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Modelo matemático de propagação da COVID-19 na população brasileira com a inserção da vacina contra a doença

Mathematical Model for the Propagation of COVID-19 in the Brazilian Population with the Insertion of the Vaccine Against Disease

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RESUMO

A aplicação de campanhas de vacinação contra doenças epidemiológicas é de grande importância para o seu controle e erradicação, principalmente devido à alta taxa de infecção e mortalidade destas doenças. Este trabalho tem como objetivo a apresentação de dois modelos matemáticos do processo de transmissão da COVID-19, sem e com a vacina contra a doença, para análise sistemática do melhor cenário. Em ambos os modelos são considerados apenas a evolução temporal do processo, tendo assim, um modelo matemático descrito por um sistema de Equações Diferenciais Ordinárias (EDOs). Para a obtenção dos resultados numéricos, é utilizado o Método de Diferenças Finitas Regressivas, a fim de, determinar o período de imunidade coletiva e o impacto da vacina na população brasileira. No decorrer do trabalho, enfatizamos a importância em investimentos na fabricação de medicamentos e vacinas, e campanhas de vacinação contra a doença.

Palavras-chave: COVID-19. Modelagem matemática. Vacinação. Erradicação.

ABSTRACT

The application of vaccination campaigns against epidemiological diseases is of immense importance for its control and eradication, mainly due to the high rate of infection and mortality from these diseases. This work aims to present two mathematical models of the transmission process of COVID-19, with and without the vaccine against the disease, for systematic analysis of the best scenario. In both models, only the temporal evolution of the process is considered, thus having a mathematical model described by a system of Ordinary Differential Equations (ODEs). To obtain the numerical results, the Finite Regressive Differences Method is used to determine the period of collective immunity and the impact of the vaccine on the Brazilian population. During the work, we emphasized the importance of investments in the manufacture of medicines and vaccines, and vaccination campaigns against the disease.

Keywords: COVID-19. Mathematical modeling. Vaccination. Eradication.

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1. INTRODUCTION

Epidemiological diseases have affected the world since the beginning of its history, such as Black Death, Bubonic Plague, Measles, Dengue, Yellow Fever, Hansen's disease, Tuberculosis and Malaria. Due to the profound impact of these diseases on populations with thousands of individuals with sequelae and deaths, there is a need for further developments in research on methods of control and prevention, propagation analysis, period of herd immunity, virus mutations, among others. To assist in the development of these researches, the concept of Mathematical Epidemiology was developed, which aims to analyze the characteristics of each disease and create mathematical models that represent its transmission process, see (BERNINE et al., 2019).

According to Hamer, the development of an epidemiology depends on the rate of contact between susceptible and infected individuals with the disease, see (HAMER, 1906) and (WYSE et al., 2011). Subsequently, in (KERMACK and MCKENDREICK, 1927) it is found that the insertion of individuals infected by the disease in a region only leads to an epidemiological outbreak if the density of individuals of individuals susceptible to contracting the disease is below the pre-critical value established.

The first research on Mathematical Epidemiology started by the Swiss mathematician Daniel Bernoulli in the 18th century. His research aimed to determine a mathematical model to describe the transmission process of smallpox, an epidemiological disease of the time. However, major advances in research only took place a century later with advances in health, in particular, about the causes of infectious diseases, according to (RAMON, 2011).

In January 2021, Brazil started its vaccination campaign against the disease and has already vaccinated more than $4{,}5$ million inhabitants. However, the determination of the quantity of vaccine doses that must be distributed to each region must be analyzed based on the numbers of susceptible, infected and recovered individuals from the disease, as well as those already vaccinated against it. This determination is necessary, since, now in the initial phase of vaccination, there is not a sufficient quantity of vaccine for most of its inhabitants.

COVID-19 is a disease with a high rate of contagion and the lack of control and prevention by those susceptible to it can lead to fatality. However, to identify periods of growth, stability and decrease in the number of individuals, it is necessary to observe the characteristics of the disease, leading to a modeling of the disease and its prediction through numerical resolution.

