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Mathematical modelling for infectious viral disease: The Covid-19 perspective

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Mathematical Modelling for Infectious Viral Disease: the Covid-19 Perspective ¹

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Research Department

Mathematical Modelling for Infectious Viral Disease: the Covid-19 Perspective**Hafeez A. Adekola, Ibrahim A. Adekunle, Haneefat O. Egberongbe, Sefiu A. Onitilo
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Abstract

In this study, we examined various forms of mathematical models that are relevant for the containment, risk analysis and features of COVID-19. Greater emphasis was laid on the extension of the Susceptible-Infectious-Recovered (SIR) models for policy relevance in the time of COVID-19. These mathematical models play a significant role in the understanding of COVID-19 transmission mechanisms, structures and features. Considering that the disease has spread sporadically around the world, causing large scale socioeconomic disruption unwitnessed in contemporary ages since World War II, researchers, stakeholders, government and the society at large are actively engaged in finding ways to reduce the rate of infection until a cure or vaccination procedure is established. We advanced argument for the various forms of the mathematical models of epidemics and highlighted their relevance in the containment of COVID-19 at the present time. Mathematical models address the need for understanding the transmission dynamics and other significant factors of the disease that would aid policymakers to make accurate decisions and reduce the rate of transmission of the disease.

Keywords: Mathematical Models, SIR Models, COVID-19, COVID-19 confirmed cases, COVID-19 attributable deaths

1.0 Introduction

Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), a novel β -coronavirus is the pathogen responsible for the coronavirus disease 2019 (COVID-19) (Li et al., 2020). The novel coronavirus has spread across the globe with the attendant consequences felt in about 203 countries. As at the time of writing (June 18, 2020), there are about 8,061,550 confirmed COVID-19 cases with 440,290 attributable deaths (WHO, 2020). The Americas (North and South) account for close to 50% of global cases with values standing at 3,899,859 confirmed cases and 205,555 deaths. In Europe, there are about 2,452,247 confirmed cases with about 189,582 attributable deaths. In the Eastern Mediterranean region, cases have soared to 817,458 with fatalities around 18,057. In the Southeastern Asia region, about 503,034 cases have been recorded with around 15,498 deaths. Down in the western pacific, there are about 200,586 cases with about 7,239 attributable deaths. Across the African region, the number of confirmed cases stood at 187,625 with 4,346 deaths (WHO, 2020). Since the emergence of the virus in Wuhan, China in December 2019, the aerosolised pathogens have spread exponentially, causing a large scale and unprecedented socio and economic disruptions, threat to global public health systems, poverty, undesirable psychological depression, more considerable uncertainties among many other deep-rooted issues (Sameni, 2020). The viral genome sequence of the SARS-CoV-2 suggests the close relatedness to SARS-like bat CoVs, but most genomic encoded proteins of the SARS-CoV-2 are similar to the SARS-Covs with differences in two of the non-structural proteins (NSP2 and NSP3), spike protein and the receptor-binding domain (RBD) (Wu et al., 2020). Studies have shown that the SARS-CoV-2 is capable of mutation with two types being majorly classified as the L-type and the S-type (Tang et al., 2020). The S-type has been reported to have evolved when jumping from animal to man while the L-type evolved later. Although both are currently involved in the pandemic, the L-type has been reported to be more prevalent than the S-type (Guo et al., 2020). How mathematical models explain these chain reactions and transmission mechanisms forms the core of the foregoing.

Severity, features, structures risk analysis and containment of the virus have been studied along with various disciplines and dimensions. A notable consensus has been the adoption of social distancing and practice of good hygiene as a measure to deter virus proliferation and flatten the epidemic growth curve such that fast-rising number of COVID-19 attributable deaths can be reduced (Sameni, 2020). However, empirical ambiguity still persists on the mechanical (mathematical) nature of the transmission pattern. Mathematical models are well-

positioned to explain the evolutionary nature of epidemic outbreaks and the spread pattern. A review of the mathematical models with attendant structural evolution for the transmission dynamics of COVID-19 could be an essential finding in the containment, risk analysis and search for the cure of the disease.

