

Mathematical Modeling of Influenza Transmission Dynamics with Immigration and Control Strategy

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ABSTRACT

This paper developed a mathematical model to investigate the transmission dynamics of influenza fever with vaccination and quarantine as control strategies. In developing our model, the population was compartmentalized into susceptible-vaccinated-exposed-infected-quarantine-recovered (SVEIQR) and allowed immigrations into susceptible and exposed compartment only. The model developed in a system of differential equations. Equilibrium points of the system and basic reproduction number were obtained, existence and uniqueness of the solution, invariant region, positivity of the solution was established and we also carryout local and global stability analysis of disease free equilibrium state. Linearization method was used for proving the local stability of equilibrium while Carlo Castillo-Chavez method was adopted for proving the global stability of the equilibrium points. Analytical solution shows that, the dynamics of spread of the influenza fever is determined by the basic reproduction number R_0 if $R_0 < 1$, the influenza free equilibrium is locally asymptotically stable or otherwise, if $R_0 > 1$. In this regard, Government and non-governmental organization of every country should encourage the use of influenza vaccine among individuals.

Keyword: Positivity, existence and uniqueness, invariant region, disease free equilibrium, endemic equilibrium, basic reproductive number, stability analysis.

INTRODUCTION

Influenza is an acute contagious disease of the upper airways and lungs caused by a virus which rapidly spreads around the world as seasonal epidemics. The virus was identified in Mexico and USA in April 2009; the world health organization (WHO) declared it as a pandemic in June 11, 2009 (8, 11). The 2009 pandemic influenza A(H1N1) virus referred to as influenza A(H1N1)pdm09 which appeared for the first time in 2009 causing a global influenza pandemic, is now a seasonal influenza virus that co-circulates with other seasonal viruses (5). The virus is categorized into three main types; A, B, and C. This categorization is based on the differences that exist between matrix protein (M) and nucleoprotein (NP) (7). Type A can infect both human, pigs, whales, birds and especially wild animals. It is the most acute of all the types. It is further subdivided into subtypes based on *hemagglutinin* (HA) and *neuraminidase* (NA) proteins found on the surface of the virus. There are 16 types of *hemagglutinin* (H1 – H16) and 9 types of *neuraminidase* (N1 – N9). Influenza virus subtypes are named according to the combination of HA and NA present in them, Influenza A that has an HA1 protein and NA1 protein, In humans only three of these combinations are the most common; H1N1, H1N2, and H3N2. Type B can also infect humans and birds, and can cause epidemics. The last type C affects only humans and it can hardly be differentiated from common cold as it causes no epidemics (9). The category of influenza transmission zones, which are geographical groups of countries, areas or territories with similar influenza transmission patterns. In the temperate zone of the northern hemisphere, influenza activity remained at inter-seasonal levels in most countries. However, influenza activity continued to increase across the countries of the Arabian Peninsula but in the tropical Africa, influenza activity remained elevated in some countries of western

Africa (10). Evidence is shown that influenza viruses circulate throughout the tropical zones and contribute substantially to the respiratory disease burden in developing and impoverished country (2). Infection with influenza viruses can give rise to a wide range of clinical presentations, ranging from asymptomatic infection to severe illness and death depending on the characteristics of both the virus and the infected person. In the majority of people, influenza is an uncomplicated illness that is characterized by sudden onset of constitutional and respiratory symptoms such as fever, myalgia, cough, sore throat, rhinitis and headache (6). It can be transmitted by exposure to infectious droplets expelled by coughing or sneezing that are then inhaled, or through contaminate hands or other surfaces whereas the typical incubation period for influenza is 1-4 days but in most persons ill with influenza shed virus from a few days before symptoms begin through 5-7 days after illness onset (4).

