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Transmission and Control Dynamic Model of Influenza Virus Infection

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Abstract: ***Influenza virus infection is one of the diseases that pose a global threat and causes seasonal outbreaks and pandemics. As a result, it is associated with a high rate morbidity and mortality worldwide despite the availability of vaccine and antiviral drugs. To understand the transmission and control dynamics of this threatening infection, we formulated a six compartmental mathematical model, which incorporated vaccination and treatment parameters into the deterministic model that studies the behaviour of the infection. The mathematical analysis shows that the disease free and the endemic equilibrium point of the model exist. The model has disease free equilibrium point which is both locally and globally asymptotically stable whenever the basic reproduction number is less than unity (i.e. when*** $R_0 < 1$) ***and unstable when*** $R_0 > 1$. ***In the same way, the endemic equilibrium is also locally asymptotically stable. Numerical simulation was carried out by Maple 18 software using differential transformation method to investigate the effects of vaccine, recovery (due to body immunity), and treatment on the dynamics of the disease. Our results showed that increasing the rates of vaccination and recovery has a significant effect of reducing infection in both populations of the infected individuals and increases the recovered and susceptible populations. However, although treatment decreases infection in the symptomatic infected population, it has a negative effect of increasing infection among the asymptomatic infected individuals. This effect can be reversed by screening all individuals to know their infection status so that necessary measure will be taken. Also, our result show that vaccine wanes off after some time and so, it was recommended that influenza vaccines be taken periodically (annually, biennially or otherwise, depending on the expiry duration) for renewal sake in order to lower the rate at which vaccine wanes off.***

Keywords: Influenza, Influenza virus, Vaccination, Critical points, Basic reproduction number

1. Introduction

Influenza (simply called Flu) is a contagious respiratory disease that is caused by influenza viruses that infect the nose, throat and lungs. It causes mild to severe illness and can sometimes lead to death [5]. Influenza viruses are transmitted among humans in three ways: (1) direct contact with infected individuals; (2) contact with contaminated objects (i.e. fomites) such as toys, doorknobs, etc.; and (3) inhalation by virus-laden aerosols.

People with influenza usually feel some/all of these signs and symptoms: fever/chills, cough, sore throat, running/stuffy nose, muscle/body aches, headache, fatigue/tiredness and vomiting and diarrhoea (in children). It should be noted that not everyone with flu have fever. The time from when a person is exposed to the virus to when symptoms begins is about 1 – 4 days, with an average of about 2 days [5]. However, approximately 33% of people with influenza are asymptomatic [2]. Most infected people recover within one to two weeks without requiring medical treatment. However, in the very young, the elderly, and those with other serious medical conditions, infection can lead to severe complication of underlying condition (like asthma, diabetes, heart disease, etc.); secondary bacterial infections (like pneumonia, bronchitis, sinus, ear infection etc.); and death [18].

The influenza vaccine is recommended, to prevent influenza, by the WHO and the United states CDC to the high-risk group such as children, the elderly, health care workers and people with chronic illness, or are immuno-compromised (such as people with HIV/AIDS) among others. It can also be prevented by everybody preventive actions (such as staying away from people who are sick, covering coughs and sneezes and frequent hand washing) to help slow the spread of germs that cause respiratory (nose, throat and lungs) illness like flu [5]. There are influenza antiviral drugs (such as Neuraminidase inhibitor, Oseltamivir, among others) that can be used to treat flu illness [5] [18].

Influenza virus infections are associated with considerable morbidity and mortality worldwide. In the US alone, despite the availability of vaccine and antiviral drugs, influenza causes approximately 200,000 serious infections that require hospitalization and 36,000 deaths each year. Influenza pandemics and epidemics which mostly occur annually in the fall or winter pose threats (such as missed work, cost of hospitalisation and medical treatment and increased deaths) to the human population [18]. As a result, it is important to understand to detail, the dynamics of this disease.

A number of works has been done on the spread of multiple strains of the influenza virus with immunity [1], [13], [14]; on modelling the dynamics with different age groups [3], [6], [11], [15]. In the present study, we formulate a new model to get a better insight into the dynamical transmission and control of influenza infection.

The rest of this work is organized as follows: Section 2 gives a full description of the model and shows a domain where the model is epidemiologically well posed. Section 3 provides the existence of equilibria including a derivation of the basic reproduction number and stability analysis of the equilibria. In Section 4, we perform numerical simulations

of the model with graphical illustrations and their discussion, and give concluding remark in Section 5.

2. Model Formulation

To study the transmission and control of influenza virus infection in humans, we formulate a model which divides the total human population size at time t, denoted by N(t), into susceptible humans S(t), Vaccinated humans V(t), Exposed humans E(t), Asymptomatic infected humans $I_A(t)$, Symptomatic infected humans $I_S(t)$ and Recovered humans T(t). Hence, we have:

$$N(t) = S(t) + V(t) + E(t) + I_A(t) + I_s(t) + T(t).$$

The transmission and control of influenza Virus among human is governed by some basic epidemiological parameters. Susceptible individuals are recruited into the human population either by birth or immigration at a rate π, out of which a fraction ν is vaccinated and the remaining fraction (1–ν) receives no vaccine. The vaccine wanes off at a rate ω and individuals of the vaccinated return to susceptible. When an infected individual, either asymptomatic or symptomatic, comes in contact with a susceptible human, the virus is passed unto the human and the person moves to the exposed class E(t) at a rate β_1 and β_2 respectively (the model did not include the transmissions from virus laden aerosols).

The human natural and disease-induced death rates are denoted respectively as μ and δ. The average exposure period is $^1/\rho$, after which a fraction ε of ρE(t) shows no symptom. Other parameters are as given in table 2.1.
The figure 2.1 below shows the dynamics of the model with the inflow and outflow on each compartment of the model.

