic beginning, the serial interval was longer, possibly associated with subclinical disseminators, that is, belonging to COVID-19 asymptomatic patient, which were not detected; and the lack containment implementation measures. Oliveira, Lucas & Iquiapaza (2020), demonstrate by simulation viral circulation reduction, related to hygiene measures adoption by the population, social restriction and not agglomerations.

4. Conclusion

Based on the results obtained in this work, estimative of effective reproduction number simulations in Vitória de Santo Antão/PE municipality are important to understand the processes that involve COVID-19 dynamics in the place. That is, $R_{(t)}$ reduction in the last few weeks demonstrated that each time fewer individuals become infected, consequently, receding contagions number commonly associated with preventive measures and guidance on the novel Coronavirus. In addition, the present study provides subsidies for endemic and epidemic regulatory agencies, assisting in decision-making to reduce transmission speed of SARS-CoV-2 virus in the region.

Finally, for future work, we will use georeferencing tools in order to map the remaining municipalities that may be susceptible, thus guiding public policies aimed at health in the state of Pernambuco.

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