STOCHASTIC MODEL ON THE IMPACT OF DRUG EFFICACY ON CORONAVIRUS PANDEMIC IN NIGERIA

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ABSTRACT: *Coronavirus popularly known as COVID-19 has created a large scale of infections in Nigeria. To study the efficacy of drug response of COVID-19, we developed a continuous time stochastic model for the dynamics of infections assuming that the exposed individuals develop an active case within fourteen days. To generate the sample paths describing the Susceptible-Exposed-Infected-Recovered individuals, we use stochastic simulation using tau-leap simulator. To evaluate the efficacy of response drug to recover in treating the incidence of COVID-19 in Nigeria, we compared the predicted sample paths of coronavirus with and without ERDR. At 90 days administration, it reduced the prevalence to 85% recovery from an active exposed. To assess our model, we compared the tau-leap simulator with the coronavirus SEIR fit.*

KEYWORDS*: Coronavirus, drug efficacy, stochastic simulation, tau-leap simulator*

1. INTRODUCTION

Developing new drugs and vaccines for disease like the COVID-19 can take years; Chloroquine has gained a lot of attention after a small study of 36 COVID-19 patients published March 17 in France found that most patients taking the drug cleared the coronavirus from their system a lot faster than the control group [14]. Adding azithromycin, commonly known as a Z-pak, to the mix was significantly more efficient for virus elimination. A small study in China also found that combining Chloroquine with azithromycin was found to be more potent than Chloroquine [14]. A number of drugs have shown promise in treating other corona viruses, including SARS and MERS that may be helpful in fighting COVID-19 [15]. Some of the drugs may impact the length of disease; some impact the severity of disease. Scientist and infections disease experts say the study's finding were not definitive and a large scale trial is needed to see whether the drugs are effective.

The novel coronavirus (COVID-19) was originated in the city of Wuhan, China which is the capital of Hubei province on December 31, 2019. The first case was detected after developing the pneumonia without a clear cause and for which the vaccine or treatments were not available and effective [2]. The virus can be transmitted from human to human [3]. It takes 2 to 10 days for the appearance of the symptoms and those symptoms include coughing, difficulties in breathing, and fever. It has been reported that the virus might be originated from bat [1] and the transmission of the virus might originated to a seafood market [4,5]. In recent, the features and clinical findings of the infection have been reported [5,6]. Currently, the spread is still ongoing and has claimed 2663 lives, along with 77,658 confirmed cases and 2824 suspected cases in China as of 24 Febuary,2020 [7]. The coronavirus cases not only spread in China but to some other part of the globe such as Europe, North America, Asia specific and Africa. According to a recent report by CNN, America recorded the highest cases of coronavirus.

In Nigeria, according to a report by center for disease control (NCDC), we have almost 1000 confirmed cases, 200 recovery and 30 die as of 24th April, 2020, 11:23pm [12]. In this work, we developed a stochastic model on the impact of drug efficacy of coronavirus (COVID-19) pandemic in Nigeria.

2. LITERATURE REVIEW

A number of literature has been review on recent and related work, these include [8], [9], [13] and [10] on mathematical and stochastic modeling of novel coronavirus dynamics.

3. METHODOLOGY

We developed a stochastic model on the impact of drug efficacy on coronavirus pandemic in Nigeria. The dynamics of coronavirus (COVID-19) is considered as stochastic continuous-time birth and death process. Satisfying $\{X(t):t\}$, where $X(t)$

represent a stochastic process and the model was formulated via the schematic or model diagram below:

Model Formulation

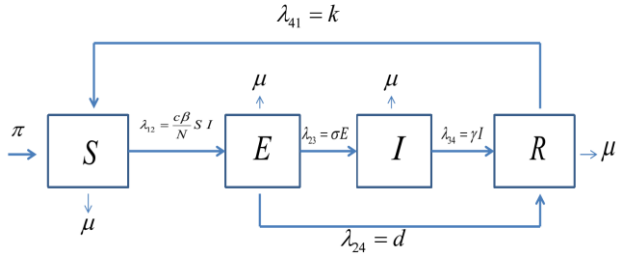

Figure 1: Model diagram of coronavirus Infectious

Table 1: Variables and Parameters Description of the Model

Parameters/ Variables	Description	Value/ Source
β	Rate of transmission	0.095[13]
c	Rate of effective contact	31[13]
σ	Rate of transmission of exposed to infected class	1/7[13]
γ	Rate of recovered from infectious	0.008[13]
k	Rate of immunity developed	0.005[Assumed]
d	Drug parameter	0.80[Assumed]
μ	Disease induced mortality rate	0.0027[13]
π	Recruitment rate	500
S	Susceptible individual (initial)	1000[Assumed]
E	Exposed cases (initial)	493[12]
I	Infected cases (initial)	277[12]
R	Recovered from infectious (initial)	159[12]