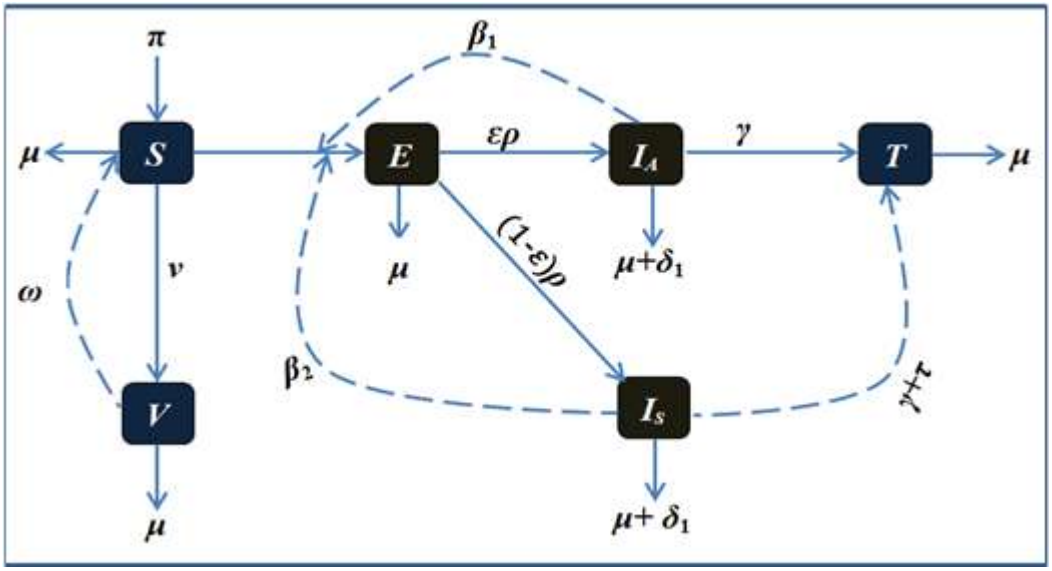

Figure 2.1: The diagrammatic representation for the dynamics of influenza virus infection

The model is formulated as a system of coupled ordinary differential equation as:

$$\begin{aligned}
\frac{dS}{dt} &= (1-\nu)\pi - \mu S - (\beta_1 I_A + \beta_2 I_S) S + \omega V \\
\frac{dV}{dt} &= \nu\pi - (\mu+\omega)V \\
\frac{dE}{dt} &= (\beta_1 I_A + \beta_2 I_S) S - (\mu+\rho)E \\
\frac{dI_A}{dt} &= \varepsilon\rho E - (\mu+\delta+\gamma) I_A \\
\frac{dI_S}{dt} &= (1-\varepsilon)\rho E - (\mu+\delta+\gamma+\tau) I_S \\
\frac{dT}{dt} &= \gamma I_A + (\gamma+\tau) I_S - \mu T;
\end{aligned} \tag{2.1}$$

together with the initial conditions:

$S(t_0) = S_0, V(t_0) = V_0, E(t_0) = E_0, I_A(t_0) = I_{A0}, I_S(t_0) = I_{S0}, T(t_0) = T_0.$

2.1Existence and Uniqueness of Solution

THEOREM 2.1 [8]: Let

$$\begin{aligned}
x_1' &= f_1(x_1, x_2, ...x_n, t), x_1(t_0) = x_{10} \\
x_2' &= f_2(x_1, x_2, ...x_n, t), x_2(t_0) = x_{20} \\
&\vdots \\
x_n' &= f_n(x_1, x_2, ...x_n, t), x_n(t_0) = x_{n0}.
\end{aligned} \tag{2.2}$$

Suppose D is the region in (n+1)-dimensional space (one dimension for t and n dimensions for the vector $\underline{x}$). If the partial derivatives $\frac{\partial f_i}{\partial x_j}, i, j = 1,2,...,n$ are continuous in $D = \{(x,t) : |t - t_0| \le a, |x - x_0| \le b\}$,

then there is a constant $\delta > 0$ such that there exists a unique continuous vector solution $\underline{x} = [x_1(t), x_2(t), ..., x_n(t)]$ in the interval $|t - t_0| \le \delta$

Table 2.1: Description of Variables and parameters used in the model

State Variables and Description Parameters		*Values*	*Sources*
S(t)	Number of individuals susceptible to influenza infection at time t		
V(t)	Number of individuals vaccinated against influenza infection at time t		
E(t)	Number of individuals exposed to influenza infection at time t		
$I_A(t)$	Number of asymptomatic infected individuals at time t		
$I_S(t)$	Number of symptomatic infected individuals at time t		
T(t)	Number of recovered individuals at time t		
N	Total human population		
π	Recruitment term of the susceptible individuals	0.01547	Assumed
ν	Per capita rate of vaccination	0.4	Estimated
ω	Per capita rate of vaccine wanes off	0.01	Estimated
β_1	Rate of transmission from contact between susceptible and asymptomatic infected individuals	0.30	Assumed
β_2	Rate of transmission from contact between susceptible and symptomatic infected individuals	0.25	[10]
ρ	Per capita rates of progression from the exposed state to the infected states	$^1/_{2.6}$ = 0.385	[9]
ε	Fraction of the exposed individuals that are migrated to symptomatic infected	0.33	Estimated
δ	Disease-induced death rate	0.0005/day	[10]
μ	Natural death rate	0.009493	Assumed
γ	Natural recovery rate of the infected individuals	$½(^1/_7+^1/_{14})$	Estimated
τ	Per capita recovery rate due to treatment of influenza	$^1/_{2.4}$ = 0.417	[9]

THEOREM 2.2: Let

$$f_1 = \frac{dS}{dt} = (1-\nu)\pi - \mu S - (\beta_1 I_A + \beta_2 I_S)S + \omega V; \qquad S(t_0) = S_0$$

$$f_2 = \frac{dV}{dt} = \nu\pi - (\mu+\omega)V; \qquad V(t_0) = V_0$$

$$f_3 = \frac{dE}{dt} = (\beta_1 I_A + \beta_2 I_S)S - (\mu+\rho)E; \qquad E(t_0) = E_0$$

$$f_4 = \frac{dI_A}{dt} = \varepsilon\rho E - (\mu+\delta+\gamma)I_A; \qquad I_A(t_0) = I_{A_0}$$

$$f_5 = \frac{dI_S}{dt} = (1-\varepsilon)\rho E - (\mu+\delta+\gamma+\tau)I_S; \qquad I_S(t_0) = I_{S_0}$$

$$f_6 = \frac{dT}{dt} = \gamma I_A + (\gamma+\tau)I_S - \mu T; \qquad V(t_0) = V_0,$$

(2.3)

$$D = \{(S,V,E,I_A,I_S,T): |S-S_0| \le a, |V-V_0| \le b, |E-E_0| \le c, |I_A - I_{A_0}| \le d, |I_S - I_{S_0}| \le e, |T-T_0| \le f, |t-t_0| \le g\}.$$

Then equation (2.3) has a unique solution.