This work aims to build a mathematical model that describes the transmission process of COVID-19 for the analysis and determination of an ideal scenario, to determine the period of collective immunity and the impact of the vaccine on the Brazilian population. Note that as soon as the collective immunity period is reached the number of infected individuals starts to drop.

The work was divided as follows: in section 2, a case study regarding the disease in question is presented. Important points are addressed in relation to COVID-19, such as appearance, symptoms, forms of transmission and prevention, and studies on vaccines and treatments; in section 3, two mathematical models are constructed, using Ordinary Differential Equations, to be able to simulate the spread of the disease, without and with the insertion of the vaccine against the disease; section 4, on the other hand, is composed of the analysis and discussions on the results obtained through the numerical resolution of mathematical models. Final considerations and possible further work are presented in section 5.

2. CASE STUDY

The COVID-19 is a disease caused by the SARS-CoV-2 virus, which etymologically means Severe Acute Respiratory Syndrome – Coronavirus – 2. This disease belongs to the Coronavirus family, which is responsible for some respiratory diseases with varying levels of severity. Among the diseases belonging to this family, we can mention SARS, transmitted by the SARS-CoV virus that occurred in 2002 with its first registration in China, and MERS, transmitted by the MERS-CoV virus that occurred in 2012 with its first registration in Saudi Arabia.

Like SARS and MERS, COVID-19 is believed to have originated from a zoonotic source, that is, its virus was initially transmitted from an animal to a human. However, as defended in (NOGUEIRA, 2020), even if they have several hypotheses about the origin of the virus, it is still not possible to affirm its main parent.

The symptoms and severity of the disease vary from individual to individual. However, according to (BRASIL, 2020), the most common symptoms are: cough, runny nose, sore throat, high fever (≥ 38◦C), loss of taste and smell, gastrointestinal disorders such as vomiting, diarrhea, tiredness and difficulty breathing. However, there are also cases where the person is infected and does not develop symptoms, that is, he is asymptomatic. In both situations, the infected individual has the same chance of transmitting the virus.

2.1. TRANSMISSION AND PREVENTION

The high contagion power of COVID-19 is a worrying factor, since after a few days of its first registration, which took place on December 31, 2019 in Wuhan, China, the World Health Organization (WHO) declared that the epidemic was of a Public Health Emergency of International Importance (PHEII), according to (WHO, 2020).

The transmission of COVID-19, like most respiratory diseases, occurs through saliva, through droplets expelled during speech, sneezing, or coughing from individuals infected with the virus. Contagion can occur directly, where an infected individual infects an individual susceptible to the disease, or indirectly, which is when an individual susceptible to the disease encounters surfaces or objects that have been contaminated by the virus.

It is worth mentioning that there is a difference between the time that the virus remains alive on surfaces and objects, this differs in relation to the material that constitutes the surface or the object. The oscillation of time that the virus can stay alive on each surface is shown in Table 1.

Starting from a demographic perspective, the transmission of the disease can occur in an imported way, which is when an individual who became infected in another region is in a region that until then had no record of the disease; locally, which occurs when the region already has a record of contamination by the virus, but in a reduced form, capable of screening the disease and susceptible individuals who possibly came into contact with individuals infected by the disease; or in a community way, which is when the number of infected people is high enough that it is not possible to screen the disease in a given region.

Table 1. Time of the active virus in relation to the material.

Material	**Tempo**
Aluminum	2 - 8 hours
Copper	4 hours
Stainless steel	2 days
Wood	4 days
Glass	4 days
Metal	5 days
Plastic	5 days

Source: Adapted from (KAMPF et al.,2020).

Due to its high spread, the form of disease control occurs through the quarantine mechanisms to reduce the flow of people in non-essential activities. With this, cities can declare Lockdown to prohibit any non-essential activity for a specified period taking into account the contamination rates in the region in question. This modality is considered the most severe and occurs when its contamination rates are high.

In case of infection by the virus, the individual must perform isolation, which can occur in a hospital or at home, considering the clinical condition of the patient, not to spread the virus. However, during the pandemic, Social Distancing is recommended by all, since the majority of infected individuals are asymptomatic and still transmit the disease virus.

