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Stability Analysis of the Effect of Vaccination in the Transmission of Swine Flu

[1]Nita H. Shah, [2]Ankush H. Suthar and [3]Moksha H. Satia
[1]*Professor, Department of Mathematics, Gujarat University, Ahmedabad-380009, Gujarat, India.*
[2,3]*Research Scholar (Reg. No: 8487)[2](Reg. No: 7885)[3], Department of Mathematics, Gujarat University, Ahmedabad-380009, Gujarat, India.*
Corresponding Author: Nita H. Shah

ABSTRACT
In this study, a deterministic model for swine flu is formulated and analysed to study the effects of vaccination in the spread of the disease. The model parameters of the swine flu are investigated in depth. The threshold and equilibrium points for the model are computed and stabilities are studied. The swine flu free equilibrium is proved to be globally stable. Centre manifold theory is used to established local stability of endemic equilibrium, the global stability is proved using Lyapunov function. Through numerical simulation, it is observed that swine flu individuals in the population for a non-vaccinated community are at risk. The result reveals that vaccination should be encouraged to reduce the vitality of the disease.
KEYWORDS: *Swine-Flu model, Vaccination, Basic reproduction number, Equilibria, Stability, Sensitivity analysis, Simulation*
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I. INTRODUCTION

Influenza virus is a respiratory pathogen belonging to the family Orthomyxoviridae (Wright, 2001). The novel influenza type A (H1N1) virus that affects pigs (swine) was named as Swine flu. It is a new flu virus, which is a combination of swine, avian (bird), and human genes that mixed together in pigs and spread to humans. The flu can pass through infected individuals to the humans, through inhaling air that is contaminated with the virus, or touches a surface that an infected individual has recently touched. Since humans have low immunity to influenza virus, it spread quickly and can cause more serious health problems for humans. On 15th and 17th April, 2009, the first two cases of human infection with a H1N1 virus was confirmed by the Centres for Disease Control and Prevention (CDC) in the United States (synonymous 2009). The virus contained a unique combination of gene segments that had never been identified earlier in the state (Nguyen-Van-Tam et al, 2010 and Garten et al, 2009). The virus soon spread to the rest of the world, it had been identified in 191 countries and territories as of September 20, 2009. In 2011, CDC published estimation of numbers of hospitalizations and death cases in this outbreak. This finding estimates from April 12, 2009 to April 10, 2010 confirm 274,304 hospitalizations cases and 12,469 deaths in the United States due to pandemic influenza (Shrestha et al, 2011). During the first 12 months of the eruption by reason of 2009 H1N1 virus, it was estimated by CDC that 0.001–0.007% of the world's population died.

There are three types of influenza virus (A, B and C), differ in their pathogenicity and genome organization. Virus of type A is found in a warm-blooded animal, whereas types B and C are predominantly human pathogens. Viruses that most commonly cause human disease Influenza are of type A and B. Despite the up-gradation in antiviral therapy, nowadays vaccination is still the most effective method of defence. For those at risk of influenza, annual vaccination is recommended due to the antigenic variations. However, there is still scope for improvement in vaccine efficiency. To support studies on vaccination, Cox et al. (2004) tried to study the nature of vaccine observing different groups of variously vaccinated pigs. When disease is caused by an infective agent, then one can build a mechanistic model for spread of the agent and use it to disentangle how this spread is influenced by various factors. It is also used to predict the effect of different dynamics on mitigating future epidemics or pandemics.

A number of dynamical models have been developed to understand behaviour of infectious diseases under impact of different factors related to it. Vardavas et al. (2007) constructed a dynamic individual-level model of human understanding and behaviour where individuals are allowed to decide, whether to vaccinate or not each

year. Galvani et al. (2007) took a different approach and developed a static model based on game theory, both of them showed that proper immunity against diseases could be attained by implementing vaccination programs. Dynamical models of influenza transmission are analyzed by Ferguson et al. (2005) and Mills et al (2004), to determine what proportion of the population would need to be vaccinated to prevent influenza epidemics. Longini et al. (2004) modeled the effects of age-specific targeting strategies and found that vaccinating 80% of children (less than 19 years old) would be nearly as effective as vaccinating 80% of the entire population, also different approaches in order to reduce infection are specified. Pongsumpun and Tang (2011) has deliberated a dynamical model for the transmission of Swine flu and tried to find a substitute way of outbreak. Tracht et al. (2010) have formulated a mathematical model for a population wearing facemasks during the pandemic and calculate impact of wearing mask on the spread of influenza and suggested that facemasks are an effective strategy to diminish the spread of influenza.