Proof:

We find the partial derivatives, evaluated at the origin thus:

$$\left.\frac{\partial f_1}{\partial S}\right|_{(0,0,0,0,0,0)} = -\mu \quad \left.\frac{\partial f_2}{\partial S}\right|_{(0,0,0,0,0,0)} = 0$$

$$\left.\frac{\partial f_1}{\partial V}\right|_{(0,0,0,0,0,0)} = -\omega \quad \left.\frac{\partial f_2}{\partial V}\right|_{(0,0,0,0,0,0)} = -(\mu+\omega)$$

$$\left.\frac{\partial f_1}{\partial E}\right|_{(0,0,0,0,0,0)} = 0 \quad \left.\frac{\partial f_2}{\partial E}\right|_{(0,0,0,0,0,0)} = 0$$

$$\left.\frac{\partial f_1}{\partial I_A}\right|_{(0,0,0,0,0,0)} = 0 \quad \left.\frac{\partial f_2}{\partial I_A}\right|_{(0,0,0,0,0,0)} = 0$$

$$\left.\frac{\partial f_1}{\partial I_S}\right|_{(0,0,0,0,0,0)} = 0 \quad \left.\frac{\partial f_1}{\partial I_S}\right|_{(0,0,0,0,0,0)} = 0$$

$$\left.\frac{\partial f_1}{\partial T}\right|_{(0,0,0,0,0,0)} = 0 \quad \left.\frac{\partial f_2}{\partial T}\right|_{(0,0,0,0,0,0)} = 0$$

$$\left.\frac{\partial f_3}{\partial S}\right|_{(0,0,0,0,0,0)} = 0$$

$$\left.\frac{\partial f_3}{\partial V}\right|_{(0,0,0,0,0,0)} = 0$$

$$\left.\frac{\partial f_3}{\partial E}\right|_{(0,0,0,0,0,0)} = -(\mu+\rho)$$

$$\left.\frac{\partial f_3}{\partial I_A}\right|_{(0,0,0,0,0,0)} = 0$$

$$\left.\frac{\partial f_3}{\partial I_S}\right|_{(0,0,0,0,0,0)} = 0$$

$$\left.\frac{\partial f_3}{\partial T}\right|_{(0,0,0,0,0,0)} = 0$$

$$\left.\frac{\partial f_4}{\partial S}\right|_{(0,0,0,0,0,0)} = 0$$

$$\left.\frac{\partial f_4}{\partial V}\right|_{(0,0,0,0,0,0)} = 0$$

$$\left.\frac{\partial f_4}{\partial E}\right|_{(0,0,0,0,0,0)} = \varepsilon\rho$$

$$\left.\frac{\partial f_4}{\partial I_A}\right|_{(0,0,0,0,0,0)} = (\mu+\delta+\gamma)$$

$$\left.\frac{\partial f_4}{\partial I_S}\right|_{(0,0,0,0,0,0)} = 0$$

$$\left.\frac{\partial f_4}{\partial T}\right|_{(0,0,0,0,0,0)} = 0$$

$$\left.\frac{\partial f_5}{\partial S}\right|_{(0,0,0,0,0,0)}=0 \qquad \left.\frac{\partial f_6}{\partial S}\right|_{(0,0,0,0,0,0)}=0$$

$$\left.\frac{\partial f_5}{\partial V}\right|_{(0,0,0,0,0,0)}=0 \qquad \left.\frac{\partial f_6}{\partial V}\right|_{(0,0,0,0,0,0)}=0$$

$$\left.\frac{\partial f_5}{\partial E}\right|_{(0,0,0,0,0,0)}=-(1-\varepsilon)\rho \qquad \left.\frac{\partial f_6}{\partial E}\right|_{(0,0,0,0,0,0)}=0$$

$$\left.\frac{\partial f_5}{\partial I_A}\right|_{(0,0,0,0,0,0)}=0 \qquad \left.\frac{\partial f_6}{\partial I_A}\right|_{(0,0,0,0,0,0)}=\gamma$$

$$\left.\frac{\partial f_5}{\partial I_S}\right|_{(0,0,0,0,0,0)}=-(\mu+\delta+\gamma+\tau) \qquad \left.\frac{\partial f_6}{\partial I_S}\right|_{(0,0,0,0,0,0)}=\gamma+\tau$$

$$\left.\frac{\partial f_5}{\partial T}\right|_{(0,0,0,0,0,0)}=0 \qquad \left.\frac{\partial f_6}{\partial T}\right|_{(0,0,0,0,0,0)}=-\mu$$

Obviously, $\left|\frac{\partial f_i}{\partial x_j}\right|, i, j=1,2,...,6$ are continuous and bounded in

$$D=\left\{(S,V,E,I_A,I_S,T):|S-S_0|\le a,|V-V_0|\le b,|E-E_0|\le c,|I_A-I_{A_0}|\le d,|I_S-I_{S_0}|\le e|T-T_0|\le f,|t-t_0|\le g\right\}.$$

Hence, following Derrick and Grossman [8] of theorem 2.1 above, the problem (2.3) has a unique solution and so the model (2.1) is both epidemiologically feasible and mathematically well posed.

3. Mathematical Analysis of the Model

In this section we carry out qualitative analysis of the model (2.1) to investigate existence and stability of the steady states.

3.1 Existence of Equilibrium Points

Let $E=\left(S^*,\ V^*,\ E^*,\ I_A^*,\ I_S^*,\ T^*\right)$ represent any arbitrary equilibrium point of system (2.1) obtained by setting $\frac{dS}{dt}=\frac{dV}{dt}=\frac{dE}{dt}=\frac{dI_A}{dt}=\frac{dI_S}{dt}=\frac{dT}{dt}=0$; i.e.

$$\begin{aligned}
(1-\nu)\pi-\mu S^*-\left(\beta_1 I_A^*+\beta_2 I_S^*\right)S^*+\omega V^* &= 0\\
\nu\pi-(\mu+\omega)V^* &= 0\\
\left(\beta_1 I_A^*+\beta_2 I_S^*\right)S^*-(\mu+\rho)E^* &= 0\\
\varepsilon\rho E^*-(\mu+\delta+\gamma)I_A^* &= 0\\
(1-\varepsilon)\rho E^*-(\mu+\delta+\gamma+\tau)I_S^* &= 0\\
\gamma I_A^*+(\gamma+\tau)I_S^*-\mu T^* &= 0
\end{aligned} \qquad (2.4)$$

3.1.1 Disease-free Equilibrium Points, R_0

Disease-free equilibrium points are steady-state solutions in the absence of influenza virus infection (i.e. $I_A = I_S = 0$). Thus, the disease-free equilibrium point, E_0, for the influenza virus model (2.1) when $I_A = I_S = 0$ yields:

$$E_0=\left(\frac{\pi}{\mu}\left[1-\nu+\frac{\omega\nu}{\mu+\omega}\right],\ \frac{\nu\pi}{\mu+\omega},\ 0,\ 0,\ 0,\ 0\right) \qquad (2.5)$$