From our model, we obtain the Kolmogorov forward Equations for the dynamics of coronavirus as follows: Let $i = S, k = E, l = I, m = R$ for the disease compartments.

$$\begin{cases} P_i(t+\Delta t) = (\pi+\lambda_{12})(i-1)\Delta t P_{i-1}(t) + (\lambda_{41}+\mu_1)(i+1)\Delta t P_{i+1}(t) + \left[1-(\pi+\lambda_{12}+\lambda_{41}+\mu_1)(i)\Delta t\right]P_i(t) + o(\Delta t) \\ P_k(t+\Delta t) = (\lambda_{23}+\lambda_{24})(k-1)\Delta t P_{k-1}(t) + (\lambda_{12}+\mu_2)(k+1)\Delta t P_{k+1}(t) + \left[1-(\lambda_{23}+\lambda_{24}+\lambda_{12}+\mu_2)(k)\Delta t\right]P_k(t) + o(\Delta t) \\ P_l(t+\Delta t) = \lambda_{34}(l-1)\Delta t P_{l-1}(t) + (\lambda_{23}+\mu_3)(l+1)\Delta t P_{l+1}(t) + \left[1-(\lambda_{34}+\lambda_{23}+\mu_3)(l)\Delta t\right]P_l(t) + o(\Delta t) \\ P_m(t+\Delta t) = \lambda_{45}(m-1)\Delta t P_{m-1}(t) + \mu_4(m+1)\Delta t P_{l+1}(t) + \left[1-(\lambda_{45}+\mu_4)(m)\Delta t\right]P_m(t) + o(\Delta t) \end{cases} \quad (1)$$

And the Kolmogorov Forward Differential Equations for the dynamics of coronavirus in our model are obtained as follows:

$$\begin{cases} \frac{dP_i(t)}{dt} = (\pi+\lambda_{12})(i-1)P_{i-1}(t) + (\lambda_{41}+\mu_1)(i+1)P_{i+1}(t) - (\pi+\lambda_{12}+\lambda_{41}+\mu_1)(i)P_i(t) \\ \frac{dP_k(t)}{dt} = (\lambda_{23}+\lambda_{24})(k-1)P_{k-1}(t) + (\lambda_{12}+\mu_2)(k+1)P_{k+1}(t) - (\lambda_{23}+\lambda_{24}+\lambda_{12}+\mu_2)(k)P_k(t) \\ \frac{dP_l(t)}{dt} = \lambda_{34}(l-1)P_{l-1}(t) + (\lambda_{23}+\mu_3)(l+1)P_{l+1}(t) - (\lambda_{34}+\lambda_{23}+\mu_3)(l)P_l(t) \\ \frac{dP_m(t)}{dt} = \lambda_{45}(m-1)P_{m-1}(t) + \mu_4(m+1)P_{m+1}(t) - (\lambda_{45}+\mu_4)(m)P_m(t) \end{cases} \quad (2)$$

The above equations can also be reduced as follows:

$$\begin{cases} \frac{dP_i(t)}{dt} = b(i-1)P_{i-1}(t) + d(i+1)P_{i+1}(t) - (b+d)(i)P_i(t) \\ \frac{dP_k(t)}{dt} = b(k-1)P_{k-1}(t) + d(k+1)P_{k+1}(t) - (b+d)(k)P_k(t) \\ \frac{dP_l(t)}{dt} = b(l-1)P_{l-1}(t) + d(l+1)P_{l+1}(t) - (b+d)(l)P_l(t) \\ \frac{dP_m(t)}{dt} = b(m-1)P_{m-1}(t) + d(m+1)P_{m+1}(t) - (b+d)(m)P_m(t) \end{cases} \quad (3)$$

To solve the system of our equations describe above, we use moment generating function (mgf) so as to obtain our mean and variance of coronavirus from our model.