II. MATHEMATICAL MODELING

The swine-flu model is categorized into the host population at time t, denoted by $N(t)$, into susceptible vaccinated individuals $S_1(t)$, susceptible non-vaccinated individuals $S_2(t)$, vaccinated infected individuals $I_1(t)$, non-vaccinated infected individuals $I_2(t)$,vaccinated recovered individuals $R_1(t)$ and non-vaccinated recovered individuals $R_2(t)$. The birth rate of vector population $V(t)$ at time t is B. A proportion p of these individuals are vaccinated and hence they are in the $S_1(t)$ class. The remaining $(1-p)$ are non-vaccinated and are part of $S_2(t)$ class. Non-vaccinated susceptible may get vaccinated and become a member of vaccinated susceptible at a constant rate α_1. Both vaccinated individuals $S_1(t)$ and non-vaccinated individuals $S_2(t)$ catch swine flu by coming in contact with vector at rates λ and $\theta\lambda$, where θ represents the rate at which immunity decreases. The infected rate λ is given by $\lambda = \frac{eV}{K+V}$, where e denotes the rate of vector bite per unit time, K is the concentration of vector population and $\lambda = \frac{eV}{K+V}$ is the probability that an individual gets infected by vector bite. Vaccinated and non-vaccinated individuals suffer from swine-flue move to swine flu infected classes $I_1(t)$ and $I_2(t)$ at the rate λ and $\theta\lambda$. We assume $\theta > 1$ to assume increased susceptibility to swine flu infection of the non-vaccinated individuals.

Infected individuals recover at a rate α_2 and α_3 for the vaccinated and non-vaccinated individuals in the recovered classes respectively. μ_d and $\tau\mu_d$ are the disease induced death rates in respective classes. $\tau > 1$ justifies that the increase death rate in the non-vaccinated swine-flu infected class. μ denotes natural death rate. The growth rate of vector population is $\alpha_4 V(t)$ and it spreads by the swine flu infected individuals $\left(I_1(t) + I_2(t)\right)$ at a constant rate α_5 which is a measure of the contribution of each swine flu infected individual to the population of vector in the specified area. The natural death rate of vector is μ_V. To satisfy the condition that vector population decreases due to death but can also transit towards non-harmful state, we assume $\mu_V > \alpha_4$. Thus, the density of the vector is the balance between birth and death rates and the contribution of the infected individuals.

This gives the system of differential equations,

$$\begin{aligned}
\frac{dS_1(t)}{dt} &= pB - \frac{eVS_1}{K+V} - (\mu + \alpha_1)S_1 \\
\frac{dS_2(t)}{dt} &= (1-p)B + \alpha_1 S_1 - \frac{\theta eVS_2}{K+V} - \mu S_2 \\
\frac{dI_1(t)}{dt} &= \frac{eVS_1}{K+V} - (\alpha_2 + \mu + \mu_d) I_1 \\
\frac{dI_2(t)}{dt} &= \frac{\theta eVS_2}{K+V} - (\alpha_3 + \mu + \tau\mu_d) I_2 \qquad (1) \\
\frac{dR_1(t)}{dt} &= \alpha_2 I_1 - \mu R_1 \\
\frac{dR_2(t)}{dt} &= \alpha_3 I_2 - \mu R_2
\end{aligned}$$

$$\frac{dV(t)}{dt} = \alpha_4 V + \alpha_5 \left(I_1 + I_2\right) - \mu_V V$$

We reduce the system (1) to following system without loss in mathematical generality,

$$\frac{dS_1(t)}{dt} = pB - \frac{eVS_1}{K+V} - \left(\mu + \alpha_1\right) S_1$$

$$\frac{dS_2(t)}{dt} = \left(1-p\right) B + \alpha_1 S_1 - \frac{\theta eVS_2}{K+V} - \mu S_2$$

$$\frac{dI_1(t)}{dt} = \frac{eVS_1}{K+V} - \left(\alpha_2 + \mu + \mu_d\right) I_1 \qquad (2)$$

$$\frac{dI_2(t)}{dt} = \frac{\theta eVS_2}{K+V} - \left(\alpha_3 + \mu + \tau\mu_d\right) I_2$$

$$\frac{dV(t)}{dt} = \alpha_4 V + \alpha_5 \left(I_1 + I_2\right) - \mu_V V$$

This represent non-negative R_+^5 manifold which is positively invariant, thus, we have following theorem

Theorem 2.1: Let $\left(S_1(t), S_2(t), I_1(t), I_2(t), V(t)\right)$ be the solution of the system (2), with initial condition $\left(S_1(0), S_2(0), I_1(0), I_2(0), V(0)\right)$ and the compact set Ω is a positively invariant set where all solutions in R_+^5 converge

$$\text{Where, } \Omega = \left\{ \left(S_1, S_2, I_1, I_2, V\right) \in R_+^5, L_H \le \frac{B}{\mu}, L_V \le \frac{\alpha_5 B}{\mu\left(\mu_V - \alpha_4\right)} \right\} \qquad (3)$$

Proof: Define $L(t) = \left(L_H, L_V\right) = \left(S_1 + S_2 + I_1 + I_2, V\right)$, by differentiating it with respect to t,

$$\frac{dL}{dt} = \left(\frac{dL_H}{dt}, \frac{dL_V}{dt}\right) = \left(\frac{dS_1}{dt} + \frac{dS_2}{dt} + \frac{dI_1}{dt} + \frac{dI_2}{dt}, \frac{dV}{dt}\right)$$

$$= \left(B - \mu\left(S_1 + S_2 + I_1 + I_2\right) - \left(\alpha_2 + \mu_d\right) I_1 - \left(\alpha_3 + \tau\mu_d\right) I_2,\ \left(\alpha_4 - \mu_V\right) V + \alpha_5 \left(I_1 + I_2\right)\right)$$