3.1.2 Endemic Equilibrium Point, E_e

In addition to the disease-free equilibrium point E_0, we shall show that the model (2.1) has an endemic equilibrium point, E_e. The endemic equilibrium point is a positive steady state solution where the disease persists in the population (i.e. if $I_A \neq I_S \neq 0$). Therefore, solving the system (2.4) simultaneously gives the endemic equilibrium defined by:

$$E_e=\left(S^*,\ V^*,\ E^*,\ I_A^*,\ I_S^*,\ T^*\right); \qquad (2.6)$$

where

$$S^*=\frac{1}{\mu}\left\{(1-\nu)\pi+\frac{\omega\nu\pi}{\mu+\omega}+\left[\frac{\rho}{\mu}\left(\frac{\varepsilon\gamma}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)(\gamma+\tau)}{\mu+\delta+\gamma+\tau}\right)-(\mu+\rho)\right]C\right\}$$

$$V^*=\frac{\nu\pi}{\mu+\omega};$$

$$E^*=C;$$

$$I_A^*=\frac{\varepsilon\rho}{\mu+\delta+\gamma}C;$$

$$I_S^*=\frac{(1-\varepsilon)\rho}{\mu+\delta+\gamma+\tau}C;$$

$$T^*=\frac{\rho}{\mu}\left(\frac{\varepsilon\gamma}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)(\gamma+\tau)}{\mu+\delta+\gamma+\tau}\right)C,$$

with

$$C=\frac{\frac{(\mu+\rho)(\mu+\delta+\gamma)(\mu+\delta+\gamma+\tau)}{\rho\left[\varepsilon(\mu+\delta+\gamma+\tau)+(1-\varepsilon)(\mu+\delta+\gamma)\right]}-\frac{\pi}{\mu}\left[1-\nu+\frac{\omega\nu}{\mu+\omega}\right]}{\frac{1}{\mu}\left\{\left[\frac{\varepsilon\gamma}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)(\gamma+\tau)}{\mu+\delta+\gamma+\tau}\right]-(\mu+\rho)\right\}}$$

.

3.2 Derivation of Basic Reproduction Number, R_0

An important notion in epidemiological models is the basic reproduction number, usually denoted by R_0. It is a threshold value that is often used to measure the spread of a disease. It is defined as the number of secondary infections in humans that arise as a result of a single infected individual being introduced in a fully susceptible population. When $R_0 < 1$, it implies that on average an infectious individual infects less than one person throughout his/her infectious period and in this case the disease is wiped out. On the other hand, when $R_0 > 1$, then on average every infectious individual infects more than one individual during his/her infectious period and the disease persists in the population.

The derivation of basic reproduction number is essential in order to assess the local stability of the system (2.1).

To do this, we employ the method of next generation matrix described by Driessche and Watmough [17].We have the transmission and transition matrices to be given respectively as

$$\mathcal{F} = \begin{pmatrix} (\beta_1 I_A + \beta_2 I_S) S \\ 0 \\ 0 \end{pmatrix} \text{ and}$$

$$\mathcal{V} = \begin{pmatrix} (\mu+\rho)E \\ -\varepsilon\rho E + (\mu+\delta+\gamma)I_A \\ -(1-\varepsilon)\rho E + (\mu+\delta+\gamma+\tau)I_S \end{pmatrix}.$$

The Jacobian matrices for $\mathcal{F}$ and $\mathcal{V}$ at DFE (E_0) are evaluated as follows:

$$F = D\mathcal{F}|_{E_0} = \begin{pmatrix} 0 & \frac{\pi\beta_1}{\mu}\left[1-\nu+\frac{\omega\nu}{\mu+\omega}\right] & \frac{\pi\beta_2}{\mu}\left[1-\nu+\frac{\omega\nu}{\mu+\omega}\right] \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

and $V = D\mathcal{V}|_{E_0} = \begin{pmatrix} \mu+\rho & 0 & 0 \\ -\varepsilon\rho & \mu+\delta+\gamma & 0 \\ -(1-\varepsilon)\rho & 0 & \mu+\delta+\gamma+\tau \end{pmatrix}$

$$F.V^{-1} = \begin{pmatrix} \frac{\pi\beta_1}{\mu}\left[1-\nu+\frac{\omega\nu}{\mu+\omega}\right].\varepsilon\rho + \frac{\pi\beta_2}{\mu}\left[1-\nu+\frac{\omega\nu}{\mu+\omega}\right].(1-\varepsilon)\rho & \frac{\pi\beta_1}{\mu}\left[1-\nu+\frac{\omega\nu}{\mu+\omega}\right] & \frac{\pi\beta_2}{\mu}\left[1-\nu+\frac{\omega\nu}{\mu+\omega}\right] \\ \hline (\mu+\rho)(\mu+\delta+\gamma) & (\mu+\delta+\gamma) & (\mu+\delta+\gamma+\tau) \\ \hline (\mu+\rho)(\mu+\delta+\gamma+\tau) & & \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

Now, the basic reproduction number, which equals $\rho(F.V^{-1})$, is obtained as the spectra radius (i.e. the dominant eigenvalue) of the product $F.V^{-1}$ thus:

$$R_0 = \frac{\pi\rho\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right)}{\mu(\mu+\rho)}.\left[\frac{\varepsilon\beta_1}{\mu+\delta+\gamma} + \frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right] \quad (2.7)$$

This quantity gives the basic reproduction number.

3.3 Local Stability of Disease-free Equilibrium Point

Theorem 3.1:

If $\frac{\pi\rho\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right)}{\mu(\mu+\rho)}.\left[\frac{\varepsilon\beta_1+(1-\varepsilon)\beta_2}{(\mu+\delta+\gamma)+(\mu+\delta+\gamma+\tau)}\right] < 1;$

and if $R_0 < 1$, then the disease-free equilibrium is locally asymptotically stable. Otherwise, it is unstable.

Proof: The stability of the disease-free equilibrium is determined by the eigenvalues of the Jacobian matrix of the full system (2.1), evaluated at the disease-free equilibrium point, given by

$$J|_{E_0} = \begin{pmatrix} -\mu & \omega & 0 & -\frac{\pi\beta_1}{\mu}\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right) & -\frac{\pi\beta_2}{\mu}\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right) & 0 \\ 0 & -(\mu+\omega) & 0 & 0 & 0 & 0 \\ 0 & 0 & -(\mu+\rho) & \frac{\pi\beta_1}{\mu}\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right) & \frac{\pi\beta_2}{\mu}\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right) & 0 \\ 0 & 0 & \varepsilon\rho & -(\mu+\delta+\gamma) & 0 & 0 \\ 0 & 0 & (1-\varepsilon)\rho & 0 & -(\mu+\delta+\gamma+\tau) & 0 \\ 0 & 0 & 0 & \gamma & \gamma+\tau & -\mu \end{pmatrix}$$

.