To avoid contamination by the disease virus, the WHO recommends that the entire area of the hands be washed frequently, using soap and water, and when this is impossible, 70% gel alcohol should be used. It is also recommended to use masks whenever you leave the house, being for individual use, avoiding crowded places and not sharing personal objects, as well as maintaining ventilated environments and disinfecting surfaces and objects of frequent contact.

2.2. VACCINES AND TREATMENTS

The growth of studies and research related to COVID-19 is notable, which consequently generates more hypotheses about the disease. Among the points studied, we must highlight research aimed at treatments to mitigate the effects of the disease, as well as vaccines against it.

In August 2020, about 203 vaccine candidates were counted, being studied and tested worldwide, as (BERNINE et al, 2020). To date, according to (MI, 2020), within the 9 categories and 5 phases for vaccine development, there are 242 vaccines under development. Among them, 10 are already in use around the world, however only 3 have authorization for application, which are

- Moderna: RNA-based vaccine that is in use in Canada, Israel, Switzerland, the European Union, USA and the United Kingdom;
- BioNTech and Pfizer: RNA-based vaccine that is in use by the European Commission and in Argentina, Mexico, Saudi Arabia, Canada, Bahrain and the USA and UK;

- Oxford and AstraZeneca: Vaccine based on the viral vector without replication that is in use in Argentina, Brazil, Dominican Republic, El Salvador, India, Mexico, Morocco, Pakistan and the United Kingdom.

Among the other vaccines used, some were released for emergency application. However, this authorization varies from country to country.

Regarding medication, WHO launched an international clinical study entitled “Solidarity”, with the aim of assisting the discovery of drugs that can help in the treatment against COVID-19 or its effects. Initially, treatment with four types of medication was proposed: Remdesivir, used to treat Ebola; Lopinavir - Ritonavir, medicine for HIV; Interferon, used to treat multiple sclerosis; and Hydroxychloroquine, a medicine against malaria. However, in July 2020, WHO decided to discontinue studies with Hydroxychloroquine and Lopinavir - Ritonavir. In October 2020, (SOLIDARITY, 2020), in a printed statement, stated the inefficiency of such drugs in relation to mortality, beginning of ventilation and the length of hospital stay, suspending the application of these drugs.

2.3. REINFECTION

COVID-19 is a disease with reinfection, since, after the patients have recovered from the disease, they acquire temporary immunity to it, where the immunity time varies from individual to individual, and at the end of immunity the individual is again susceptible to disease. Some cases of reinfection have already been recorded worldwide. Until February 12, 2021, 49 cases of reinfection by the disease had been confirmed worldwide, and among them, 5 occurred in Brazil, according to (BNO, 2021).

As a result of the reinfection of COVID-19, individuals recovered from the disease must also be vaccinated against it. We emphasize that the vaccination of individuals already infected with the disease is still under study. However, we emphasize that the best way to control the disease is through prevention and vaccination. In Section 4, we will show the analysis of scenarios without and with the insertion of vaccination, to analyze the impact caused without vaccination of the population.

3. MATHEMATICAL AND COMPUTATIONAL MODELING

To build the two mathematical models of the COVID-19 transmission process, it is necessary to use compartmental classes, where individuals are separated according to their situation regarding the disease. We advance that the models developed in this work are based on the Susceptible-Infected-Recovered (SIR) model, proposed by (KERMACK and MCKENDREICK, 1927), with a vaccinated class addition proposed by (HETHCOTE, 2000). The compartmental classes used are

- Susceptible (S): group of individuals who are healthy and able to become infected;
- Infected (I): group of individuals who became infected and are able to transmit the disease virus;
- Recovered (R): group of individuals who became infected and recovered from the disease, contracting temporary immunity to it;
- Vaccinated (V): group of individuals who received the vaccine against the disease and are immune to it.

