Transitivity of COVID-19, based on parameters R_0 and $R_{(t)}$ in Pombos/PE municipality, Brazil

Transitividade da COVID-19, a partir dos parâmetros R_0 e $R_{(t)}$ no município de Pombos/PE, Brasil

Transitividad de COVID-19, en base a los parámetros R_0 y $R_{(t)}$ en el municipio de Pombos/PE, Brasil

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Abstract

Objective: Analyze the effective reproductive number $R_{(t)}$ estimate of the Severe Acute Respiratory Syndrome triggered by the new Coronavirus (SARS-Cov-2), in Pombos/PE municipality, linked to dates in 2020. Method: Data from SARS-Cov-2 confirmed cases number, made available through epidemiological bulletins published by the Health Department of Pombos/PE, municipality, Brazil. The $R_{(t)}$ determines the potential for the spread of a virus under certain conditions. Results: The results demonstrate that, until July 22, 2020, preventive

measures and health guidance were not enough to reduce the disease infectivity rate in the municipality ($R_{(t)} > 1$), being a new challenge to be faced by those who act in COVID-19 combat. Conclusion: The results provide quantitative assessments to Pombos/PE municipality, Brazil, guiding interventions measures that can be carried out by other municipalities when dealing with future outbreaks, new rising waves.

Keywords: COVID-19; Effective reproductive number; Infectivity; SARS-Cov-2; Stabilization; Zoonosis.

Resumo

Objetivo: Analisar a estimativa do número reprodutivo efetivo $R_{(t)}$ da Síndrome Respiratória Aguda Grave desencadeada pelo novo Coronavírus (SARS-Cov-2), no município de Pombos/PE, Brasil, vinculados a datas em 2020. Método: Utilizaram-se dados de número de casos confirmados do SARS-Cov-2, disponibilizado através dos boletins epidemiológicos publicados pela Secretaria de Saúde de Pombos/PE, Brasil. O $R_{(t)}$ determina o potencial de propagação de um vírus sob certas condições. Resultados: Os resultados demonstram que, até 22 de julho de 2020, as medidas preventivas e orientação de saúde não foram suficientes para reduzir a infectividade da doença no município ($R_{(t)} > 1$), sendo um novo desafio a ser enfrentado por quem atua no combate da COVID-19. Conclusão: Os resultados fornecem avaliações quantitativas ao município de Pombos/PE, Brasil, norteando em medidas de intervenções que podem ser realizadas por outros municípios ao lidar com surtos futuros, novas ondas crescentes.

Palavras-chave: COVID-19; Número reprodutivo efetivo; Infectividade; SARS-Cov-2; Estabilização; Zoonose.

Resumen

Objetivo: Analizar la estimación del número reproductivo efectivo $R_{(t)}$ del Síndrome Respiratorio Agudo Severo desencadenado por el nuevo Coronavirus (SARS-Cov-2), en el municipio de Pombos/PE, Brasil, vinculado a fechas en 2020. Método: Se utilizaron datos del número de casos confirmados del SARS-Cov-2, disponible mediante del boletín epidemiológico publicado por la Secretaría de Salud de Pombos/PE, Brasil. La $R_{(t)}$ determina el potencial de propagación de un virus en determinadas condiciones. Resultados: Los resultados demuestran que, hasta el 22 de julio de 2020, las medidas preventivas y orientaciones sanitarias no fueron suficientes para reducir la infectividad de la enfermedad en el municipio

$(R_{(t)} > 1)$, siendo un nuevo desafío que enfrentar por quienes laboran en el combatir el COVID-19. Conclusión: Los resultados aportan valoraciones cuantitativas al municipio de Pombos/PE, Brasil, orientando las medidas de intervención eso puede llevarse a cabo por otros municipios al tratar con brotes futuros, nuevas olas crecientes.

Palabras clave: COVID-19; Número reproductivo efectivo; SARS-Cov-2; Infectividad; Estabilización; Zoonosis.