The eigen values of this Jacobian matrix are obtained to be

$\lambda_1 = -\mu,\ \lambda_2 = -(\mu+\omega),\ \lambda_3 = -\mu;$

together with the roots of the cubic equation

$$\lambda^3 + \left[(\mu+\rho)+(\mu+\delta+\gamma)+(\mu+\delta+\gamma+\tau)\right]\lambda^2 + \left\{(\mu+\delta+\gamma)(\mu+\delta+\gamma+\tau) + \left[1-\frac{\pi\rho\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right)}{\mu(\mu+\rho)}.\left[\frac{\varepsilon\beta_1+(1-\varepsilon)\beta_2}{(\mu+\delta+\gamma)+(\mu+\delta+\gamma+\tau)}\right]\right]\right\}\lambda$$
$$+\left\{1-\frac{\pi\rho\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right)}{\mu(\mu+\rho)}.\left[\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right]\right\} = 0$$

$$\Rightarrow \lambda^3 + \left[(\mu+\rho)+(\mu+\delta+\gamma)+(\mu+\delta+\gamma+\tau)\right]\lambda^2 + \left\{(\mu+\delta+\gamma)(\mu+\delta+\gamma+\tau)+\left[1-R^*\right]\right\}\lambda + \left\{1-R_0\right\} = 0 \quad (2.8)$$

Where

$$R^{*}= \frac{\pi\rho\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right)}{\mu(\mu+\rho)}.\left[\frac{\varepsilon\beta_1+(1-\varepsilon)\beta_2}{(\mu+\delta+\gamma)+(\mu+\delta+\gamma+\tau)}\right],$$

and R_0 is as defined in (2.7).

Now, if $R^{*} < 1$; and if $R_0 < 1$, then by Descartes' rule of sign, there exists no positive root (i.e. all the roots are negative or complex with negative real parts). Hence the disease-free equilibrium is locally asymptotically stable. Otherwise, it is unstable.

3.4 Global Stability of Disease-free Equilibrium Point

Here, we explored the global asymptotic stability (GAS) property of the disease-free equilibrium point for the influenza model.

Theorem 3.2:
If $R_0 < 1$, then the disease-free equilibrium point of the system (2.1) is globally asymptotically stable. Otherwise, it is unstable.

Proof: This proof is based on the use of comparison theorem [12] using the comparison method. Thus we have:

$$\begin{pmatrix} \frac{dE}{dt} \\ \frac{dI_A}{dt} \\ \frac{dI_S}{dt} \end{pmatrix} = (F-V)\begin{pmatrix} E \\ I_A \\ I_S \end{pmatrix} - F_i\begin{pmatrix} E \\ I_A \\ I_S \end{pmatrix}$$

where F – V is defined as

$$F\text{-}V=\begin{pmatrix} -(\mu+\rho) & \frac{\pi\beta_1}{\mu}\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right) & \frac{\pi\beta_2}{\mu}\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right) \\ \varepsilon\rho & -(\mu+\delta+\gamma) & 0 \\ (1-\varepsilon)\rho & 0 & -(\mu+\delta+\gamma+\tau) \end{pmatrix} = \tilde{J}$$

$\tilde{J}$ can be rewritten in the form $\tilde{J}$ = M – D, where

$$M=\begin{pmatrix} 0 & \frac{\pi\beta_1}{\mu}\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right) & \frac{\pi\beta_2}{\mu}\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right) \\ \varepsilon\rho & 0 & 0 \\ (1-\varepsilon)\rho & 0 & 0 \end{pmatrix}, D=\begin{pmatrix} -(\mu+\rho) & 0 & 0 \\ 0 & -(\mu+\delta+\gamma) & 0 \\ 0 & 0 & -(\mu+\delta+\gamma+\tau) \end{pmatrix}.$$

D is a diagonal matrix with positive diagonal elements and therefore it is a non-singular matrix, while M is the remainder. The eigenvalue of $\tilde{J}$ have negative real parts iff the spectra radius (i.e. the dominant eigenvalue) of the matrix $MD^{-1} < 1$ [7], where

$$MD^{-1}=\begin{pmatrix} 0 & \frac{\pi\beta_1}{\mu(\mu+\delta+\gamma)}\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right) & \frac{\pi\beta_2}{\mu(\mu+\delta+\gamma+\tau)}\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right) \\ \frac{\varepsilon\rho}{\mu+\rho} & 0 & 0 \\ \frac{(1-\varepsilon)\rho}{\mu+\rho} & 0 & 0 \end{pmatrix}$$

The eigen values of MD^{-1}, obtained by setting $|M D^{-1} - \lambda I| = 0$, where I is a 3 x 3 identity matrix, is given as the roots of the cubic equation:

$$-\lambda^3+\frac{\pi\beta_1\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right)}{\mu(\mu+\delta+\gamma)}\frac{\varepsilon\rho}{\mu+\rho}\lambda+\frac{\pi\beta_2\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right)}{\mu(\mu+\delta+\gamma+\tau)}\frac{(1-\varepsilon)\rho}{\mu+\rho}\lambda=0$$

$$\Rightarrow \quad -\lambda\left\{\lambda^2-\frac{\pi\rho\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right)}{\mu(\mu+\rho)}\left[\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right]\right\}=0$$

$$\Rightarrow \quad \lambda_1=0 \quad Or \quad \lambda_{2,3}=\pm\sqrt{\frac{\pi\rho\left(1-\nu+\frac{\omega\nu}{\mu+\omega}\right)}{\mu(\mu+\rho)}\left[\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right]}=\pm\sqrt{R_0}.$$

Obviously, the leading eigenvalue $\sqrt{R_0}<1$ if $R_0 < 1$. In other words, the spectra radius of $MD^{-1} < 1$, if $R_0 < 1$. Therefore, all the eigenvalue of $\tilde{J}$ have negative real parts.

Hence, the disease-free equilibrium point of the system (2.1) is globally asymptotically stable if $R_0 < 1$, and unstable if otherwise. This completes the proof.

3.5. Stability of Endemic Equilibrium Point, E_e

Theorem 3.3: The endemic equilibrium, E_0 is locally asymptotically stable.