We recall that $M_i(\theta) = E\left[e^{\theta i}\right] = \sum_{i=0}^{N} e^{\theta i} P_i'(t)$, multiplying both sides of equation (3) by $e^{\theta i}$ and sum over i.

$$e^{\theta i}\frac{dP_i(t)}{dt} = b(i-1)e^{\theta i}P_{i-1}(t) + d(i+1)e^{\theta i}P_{i+1}(t) - (b+d)(i)e^{\theta i}P_i(t)$$

$$\sum_{i=0}^{N} e^{\theta i}\frac{dP_i(t)}{dt} = b(i-1)\sum_{i=0}^{N} e^{\theta i}P_{i-1}(t) + d(i+1)\sum_{i=0}^{N} e^{\theta i}P_{i+1}(t) - (b+d)(i)\sum_{i=0}^{N} e^{\theta i}P_i(t)$$

For i,

$$\frac{\partial M_i(\theta)}{\partial t} = \{(e^{\theta i}-1)b(i-1) + (e^{-\theta i}-1)d(i+1)\}\frac{\partial M_i(\theta)}{\partial \theta_i} - \{bi+di\}(e^{\theta i}-1)\frac{\partial M_i(\theta)}{\partial \theta_i}$$

For k,

$$\frac{\partial M_k(\theta)}{\partial t} = \{(e^{\theta k}-1)b(k-1) + (e^{-\theta k}-1)d(k+1)\}\frac{\partial M_k(\theta)}{\partial \theta_k} - \{bk+dk\}(e^{\theta k}-1)\frac{\partial M_k(\theta)}{\partial \theta_k}$$

For l,

$$\frac{\partial M_l(\theta)}{\partial t} = \{(e^{\theta l}-1)b(l-1) + (e^{-\theta l}-1)d(l+1)\}\frac{\partial M_l(\theta)}{\partial \theta_l} - \frac{\{bl+dl\}(e^{\theta l}-1)(\partial M_l(\theta))}{\partial \theta_l}$$

For m,

$$\frac{\partial M_m(\theta)}{\partial t} = \{(e^{\theta m}-1)b(m-1) + (e^{-\theta m}-1)\,d\,(m+1)\}\frac{\partial M_m(\theta)}{\partial \theta_m} - \{bm+dm\}\,(e^{\theta m}-1)\frac{\partial M_m(\theta)}{\partial \theta_m} \quad (4)$$

Solving those moment equations, we can analytically obtain our mean and variance of the population size in our model as follows:

For ease of derivation, we let our $b = d = \lambda$ in the basic Kolmogorov forward differential equations and multiply through by i (for compartment i) and sum over i.

$$\sum_{i=1}^{\infty} iP_i'(t) = \lambda\sum_{i=1}^{\infty} i(i-1)P_{i-1}(t) + \lambda\sum_{i=1}^{\infty} i(i+1)P_{i+1}(t) - \lambda\sum_{i=1}^{\infty} i^2P_i(t) \quad (5)$$

We define following $M_1'(t) = \sum_{i=1}^{\infty} iP_i'(t)$, $M_2'(t) = \sum_{i=1}^{\infty} i^2P_i'(t)$ and substituting in (5), we have

$$\frac{M_1'(t)}{M_1(t)} = \lambda, \Rightarrow \int \frac{d}{dt}\big(ln\, M_1(t)\big)dt = \int \lambda dt,$$

$ln\big(M_1(t)\big) = \lambda t + c$, after taking exponential to both sides and solving for $M_1(t)$, we therefore have the mean as

$$M_i(t) = E\big(X(t)\big) = ie^{\lambda t} \quad (6)$$

To obtain the variance, we similarly multiply through our basic Kolmogorov forward differential equations by i^2 (for compartment i) and sum over i and obtain the variance as follows:

$$Var\big(X(t)\big) = M_2(t) - (M_1(t))^2 = ie^{\lambda t}\big(e^{\lambda t}-1\big) \quad (7)$$

Equation (6) and (7) are the mean and variance of the continuous time birth and death stochastic process of the coronavirus spread.