The entire population, denoted by N (t), is contained in the model, so that everyone must belong to only one of the classes at each time point (t), which represents their situation in relation to the disease. This way,

$$N(t) = S(t) + I(t) + R(t) + V(t) \quad (1)$$

The class of vaccinees is of paramount importance due to the significant attempt to control and eradicate the disease. This can also be seen when comparing the models and results obtained from the studies (FERREIRA et al, 2020) and (BERNINE et al, 2020).

The dynamics between compartmental classes occur when individuals of the Susceptible class come into contact with individuals of the Infected class, or surfaces and objects contaminated by them, becoming infected with the virus and consequently changing from the Susceptible to the Infected class. When belonging to the Infected class, the individual remains in it until the period of transmissivity of the virus ends, which lasts an average of three to four weeks. Subsequently, the individual migrates to the Recovered class, having acquired immunity against the virus, even if temporarily. As soon as the individual in the Recovered class loses immunity, he changes from the Recovered to the Susceptible class. This dynamic is seen in the diagram in Figure 1.

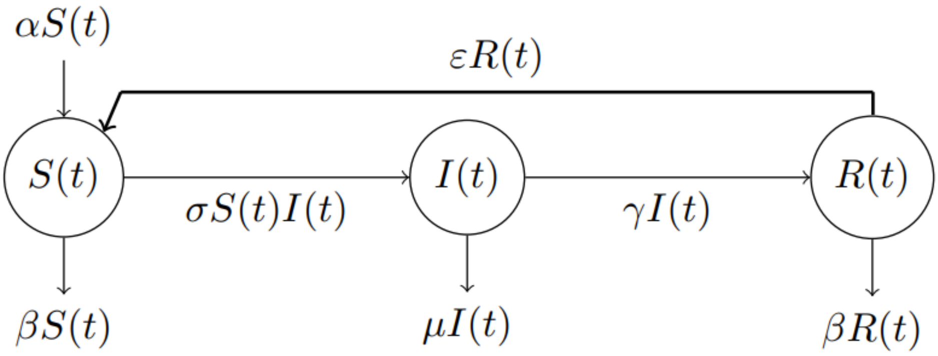

Figure 1 - COVID-19 transmission process with three compartmental classes.

However, in view of the importance of vaccination for the control and eradication of epidemiological diseases, the diagram shown in Figure 2 represents the dynamics involving vaccination, where they are considered able to receive the vaccine for those belonging to the Susceptible and Recovered class.

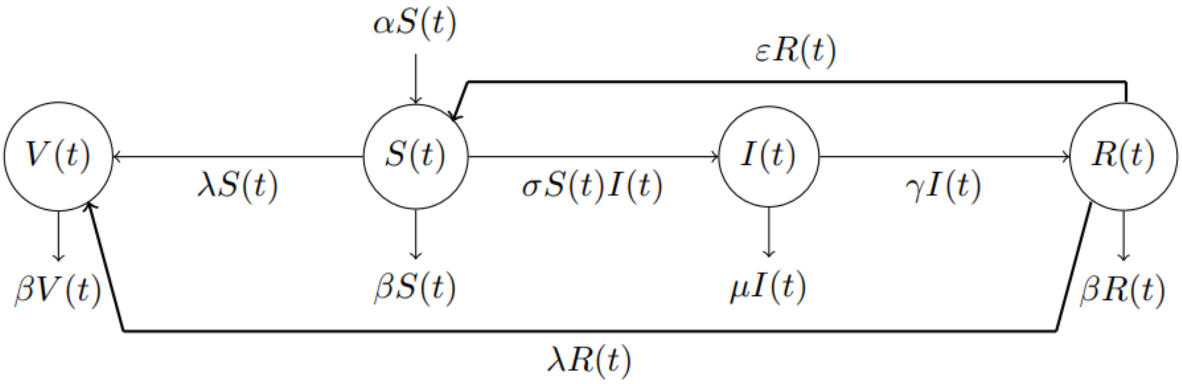

Figure 2 - COVID-19 transmission process with four compartmental classes.