The paper considers a mode depicting the transmission of influenza fever virus. The model is given by a system of six differential equations depending on parameters. It supposed that the infectious component consists of both asymptomatic and symptomatic individuals; and the birth rate is given by a constant rate Λ and natural death rates have a common rate μ . Apply the next generation matrix technique adopted by (3), it found a basic reproduction number. In general, when $R_0 < 1$, the disease can be eradicated and when $R_0 > 1$, the disease will be persists in the population. It also supposed that for the endemic equilibrium to exist there is at least one of infected classes of the model to be nonempty.

The remaining part of this paper is organized as follows; in the next section, Section 2 describes the structure of the model transmission dynamics, its basic properties and corresponding basic reproduction number; Section 3 presents the equilibria and their stability by using the linearization method and the method adopted from (1) and finally, section 4 summarizes the work.

MODEL AND ITS BASIC PROPERTIES

The structure of the model

The paper first divides a defined population under study $N(t)$ into six classes namely; Susceptible $S(t)$, Exposed $E(t)$, Infected $I(t)$, Quarantined $Q(t)$, Recovered $R(t)$ and Vaccinated $V(t)$. Hence, the total population at time t is given by $N(t) = S(t) + V(t) + E(t) + I(t) + Q(t) + R(t)$. it assumed that, the population size of susceptible is increase by a constant birth rate Λ and immigration, m_1 it reduced by a common natural death rates μ . It assumed that immigration is allowed into expose comportment at rate, m_2 susceptible individuals in contact with the virus progress to the exposed class at the rate βIS , where β is the transmission rate. The susceptible individuals after being exposed to the infection can move to the infective class. Both types of infectious individuals can move to quarantine class. Quarantine individuals may recover and after recovery it move to recovered class. However, the rates of recovery may vary from one compartment to another. Keeping these assumptions in mind, it formulates a mathematical model as follows;

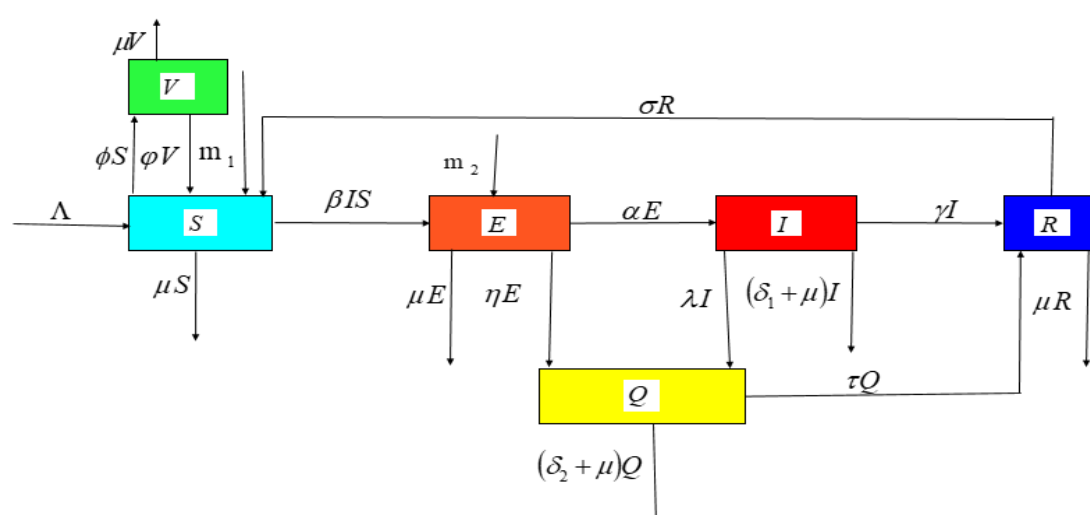


Fig 1. The schematics diagram of the model

The model is given by the following system of differential equations

$$\left. \begin{aligned} \frac{dS}{dt} &= \Lambda + \phi V + \sigma R + m_1 - \phi S - \beta IS - \mu S \\ \frac{dV}{dt} &= \phi S - \phi V - \mu V \\ \frac{dE}{dt} &= \beta IS + m_2 - \alpha E - \eta E - \mu E \\ \frac{dI}{dt} &= \alpha E - \gamma I - \theta I - (\delta_1 + \mu) I \\ \frac{dQ}{dt} &= \eta E + \theta I - \tau Q - (\delta_2 + \mu) Q \\ \frac{dR}{dt} &= \gamma I + \tau Q - \sigma R - \mu R \end{aligned} \right\} \quad 1$$

with the condition

$$S(t) + V(t) + E(t) + I(t) + Q(t) + R(t) = 1$$

Now, Because of the present of the recovered class $R(t)$ in the first equations, we can study the whole system.