1. Introduction

Infectious diseases epidemiological outbreaks are occurring more frequently and with progressively serious consequences, including zoonoses and illnesses associated with wildlife. The emergence of infectious pathogens is causally linked to anthropogenic action in nature, having a lasting effect on the human and wild populations (Schmeller et al., 2020). An example is the current outbreak of the novel SARS-CoV-2 coronavirus, whose first epicenter was in Wuhan, Hubei province capital of the People's Republic of China, spreading to many other countries (Velavan & Meyer, 2020).

Coronaviruses are enveloped, consisting of a simple positive RNA strand that infects humans and extensive animal diversity (Velavan & Meyer, 2020). SARS-CoV-2 belongs to the beta-coronavirus subfamily and is closely related to the SARS-CoV virus emerging from mammals, particularly bats (Latinne et al., 2020; Li et al., 2005).

SARS-CoV-2 genome, responsible for the COVID-19 pandemic, has several Open Reading Frames (ORFs), common to Coronaviruses and several other accessory genes (that is, genes not present in all strains of a species, considered as a flexible genome) (Zhou et al., 2020). ORFs assemble a sequence of nucleotides triads that are read as specific codons for certain amino acids. Therefore, during protein synthesis, OFRs are translated according to codon positions, encoding the following SARS-CoV-2 proteins: ORF1a, ORF1b, S, ORF3a, E, M, ORF6, ORF7a, ORF7b, ORF8, N and ORF10 (Ahmed et al., 2020).

Considering the extensive genome size (the largest non-segmented RNA viral genome ever coded), high genomic plasticity (great capacity for genetic change), and frequent recombination (exchange of genes between homologous chromosomes during the meiosis stage), CoVs have predisposition to transmission between species, with the ability to quickly adapt to new hosts (Latinne et al., 2020). Thus, the rapid transmission and SARS-CoV-2 worldwide spread signalize concern points about adaptation and evolution of the viral genome, promoted by mutations, recombination and/or deletions; the proportion at which the virus

spreads globally, finding multiple immune responses in the hosts and several countermeasures (Islam et al., 2020).

Scientists are running out of time in the development of effective vaccines or antiviral compounds to control and prevent COVID-19 based on the genomic, functional structure and aspects related to the immune response from pathogen-host interactions; however, the results are still uncertain (Rahman et al., 2020). According to the World Health Organization, 34 vaccine candidates against SARS-CoV-2 are in clinical trial and another 142 in pre-clinical evaluation (WHO, 2020), being the most promising products to date.

Being a severe disease, government institutions need to increasingly provide the necessary contribution in public health and socioeconomic policies, to develop more efficient strategies to face the epidemic outbreak of COVID-19.

Therefore, the study aims to analyze the COVID-19 transmission rate in Pombos/PE municipality, Brasil, through the effective reproductive number of the novel Coronavirus.

2. Methodology

The nature of the work is data exploratory analysis using quantitative methods (Pereira et al., 2018), characterized as a descriptive observational epidemiological study, in which it is possible to analyze the Coronavirus (COVID-19) data, without interventions in the original information. Therefore, it aims to determine the disease distribution, examining how the COVID-19 incidence (new cases) is related to the health of the population from Pombos/PE municipality, Brazil.

The analysis was performed using COVID-19 incidence database, using the R software and *EpiEstim* package, presented by Cori et al. (2013). Data were daily collected from the first confirmed case, for a period of 107 days, made available by epidemiological bulletins published by Pombos/PE Health Department, Brazil. 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 average number of secondary (infected) cases generated by a typical primary (contaminated) case at time t in a population, over a 5-day moving average (Pan et al., 2020). If this measure is greater than 1, there is an accelerated growth of the epidemic. Therefore, if this measure is less than 1, it is expected to slow the growth of the epidemic. The threshold value of 1 presents a growth in constant rhythm called the epidemic threshold (Nishiura & Chowell, 2009). This value allows us to estimate

secondary infections cases number, caused by an individual infectious in a time interval (Barros et al., 2020), being metrics for infectious diseases dynamics study (Keeling & Grenfell, 2000).

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. The R_0 is calculated when there is no immunity from past exposures or vaccination, nor any deliberate intervention in disease transmission, according to Becker et al. (2006).

