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Stability Analysis of a relapse covid-19 mathematical model

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Abstract

Coronavirus disease is a twenty-first century disease that forced the whole of human race into a compulsory recess during its pandemic. It is a global pandemic with several millions reported fatality cases. Efforts at curtailing the spread and reducing new infections eventually paid off when vaccines and therapeutic drugs were developed. However, battle against this disease is yet to be over, with statistics revealing that millions are still battling with the infection. One of the reasons for this is relapse, a condition of disease aggravation after it seems to subside. In this work, a mathematical model of covid-19 with relapse and immunity loss was developed and analyzed qualitatively. The equilibrium state of the model was found to exist distinctly as Disease Free Equilibrium (DFE) and Endemic Equilibrium (EE) respectively. Effective reproduction number of the model was computed, and numerical simulation showed a value that is greater than unity; an indicator that a break-out is certain whenever there is a contact with an infectious individual. Stability analysis of the model was computed and the system was numerically simulated. It was found that both recruitment and contact rates are major factors through which the disease can either be spread or curtailed.

Keywords: Coronavirus, Relapse, Immunity loss, Simulation, Stability

1. Introduction

COVID-19 became a menace for humanity in the latter part of year 2019, after it was first discovered in Wuhan, China. Since its outbreak, several variants of the causative virus were discovered, with each of them having their unique mode of spread and severity. According to World Health Organization (WHO), since 2020, SARS-CoV-2, the virus that causes COVID-19, has been spreading and changing globally. These changes have led to the detection of variants in many countries around the world. This development implies that, getting a unified single drug that can take out the infection becomes problematic, as each variant has its peculiar characteristics. However, classification of these variants is done in their order of significance, namely: – variants under monitoring, variants of interest and variants of concern in order to determine the best method of treatment (WHO, 2024).

According to report on Worldometer, total estimated cases of the infection stand above seven hundred million, with fatality cases of over seven million globally (Worldometer, 2024). WHO (2024) affirmed that "emergence and reemergence of infectious disease pathogens, undoubtedly remain a monumental problem to global public health and socioeconomic wellbeing of people." Relapse is a deterioration of one's state of health

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condition after some signs of improvement. There are several factors that may be responsible for this condition, depending on the type of ailment, the immune system of the patient, and other factors such as environmental, physical or state of mind. According to Buskermolen *et al.* (2021), they investigated the probable cause of relapse in COVID-19 outpatient between eight weeks after treatment, by considering two factors; namely viral reactivation and inflammatory rebound. Their study indicated an uncertainty of the probable cause of reinfection in mildly infected outpatients without the associated risk factor(s).

Model is an abstraction of physical task to be executed, a skeletal picture of problem to be solved, a sketch of basic steps needed to accomplish a task and a pictorial representation of problem-solving algorithm. Mathematical model has been a useful tool by which real life issues are mathematically presented for analysis, solution, interpretation and subsequent recommendation for way out of a crisis.

In this work, a mathematical model to study and analyze the effect of relapse on new cases of COVID-19 was formulated by adopting and extending a standard SIR model. Akinyemi *et al.* (2016) analyzed a general SIR model with consideration of relapse and immunity loss. Their model's qualitative properties established the role of relapse in disease dynamics. Odetunde *et al.* (2021) applied a semi-analytic method to solve a mathematical model of COVID-19 in the presence of reinfection. Several other mathematical models on COVID-19 were presented by different authors to consider different factors that can propagate the spread and means of eradicating the disease (Abioye *et al.*, 2021, Adewole *et al.*, 2021, Ivorra *et al.*, 2020, Musa *et al.*, 2022, Ogunlade *et al.*, 2024 and Subhas *et al.*, 2021).