Table 1: Parameters and their description in the model

Parameters	Description
Λ	The individual constant recruitment rate.
β	The rate of susceptible becomes exposed.
α	The rate of transition from exposed to infected individual.
γ	The rate of transition from infected to recovered individual.
ϕ	The rate of transition from susceptible individual to vaccinated individual.
ϕ	The rate of transition from vaccinated to susceptible individual.
σ	The rate of transition from recovered to susceptible individual.
η	The rate of transition from exposed to quarantined individual.
θ	The rate of transition from infected to quarantined individual.
τ	The rate of transition from quarantined to recovered individual.
m_1	The rate of exposed immigrated with influenza A(H1N1)pdm09.
m_2	The rate of infected immigrated with influenza A(H1N1)pdm09.
μ	The Natural mortality rate.
δ_1	The infected individual A(H1N1)pdm09 influenza mortality rate
δ_2	The quarantined individual A(H1N1)pdm09 influenza mortality rate

Positivity of solution of the model

Since the model given by (1) monitors human population, it is significant to show that all the state variables in the model are non-negative for all time $t \geq 0$

Theorem 1 If $\{S(0) \geq V(0) \geq E(0) \geq I(0) \geq Q(0) \geq R(0)\} \in \Omega$ the solutions (S, V, E, I, Q, R) of the model equations (1) are all non-negative for all time $t \geq 0$

Proof

From the model equation (1)

$$\frac{dS}{dt} = \Lambda + \phi V + \sigma R + m_1 - (\phi + \beta I + \mu)S$$

By comparison theorem, we deduced that

$$\frac{dS}{dt} \geq -(\phi + \beta I + \mu)S$$

Using method of separation of variables and upon simplification we get

$$S \geq e^{-\int (\phi + \beta I + \mu) dt}$$

therefore $S \geq 0, \forall t > 0$

Using the same processes, the paper will show that the solution of the remaining classes of the model equations with non-negative initial condition will remain non-negative for all time $t > 0$.

Existence and uniqueness of the model solution

The validity and authenticity of any mathematical model depends on whether the given system of equation has a solution, And if the solution exists is unique. The paper uses the theorem of Lipchitz continuity to establish the existence and uniqueness of solution to the system.

Theorem 2 Let D denote the region

$$|t - t_0| \leq a, \|x - x_0\| \leq b, \quad x = (x_1, x_2, \dots, x_n), \quad x_0 = (x_{10}, x_{20}, \dots, x_{n0})$$

And suppose that $F(t, x)$ satisfies the Lipchitz condition

$$\|f(t, x_1) - f(t, x_2)\| \leq k \|x_1 - x_2\|$$

Whenever the pairs (t, x_1) and (t, x_2) belong to D , there is a constant $\delta > 0$ such that there exist a unique continues vector solution $X(t)$ of the system in the interval $|t - t_0| \leq \delta$.

Proof

It is sufficient to show that $\frac{\partial f_i}{\partial x_j}, i, j = 1, 2, \dots, 6$ the model equations (1) are continuous. Where $x = (S, V, E, I, Q, R)$