4. NUMERICAL SIMULATION OF THE MODEL

To generate the sample paths describing the spread of Coronavirus in Nigeria, We perform numerical simulations of our model using tau-leap simulator and compare it with SEIR coronavirus fit using Nigeria data from daily report of Nigeria Center for Disease Control (NCDC) using parameters values in Table 2. We equally obtained the mean and variance of probability distribution describing the transition probabilities of our model using moment generating function so as to study the prevalence of the disease with and without intervention.

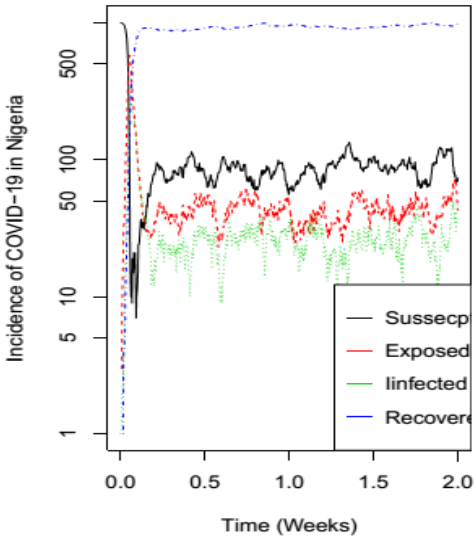

Figure 2: Plot showing sample path incidence for Susceptible-Exposed-Infected-Recovered

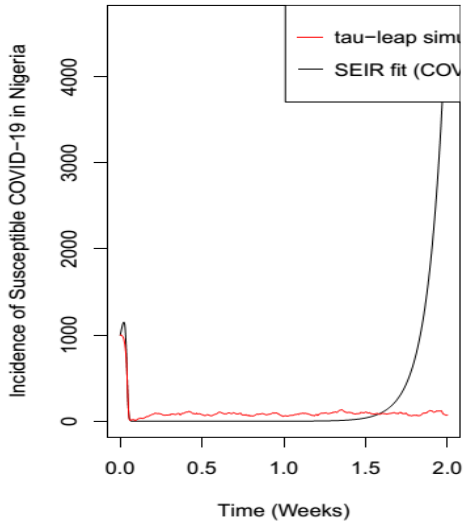

Figure 3: Plot showing sample path incidence for Susceptible in SEIR fit (COVID-19) & tau-leap simulator

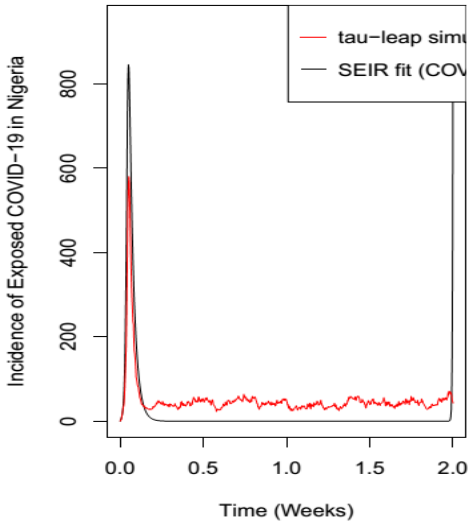

Figure 4: Plot showing sample path incidence for in SEIR fit (COVID-19) & tau-leap simulator

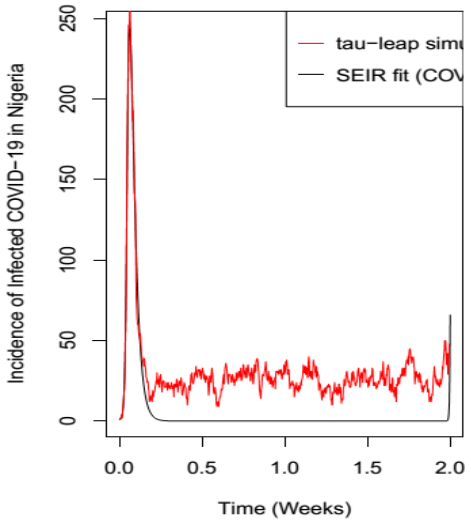

Figure 5: Plot showing sample path incidence for Exposed Infected in SEIR fit (COVID-19) & tau-leap simulator