2. Materials and Methods

The dynamics of COVID-19 transmission within human population was modeled by stratifying the total population present at any time t, denoted as N(t) into three disjoint epidemiological classes, based on their coronavirus status as Susceptible S(t), Infected and infectious class I(t) and the recovered class R(t). It was established that new cases of the infection arises when there is a contact between the S(t) class and the droplet from I(t) class. This contact can be a direct contact through sneezing, coughing, kissing etc., or an indirect one through touching or using a contaminated material from an infectious individual. Due to high rate of infectiousness of the coronavirus, social distancing, wearing of protective nose mask and other prevention measures were clinically advised to reduce new infection within the population. The S-class increased by recruitment rate π, which encompasses all forms of addition to the population, either by birth or immigration, and decreases by newly contracted infection, and natural death. The I-class increases by newly infectious individual from the S-class and reduced by $\sigma -$COVID-19 induced death rate, $\mu -$ natural death rate (other death not related to COVID-19) and $\phi -$recovered rate (either through treatment or body immunity). The R-population increased by ϕ, reduced by $\tau -$immunity loss rate, $\omega -$relapse rate and $\mu -$natural mortality. The relapse rate ω increases the population of the I-class while τ is added to the S-population. Some of the assumptions taken while formulating the models are:

(a) Proper sensitization and adequate precautions are enforced globally to reduce the risk of imported cases into a population. Imported cases are detected and properly quarantined, hence recruitment is only to the S-class
(b) Treatment of the virus does not guarantee immunity, hence recovered individual can be re-infected again.
(c) Relapse can either be a result of ineffective therapeutic drug or attitudinal disposition of the individual by deliberately abandoning the prescription at the slightest feeling of

recuperation. Some patients will not complete the dosage given to them once they feel their health is restored to normal, which can actually sabotage the total healing process.

(d) Natural mortality occurs across all the compartments at a rate lower than the recruitment rate, hence human population is always greater than zero for all time t.

Arising from the model assumptions, some of the listed points below constitute the limitation of the model:

(i) In the effect that sensitization program is not appropriately done, imported cases are not adequately monitored, hence there is a break-out of the infection

(ii) Quarantining individuals that are exposed to COVID-19 may not be effectively done without trained personnel, hence this can increase the disease burden and its spread within the community.

The dynamics of the model is pictorially presented below:

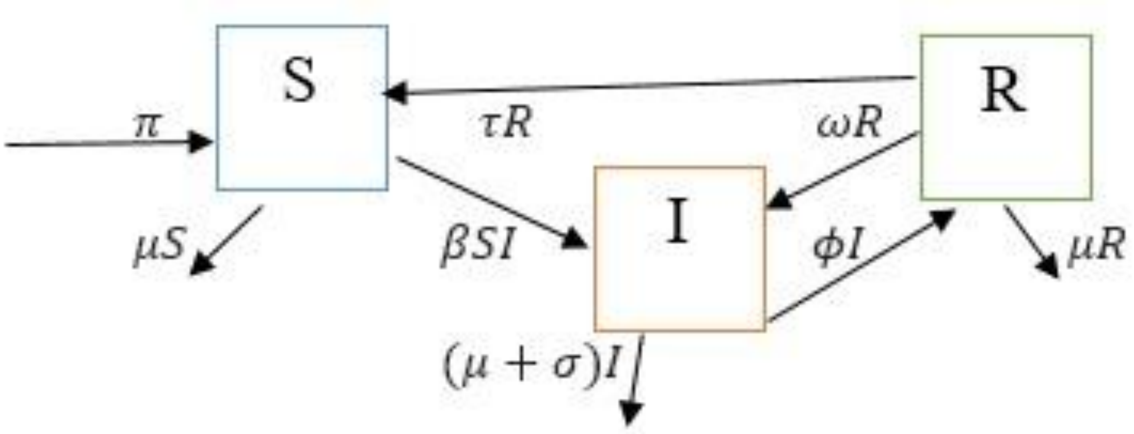

Figure 1: Model flow diagram

The model is presented as a system of first order ordinary differential equation below:

$$\frac{dS}{dt} = \pi - \beta SI - \mu S + \tau R$$
$$\frac{dI}{dt} = \beta SI - (\sigma + \mu + \phi)I + \omega R \qquad (1)$$
$$\frac{dR}{dt} = \phi I - (\tau + \omega + \mu)R$$

System of equation (1) is mathematically analyzed by scrutinizing its qualitative properties.

3. Result and Discussion

In this section, basic analysis of the model equation shall be discussed.

3.1 Positivity of Solution

Corollary 1: For the system of equations of the model to be mathematically meaningful, epidemiologically well posed and useful, the total human population at any time t, must be non-negative.

Proof: Suppose that $\mathrm{N(t) = S(t) + I(t) + R(t)}$ denote the total human population at any time t.