By considering the partial derivatives for $f_1, f_2, \dots, f_6$ as follows

$$\text{where } f_1 = \Lambda + \phi V + \sigma R + m_1 - (\phi + \beta I + \mu)S$$

$$\frac{\partial f_1}{\partial S} = |-(\phi + \beta I + \mu)| < \infty, \quad \frac{\partial f_1}{\partial V} = |\phi| < \infty, \quad \frac{\partial f_1}{\partial I} = |-\beta S| < \infty, \quad \frac{\partial f_1}{\partial Q} = |\sigma| < \infty, \quad \frac{\partial f_1}{\partial E} = \frac{\partial f_1}{\partial R} = 0 < \infty \quad \text{Clearly,}$$

$$\frac{\partial f_1}{\partial S}, \frac{\partial f_1}{\partial V}, \frac{\partial f_1}{\partial E}, \frac{\partial f_1}{\partial I}, \frac{\partial f_1}{\partial Q} \text{ and } \frac{\partial f_1}{\partial R} \text{ it's continuous and bounded.}$$

Using the same processes, the paper will show that partial derivatives of the remaining classes of the model equations are continues and bounded in the region D. Hence, there exist unique solutions of the model

equations.

Invariant region

The Paper establish the invariant region of the system (1) using the feasible region Ω

Theorem 3. The feasible region Ω defined by $\Omega = \left\{ S(t), V(t), E(t), I(t), Q(t), R(t) \in \mathbb{R}_+^6 \mid 0 \leq N \leq \max \left\{ N(0), \frac{\Lambda}{\mu} \right\} \right\}$ with initial conditions $S(0) \geq 0, V(0) \geq 0, E(0) \geq 0, I(0) \geq 0, Q(0) \geq 0$ and $R(0) \geq 0$, is positively invariant and attracting with respect to system of equations for all $t > 0$.

Proof:

Let $N(t) = S(t) + V(t) + E(t) + I(t) + Q(t) + R(t)$ Where m_1 is the immigration into susceptible compartment and m_2 is the immigration into exposed compartment, summing up the model equations (1), we obtain the total population satisfies as $\frac{dN(t)}{dt} \leq \Lambda + m_1 - \mu N$

$$\frac{dN}{dt} = \Lambda - \mu N + m_1 + m_2 - \delta_1 I - \delta_2 Q$$

In the absence of influenza it follows that

$$\frac{dN}{dt} + \mu N \leq \Lambda + m_1$$

which shows that as $t \rightarrow \infty$ the population size $N(t) \rightarrow \frac{\Lambda + m_1}{\mu}$. So if $N(0) \leq \frac{\Lambda + m_1}{\mu}$, then $\lim_{t \rightarrow \infty} N(t) = \frac{\Lambda + m_1}{\mu}$, so also if $N(0) > \left(\frac{\Lambda + m_1}{\mu} \right)$, then N will decrease to $\left(\frac{\Lambda + m_1}{\mu} \right)$ as $t \rightarrow \infty$. This means that $N(t) \leq \max \left\{ N(0), \left(\frac{\Lambda + m_1}{\mu} \right) \right\}$.

Therefore, $N(t)$ is bounded above. Subsequently $S(t), V(t), E(t), I(t), Q(t)$ and $R(t)$ are bounded above. Thus, in Ω system (1) is well posed. Hence, it is sufficient to study the dynamics of the system in Ω .

Disease free equilibrium

To obtain the equilibria system (1), we set the right-hand side of the system equations equal to zero. Thus; the disease free equilibrium;

$$E_0 = (S^*, V^*, E^*, I^*, Q^*, R^*) = \left(\frac{(\Lambda + m_1)(\phi + \mu)}{(\phi + \mu)(\phi + \mu) - \phi\phi}, \frac{\phi(\Lambda + m_1)}{(\phi + \mu)(\phi + \mu) - \phi\phi}, 0, 0, 0, 0 \right)$$

It is observed that the disease free equilibrium E_0 of the model exist when $R_0 < 1$ then $(\phi + \mu)(\phi + \mu) > \phi\phi$, this implies the endemic equilibrium always exists when $R_0 > 1$.