With the global pandemic leading to the increase in morbidity and mortality of the global population, socioeconomic and public health disarray (Zandvoort et al., 2020), the agonising consequences of the novel coronavirus on public health are influencing new waves of research on the relevance of mathematical models in predicting the sequence of the virus and its propagation pattern. With the proper understanding of the evolutionary and dynamic growth pattern of COVID-19 using mathematical models, public health officials, government and the society at large can take a giant step forward in their fight against COVID-19 amidst global uncertainties (Nandal, 2020). Several researchers in the scientific community have carried out interdisciplinary studies in order to understand the virus propagation pattern using various mathematical models (see Ivorra, Ferrández, Vela-Pérez, & Ramos, 2020; Kim, Seo, & Jung, 2020; Ndaïrou, Area, Nieto, & Torres, 2020; Torrealba-Rodriguez, Conde-Gutiérrez, & Hernández-Javier, 2020 for some examples). However, a holistic approach of mathematical instrumentalisation models in the analysis of COVID-19 growth curve and its containment strategies remains grossly understudied in extant literature. The intricacies of this unobserved factor underpin this study. We complement available studies on the subject matter and extend the SIR models and rely on inferences drawn from available studies using the extensions of SIR models. The application of these models consists of the use of mathematical tools and a specific language to explain and predict the behaviour of the infectious viral disease. These models could be deterministic, non-deterministic or could contain branching processes that aid the prediction of the infectious disease.

2.0 Mathematical Models

Mathematical models help to make mental models quantitative; it involves writing down a set of equations that mimics reality which is then solved for specific values of the parameters within the equations (Panovska-Griffiths, 2020; Revathi & Rangnathan, 2020). Mathematical modelling simplifies reality and answers questions using subsets of data (Panovska-Griffiths, 2020). Predictive mathematical models are essential for understanding the course of an epidemic. One of the most commonly used models is the Susceptible-Infectious-Recovered (SIR) models for the human to human transmission (Giordano et al., 2020). However,

modellers need to acquire at least one dataset with relevant data points before developing or validating a model (Nandal, 2020). Predictive models for large countries could be problematic because they aggregate heterogeneous sub-epidemics (Jewell et al., 2020). Various factors, such as individual characteristics and population distribution, have a significant contribution, thus affecting the model prediction (Jewell et al., 2020).

2.1 Models for Airborne Viral Diseases

a) Susceptible – Infectious – Recovered (SIR)

The underlying mathematical model which has been developed as far back in the 1920s is still in use today, and this basic model is referred to as the SIR model (Freiberger, 2014). The SIR model divided the population into three groups as in Shil (2016); the susceptible (S), the infectious (I) and the recovered (R). It was developed by Kernack and McKendrick to describe an influenza epidemic (Bauer, 2017). It assumes the introduction of an infected individual into a population where the members have not been previously exposed to the pathogen. Therefore all are susceptible (S), each infected individual (I) transmits to susceptible members of the population with a mean transmission rate β . At the end of the infectious period, individuals who recover from the infections are referred to as the recovered (R) member of the population, if the mean recovery rate is α , then the mean transmission period in any individual is given by $1/\alpha$. The differential equations describing the transmission as per the basic SIR model is given by

$$\frac{dS(t)}{dt} = \beta S(t)I(t) \quad (1)$$

$$\frac{dI(t)}{dt} = \beta S(t)I(t) - \alpha I(t) \quad (2)$$

$$\frac{dR(t)}{dt} = \alpha I(t) \quad (3)$$

Where $S(t)$ and $I(t)$ represents the number of individuals in the susceptible and infectious states respectively at any time t , while the rates of change of $S(t)$ and $I(t)$ with time is represented by $dS(t)$ and $dI(t)$ respectively.