Then, $\frac{dN}{dt} = \frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt}$

Using (1),

$$\frac{dN}{dt} = \pi - \mu(S + I + R) - \sigma I$$

$$\frac{dN}{dt} = \pi - \mu N - \sigma I$$

$$\frac{dN}{dt} \leq \pi - \mu N$$

Which implies that $N(t) \leq N_0 e^{-\mu t} + \frac{\pi}{\mu}[1 - e^{-\mu t}]$. For any time $t, e^{-\mu t} > 0$ and as $t \longrightarrow \infty, e^{-\mu t} \to 0$, hence, by Akinyemi et al. (2016), $N(t) \to \frac{\pi}{\mu}$. Thus, for all time t the system of equations in (1) is non-negative. This completes the proof.

3.2 Steady State Solution of the Model

Proposition 1: For a well posed dynamical system, the model equation in (1) must consist of at least a steady state solution, feasible at any time t.

Proof: At equilibrium point, rate of change is zero, that is $\frac{dS}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = 0$. Thus, system in (1) becomes

$$\begin{aligned} &\pi - \beta SI - \mu S + \tau R = 0 \\ &\beta SI - (\sigma + \mu + \phi)I + \omega R = 0 \\ &\phi I - (\tau + \omega + \mu)R = 0 \end{aligned} \tag{2}$$

For easy computation, setting $c_1 = (\sigma + \mu + \phi), c_2 = (\tau + \omega + \mu)$ and using $R = \frac{\phi}{c_2}I$ in the second equation of (2), we have: $\beta SI - c_1 I + \frac{\omega\phi}{c_2}I = 0$,

$$\Rightarrow I\left[\beta S - c_1 + \frac{\omega\phi}{c_2}\right] = 0 \tag{3}$$

From (3), it is obvious that two independent solutions of the dynamical system (1) exist. Hence, the model equation in (1) is well posed and have two unique solutions as the steady state solution.

3.2.1 Disease Free Equilibrium Point

This is the first equilibrium state of the model, obtained from (3) at $I = 0$ denoted as:

$$E^0 = (S^0, I^0, R^0) = \left(\frac{\pi}{\mu}, 0, 0\right) \tag{4}$$

In this steady state, change in population depends solely on the ratio of recruitment rate to the natural mortality rate. This is an equilibrium state where COVID-19 infection is not persistent and the human population interact normally without fear of contracting the virus.

3.2.2 Endemic Equilibrium State

For the case $\mathrm{I} \neq 0$, equating the second expression in (3) to zero and solving for I and R, to obtain the second steady state solution known as the endemic equilibrium state of system (1) as:

$$E^* = \begin{pmatrix} S^* \\ I^* \\ R^* \end{pmatrix} = \begin{pmatrix} \frac{c_1 c_2 - \omega\phi}{\beta c_2} \\ \frac{\mu c_1 c_2 - \omega\phi - \beta c_2 \pi}{\beta c_1 c_2 - \beta\omega\phi + \beta\tau\phi} \\ \frac{\phi}{c_2}\left(\frac{\mu c_1 c_2 - \omega\phi - \beta c_2 \pi}{\beta c_1 c_2 - \beta\omega\phi + \beta\tau\phi}\right) \end{pmatrix} \tag{5}$$

In the presence of coronavirus disease, the dynamics of the model in (1) is given in (5). This is the state of COVID-19 prevalent within the population. The spread of the infection can better be understood by the threshold parameter, called the basic reproduction number.

3.3 Basic Reproduction Number

This is epidemiologically defined as the number of new infections generated by a single infected individual introduced into a population of susceptible individuals. It is mathematically represented as R_0 and computed by the formula $\mathrm{R}_0 = \rho(\mathrm{FV}^{-1})$, where $\rho(\mathrm{FV}^{-1})$ denotes the largest eigenvalue of the matrix multiplication F and V^{-1}. Since there is only one compartment with infection in the model considered, both F and V are given as: $\mathrm{F} = \beta \mathrm{S}^0; \mathrm{V} = \mathrm{c}_1 = (\sigma + \mu + \phi)$. The basic reproduction number for system of equations in (1) is then computed as:

$$R_0 = \frac{\beta S^0}{c_1} = \frac{\beta\pi}{\mu(\sigma + \mu + \phi)} \tag{6}$$