This parameter is an epidemiologic metric used to describe the contagiousness or transmissibility of infectious agents, but is affected by numerous biological, socio-behavioral, and environmental factors that govern pathogen transmission, so its estimation must be done with caution, as seen in Delamater et al. (2019). 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 et al. (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:

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

(2)

$R_{(t)}$ is used to understand the behavior of an infectious disease in a moment of time t, because it is changed by control measures, according to Becker et al. (2006). That distribution depends on intrinsic individual biological factors and explains the disease infectivity pattern, therefore, the higher the $w_{(s)}$ at a time s, the more infectious an individual is (Cori et al., 2013).

2.3. Model

The model was developed by Wallinga and Teunis (2004) to analyze SARS cases reproduction number, being expanded to state space models by Durbin and Koopman (2012). Based on that study, Cori et al. (2013) developed the *EpiEstim* package for the R software, used in estimation and analysis of $R_{(t)}$ reproduction numbers of epidemic curves for numerous diseases in several studies in different periods and places, shown in Table 1.

Table 1. Scientific articles that address effective reproductive number theme, published in the period 2016-2020, and deposited on Scielo platform.

Study	Disease	Region	Period
Muñoz et al. (2016)	Dengue Fever	Colombia	2012-2013
Thompson et al. (2019)	Influenza H1N1	United States	2019
Thompson et al. (2019)	Middle East Respiratory Syndrome (MERS)	Saudi Arabia	2014-2015
Thompson et al. (2019)	Ebola	West Africa	2013-2016
Najafi (2020)	COVID-19	Iran	2020
Moirano et al. (2020)	COVID-19	Northern Italy	2020
Moon et al. (2020)	COVID-19	Seoul, South Korea	2020

Source: Authors (2020).

Table 1 highlights a survey of articles published on the Scielo platform, given their importance in the scientific community, addressing public health thematic areas with emphasis on human health, in which the expressions basal reproduction number and effective reproductive number were included in their keywords.

The main challenges of this approach are the quality of data and parametrize mean and standard deviation consistently. The lack of available tests in the Brazilian public health system was a factor leading the strategy that prioritized only severe cases. Besides, most of the tests were performed in private laboratories, and the public institutions relied also on rapid tests, whose accuracy is weaker than RT-PCR tests, leading towards a serious underreporting of both cases and deaths.

To determine the mean and standard deviation, it was chosen the parameters found in Ainslie et al. (2020); Nishiura, Linton, & Akhmetzhanov (2020); and Gupta et al. (2020), which are determined using Monte Carlo's simulations. Using minimums and maximums established in the previous parameters, uncertain parameterization was performed to obtain more exact results.

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:

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

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 $P\left(W > W_{(\alpha,n)}|H_0\right) > \alpha$, 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 statistical value.

3. Results and discussion

Cumulative cases that were confirmed for COVID-19 in Pombos/PE municipality, Brazil, are shown in Figures 1a and 1b, over the analyzed time. The graphs assist the understanding of local disease behavior, being the first step in a more accurate epidemiological investigation.