The basic reproductive ratio

The transmission dynamics of the model is decided by the basic reproductive ratio R_0 , which is defined as the expected number of secondary cases produced in a completely susceptible population by a typical infective

individual. By using the method of next generation matrix (3), we found that

$$R_0 = \frac{\beta(\Lambda + m_1)(\varphi + \mu)}{((\phi + \mu)(\varphi + \mu) - \phi\varphi)(\alpha + \eta + \mu)(\gamma + \theta + \delta_1)}$$

For R_0 to exist

$$(\phi + \mu)(\varphi + \mu) > \phi\varphi$$

For $R_0 < 1$;

$$[(\phi + \mu)(\varphi + \mu) - \phi\varphi](\alpha + \eta + \mu)(\gamma + \theta + \delta_1 + \mu) > \beta(\Lambda + m_1)(\varphi + \mu)$$

For $R_0 > 1$;

$$[(\phi + \mu)(\varphi + \mu) - \phi\varphi](\alpha + \eta + \mu)(\gamma + \theta + \delta_1 + \mu) < \beta(\Lambda + m_1)(\varphi + \mu)$$

Thus, R_0 is clearly a threshold parameter that can be used as an indicator for disease control.

STABILITY OF EQUILIBRIA

Local stability of equilibrium

Theorem 4 The influenza fever free equilibrium point given E_0 is locally asymptotically stable whenever $R_0 < 1$, unstable equilibrium exists, if otherwise.

Proof:

The Jacobean matrix at E_0 is given by

$$J(E_0) = \begin{bmatrix} -(\varphi + \mu) & \phi & 0 & \frac{\beta(\Lambda + m_1)(\varphi + \mu)}{(\phi + \mu)(\varphi + \mu) - \phi\varphi} & 0 & \sigma \\ \varphi & -(\phi + \mu) & 0 & 0 & 0 & 0 \\ 0 & 0 & -(\alpha + \eta + \mu) & \frac{\beta(\Lambda + m_1)(\varphi + \mu)}{(\phi + \mu)(\varphi + \mu) - \phi\varphi} & 0 & 0 \\ 0 & 0 & \alpha & -(\gamma + \theta + \delta_1 + \mu) & 0 & 0 \\ 0 & 0 & \eta & \theta & -(\zeta + \delta_1 + \mu) & 0 \\ 0 & 0 & 0 & \gamma & 0 & -(\sigma + \mu) \end{bmatrix}$$

Eigenvalues of the above matrix are;

$$\lambda_1 = -c_7 \quad \lambda_2 = -c_6 \quad \lambda_3 = -\frac{1}{2} \left(C_1 + C_3 - \sqrt{4\phi\varphi + c_1^2 - 2c_1c_3 + c_3^2} \right) \quad \lambda_4 = -\frac{1}{2} \left(C_1 + C_3 + \sqrt{4\phi\varphi + c_1^2 - 2c_1c_3 + c_3^2} \right)$$

$$\lambda_5 = -\frac{1}{2} \left(C_4 + C_5 - \sqrt{4\alpha c_1 + c_4^2 - 2c_4c_5 + c_5^2} \right) \quad \lambda_6 = -\frac{1}{2} \left(C_4 + C_5 + \sqrt{4\alpha c_1 + c_4^2 - 2c_4c_5 + c_5^2} \right)$$

where

$$C_1 = (\varphi + \mu), C_2 = \frac{\beta (\Lambda + m_1)(\varphi + \mu)}{(\phi + \mu)(\varphi + \mu) - \phi\varphi}, C_3 = (\phi + \mu), C_4 = (\alpha + \eta + \mu), C_5 = (\gamma + \theta + \delta_1 + \mu), C_6 = (\tau + \delta_2 + \mu), C_7 = (\sigma + \mu) \quad \text{Eigenvalues}$$

$\lambda_1, \lambda_2, \lambda_4, \lambda_6$ are always negative. If $R_0 < 1$, then c_2, c_3, c_4 and c_5 must be less than zero, it implies $\lambda_3 < 0$ and $\lambda_5 < 0$. Therefore, E_0 is locally asymptotically stable. Whereas, for $R_0 > 0$ then $\lambda_3 > 0$ and $\lambda_5 > 0$ and E_0 is unstable.