The parameters expressed in Figures 1 and 2 to describe the rates during the disease transmission process are:

- α - Brazilian birth rate;
- β - mortality rate of the Susceptible, Recovered and Vaccinated classes;
- μ - mortality rate of the Infected class;
- σ - rate related to contact between members of the Susceptible class with to members of the Infected class;
- γ - disease recovery rate;
- λ - vaccination rate;

- ε - rate of individuals who have lost immunity against the disease and have returned to the Susceptible class and are eligible for reinfection of the disease.

The diagrams, shown in Figures 1 and 2, are represented by systems of Ordinary Differential Equations corresponding to the systems of Equations (2) and (3), which represent the scenarios without and with insertion of the vaccine against the disease, respectively.

$$\begin{cases} \dfrac{dS(t)}{dt} = \alpha S(t) + \varepsilon R(t) - \sigma S(t)I(t) - \beta S(t) \\ \dfrac{dI(t)}{dt} = \sigma S(t)I(t) - \gamma I(t) - \mu I(t) \\ \dfrac{dR(t)}{dt} = \gamma I(t) - \varepsilon R(t) - \beta R(t) \\ S(0) = S_0 \quad I(0) = I_0 \quad R(0) = R_0 \end{cases} \tag{2}$$

$$\begin{cases} \dfrac{dS(t)}{dt} = \alpha S(t) + \varepsilon R(t) - \sigma S(t)I(t) - \lambda \mathrm{S(t)} - \beta S(t) \\ \dfrac{dI(t)}{dt} = \sigma S(t)I(t) - \gamma I(t) - \mu I(t) \\ \dfrac{dR(t)}{dt} = \gamma I(t) - \lambda \mathrm{R(t)} - \varepsilon R(t) - \beta R(t) \\ \dfrac{dV(t)}{dt} = \lambda\big(\mathrm{S(t)} + \mathrm{R(t)}\big) - \beta \mathrm{V(t)} \\ S(0) = S_0 \quad I(0) = I_0 \quad R(0) = R_0 \quad V(0) = V_0 \end{cases} \tag{3}$$

3.1. BASAL REPRODUCIBILITY

The value of the Basal Reproducibility rate (R_b) represents the spread of an epidemiological disease and it is through it that we identify whether the spread of a disease is growing, stable or fall. This value is expressed by the ratio between the amount of the Susceptible class with of the Infected class transmits the disease, as (WYSE et al., 2011).

Thus, we have $R_b = \frac{\sigma S_0 I_0}{\gamma I_0}$, where σ and γ are the parameters mentioned above. Regarding the periods of growth, stability and fall of the disease, we have the following conditions:

- $R_b > 1$ – the number of individuals in the infected class is growing;
- $R_b = 1$ – the number of individuals in the infected class is stable;
- $R_b < 1$ – the number of individuals in the infected class is falling.

3.2. NUMERICAL DISCRETIZATION

The discretization of the analyzed interval $[0, T]$ occurs by dividing m subintervals of the same size, that is, $\Delta t = {}^{T}/_{m}$, where $t_0 = 0,\ t_1 = \Delta t,\ t_2 = 2\Delta t, \dots ,\ t_m = m\Delta t = T$.

To approximate the first order derivatives present in Equations 2 and 3, the Finite Differences Method was used, due to its stability according to (BURDEN and FAIRES, 2015). Since all functions are considered C^1 in the range, we can rewrite, to:

$$S_i \approx S(t_i), \quad I_i \approx I(t_i), \quad R_i \approx R(t_i) \quad e \quad V_i \approx V(t_i) \tag{4}$$

Then resulting in Equations 5 and 6, which is the discretization of the S, I, R and V functions of the model without and with insertion of the vaccine, respectively.