Then, $\frac{dL_H}{dt} = B - \mu L_H - \left(\alpha_2 + \mu_d\right) I_1 - \left(\alpha_3 + \tau\mu_d\right) I_2 \le B - \mu L_H \le 0$, for $L_H \ge \frac{B}{\mu}$. (4)

$$\frac{dL_V}{dt} = \left(\alpha_4 - \mu_V\right) L_V + \alpha_5 \left(I_1 + I_2\right) \le \left(\alpha_4 - \mu_V\right) L_V + \alpha_5 L_H \le 0, \qquad (5)$$

when $L_V \ge \frac{\alpha_5 B}{\mu\left(\mu_V - \alpha_4\right)}$ for $L_H \ge \frac{B}{\mu}$ and $\mu_V > \alpha_4$.

From equation(4) and (5), we have establishing that Ω is a positively invariant set.

$\frac{dL_H}{dt} \le B - \mu L_H$ gives $L_H(t) = \frac{B}{\mu} + L_H(0) e^{-\mu t}$ and $\frac{dL_V}{dt} \le \left(\alpha_4 - \mu_V\right) L_V + \alpha_5 L_H$ gives

$L_V(t) = \frac{\alpha_5 B}{\mu\left(\mu_V - \alpha_4\right)} + L_V(0) e^{-\left(\alpha_4 - \mu_V\right)t}$, where, $L_H(0)$ and $L_V(0)$ are the initial conditions of $L_H(t)$ and $L_V(t)$ respectively. As $t \to \infty$, $0 \le \left(L_H(t), L_V(t)\right) \le \left(\frac{B}{\mu}, \frac{\alpha_5 B}{\mu\left(\mu_d - \alpha_4\right)}\right)$ and hence ϕ is an attractive set.

2.1 Local stability of the disease-free equilibrium

The disease-free equilibrium of the system (2) is

$$X_0 = \left(S_{1_0}, S_{2_0}, I_{1_0}, I_{2_0}, V_0\right) = \left(\frac{pB}{\mu + \alpha_1}, \frac{B\left(\alpha_1 + \left(1-p\right)\mu\right)}{\mu\left(\mu + \alpha_1\right)}, 0, 0, 0\right). \qquad (6)$$

The local stability of X_0 is govern by the threshold (Hethcote, 2000). We will use next generation matrix to establish the stability of equilibrium (Diekmann et al., 1990; Driessche and Watmough, 2002).

The matrix of the new infections F and the matrix of transmission V are given by

$$F=\begin{bmatrix} 0 & 0 & \dfrac{epB}{K(\mu+\alpha_1)} \\ 0 & 0 & \dfrac{e\phi B(\alpha_1+(1-p)\mu)}{K\mu(\mu+\alpha_1)} \\ 0 & 0 & 0 \end{bmatrix} \text{ and } V=\begin{bmatrix} \mu+\mu_d+\alpha_2 & 0 & 0 \\ 0 & \mu+\tau\mu_d+\alpha_3 & 0 \\ -\alpha_5 & -\alpha_5 & \mu_V-\alpha_4 \end{bmatrix} \quad (7)$$

and $R_0=\rho(FV^{-1})=\dfrac{e\alpha_5\left((\mu+\tau\mu_d+\alpha_3)S_{1_0}+\theta(\mu+\mu_d+\alpha_2)S_{2_0}\right)}{K(\mu_V-\alpha_4)(\mu+\mu_d+\alpha_2)(\mu+\tau\mu_d+\alpha_3)}$, with $\mu_V>\alpha_4$.

Theorem 2.1.1: The disease-free equilibrium of (2) is locally asymptotically stable if $R_0<1$ and unstable if $R_0>1$.

Proof: R_0 denotes the average number of new infections generated by a single infected individual is a susceptible population. Thus, theorem 2 implies that swine-flu can be eliminated from the population (when $R_0<1$) if the initial sizes of the sub-populations of the model are in basin of attraction of the disease-free equilibrium. To ensure that elimination of the vector is independent of the initial sizes of the sub-populations, it is necessary to show that the disease-free equilibrium is globally asymptotically stable.

2.2 Global stability of the disease-free equilibrium

Theorem 2.2.1: If $R_0<1$, the disease-free equilibrium is globally asymptotically stable and unstable if $R_0>1$.

Proof: The comparison theorem is used to prove this result.

The rate of change of variables governing the infected compartments of system (2) are rewritten as,

$$\begin{bmatrix} \dfrac{dI_1(t)}{dt} \\ \dfrac{dI_2(t)}{dt} \\ \dfrac{dV}{dt} \end{bmatrix}=(F-V)\begin{bmatrix} I_1 \\ I_2 \\ V \end{bmatrix}-\begin{bmatrix} eV\left(\dfrac{pB}{K(\mu+\alpha_1)}-\dfrac{S_1}{K+V}\right) \\ \theta eV\left(\dfrac{B(\alpha_1+(1-p)\mu)}{\mu K(\mu+\alpha_1)}-\dfrac{S_2}{K+V}\right) \\ 0 \end{bmatrix}$$

where F and V are as defined in (7).