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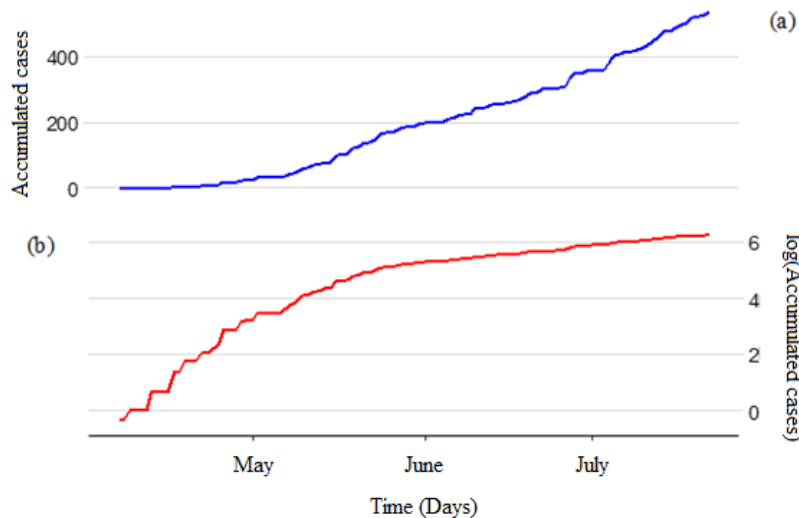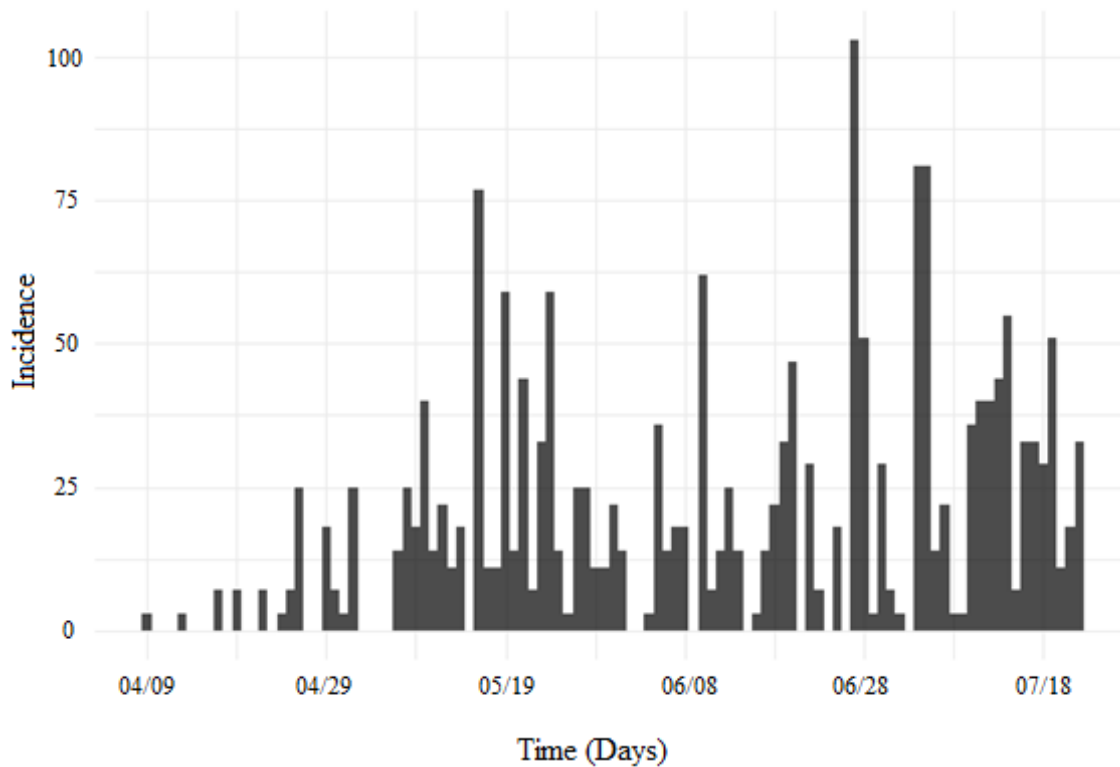

Source: Authors (2020).

In Figure 1a, checks the cumulative number of COVID-19 confirmed cases in Pombos/PE municipality, Brazil, between April 7, 2020 and July 22, 2020. Between these two dates, the accumulated cases number increased from 1 to 534. The observed growth has characteristics of an exponential distribution, with parameter $\lambda = 0.20$, which implies a doubling time in cases number in $\ln(2) / \lambda = 3.46$ days.

When analyzing the last 53 days, λ corresponded to 0.28, which implies a doubling time in case number of 2.47 days. Therefore, the increase in λ value, implies a growth rate deceleration.

Examining Figure 1b, confirmed coronavirus cases in Pombos/PE municipality, Brazil, 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. This strength loss indicates that the number of people being infected by the already sick is reducing. Due to underreporting, projections of the epidemiological outbreak advance based only on documented cases tend to generate results that are far from reality (Nogueira et al., 2020).