$$\begin{cases} (1 - \alpha\Delta t + \beta\Delta t)S_i - (1 - \sigma I_{i-1}\Delta t)S_{i-1} = \varepsilon R_{i-1}\Delta t \\ (1 + \gamma\Delta t + \mu\Delta t)I_i - (1 + \sigma S_{i-1}\Delta t)I_{i-1} = 0 \\ (1 + \beta\Delta t)R_i - (1 - \varepsilon\Delta t)R_{i-1} = \gamma I_i \Delta t \end{cases} \tag{5}$$

$$\begin{cases} (1 - \alpha\Delta t + \beta\Delta t)S_i - (1 - \sigma I_{i-1}\Delta t)S_{i-1} = \varepsilon R_{i-1}\Delta t \\ (1 + \gamma\Delta t + \mu\Delta t)I_i - (1 + \sigma S_{i-1}\Delta t)I_{i-1} = 0 \\ (1 + \lambda\Delta t + \beta\Delta t)R_i - (1 - \varepsilon\Delta t)R_{i-1} = \gamma I_i \Delta t \\ (1 + \beta\Delta t)V_i - V_{i-1} = \lambda\Delta t(S_i + R_i) \end{cases} \tag{6}$$

To obtain values, both for parameters and boundary conditions, the data provided by the Ministry of Health of Brazil until February 12, 2021 were used. These values were used in both models.

Table 2. - Values of initial conditions and parameters used in the simulation of the proposed models, in day^{-1}, based on data released by the Ministry of Health of Brazil.

Initial Parameters / Conditions	Value considered in the model without vaccine insertion	Value considered in the model with vaccine insertion
$S(0)$	202680566	198180566
$I(0)$	1110833	1110833
$R(0)$	8657818	8657818
$V(0)$	-	4500000
α	$3{,}8011497 \times 10^{-5}$	$3{,}8874607 \times 10^{-5}$
β	$1{,}7267419 \times 10^{-5}$	$1{,}7267419 \times 10^{-5}$
μ	$6{,}6624081 \times 10^{-5}$	$6{,}6624081 \times 10^{-5}$
σ	$1{,}188723 \times 10^{-10}$	$1{,}215715 \times 10^{-10}$
γ	$2{,}428280 \times 10^{-3}$	$2{,}428180 \times 10^{-3}$
λ	-	000870244×10^{-4}
ε	$1{,}1982269 \times 10^{-5}$	$1{,}1716233 \times 10^{-5}$
T	800	800

In Brazil, vaccination campaigns started on January 18, 2021 and only two vaccines were authorized for application: from Oxford and Sinovac. In both cases, for the vaccine to be effective, the patient must take two doses, where the interval varies according to the vaccine, 28 days for Sinovac and up to 3 months for Oxford, according to (CNN, 2021). Until February 12, 2021, approximately $4{,}5$ million individuals were vaccinated in the first phase of the campaign, that is, $2{,}12\%$ of the Brazilian population, according to (CORONAVIRUS, 2021).

4. RESULTS AND DISCUSSIONS

4.1. PROPOSED MODEL

The mathematical models that represent the transmission process of COVID-19, without and with the insertion of the vaccine against the disease, are represented by two graphs, expressed by Figures 3 and 4, respectively. The graphs are obtained from the numerical resolution of the systems of different ordinary equations (2) and (3) through the method of Finite Differences Regressive, with the aid of the *Octave* software, a free alternative software to *MATLAB*.