Since $S_1\le\dfrac{pB}{\mu+\alpha_1}$, we have $\dfrac{S_1}{K+V}\le\dfrac{pB}{\mu+\alpha_1}$ for all $t\ge0$ in Ω. Also, $S_2\le\dfrac{B(\alpha_1+(1-p)\mu)}{\mu(\mu+\alpha_1)}$ then $\dfrac{S_2}{k+V}\le\dfrac{B(\alpha_1+(1-p)\mu)}{\mu(\mu+\alpha_1)}$.

Thus, $$\begin{bmatrix} \dfrac{dI_1(t)}{dt} \\ \dfrac{dI_2(t)}{dt} \\ \dfrac{dV}{dt} \end{bmatrix}\le(F-V)\begin{bmatrix} I_1 \\ I_2 \\ V \end{bmatrix} \quad (8)$$

Given that all the eigenvalues of the matrix $F-V$ have negative real parts, (8) holds for $R_0<1$. This implies that as $t\to\infty$, $(I_1,I_2,V)\to0$. By the comparison theorem, it follows that $(I_1,I_2,V)\to(0,0,0)$ and hence $S_{1_0}\to\dfrac{pB}{\mu+\alpha_1}$ and $S_{2_0}\to\dfrac{B(\alpha_1+(1-p)\mu)}{\mu(\mu+\alpha_1)}$ for $R_0<1$. So X_0 is globally asymptotically stable.

2.3 Endemic Equilibrium (EE)

The EE is given by $X^* = \left(S_1^*, S_2^*, I_1^*, I_2^*, V^*\right)$

where, $S_1^* = \dfrac{pB}{\lambda^* + \alpha_1 + \mu}$, $S_2^* = \dfrac{\left(\alpha_1 + (1-p)\left(\mu + \lambda^*\right)\right)B}{\left(\delta + \mu + \lambda^*\right)\left(\mu + \theta\lambda^*\right)}$, $I_1^* = \dfrac{pB\lambda^*}{\left(\alpha_1 + \mu + \lambda^*\right)\left(\mu + \mu_d + \alpha_2\right)}$,

$I_1^* = \dfrac{\theta B\lambda^*\left(\alpha_1 + (1-p)\right)\left(\mu + \lambda^*\right)}{\left(\alpha_1 + \mu + \lambda^*\right)\left(\mu + \theta\lambda^*\right)\left(\mu + \tau\mu_d + \alpha_3\right)}$ and $V^* = \dfrac{\sigma}{\mu_V - \alpha_4}\left(I_1^* + I_2^*\right)$ with $\lambda^* = \dfrac{eV^*}{K + V^*}$.

To investigate the local asymptotic stability of EE, we will use centre manifold theory (J. Carr, 1981).

Write $S_1 = x_1$, $S_2 = x_2$, $I_1 = x_3$, $I_2 = x_4$ and $V = x_5$. So, vector notation is $X = \left(x_1, x_2, x_3, x_4, x_5\right)^T$.

The system takes the form $\dfrac{dX}{dt} = F = \left(f_1, f_2, f_3, f_4, f_5\right)^T$ such that $\lambda = \dfrac{ex_5}{K + x_5}$ and

$$
\begin{aligned}
x_1'(t) &= f_1 = pB - \lambda x_1 - \mu x_1 \\
x_2'(t) &= f_2 = (1-p)B + \alpha_1 x_1 - \theta\lambda x_2 - \mu x_2 \\
x_3'(t) &= f_3 = \lambda x_1 - \left(\alpha_2 + \mu + \mu_d\right)x_3 \\
x_4'(t) &= f_4 = \theta\lambda x_2 - \left(\alpha_3 + \mu + \tau\mu_d\right)x_4 \\
x_5'(t) &= f_5 = \alpha_4 x_5 + \alpha_5\left(x_3 + x_4\right) - \mu_V x_5
\end{aligned}
\tag{9}
$$

The Jacobian matrix of system (9) is given by

$$
J\left(X_0\right) = \begin{bmatrix}
-\mu - \alpha_1 & 0 & 0 & 0 & 0 \\
\alpha_1 & \mu & 0 & 0 & 0 \\
0 & 0 & -\alpha_2 - \mu - \mu_d & 0 & 0 \\
0 & 0 & 0 & -\alpha_3 - \mu - \tau\mu_d & 0 \\
0 & 0 & 0 & 0 & \alpha_4 - \mu_V
\end{bmatrix}
$$

Let us consider e as a bifurcation parameter and $R_0 = 1$, then

$$
e = e^* = \frac{\mu K\left(\mu_V - \alpha_4\right)\left(\mu + \alpha_1\right)\left(\mu + \mu_d + \alpha_2\right)\left(\mu + \tau\mu_d + \alpha_3\right)}{\alpha_5 BQ}
$$

where, $Q = \theta\left(\left(\alpha_1 + \mu(1-p)\right)\left(\mu + \mu_d + \alpha_2\right) + \mu p\left(\mu + \tau\mu_d + \alpha_3\right)\right)$.