If the population is considered constant with no agent leaving or coming into the system, the equation is given by:

$$N = S(t) + I(t) + R(t) \quad (4)$$

The number of susceptible individuals decreases as the number of incidences increases, so also the epidemic declines, as more individuals recover from the disease (Shil, 2016). Basic reproduction number is a phenomenon where the average number of secondary infections generated by one infectious individual when introduced into a fully susceptible population is measured, R_0 denotes it. The severity of an epidemic and rate of progression depends on the value of the basic reproduction number, so if R_0 is greater than 1, the epidemic will continue, but if it is less than 1 then the epidemic would fade out (Delamater et al., 2019). The basic reproduction number can be calculated from the growth rate (r) of the epidemic obtained from the cumulative incidences data in the initial growth phase of the outbreak as

$$R_0 = \left(1 + \frac{r}{\alpha}\right) \quad (5)$$

The numerical solutions of the ordinary differential equations can be obtained with an appropriate application using computer simulations, and this model has been used to explain the transmission and repeated outbreaks of measles in New York between 1930 and 1962. The SIR model can be further modified considering demographics and weather/seasonal variations. Modified SIR has been used to explain viral epidemics such as Influenza justifying its applicability to the COVID-19 context.

b) Susceptible – Exposed – Infectious – Recovered (SEIR)

Certain infectious diseases have an incubation period or exposed state in an individual following infection until the symptoms are observed. In other words, the SEIR account for the exposed or latent stage (Shil, 2016). Here each individual who receives the virus exist in the exposed or latent state (E) during which the virus is incubated but do not transmit the infection to anyone, so with the onset of symptoms the individual makes a transition to the infectious state. Considering the constant population size

$$N = S + E + I + R \quad (6)$$

and the set of differential equations as;

$$\text{Recall Equ(1)} \quad \frac{dS(t)}{dt} = \beta S(t)I(t)$$

and

$$\text{Equ(2)} \quad \frac{dI(t)}{dt} = \beta S(t)I(t) - \alpha I(t)$$

to generate

$$\frac{dE(t)}{dt} = \beta S(t)I(t) - kE(t) \quad (7)$$

While

$$\text{Equ(3)} \text{ remains as } \frac{dR(t)}{dt} = \alpha I(t)$$

The basic reproduction of the SEIR model can be determined using the formula

$$R_0 = \left(1 + \frac{r}{\alpha}\right) \left(1 + \frac{r}{k}\right) \quad (8)$$

Where the mean infective period is $1/\alpha$ while the mean incubation period is $1/k$

The SEIR model with suitable adaptations has been widely applied for various disease epidemics such as chickenpox and SARS, and its relevance has been advanced for the analysis of the dynamic transmission of COVID-19 in this context.

c) Susceptible – Exposed – Infectious – Asymptomatic – Recovered (SEIAR)

This is a simple model for viral epidemics involving asymptomatic individuals in the population in a situation without any interventions. Individuals testing positive in serological tests or blood tests for disease without symptoms is referred to as asymptomatic and is denoted as A in the SEIAR model, so considering a constant population;

$$N = S(t) + E(t) + I(t) + A(t) + R(t) \quad (9)$$

This indicates the total population was susceptible, and there was no transmission from individuals at the latent state and a fraction of the proceeds to the infectious state. In contrast, other fractions $(1 - p)$ proceed to the asymptomatic state at the same time (k) with the asymptomatic individuals having a reduced ability to transmit the infection. If q is the factor that determines transmissibility in asymptomatic individuals, then $0 < q < 1$. The ordinary differential equation of the transmission process can be described as the following.

$$\frac{dS}{dt} = -\beta S(1 + qA) \quad (10)$$

$$\frac{dE}{dt} = \beta S(1 + qA) - kE \quad (11)$$

$$\frac{dI}{dt} = pkE - \alpha I \quad (12)$$

$$\frac{dA}{dt} = (1 - p)kE - \eta A \quad (13)$$

$$\frac{dR}{dt} = \alpha I + \eta A \quad (14)$$

$$\frac{dC}{dt} = \alpha I \quad (15)$$

C denotes the cumulative number of infectives. This model was used to explain the transmission dynamics of the swine flu outbreak in 2009 at a residential school in Maharashtra, India (Shil *et al.*, 2011).