In Figure 2, features new cases incidence rate in Pombos/PE municipality, Brazil. On April 9, 2020, the municipality registered its first three COVID-19 infection cases, whose incidence rate was approximately 3.69% (labeled as day 1); up to 534 confirmed cases, on July 22, 2020 (day 107) with an 33.22% incidence.

Figure 2. COVID-19 daily incidence in Pombos/PE municipality, Brazil, 2020, in which the curve still shows resistance.
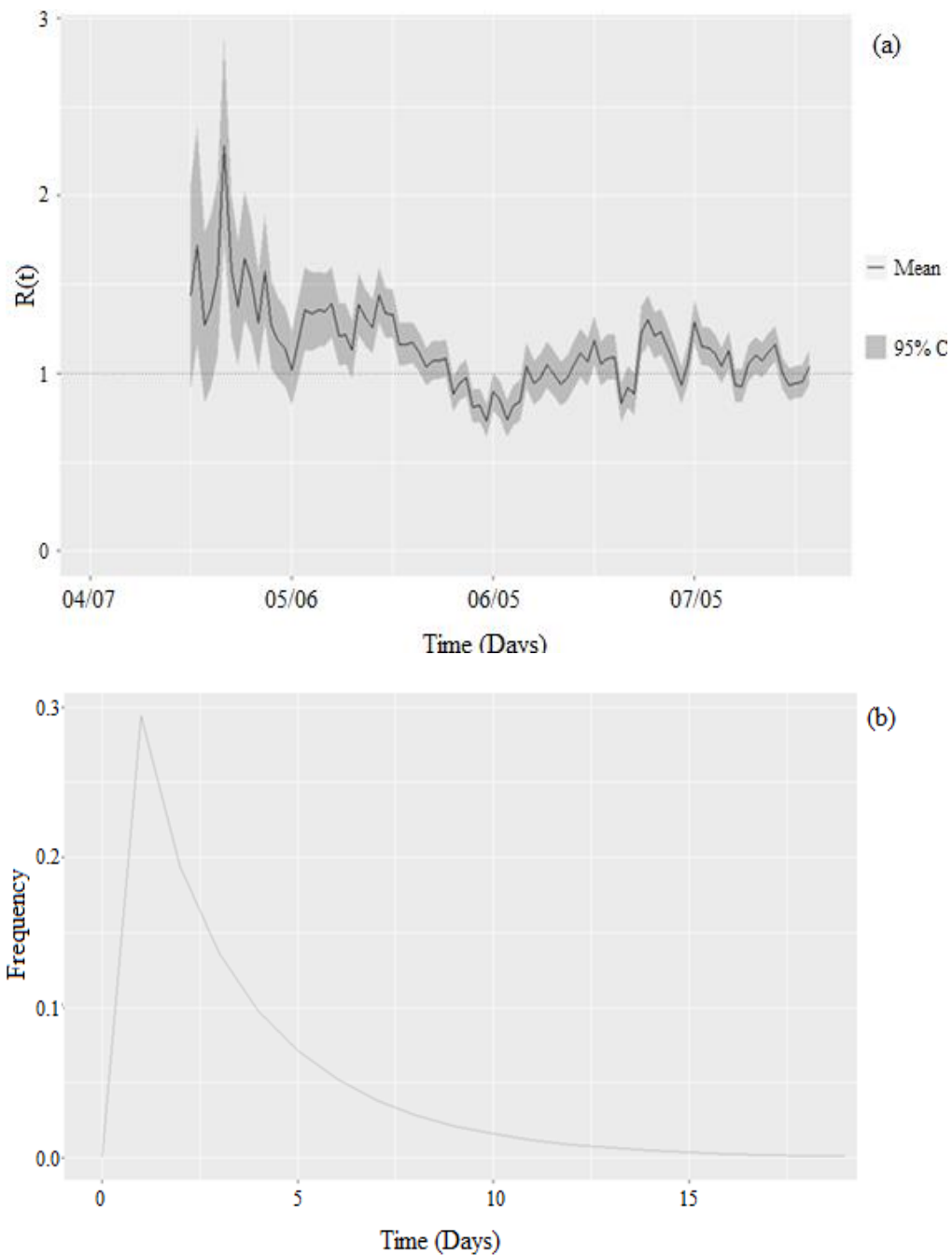

Source: Authors (2020).