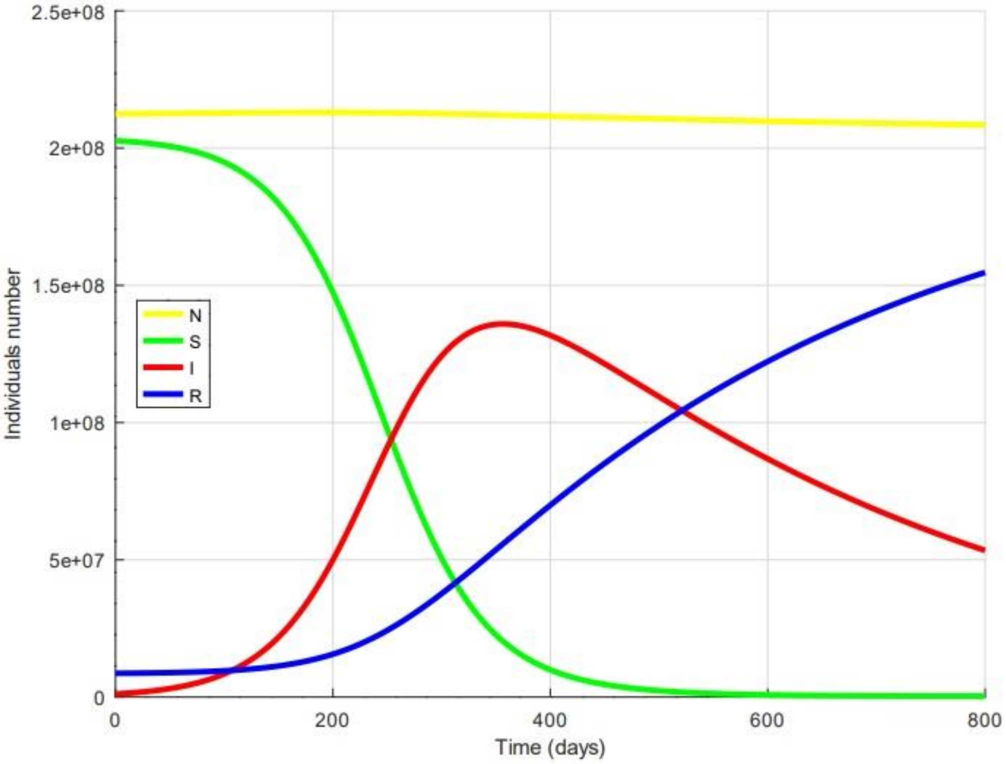

Figure 3 - COVID-19 transmission process in the Brazilian population without the insertion of the vaccine against the disease.

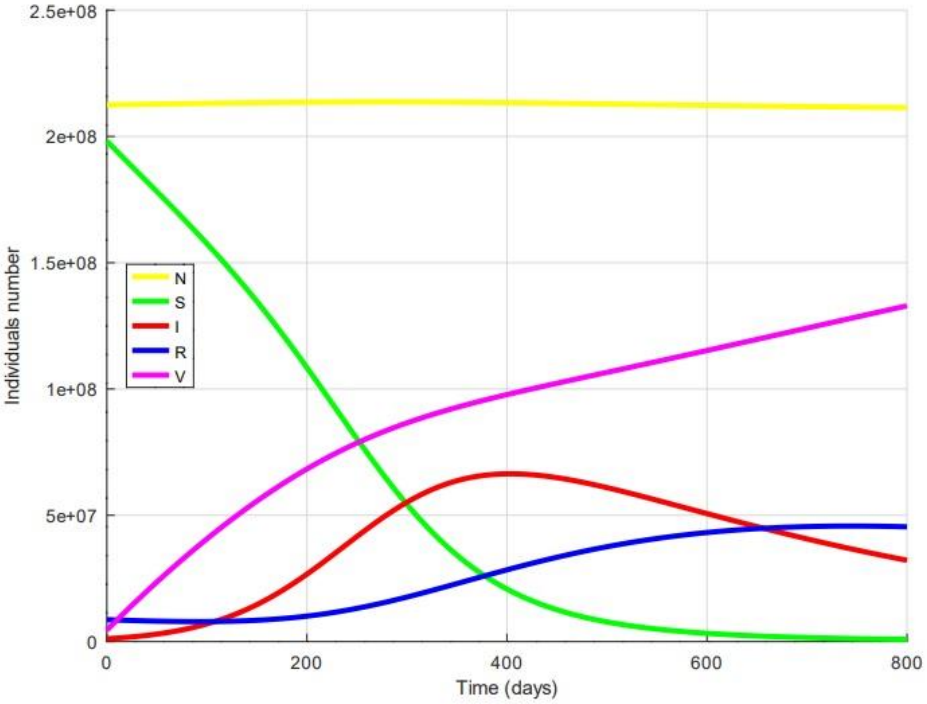

Figure 3 - COVID-19 transmission process in the Brazilian population with the insertion of the vaccine against the disease.