d) Complex SEIAR (Hospitalisation)

This model describes the incorporation of the hospitalisation of a fraction of infectious individuals. Here the population is classified into SEIAR with $J(t)$ and $D(t)$ denoting the hospitalised and dead respectively. Considering the total population is constant at any time,

$$N = S(t) + E(t) + I(t) + A(t) + J(t) + D(t) \quad (16)$$

The ordinary differential equation of the transmission process is described as the following

$$\frac{dS}{dt} = \mu N(t) - \frac{\beta S(t) \cdot (I(t) + J(t) + qA(t))}{N} - \mu S(t) \quad (17)$$

$$\frac{dE}{dt} = \frac{\beta S(t) \cdot (I(t) + J(t) + qA(t))}{N} - (k + \mu)E(t) \quad (18)$$

$$\frac{dA}{dt} = k(1 - p)E(t) - (y_1 + \mu)A(t) \quad (19)$$

$$\frac{dI}{dt} = kpE(t) - (\alpha + y_1 + \mu)I(t) \quad (20)$$

$$\frac{dJ(t)}{dt} = \alpha I(t) - (\delta + y_2 + \mu)J(t) \quad (21)$$

$$\frac{dR(t)}{dt} = y_1(A(t) + I(t)) + y_2 J(t) - \mu R(t) \quad (22)$$

$$\frac{dD(t)}{dt} = \delta J(t) \quad (23)$$

$$\frac{dC(t)}{dt} = \alpha I(t) \quad (24)$$

The μ represents the rate of birth and natural death, while the cumulative number of infections is represented by $C(t)$. Epidemic data of the Spanish Flu pandemic in Geneva was obtained using the Complex SEIAR model, and all parameters of the model were determined.

The SEIR and SEIAR models have been further extended by involving various parameters to play crucial roles in public health interventions, quarantine, travel restrictions, vaccination or dosage of antivirals (Shil, 2016).

3.0 Modelling the COVID-19 pandemic

Globally, radical alteration with rapidly changing socioeconomic dynamics has been occurring due to the COVID-19 Pandemic, Several countries have been on full or partial lockdown while adhering to social distancing measures as they wait for a specific treatment modality such as vaccines (Sinha, 2020). Public information such as incidence or prevalence of infection, morbidity or mortality due to COVID-19 could be used to solve mathematical

models, solutions from these models are then recalibrated repetitively until it is suitable for prediction of the future behaviour of SARS-CoV-2 (Panovska-Griffiths, 2020).

The COVID-19 Pandemic has been modelled by various researchers with the aim of stimulating the infections within the population (Shaikh et al., 2020). Most models represent individual to transition between compartments in a given community, these compartments are based on each individual's infectious state, and related population sizes with respect to time (Shaikh et al., 2020). Lin et al. had suggested a conceptual model for COVID-19, this model effectively catches the timeline of the disease epidemic while Chen et al. (2020) examined a model based on stage based transmissibility of the SARS-CoV-2 (Chen et al., 2020; Lin et al., 2020). Whereas Khan et al. (2020) formulated a model of people versus COVID 19, the model is given as

$$D_t S(t) = \Delta - \lambda S - \frac{\alpha S(I+\beta A)}{N} - \gamma S Q, \quad (25)$$

$$D_t E(t) = \alpha \frac{S(I+\beta A)}{N} + \gamma S Q - (1 - \phi)\delta E - \phi\mu E - \lambda E, \quad (26)$$

$$D_t I(t) = (1 - \phi)\delta E - (\sigma + \lambda)I, \quad (27)$$

$$D_t A(t) = \phi\mu E - (\rho + \lambda)A, \quad (28)$$

$$D_t R(t) = \sigma I + \rho A - \lambda R, \quad (29)$$

$$D_t Q(t) = \kappa I + \nu A - \eta Q, \quad (30)$$

Where N represents the total population and is further divided into five subclasses which include susceptible people $S(t)$, exposed people $E(t)$, Infected people $I(t)$, Asymptomatic people $A(t)$ and Recovered people $R(t)$, The reservoir population is denoted as $Q(t)$.