Global stability of disease free equilibrium (DFE)

To prove the global stability of disease free equilibrium, we are using the theorem by (1).

Theorem 5 If the given mathematical model can be putting in the form:

$$\frac{dX}{dt} = F(X, Z) \quad \text{and} \quad \frac{dZ}{dt} = G(X, Z), \hat{G}(X, 0) \geq 0$$

Where $X \in R^m$ denoted the number of uninfected individuals and $Z \in R^n$ denoted the number of infected individuals respectively.

$$\text{The DFE is represented here by } E_0 = (X_0, 0) = \left(\frac{(\Lambda + m_1)(\varphi + \mu)}{(\phi + \mu)(\varphi + \mu) - \phi\varphi}, \frac{\phi(\Lambda + m_1)}{(\phi + \mu)(\varphi + \mu) - \phi\varphi}, 0, 0, 0, 0 \right)$$

For the global asymptotic stability of E_0 the conditions (H1) and (H2) given below must be satisfied.

(H1) for $\frac{dX}{dt} = F(X, 0)$, X^* Is globally asymptotically stable (GAS)

(H2) for $G(X, Z) = KZ - \hat{G}(X, Z)$, $\hat{G}(X, Z) \geq 0$ For $(X, Z) \in \Omega$,

Here $K = \Delta_Z G(X^*, 0)$ is an M -matrix (the off diagonal elements of K are non-negative) and Ω is the region where the model makes biological sense.

Theorem 6 The fixed point $E_0 = (X^*, 0)$ is a globally asymptotic stable equilibrium of model equations (1) provide that $R_0 < 1$ and the assumption that (H1) and (H2) are satisfied.

Proof By using Theorem 1 to our model equations (1), we get

$$F(X, 0) = \begin{bmatrix} \Lambda + m_1 + \varphi V - (\phi + \mu)S \\ \phi S - (\varphi + \mu)V \\ 0 \end{bmatrix}, \quad G(X, Z) = KZ - \hat{G}(X, Z)$$

Where

$$K = \begin{bmatrix} -(\alpha + \eta + \mu) & \frac{\beta(\Lambda + m_1)(\varphi + \mu)}{(\phi + \mu)(\varphi + \mu) - \phi\varphi} & 0 \\ \alpha & -(\gamma + \lambda + \delta_1 + \mu) & 0 \\ \eta & \lambda & -(\tau + \delta_2 + \mu) \end{bmatrix}$$

And

$$G(X, Z) = \begin{pmatrix} G_1(X, Z) \\ G_2(X, Z) \\ G_3(X, Z) \end{pmatrix} = \begin{bmatrix} m_2 \\ 0 \\ 0 \end{bmatrix}$$

Since $S(t) < N$, We have $\hat{G}(X, Z) \geq 0$ for all (X, Z) can also notice that the matrix K is M matrix by definition. Hence the DFE (E_0) is globally stable. (X, Z)

CONCLUSION

This paper developed a mathematical model for transmission dynamics of influenza fever that account for vaccination of susceptible individuals, quarantine of infected individuals and immigrations into susceptible and expose compartment only. It carried out analytical solution of the model where the population comprises of six compartments: Susceptible individuals, Exposed individuals, infected individuals, quarantine individuals, Recovered individuals and Vaccinated individuals. The Disease Free Equilibrium (DFE), existence and uniqueness, invariant region, positivity of solution and basic reproduction number were obtained. It also carried out the stability analysis for the disease free equilibrium using linearization method and the results indicated that the disease free equilibrium (DFE) points are locally asymptotically stable (LAS) whenever $R_0 < 1$ and global asymptotically stable (GAS) whenever $R_0 > 1$. The global analysis depends on the threshold quantities, basic reproduction ratio denoted by R_0 and if basic reproduction number less than 1, the disease dies out and if the basic reproduction number greater than 1, the epidemic occurs with respect to influenza fever disease will persists in community. In this regard Government and non-governmental organization should encourage the use of influenza fever vaccine among individuals because it plays a vital role in reducing or stopping the spread of virus.

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