Then the linearized system of transformed equations (10) with $e = e^*$ has a simple zero eigenvalue. Hence, the centre manifold theory can be used to study the dynamics of (10) near $e = e^*$ (Castillo-Chavez & Song, 2004). The Jacobian at $e = e^*$ has a right eigenvector $u = \left(u_1, u_2, u_3, u_4, u_5\right)^T$ associated with the zero eigenvalue as

$u_1 = \dfrac{e^* pB}{K\left(\mu + \alpha_1\right)^2}u_5$, $u_2 = \dfrac{-e^* pB}{K\mu\left(\mu + \alpha_1\right)}\left(\dfrac{\alpha_1}{\left(\mu + \alpha_1\right)} + \dfrac{\theta\left(\alpha_1 + \mu(1-p)\right)}{\mu}\right)u_5$,

$u_3 = \dfrac{e^* pB}{K\mu\left(\mu + \mu_d + \alpha_2\right)}u_5$, $u_4 = \dfrac{e^*\theta B\left(\alpha_1 + \mu(1-p)\right)}{K\mu\left(\mu + \delta\right)\left(\mu + \tau\mu_d + \alpha_3\right)}u_5$ and $u_5 = u_5 > 0$.

The left eigenvector of $J(X_0)$ associated with the zero eigenvalue at $e = e^*$ is $v = \left(v_1, v_2, v_3, v_4, v_5\right)^T$ where,

$v_1 = 0$, $v_2 = 0$, $v_3 = \dfrac{\alpha_5 v_5}{\left(\mu + \mu_d + \alpha_2\right)}$, $v_4 = \dfrac{\alpha_5 v_5}{\left(\mu + \mu_d + \alpha_3\right)}$ and $v_5 = v_5 > 0$.

For existence of a bifurcation, consider system of ordinary differential equations with a parameter ψ,

$$
\frac{dX}{dt} = f\left(X, \psi\right),\ f : \mathbb{R}^n \times \mathbb{R} \text{ and } f \in \mathbb{C}^2\left(\mathbb{R}^n \times \mathbb{R}\right) \tag{10}
$$

where 0 is an equilibrium of the system. i.e. $f\left(0, \psi\right) = 0$ for all ψ and we assume

- A1: $A = D_X f\left(0,0\right) = \left(\dfrac{\partial f_i\left(0,0\right)}{\partial X_j}\right)$ is the linearization of (10) around the equilibrium 0 with ψ evaluated at zero. Zero is a simple eigenvalue of A and all the other eigenvalues have negative real parts.

- A2: Matrix A has a right eigenvector u and a left eigenvector v corresponding to the zero eigenvalue.

Let f_k be the k^{th} - component of f and

$$a = \sum_{k,i,j=1}^{n} v_k u_i u_j \frac{\partial^2 f_k(0,0)}{\partial x_i \partial x_j},\ b = \sum_{k,i=1}^{n} v_k u_i \frac{\partial^2 f_k(0,0)}{\partial x_i \partial \psi} \tag{11}$$

The local dynamics of (15) around zero is determined by a and b.

(i) $a > 0, b > 0$. When $\psi < 0$ with $|\psi| \le 1$, 0 is locally asymptotically stable, and there exist a positive unstable equilibrium, when $0 < \psi \le 1$, 0 is unstable and there exists a negative and locally asymptotically stable equilibrium.

(ii) $a < 0,\ b < 0$. When $\psi < 0$ with $|\psi| \le 1$, 0 is unstable, when $0 < \psi \le 1$, it is asymptotically stable, and there exist a positive unstable equilibrium.

(iii) $a > 0,\ b < 0$. When $\psi < 0$ with $|\psi| \le 1$, 0 is unstable, and there exist a locally asymptotically stable negative equilibrium. When $0 < \psi \le 1$, 0 is stable and a positive unstable equilibrium exists.

(iv) $a < 0,\ b > 0$. When ψ changes from negative to positive, 0 changes its stability from stable to unstable. Hence, a negative equilibrium becomes positive and locally asymptotically stable.

Computations of a and b:

The associated non-zero partial derivatives of F at disease-free equilibrium point are given by

$$\frac{\partial^2 f_1}{\partial x_1 \partial x_5} = -\frac{e^*}{K} = \frac{\partial^2 f_1}{\partial x_5 \partial x_1},\ \frac{\partial^2 f_1}{\partial x_5^2} = -\frac{2e^* pB}{K^2(\alpha_1 + \mu)},\ \frac{\partial^2 f_2}{\partial x_5 \partial x_2} = -\frac{\theta e^*}{K} = \frac{\partial^2 f_2}{\partial x_2 \partial x_5}$$

$$\frac{\partial^2 f_2}{\partial x_5^2} = \frac{2\theta e^* B(\alpha_1 + \mu(1-p))}{K^2 \mu(\alpha_1 + \mu)},\ \frac{\partial^2 f_3}{\partial x_1 \partial x_5} = \frac{e^*}{K} = \frac{\partial^2 f_3}{\partial x_5 \partial x_1},\ \frac{\partial^2 f_3}{\partial x_5^2} = -\frac{2e^* pB}{K^2(\alpha_1 + \mu)},$$

$$\frac{\partial^2 f_4}{\partial x_2 \partial x_5} = \frac{\theta e^*}{K} = \frac{\partial^2 f_4}{\partial x_5 \partial x_2} \text{ and } \frac{\partial^2 f_4}{\partial x_5^2} = -\frac{2\theta e^* B(\alpha_1 + \mu(1-p))}{K^2 \mu(\alpha_1 + \mu)} \tag{12}$$