Since most mathematical models utilise ordinary differential equations with integer order for understanding dynamics of biological systems, every model depending on such classical derivatives has been discovered to have restrictions (Shaikh et al., 2020). These restrictions could be overcome using fractional calculus, as recommended by Caputo and Fabrizio. Researchers such as Shaikh et al. (2020) applied the Caputo-Fabrizio fractional derivative operator to study the dynamics of COVID-19 using the mathematical model suggested by Khan et al. (2020) in the form of the system of nonlinear differential equations involving the Caputo-Fabrizio operator (Khan & Atangana, 2020; Shaikh et al., 2020). The model is given as

$${}^{\text{CF}}D_t^\tau S(t) = \Delta - \lambda S - \frac{aS(I+\beta A)}{N} - \gamma SQ, \quad (31)$$

$${}^{\text{CF}}D_t^\tau E(t) = \alpha \frac{S(I+\beta A)}{N} + \gamma SQ - (1 - \phi)\delta E - \phi\mu E - \lambda E, \quad (32)$$

$${}^{\text{CF}}D_t^\tau I(t) = (1 - \phi)\delta E - (\sigma + \lambda)I, \quad (33)$$

$${}^{\text{CF}}D_t^\tau A(t) = \phi\mu E - (\rho + \lambda)A, \quad (34)$$

$${}^{\text{CF}}D_t^\tau R(t) = \sigma I + \rho A - \lambda R, \quad (35)$$

$${}^{\text{CF}}D_t^\tau Q(t) = \kappa I + \nu A - \eta Q, \quad (36)$$

With initial conditions

$$S(0) = \theta_1, E(0) = \theta_2, I(0) = \theta_3, A(0) = \theta_4, R(0) = \theta_5, Q(0) = \theta_6.$$

Early dynamics of COVID-19 transmission were studied by researchers such as Kucharski et al. (2020), where a combination of a stochastic transmission model with data on both cases in Wuhan and international cases that originated from Wuhan were used to estimate how transmission had varied between January to February 2020, these estimates were then used to calculate the probability of new cases that might generate outbreaks in new areas (Kucharski et al., 2020). Their findings estimated that daily reproduction number (R_t) in Wuhan declined from 2.35 to 1.05 between 1 week before and after travel restrictions were introduced respectively (Kucharski et al., 2020). based on these estimates, locations with similar transmission potential to Wuhan have at least a 50% chance of an outbreak for very four independently introduced cases (Kucharski et al., 2020).

Several modelling studies have used the Susceptible-Exposed-Infectious-Recovered (SEIR) model to study the transmission dynamics of COVID-19. Wu et al. (2020) used the SEIR model to describe the transmission dynamics and forecast the spread of the disease using reported data between December 31, 2019, to January 28, 2020. The study also estimated the basic reproductive number to be 2.68 (Wu et al., 2020). Another study by Read et al. (2020) using the SEIR model reported a basic reproductive number value of 3.1 using an assumption of Poisson-distributed daily time increments (Read et al., 2020). In contrast, Tang et al. (2020) obtained a basic reproductive number value as high as 6.47 when the clinical progression of the disease, individual epidemiological status and intervention measures were incorporated into a deterministic compartmental model based on the SEIR model (Tang et al., 2020). A different approach was used by Zandvoort et al. (2020), An age-stratified SEIR model was used to study the effectiveness of non-pharmaceutical interventions in three African countries (Zandvoort et al., 2020). Most African countries have resource-limited