Since all parameters of the model are non-negative, hence the basic reproduction number as obtained in (6) is positive, thus, it can be concluded that COVID-19 infection is highly contagious if no proper precaution is taken, it can become a pandemic. From (6), it was observed that two parameters are highly important to determine the value of the basic reproduction number, they are: β and π. Recruitment rate π cannot be zero (since the entire population will vanish if $\pi = 0$) but can only be monitored for proper screening of everyone entering the population. On the other hand, contact rate β can be adequately reduced through various preventive measures, such as sensitization, educational campaign, quarantine of detected cases and other measures so that new infection can be curtailed. Whenever $\mathrm{R}_0 < 1$, the disease free equilibrium position is maintained, when $\mathrm{R}_0 = 1$, there is a shift in the equilibrium point from E^0 to E^* (mathematically referred to as the bifurcation point), whereas, when $\mathrm{R}_0 > 1$, the endemic equilibrium point is achieved. Next, we shall consider the stability analysis of the equilibrium position based on R_0.

3.4 Stability Analysis of the Equilibrium Point

In this section, attention is given to the criteria that shift the equilibrium position from one point to another. The local stability analysis of the model at the steady state point E^0 shall be discussed.

3.4.1 Local Stability Analysis of the Disease Free Equilibrium Point

Theorem 1: Equilibrium point E^0 of the system (1) is locally asymptotically stable if and only if $R_0 < 1$, and unstable otherwise.

Proof: Consider the Jacobian matrix of system (1), evaluated at E^0, given as:

$$J(E^0) = \begin{bmatrix} -\mu & -\frac{\beta\pi}{\mu} & \tau \\ 0 & \frac{\beta\pi}{\mu} - c_1 & \omega \\ 0 & \phi & -c_2 \end{bmatrix} \qquad (7)$$

The characteristic polynomial corresponding to $|J(E^0) - \lambda I| = 0$, is given as:

$$(\lambda + \mu)(\lambda^2 + k_1\lambda + k_2) = 0 \qquad (8)$$

where

$$k_1 = c_1 + c_2 - \frac{\beta\pi}{\mu}$$
$$k_2 = c_1c_2 - \phi\omega - \frac{\beta\pi c_2}{\mu}$$

Clearly, one of the eigenvalues of (8) is negative $(-\mu)$. Using Routh-Hurwitz criterion for negative real roots of a quadratic equation to establish the stability of E^0 equilibrium point. Using (6) to express k_1 and k_2 in terms of R_0, to get:

$$k_1 = \frac{{c_1}^2 + \phi\omega R_0 + c_1c_2(1 - R_0)}{c_1}$$
$$k_2 = (c_1c_2 - \phi\omega)(1 - R_0)$$

Using the original expressions of c_1, c_2, it was established that $c_1c_2 - \phi\omega = (\sigma + \mu)c_2 + \phi(\tau + \mu) > 0$. Obviously, both k_1 and k_2 are positive whenever $R_0 < 1$, which affirmed that (8) has all negative real roots. Hence, the proof.

The analysis of the stability of equilibrium point E^0 implies that, for all time t, if the basic reproduction number of COVID-19 infection is maintained below the threshold value of 1, the system is stable, and no disease break-out is expected within the population. However, there is a shift in equilibrium position once $R_0 > 1$.

3.5 Runge-Kutta Numerical Solution of the Model

The system (1) was numerically simulated, using Maple 18 in-built Runge-Kutta order 4 scheme. The table of parameter value used in the numerical simulation is given in table 1. The graphical result obtained for each class is displayed in Figures 2 - 4, with their interpretations.

Based on parameter values in Table 1, the basic reproduction number is estimated as $R_0 = 20.04 > 1$. However, the following are the assumed initial conditions used for each of the three compartments, i.e. $S(0) = 20000, I(0) = 500$ and $R(0) = 10$. Below are the graphical result obtained from the numerical simulation of system (1) based on Table 1 and the initial conditions.

In Figure 2 the initial population, $S(0) = 20000$ reduces drastically within few days due to high infectivity of the coronavirus. This implies that introduction of 500 infectious individuals into a population of largely susceptible individuals, without restriction, will lead to a pandemic and the entire population will contract the infection. After zero equilibrium is obtained, newly recruited and recovered individuals are re-introduced into the S −population.