Based on the data exposed by the graphs, we can identify the best scenario, with the insertion of the vaccine against the disease, and from it seek better proposals for the control and prevention of the disease. As can be seen, in both scenarios there is a period of growth, stability and decrease in the number of individuals in the infected class (red color) between days 1 and 350, 351 and 450, and 451 and 800, respectively. These periods occur due to the immunity provided after recovery from the disease, that is, as individuals recover from the disease, they acquire temporary immunity to it and cannot be infected during that time.

Comparing the two graphs, it is noted that the number of individuals in the Infected class in Figure 4 is approximately double that of Figure 3. This smaller amount of infected in Figure 4 is obtained due to the introduction of the vaccine against the disease, where vaccination of the Susceptible class and Recovered from the disease is considered. Remember that the mortality rate of the Infected class is higher than the other classes and that COVID-19 has grave consequences for most of those infected by it.

The amount of infected in each iteration depends on the amount of the Susceptible class (green color), since the infection occurs due to the contact between becoming infected ones with the susceptible ones. Thus, as the number of individuals in the Susceptible class falls, the number of individuals in the Infected class has a proportional drop, that is, there is a smaller number of individuals able to be infectedThe same occurs with the amount of necessary for the Recovered class, which depends on the recovery of those belonging to the Infected class. However, after the 400-day period, the Susceptible class has more individuals in scenario 2 than in scenario 1, due to the smaller number of individuals in the Infected class and the loss of immunity of individuals in the Recovered class.

Note that the total number of individuals (yellow) has a small decrease in Figure 3 (graph without inserting the vaccine against the disease). This fact occurs due to the greater number of infected and its high mortality rate. In Figure 4, there is a smaller amount of susceptible in each interaction to be infected, due to the insertion of this population's vaccination against the disease.

4.2. VACCINE IMPACT

Vaccination of the population against infectious diseases is extremely important to reduce cases of infection with these diseases, leading to its eradication. As an example of diseases eradicated with the help of the vaccine, we can mention Smallpox, Polio, Measles and Tetanus.

With the model described in this work, we confirm the importance of applying the vaccine against the disease as a way of controlling and preventing COVID-19. We emphasize that vaccination is a collective pact and anti-vaccine movements contribute to the growth of cases of people infected with the disease virus.

We are facing a period of doubts and uncertainties regarding the quantity of vaccine doses that must be distributed in each region. However, this distribution must occur taking into account the number of inhabitants of each region, as well as the number of infected and recovered, and giving priority to the groups of risks present. For this, the baseline reproducibility value of each of the regions must be analyzed, to approach a stability or a decrease in the amount of missing infected in relation to the disease.

The current scenario in Brazil has a baseline reproducibility rate greater than 1 and this factor can be seen in the graph in Figure 4 with the growth of the Infected class up to approximately the first 350 days. However, some regions of the country were found to be stable and even declining in the number of infected. We highlight the need for greater investments in vaccination campaigns in the most affected regions, to obtain control of the number of general cases.

5. FINAL CONSIDERATIONS

In the present work, two mathematical models were constructed that represent the transmission process of COVID-19 and later, an analysis of the graphs using the resolutions of the two models. In both scenarios, we found the need for greater investments in vaccine manufacturing and vaccination campaigns, since even with the insertion of the vaccine against the disease, in scenario 2, it takes an average of three years to get the disease eradicated.

It was also found that the number of individuals in the Infected class in scenario 2 is approximately double compared to the same class in scenario 1. This fact is worrying, given that the mortality rate of the Infected class is much higher than that of the other classes and that this disease leaves severe sequelae in most of the recovered from it. We emphasize that vaccination campaigns must take place in all regions, but the doses must be distributed according to the quantitative reports of the inhabitants, infected and recovered from each region.

As future work, we seek to improve the mathematical models presented in this work, to obtain results closer to reality. To this end, we will analyze data related to those infected, recovered with and without sequelae, vaccinated with and without sequelae, and the dead by disease. We also seek to develop an epidemiological model of transmission of COVID-19 with the application of the Totally Homomorphic Cryptography (FHE) used method on the Finite Differences method, to obtain the integrity of the data on the disease.

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