Now,

$$\begin{aligned} a &= \sum_{k,i,j=1}^{5} v_k u_i u_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(X_0) = \sum_{i,j=1}^{5} v_3 u_i u_j \frac{\partial^2 f_3}{\partial x_i \partial x_j}(X_0) + \sum_{i,j=1}^{5} v_4 u_i u_j \frac{\partial^2 f_4}{\partial x_i \partial x_j}(X_0) \\ &= \frac{-2e^* u_5}{K}\left[v_3 \left(\frac{epBu_5}{K(\alpha_1 + \mu)^2} + \frac{pBu_5}{K(\alpha_1 + \mu)} \right) \right. \\ &\quad \left. -\theta v_4 \left(\frac{epBu_5}{K\mu(\alpha_1 + \mu)} \left\{ \frac{\alpha_1}{(\alpha_1 + \mu)} + \frac{\theta(\alpha_1 + \mu(1-p))}{\mu} \right\} + \frac{u_5 B(\alpha_1 + \mu(1-p))}{K\mu(\alpha_1 + \mu)} \right) \right] < 0 \end{aligned} \tag{13}$$

As regards the sign of b, it is associated with the following non-vanishing partial derivatives of F:

$$\frac{\partial^2 f_1}{\partial x_5 \partial e^*} = \frac{-pB}{K(\alpha_1 + \mu)},\ \frac{\partial^2 f_2}{\partial x_5 \partial e^*} = -\frac{\theta B(\alpha_1 + \mu(1-p))}{K\mu(\alpha_1 + \mu)},$$

$$\frac{\partial^2 f_3}{\partial x_5 \partial e^*} = \frac{pB}{K(\alpha_1 + \mu)} \text{ and } \frac{\partial^2 f_4}{\partial x_5 \partial e^*} = \frac{\theta B(\alpha_1 + \mu(1-p))}{K\mu(\alpha_1 + \mu)}$$

From (19), $b = \sum_{k,i=1}^{5} v_k u_i \frac{\partial^2 f_k}{\partial x_i \partial e^*}(0,0) = v_3 u_5 \frac{\partial^2 f_3}{\partial x_5 \partial e^*} + v_4 u_5 \frac{\partial^2 f_4}{\partial x_5 \partial e^*}$

$$= \frac{Bu_5}{K(\alpha_1 + \mu)}\left[pv_3 + \frac{\theta v_4(\alpha_1 + \mu(1-p))}{\mu} \right] > 0 \tag{14}$$

(iv) reveals that swine-flu model undergoes a trans-critical bifurcation at $R_0 = 1$ whenever (13) and (14) holds.

2.4 Global stability of Endemic equilibrium point

Theorem 2.4.1: The disease free equilibrium point E^* is globally asymptotically stable.

Proof: let consider a Lyapunov function L, given by $L = w_1 S_1 + w_2 S_2 + w_3 I_1 + w_4 I_2 + w_5 V$.

$$L' = B\left(w_1 p + (1-p)w_2\right) + \frac{eVS_1}{K+V}\left(w_3 - w_1\right) + \frac{\theta eVS_2}{K+V}\left(w_4 - w_2\right) + \alpha_1 S_1\left(w_2 - w_1\right) - \mu S_1 w_1 - \mu S_2 w_2$$
$$I_1\left(w_5\alpha_5 - w_3(\alpha_2 + \mu + \mu_d)\right) + I_2\left(w_5\alpha_5 - w_4(\alpha_3 + \mu + \tau\mu_d)\right) + Vw_5\left(\alpha_4 - \mu_V\right)$$

By assuming $w_5 = \frac{1}{\alpha_5}$, $w_3 = w_4 = \frac{1}{\mu}$ and $w_2 = w_1 = \frac{1}{\tau\mu_d}$, we get

$$= \frac{B}{\tau\mu_d} + \frac{eVS_1}{K+V}\left(\frac{1}{\mu} - \frac{1}{\tau\mu_d}\right) + \frac{\theta eVS_2}{K+V}\left(\frac{1}{\mu} - \frac{1}{\tau\mu_d}\right) - \frac{\mu}{\tau\mu_d}\left(S_1 + S_2\right) - \frac{I_1}{\mu}(\alpha_2 + \mu_d) - \frac{I_2}{\mu}(\alpha_3 + \tau\mu_d)$$
$$+ \frac{V}{\alpha_5}\left(\alpha_4 - \mu_V\right)$$

Since $\tau\mu_d < \mu$ and $\alpha_4 < \mu_V$, $L \le 0$ and hence the endemic equilibrium point is globally asymptotically stable.