Proof: The stability of the endemic equilibrium is determined by the eigenvalues of the Jacobian matrix of the full system (2.1), evaluated at the endemic equilibrium point, given by

$$J\big|_{E_e}=\begin{pmatrix} -\left(\mu+\rho C\left[\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right]\right) & \omega & 0 & -\beta_1 S^* & -\beta_2 S^* & 0 \\ 0 & -(\mu+\omega) & 0 & 0 & 0 & 0 \\ \rho C\left[\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right] & 0 & -(\mu+\rho) & \beta_1 S^* & \beta_2 S^* & 0 \\ 0 & 0 & \varepsilon\rho & -(\mu+\delta+\gamma) & 0 & 0 \\ 0 & 0 & (1-\varepsilon)\rho & 0 & -(\mu+\delta+\gamma+\tau) & 0 \\ 0 & 0 & 0 & \gamma & \gamma+\tau & -\mu) \end{pmatrix}$$

where S^* is as defined in (2.6).

This gives an eigenvalue $\lambda_1=-(\mu+\omega)$; others being the roots of the polynomial equation:

$$\lambda^5+a_4\lambda^4+a_3\lambda^3+a_2\lambda^2+a_1\lambda+a_0=0; \qquad (2.9)$$

Where $a_4=(\mu+\kappa)+\left[(\mu+\delta+\gamma)+(\mu+\delta+\gamma+\tau)\right]+(\mu+\rho)+\left[\mu+\rho C\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)\right]$,

$$a_3=\mu\left(\left[\mu+\rho C\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)\right]+(\mu+\rho)\right)+\mu\left[(\mu+\delta+\gamma)+(\mu+\delta+\gamma+\tau)\right]$$
$$+\left[\mu+\rho C\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)\right]+\left[(\mu+\delta+\gamma)+(\mu+\delta+\gamma+\tau)\right]\left(\left[\mu+\rho C\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)\right]+(\mu+\rho)\right)$$
$$+(\mu+\delta+\gamma)(\mu+\delta+\gamma+\tau)+(1-\varepsilon)\rho\beta_2 S^*,$$

$$a_2=\mu\left[\mu+\rho C\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)\right]+\left[(\mu+\delta+\gamma)+(\mu+\delta+\gamma+\tau)\right]\left(\left[\mu+\rho C\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)\right]+(\mu+\rho)\right)$$
$$+\mu\left[1+(\mu+\delta+\gamma)(\mu+\delta+\gamma+\tau)\right]+\left[\mu+\rho C\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)\right](\mu+\rho)\left[(\mu+\delta+\gamma)+(\mu+\delta+\gamma+\tau)\right]$$
$$+(\mu+\delta+\gamma)(\mu+\delta+\gamma+\tau)\left(\left[\mu+\rho C\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)\right]+(\mu+\rho)\right)+(1-\varepsilon)\rho\beta_2\left[\mu+\rho C\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)\right]S^*$$
$$+(1-\varepsilon)\rho\beta_2\left[(\mu+\delta+\gamma)+(\mu+\kappa)\right]S^*+(1-\varepsilon)\beta_2\rho^2 C\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)S^*,$$

$$a_1=\mu\left[(\mu+\delta+\gamma)+(\mu+\delta+\gamma+\tau)\right](\mu+\rho)\left[\mu+\rho C\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)\right]+(\mu+\delta+\gamma)(\mu+\delta+\gamma+\tau)$$
$$+\mu\left(\left[\mu+\rho C\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)\right]+(\mu+\rho)\right)+(\mu+\rho)(\mu+\delta+\gamma)(\mu+\delta+\gamma+\tau)\left[\mu+\rho C\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)\right]$$
$$+(1-\varepsilon)\rho\beta_2\left[(\mu+\delta+\gamma)+\mu\right]\left[\mu+\rho C\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)\right]S^*+(1-\varepsilon)\rho\beta_2\left[(\mu+\delta+\gamma)+\mu\right]S^*$$
$$+\varepsilon\rho C\beta_2\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)S^*+(1-\varepsilon)\rho^2 C\beta_2\left[(\mu+\delta+\gamma)+\mu\right]\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)S^*,$$

$$a_0 = \mu\left[\mu+\rho C\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)\right](\mu+\rho)(\mu+\delta+\gamma)(\mu+\delta+\gamma+\tau)$$
$$+(1-\varepsilon)\rho\beta_2\mu(\mu+\delta+\gamma)\left[\mu+\rho C\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)\right]S^*+\varepsilon\rho^2C\beta_1\mu\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)S^*$$
$$+(1-\varepsilon)\rho^2\beta_2C\mu(\mu+\delta+\gamma)\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right)S^*+(1-\varepsilon)\rho^2\beta_2C(\gamma+\tau)(\mu+\omega)(\mu+\delta+\gamma)\left(\frac{\varepsilon\beta_1}{\mu+\delta+\gamma}+\frac{(1-\varepsilon)\beta_2}{\mu+\delta+\gamma+\tau}\right);$$

and S^* is as defined in (2.6).

Obviously, from the polynomial equation (2.9), there is no sign change, and so by Descartes' rule of sign, there exists no positive root (i.e. all the roots are negative or complex with negative real parts). Hence the endemic equilibrium is locally asymptotically stable.

Numerical Results and Discussion

The numerical simulation for the model was carried out by Maple 18 software using differential transformation method to show the effects of vaccination, recovery and treatment rates on the dynamics of influenza virus disease.
$S(0)=500,\ V(0)=175,\ E(0)=250,\ I_A(0)=100,\ I_S(0)=150,\ T(0)=200.$

4.1 Presentation of Results

The results are given in Figures 4.1 – 4.16 to illustrate the system's behaviour for different values of the model's parameters.

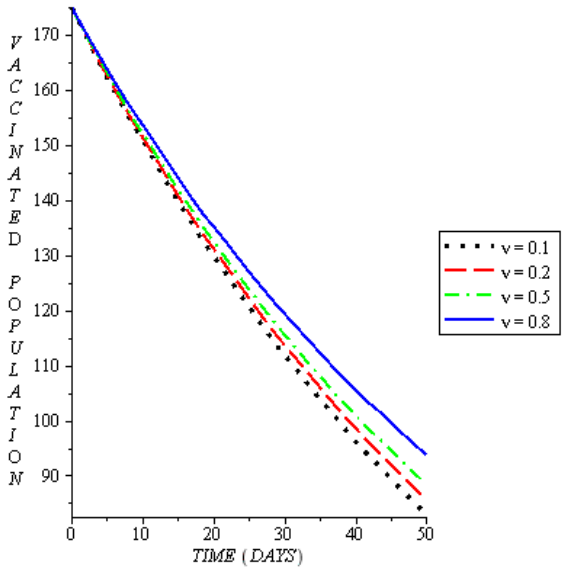

Figure 4.1: The behaviour of vaccinated population for varied values of vaccination rate, .