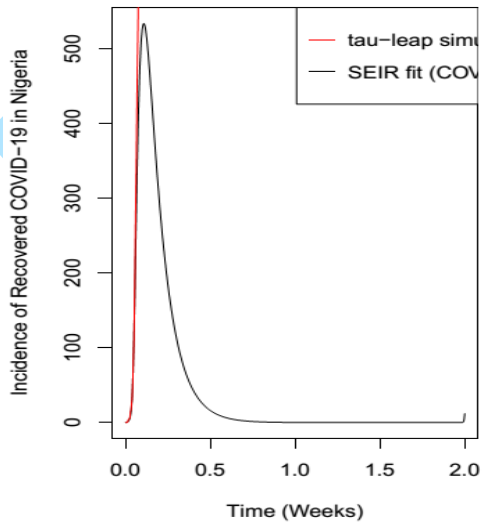

Figure 6: Plot showing sample path incidence for Recovered in SEIR fit (COVID-19) & tau-leap simulator

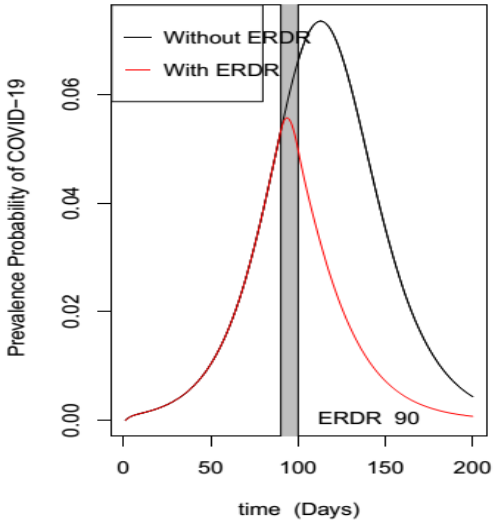

Figure 7: Plot showing Prevalence probability with & without effective response drug to recovery (ERDR)

5. DISCUSSION

From the graphical result of our simulation, Figure 2 is showing the sample path incidence for Susceptible -Exposed-Infected-Recovered individuals, Figure 3 is showing sample path incidence for Susceptible in SEIR fit (COVID-19) and sample path obtained from tau-leap simulator, Figure 4 is showing sample path incidence for Exposed in SEIR fit (COVID-19) and sample path obtained from tau-leap simulator, Figure 5 is showing sample path incidence for Infected in SEIR fit (COVID-19) and sample path obtained from tau-leap simulator, Figure 6 is showing sample path incidence for Recovery in SEIR fit (COVID-19) and sample path obtained from tau-leap simulator and Figure 7 is showing the prevalence probability active exposed with and without effective response drug to recovery (ERDR).

From Figure 2, we observed that the incidence of susceptible individuals population decline and maintain some steadily up to 11th day and then begins to increase largely due to COVID-19 transmission and movement of infected susceptible individuals into the Latently Infected population. Figure 3, shows the Exposed individuals incline and decline initially then maintain some steadily state due to the fact that they have been trace and start receiving medication and raises up as a result new cases are being reported daily as a result of more contacts. Figure 4 has similar properties with that of figure 3. Figure 5, we observed that the incidence of recovery individuals population incline and decline then maintain some steadily and then begins to increase slowly due large proportion of new confirmed cases and possibility of new re-infections of individuals or if the vaccine given to susceptible are not yet developed. Figure 6; indicate that the

effective response drug to recovery if given for 3 month (90 days) will reduced the prevalence of infections in a population when compared to prevalence without intervention.

CONCLUSION

Considering the randomness in the transmission of the COVID-19 infection, we construct a continuous-time stochastic compartment system to study the dynamic behavior of the disease outbreak since transition of an individual from one state to the next state can be considered as a stochastic process, in which the population in each compartment was assumed to follow a binomial distribution. We numerically study the model and see the impact of 3 month (90 days) intervention by use of effective response drug to recovery on the spread of COVID-19 cases and were found to have efficacy of almost 85% on recovery when compared to prevalence without intervention of active exposed. There is still need for government to develop a vaccine to prevent the susceptible population from being infected or re-infected; reducing exposure is one of the effective measures to control the spread of disease through quarantined at home, minimizing contacts to two person, social distancing, wearing a mask and staying indoor can reduce the risk of getting infected. Lastly, the stochastic SEIR COVID-19 model fits show that the reported data are much than the simulated data. We recommend a need for future work to investigate the possibility of coronavirus re-infections and co-infections with related disease.

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