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 27/06/2020, 04/07/2020 and 05/07/2020, presenting 103.35% and 81.20%, demonstrating that pandemic reveals random behavior. Therefore, containment measures are essential, eliminating to the maximum the community broadcasts to cushion the disease spread (Pimentel et al., 2020). Moreover, when applying the Shapiro-Wilk test, was checked non-normality in incidence rates (p-valor < 0.05).

In Figures 3a and 3b, is demonstrated how the effective reproduction number $R_{(t)}$ changes over time and the serial interval distribution that was generated to estimate it. In Figure 3a, the black line represents the effective reproduction number on a given time t, and the gray region the 95% confidence interval for that number. In 3b, plot shows an adjusted Gamma distribution with parameters observed in Prete et al. (2020), with mean 2.97 days, standard deviation 3.29 days and non-symmetry.

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* (Prete et al., 2020).

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 (between May 28th, 2020 and June 06th, 2020), strongly suggesting that containment efforts are progressively reducing disease transmission in Pombos/PE municipality, Brazil.

In addition, in the following weeks there was an accelerated growth with fluctuations in the estimates. Around June 25th, that number dropped to a value close to 1, remaining at that level for a week. This data indicates a stabilization in the disease speed progression. However, in the last weeks analyzed the effective reproductive number has grown at a steady pace, and no longer accelerated.

It is observed that daily variation may be large (95% Crl), especially in epidemic earlier phases, with strong variations over time. This result is possibly associated with subclinical manifestations, that is, belonging to COVID-19 asymptomatic patient, which were not detected or did not present to hospitals for treatment may be substantial. These cases possibly represent most COVID-19 infections.

Normally, $R_{(t)}$ decreases over time starting from R_0, the basic reproductive number, because of both the depletion of susceptible individuals and effective control efforts (Nishiura & Chowell, 2009).

The discrete daily distribution of the serial interval (period between symptoms onset in a case and in their infector) for COVID-19, assuming the adjusted Gamma distribution is shown in Figure 3b. In this result, it is possible to verify that the distribution assumes frequencies between 0 and 0.3, and greater probabilities in the pandemic initial phases.

According to the Survey of Territorial Information (LIT), carried out based on the Demographic Census of the Brazilian Institute of Geography and Statistics (IBGE, 2000), the Northeast region concentrates 28.7% of the 926 thousand private households occupied in subnormal agglomerates, with irregular urban pattern, lack of essential public services and location in areas restricted to occupation (Fiorillo & Ferreira, 2016), a possible factor associated with the progressive increase of the pandemic in Brazil, $R_{(t)} > 1$.

4. Conclusion

Based on the results obtained in this study, it was observed that the $R_{(t)}$ estimates showed a decline. However, in the last weeks, the values showed an epidemic accelerated growth. Therefore, estimates simulations are important to understand the processes that occur, in this case the $R_{(t)}$ reduction, commonly due to sanitary measures. Although, this was not enough to reduce it effectively, with $R_{(t)} < 1$.

Given the above information, the effective breeding number estimation in Pombos/PE, Brazil, was applied to evaluate the epidemic transmissivity, and so, plan measures that prevent

transmission, provide information to society to face the pandemic, especially in vulnerable areas, and support decision-making in the adoption of policies and intervention actions.

In addition, for future work it is necessary to approach non-linear models to predict possible municipalities that tend to leave stability as a proposal for more assertive monitoring of the epidemic. Furthermore, it is interesting to address the application of the same quantitative methods in areas close to the municipality of Pombos/PE, Brazil, in order to verify whether the exodus of the potentially infected population does indeed have a direct influence on COVID-19 cases in neighboring municipalities.

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