III. SENSITIVE ANALYSIS

Mathematical models are characterized by a certain degree of uncertainty, as a result of uncertainty in modeled developments and observation errors, or the structural and numerical errors of the mathematical model. Sensitivity analysis is the study of how the uncertainty in the output of a model can be apportioned to different sources of uncertainty in the model input. It is based on estimating the fractional contribution of each input factor to the variance of the model output, also accounting for interaction terms (Saltelli, (2002)). In determining how best to reduce human mortality and morbidity due to swine-flu, it is necessary to know the relative importance of the different factors responsible for its transmission and prevalence. We calculate the sensitivity indices of the reproductive number, to the parameters used in the model. These indices tell us how crucial each parameter is to disease transmission and prevalence (Chitniset al.,2008).

In Table 1, the intensity of variations in basic reproductive number with respect to the respective parameters and its reflections and observations, where positive (negative) sign of value indicates increment (decrement) in transmission is presented. The parameters are ordered from most sensitive to least. In both cases, of high and low transmission, the most sensitive parameter is the natural death rate, μ_V of vector and the least sensitive parameter is α_1.

Parameters	**Sensitivity of R_0**	**Observations**
μ_V	-2	Spread of influenza virus has a very high influence on human life and mortality rate and it can be controlled or enhanced by regulating the factors related to spread of the infection.
B, e, α_4, α_5	1	Transmission of swine-flu is directly affected by birth rate of population (B), rate of vector bite per unit time (e), growth rate of vector population (α_4) and rate at which infected individual affects vector population (α_5) at the same rate.
K	-1	Minimization of transmission of swine-flu helps to control overall mortality rate, which results in significant growth in concentration of vector population.
θ	0.983861	Immunity helps to revive the disease spread.
α_3	-0.829762	Rate at which infected non-vaccinated individuals are getting recovered is one of the affective aspects to control the spread of swine-flu.
μ_d	-0.076273	By controlling transmission of virus, death rate due to swine influenza virus is reduced.
τ	-0.071122	Increase death rate in the non-vaccinated swine-flu infected class is given by τ, which is inversely proportional to the transmission rate of swine-flu.
α_2	-0.008584	Outbreak can be controlled at minor rate by paying attention on recovering infected vaccinated individuals.
p	0.005172	More fraction of population needs to be vaccinated to reduce transmission of swine-flu.
α_1	-0.004887	Vaccination is an effective step to reduce the disease spread.

Table 1: Sensitive analysis of swine-flu model

IV. NUMERICAL SIMULATION

To study the dynamical behaviour of model (2), numerical simulation of the model is carried out by integration set of equations by Runge-Kutta method.

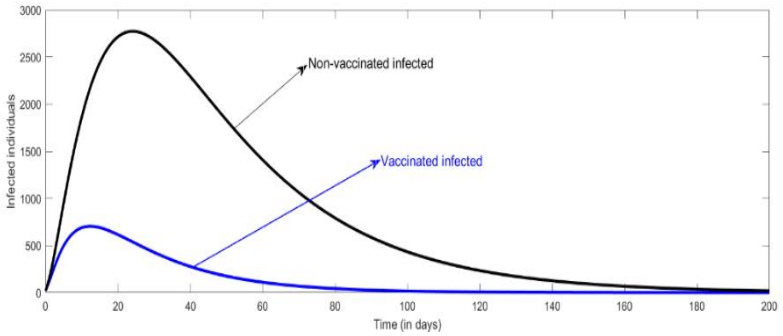


Figure 1. Class of vaccinated and non-vaccinated infected at time t

Effect of vaccination on infected individual is graphically observed in Figure 1. Almost 25% population of infected non-vaccinated is equal to total population of infected vaccinated individuals that indicates, vaccinated individuals have comparatively higher immunity towards swine-flu virus. Further similar analysis is done for different values in some significant epidemiological parameters like α_1, θ and τ.

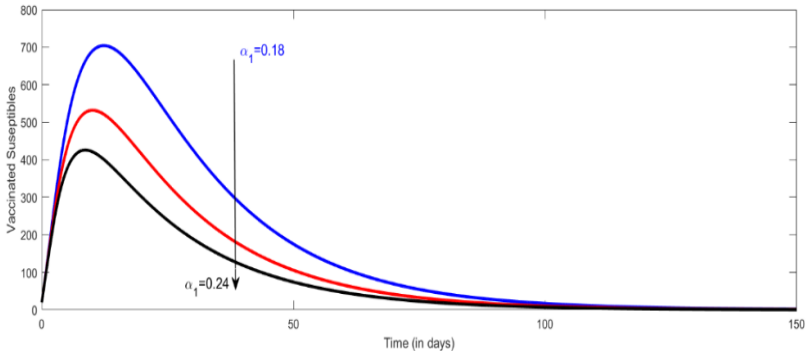


Figure 2. Variation in class of vaccinated susceptible for different inflow rates of α_1

In figure 2, simulation results showing that susceptibility of vaccination is continuously decreasing with increase in the value of alpha1 from 0.18 to 0.24.