Table 1: Table of Parameter Value

Symbol	Parameter Meaning	Values	Source
π	Recruitment rate	5.2	World Bank (2021)
β	Contact rate	0.05	Assumed
σ	Disease induced death	0.012	Worldometer (2024)
μ	Natural mortality rate	0.013	World Bank (2021)
ϕ	Recovery rate	0.9729	Worldometer (2024)
τ	Loss of immunity	0.15	Assumed
ω	Relapse rate	0.15	Assumed

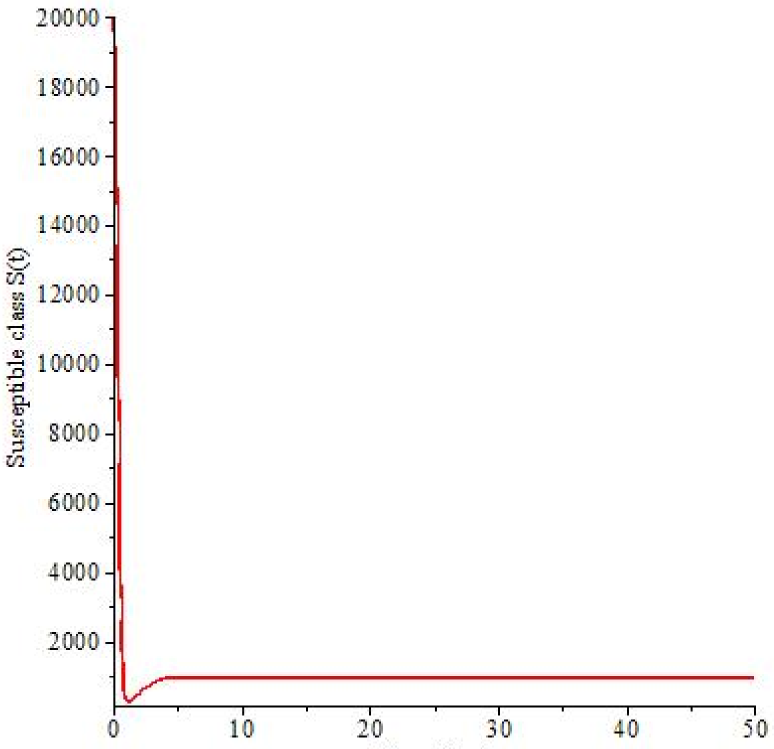

Figure 2: RK4 simulation of S-class

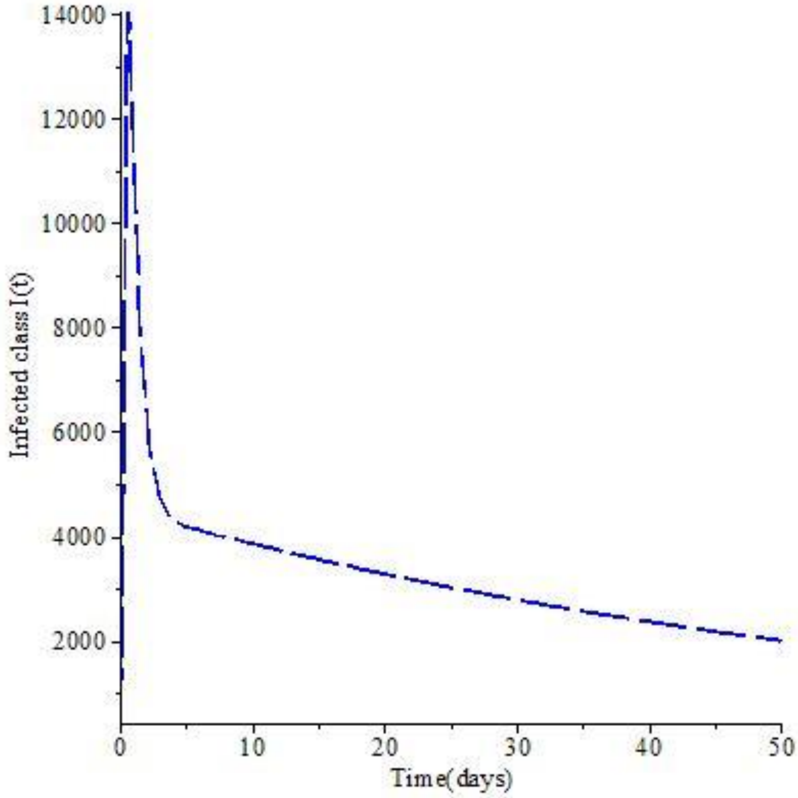

Figure 3: RK4 simulation of $\mathrm{I}-$class

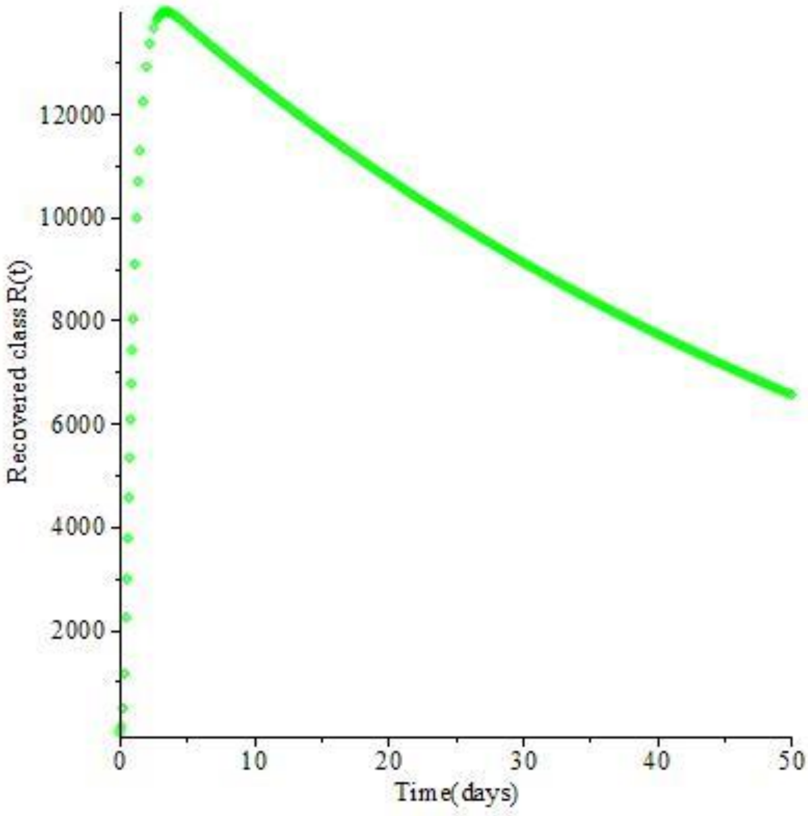

Figure 4: RK4 simulation of $\mathrm{R}-$compartment

As observed from the graph above, the infectious population increases rapidly from its initial population of $I(0) = 500$ until the entire susceptible class was wiped out. Based on Fig. 3, an endemic equilibrium point was attained at the peak before there is a shift and downward trend begins. This can be attributed to effective treatment mechanism adopted and removal rate due to death, quarantining or otherwise (as a result of sensitization, case detection or other mechanism). It decreases slowly until it attains a steady value around the 20 days. The estimated R_0 from the data used (being greater than unity) affirmed the behavior of the model.

From its initial value of 10, the recovered class increase astronomically until it reaches the peak and start to decline due to immunity loss, relapse and other factor. Larger percentage of the recovered class stayed in the compartment for a longer period. This can imply that immunity obtained from successful treatment might have contributed to their body resistance against reinfection.

4. Conclusion

In this work, a classical SIR model was considered to include immunity loss and possibility of relapse. The system of equation governing the extended model was analyzed for the existence of positive solution at all time t, which was found to exist. The steady state solution of the model equations was computed, and it was observed that the model possesses two unique equilibrium states, which was tagged as the disease free equilibrium and COVID-19 endemic equilibrium states. The basic reproduction number of the model was computed and numerically simulated to obtain a value. The stability analysis of the model at the disease free equilibrium was deduced to be stable if the basic reproduction number $R_0 < 1$ and unstable otherwise. The model was numerically simulated using data from literature and the graph presented. The population changes sporadically in a short period of time when five hundred infected individuals were introduced into a population of twenty thousand susceptible group. This attest to the fact that the disease is highly infectious, albeit treatable and recovery does not guarantee immunity against reinfection. The basic reproduction number obtained, depict that both recruitment and contact rates play a pivotal role in COVID-19 transmission dynamics and can be monitored to reduce the risk of pandemic.

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