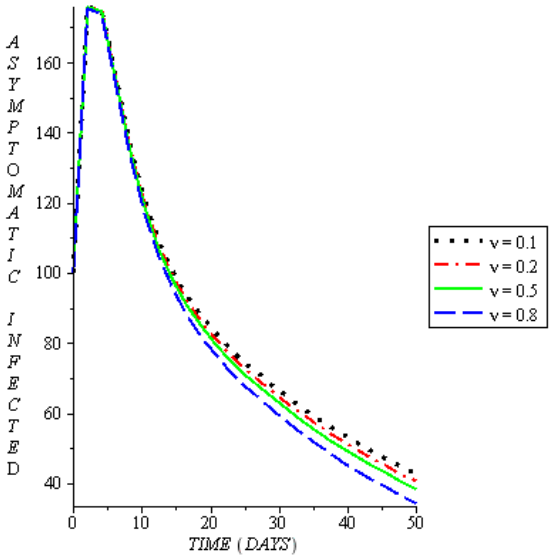

Figure 4.2: The behaviour of asymptomatic infected population for varied values of vaccination rate, ν

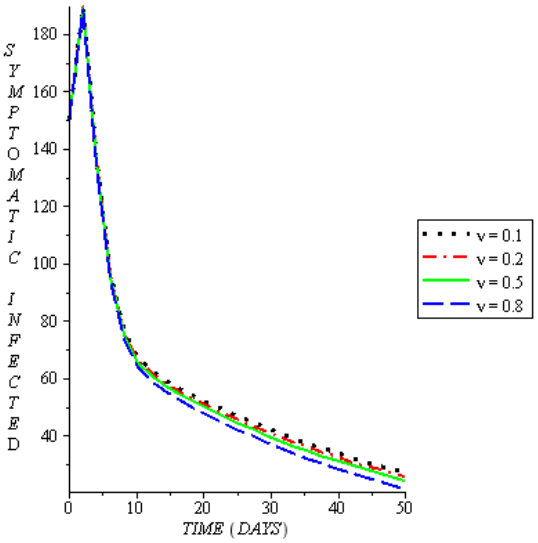

Figure 4.3: The behaviour of symptomatic infected population for varied values of vaccination rate,

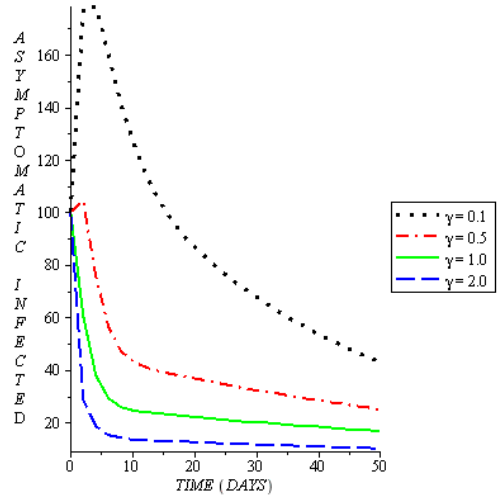

Figure 4.5: The behaviour of asymptomatic infected population for varied values of recovery rate, γ

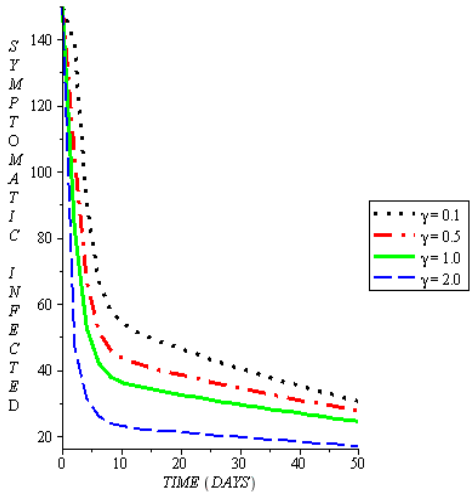

Figure 4.6: The behaviour of symptomatic infected population for varied values of recovery rate, γ

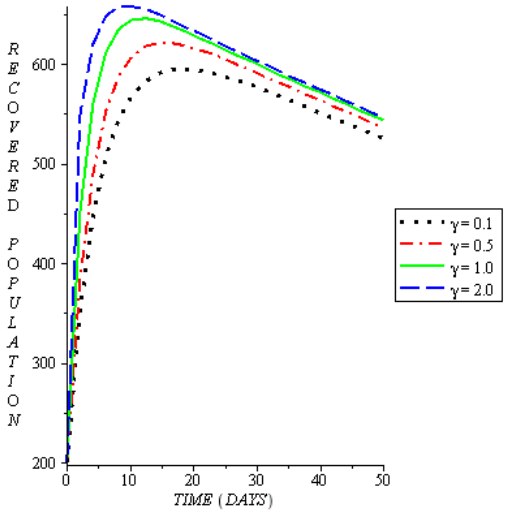

Figure 4.7: The behaviour of recovered population for varied values of recovery rate, γ

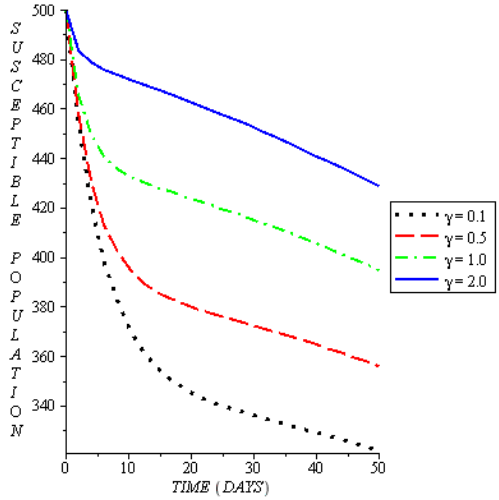

Figure 4.8: The behaviour of the susceptible population for varied values of recovery rate, γ

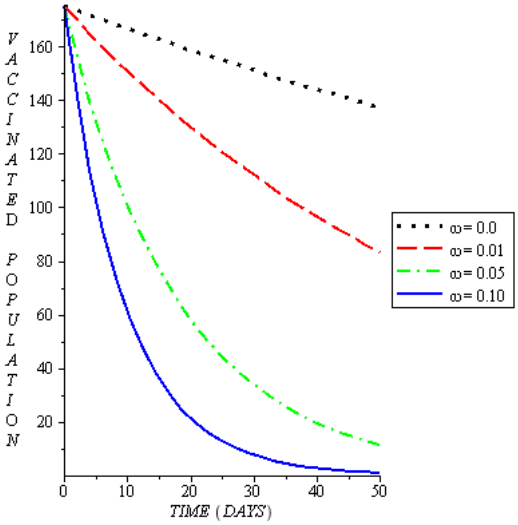

Figure 4.4: The behaviour of vaccinated population for varied values of vaccine wanes off rate, ω