settings and have fewer means to suppress virus propagation, and the study observed that isolating infected individual is the most effective way of reducing transmission in African countries (Zandvoort et al., 2020). All these studies are based on the human-to-human transmission and did not take in to account the significance of the environment in COVID-19 transmission (Yang & Wang, 2020). Yang and Wang examined proposed an SEIR model that describes multiple transmission pathways in the infection dynamics. It also emphasised the role of the environmental reservoir in the propagation of COVID-19 (Yang & Wang, 2020). The model employed non-constant transmission rates that change with the epidemiological status and environmental conditions while reflecting the impact of the on-going control measures. Using public data, the study concluded that COVID-19 would remain endemic, and this demands long term prevention and intervention measures (Yang & Wang, 2020).

A different mathematical model approach was employed by Li et al. (2020) where a Susceptible-Exposed-Infectious-Quarantined-Diagnosed-Recovered (SEIQDR) based model, which is an expansion of the SEIR model was used (Li et al., 2020). This six-chambered model was used to study the transmission mechanism of COVID-19 and the implemented prevention and control measures, with the aid of time series and kinetic modal analysis, a basic reproductive number value of 4.01 was obtained (Li et al., 2020). The findings of the study suggested that while recovered individuals might not be re-infected due to the presence of antibodies to COVID-19, bodies of deceased individuals should be well treated to prevent viral transmission (Li et al., 2020). Kim et al. (2020) also used a SEIQR model that factored in behavioural changes to study the transmission of COVID-19 in Korea and predict the likely size and end of the epidemic (Kim et al., 2020). The model predicted over 10,000 cases over time until June, so it was suggested that a sustainable long term non-pharmaceutical interventions would significantly reduce transmission among the population (Kim et al., 2020).

Although the mathematical models for the COVID-19 have majorly forecast few areas relating to pathogen spread such as the basic reproductive number of the SARS-CoV-2, population control measures, percentage of asymptomatic people (Nandal, 2020). There is still a paucity of modelling studies focusing on predicting the magnitude of the global spread of the virus, duration of the pandemic and possible effective interventions (Nandal, 2020). Nevertheless, consumers of these models such as the public, media and politicians; have the need for this predictions in order to plan for various interventions that would be reliable in combating the disease (Jewell et al., 2020).

Models are very useful tools particularly for short term accurate predictions, and it helps policymakers to make decisions and allocate adequate resources towards disease control through predictions of disease spread and infected population (Kucharski et al., 2020; Revathi & Rangnathan, 2020). Mathematical models can be used to understand how and where the disease is most likely to spread while avoiding so many trial experiments or random guesses with the real population. Most mathematical models used during this epidemic are extensions of the Susceptible-Exposed-Infected-Recovered (SEIR) model, a compartmental model based on the behaviour of the population which enabled the simulation of how non-pharmaceutical prevention and intervention measures such as lockdowns, social distancing, self-isolation; can significantly affect the morbidity and mortality of the population over time (Sameni, 2020).

4.0 Conclusion

Although mathematical models mimic the actual reality using an equation that is solved for specific values of the user parameters within the equations, a mathematical model is as good as the data it uses. However, mathematical models are potent tools for understanding the transmission dynamics of an infectious viral disease. In other climes, there is no gainsaying to aver that the Susceptible-Exposed-Infected-Recovered (SEIR) model seems the most reliable extension of the SIR models during this pandemic due to its plausibility in explaining heterogeneous changes in features, structures, containment and risk analysis of the virus transmission. Since infectious diseases have an incubation period or exposed state in an individual following infection until the symptoms are observed, the SEIR account for the exposed or latent stage which is concomitant with real-time observation across various geography and population. During the COVID-19 Pandemic, mathematical models have played significant roles in policymaking and social life generally. Through various models, different scenarios have been explored to understand the transmission of COVID-19, basic reproductive number, case-fatality rate, duration of epidemic and significance of various prevention and intervention measures among the population. Although mathematical models rely on predictions and estimations, they are handy tools that could significantly guide the implementation of public health decisions when properly expressed and estimated.

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