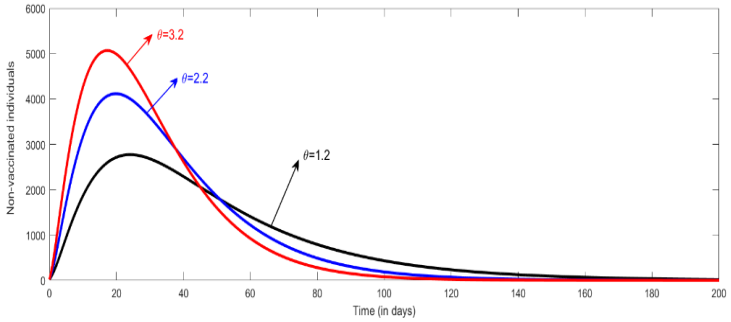


Figure 3. Variation in class of non-vaccinated susceptible for different inflow rates of θ.

Figure illustrate that immunity of vaccinated individuals is continuously increasing but at the same time non-vaccinated individuals' immunity is decreasing at a higher rate. It is observed that initially non-vaccinated class gives maximum value for higher rate of theta but after approximate 45-50 days case is different, that is more population is diverge towards infected class which concludes that lower value of θ is beneficial.

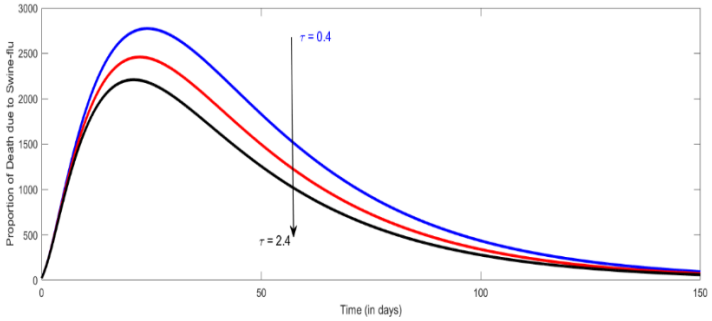
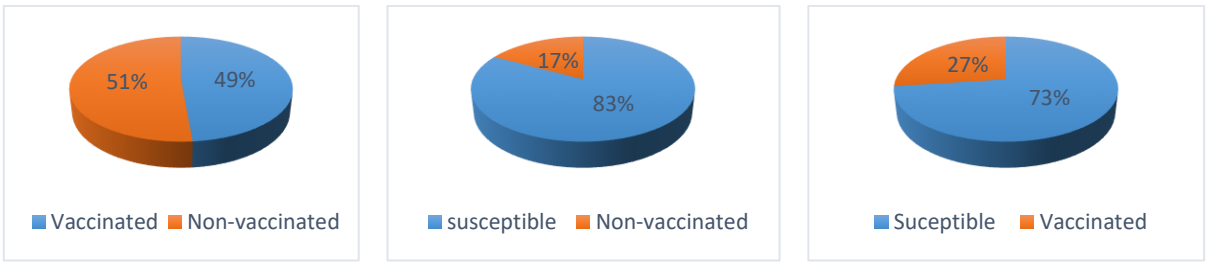


Figure 4. Variation in mortality rate due to swine-flu for different inflow rates of τ

Ratio of mortality rate due to swine-flu in non-vaccinated to vaccinated individuals is represented by τ. $\tau = 1$, when mortality is equal in both cases. The value of τ also depends on quality of vaccine, as it can trigger rare but serious reactions among people with no apparent allergies or sensitivities. It may also happen that people get reaction in long-term due to improper vaccination and increase mortality rate, in that case value of τ is from $(0,1)$, which is a very rare situation. In normal cases, vaccination gives positive response hence $\tau > 1$, and when it is not effective $\tau = 1$. Figure 4 depicts that overall mortality due to infection is minimised by increasing the value of τ at some point. We can also improve the value of τ by improving quality and quantity of vaccine and also make it publically available.



(a) (b) (c)

Figure 5. Impact of vaccination on human health

World-wide, only 49% population is vaccinated. Figure 5(b, c) shows that 83% population of non-vaccinated are getting affected by swine-flu virus while in the case of vaccinated class, 73% is getting affected by the virus and the effectiveness of influenza vaccination to prevent disease or death among the total population for influenza is 27%. The infection can be reduced up to 10% by making people aware of swine flu vaccines.

V. CONCLUSION

In the present work, a transmission of swine-flu in vaccinated and non-vaccinated class is studied using dynamical system of differential equations formed using mathematical modeling. Local and global stability of system is proved using different methods like central manifold theory and Lyapunov function. With the help of sensitive analysis, we come to know the factors or parameters which are most effective in transmission of swine-flu. Moreover effect of each parameter is also analyzed in this section. Amongst the practically controllable and most sensitive parameters are the rate of vector bite per unit time (e), the rate at which infected individual affects vector population (α_5), immunity (θ), and the rate at which infected non-vaccinated individuals are getting recovered (α_3). So, by possibly controlling or improving on these factors we can certainly improve the present situation and definitely control the spread of swine-flu at a certain level. Numerical simulation shows the relationship between parameters and compartmental variables and also gives its graphical visualization. This further suggests that vaccination is an effective step to reduce the disease spread. Whereas the infection can be controlled up to 10% by making people aware of anti-influenza vaccines and improving quality and availability of vaccine. Thus, from the present study, we can conclude that vaccination issues should be more addressed in impoverished communities affected with swine-flu in order to reduce the encumbrance of the disease. This analysis would be helpful to the governmental health department in improving the conditions during the outbreak.

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