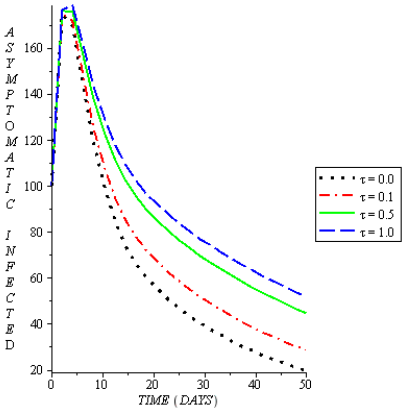

Figure 4.9: The behaviour of asymptomatic infected population for varied values of treatment rate, τ

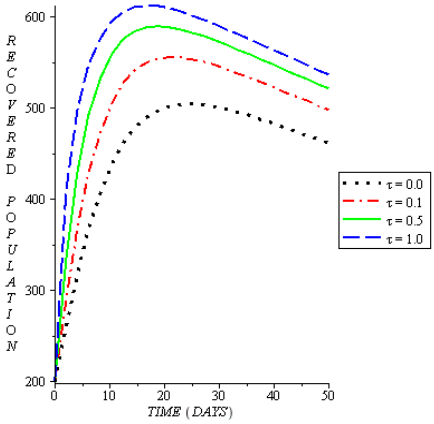

Figure 4.11: The behaviour of recovered population for varied values of treatment rate,

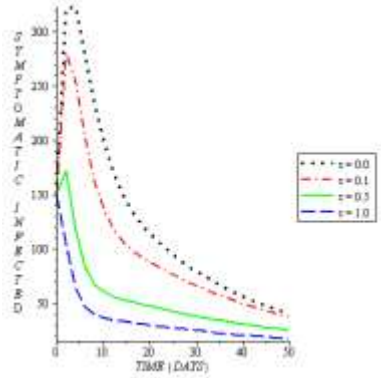

Figure 4.10: The behaviour of symptomatic infected population for varied values of treatment rate, τ

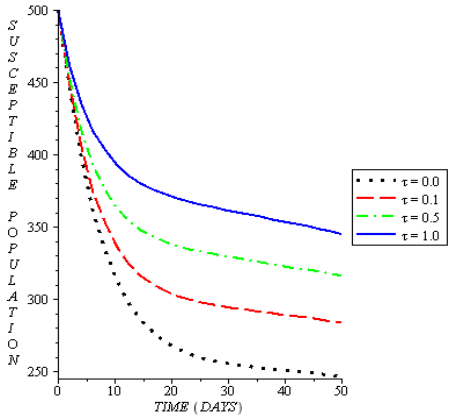

Figure 4.12: The behaviour of susceptible population for varied values of treatment rate, τ

4.2 Discussion of Results

Figure 4.1 to figure 4.3 illustrate the effect of administering influenza vaccine at birth on the populations. From figure 4.1, we observed that increasing the vaccination rate, ν, increases the vaccinated population, which in turn lowers the population of both asymptomatic and symptomatic infected populations. This can be seen as shown in figures 4.2 and 4.3 respectively. However from figure 4.4, which is the plot of vaccinated population against time for varied values of the rate of vaccine wane-off (ω), it was seen that the vaccinated population decreases as ω increases. This will in turn has the effect of increasing influenza infection in the population and hence the need for more medical research in order to increase the efficacy and/or expiry duration of influenza vaccines. Also, while such research is on-going, influenza vaccines should be retaken for renewal sake and should not be once in a lifetime. In these ways, the rate at which vaccines wane off will be greatly lowered, and the infection will be lowered in the population as well.

Also, from figures 4.5 and 4.6, the plots of asymptomatic and symptomatic infected population respectively against time for varied values of the recovery rate γ, we observed a declining infection as the recovery rate, γ, increases. This recovery is due to the body immunity of the infected individuals. Figure 4.7 is the plot of recovered population against time when recovery rate is varied and it shows that the recovered population increases as γ increases. From figure 4.8, which is the plot of susceptible population against time when recovery rate is varied, it was shown that the susceptible population increases as γ increases.

Furthermore, we investigated the effect of treatment on the dynamics of influenza virus infection. Figure 4.9 shows the behaviour of the asymptomatic infected population for varied values of treatment rate, τ, and it shows that there is increase in the number of asymptomatic infected individuals per time. This can attributed to the fact that this group of individuals are not treated since their infection status is not known, in addition to the fact that they are also able to transmit the infection even though they show no symptom of the infection. So they contribute to an increase infection in the population. Figure 4.10 shows that there is a decline in infection in the symptomatic infected population as the rate of treatment increases. From figure 4.11, which is the plot of the recovered population against time for varied values of the treatment rate, τ, it was observed that there was an increase in the population of the recovered individuals as τ increases.

5. Conclusion

In this paper, we have formulated and analysed a compartmental model for influenza virus control among humans. The total human population was divided into six compartments: susceptible, vaccinated, exposed, asymptomatic infected, symptomatic infected and recovered sub-populations. We established a region where the model is epidemiologically feasible and mathematically well-posed. The existence and stability of a disease-free equilibrium point as well as the endemic equilibrium point were determined.

The numerical simulations were performed to see the effects of vaccine, recovery (due to body immunity), and treatment on the dynamics of the disease. Our results showed that increasing the rates of vaccination and recovery has a significant effect of reducing infection in both populations of the infected individuals and increases the recovered and susceptible populations. However, although treatment decreases infection in the symptomatic infected population, it has a negative effect of increasing infection among the asymptomatic infected individuals. This effect can be reversed if screening programmes are organized for all individuals irrespective of whether they show symptoms or not. This will help in knowing the infection status of all individuals and as such, necessary measure will be taken.

In order to lower the rate at which vaccines wane off, it is recommended that influenza vaccines be taken periodically (annually, biennially or otherwise, depending on the expiry duration) for renewal sake, and it should be administered to a higher proportion of individual. It was proposed by the CDC's Advisory Committee on Immunization Practices (ACIP) that priorities should be given to young people aged 6months to 25years, who are the most efficient at transmitting influenza viruses [4]. However, in administering vaccines, a wide range of ages from 5 months to 65 years should be considered [15]. These control measures will greatly reduce the transmission of the influenza virus infection. However, efforts should be intensified in developing improved vaccines with higher efficacy and longer expiry duration for influenza virus disease as this would facilitate the stimulation of the immune system in producing antibodies against influenza virus infection.

6. Acknowledgement

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