MSC 92B05 DOI: 10.14529/mmp200207

MODELLING THE HUMAN PAPILLOMA VIRUS TRANSMISSION IN A BISEXUALLY ACTIVE HOST COMMUNITY

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In this article, we construct a mathematical model describing the transmission dynamics of Human Papilloma Virus (HPV) in a bisexually active host community. Comprehensive mathematical techniques are used to qualitatively and quantitatively analyze the model. We analyze the local and global stabilities of the model's equilibria and show that if the basic reproduction number is less than unity, then the model is locally and globally asymptotically stable at the HPV-free static states. Also, if the basic reproduction number is less than unity, then the HPV-endemic static state is globally asymptotically stable. Numerical simulations are carried out and graphical illustrations are presented to validate the theoretical results.

Keywords: HPV; basic reproduction number; local stability; global stability.

Introduction

Human papilloma virus (HPV) is a viral infection of the genitals of sexually active male and female. Penetrative sex and skin to skin genital contact serves as the mode of transmission of this disease. HPV have been known to be the cause of cervical cancer in women, and other types of HPV causes cancer of the anus, vulva, vagina, penis and genital warts, respiratory human papillomatosis [1]. According to the Center for Disease Control (CDC) [2], 79 million Americans are infected in their early $20s$. HPV is prevented by taking appropriate vaccines, surgical removal, sexual abstinence and condom usage, respectively [3]. Mathematical models are important tools used in exploring epidemic breakout and health consequences of interventions in human and environmental host populations with time [4–6]. S.L. Lee and A.M. Tameru [7] worked on mathematical model of HPV in United States of America with its special impact on cervical cancer. Also, E.J. Dasbach, E.H. Elbasha and R.P. Insinga [8] discussed the epidemiologic and economic impact of vaccination against HPV. Recently published works of A. Omame, R.A. Umana, D. Okounghae [9], A.E. Sado [10], N. Ziyadi [11], M. Dyser, P. E. Granitt, E.R. Myers [12], H.F. Brower [13], O. Sharomi, T. Malik [14], E.H. Elbasha [15], proved effective to this study. Having consulted the aforementioned literature, this work extends the existing HPV models by considering the infectious transmission of HPV in an active bisexually intimate human host community, see [16, 17]. The paper is organized as follows. Section 1 discusses the model formulation, mathematical analysis and the basic reproduction number. Section 2 involves the local and global analysis of the model at the HPV-free steady-state solutions. Finally, Section 3 uses mathematical computational software MAPLE 18 for numerical simulation of the theoretical results with the data available in recent literature.

1. Model Formulation

In this section, the model system of equations describing the transmission of HPV is based on the system of ordinary differential equations of the first order. The total bisexually

active human host is divided into sub-populations as follows. Let M_s be a number of sexually active males who are prone to acquiring HPV, M_i be a sub-population of sexually active males who are infected with HPV, F_s be a number of sexually active females who are prone to acquiring HPV, F_i be a number of sexually active HPV infected females, R_{mf} be a number of individuals recovered from HPV. The number of total bisexually active host population is denoted by

$$N_h = N_m.N_f = M_s + M_i + F_s + F_i + R_{mf}.$$

Sexually active males who are prone to acquiring HPV are recruited into the bisexual host population at the rate A_m. There is an effective infectious sexual intimacy between sexually active male individuals who are prone to acquiring HPV and sexually active infected males and females denoted by the quantity

$$\frac{\beta_1 M_s(M_i + F_i)}{N_h}, \tag{1}$$

where β_1 is the effective transmission rate. Also, μ denotes the natural mortality rate applied to all sub-population. The sub-population of sexually active infected male is increased by $\frac{\beta_1 M_s(M_i+M_f)}{N_h}$ and decreased by the quantity $\gamma_o M_i$, where γ_o denotes the progression rate of sexually active infected males to the recovered sub-population. Furthermore, the sub-population of sexually active females who are prone to acquiring HPV is recruited into the bisexual host population at the rate A_f, while there is an effective infectious sexual intimacy between sexually active female individuals who are prone to acquiring HPV and sexually active HPV infected male and female individuals given by the quantity

$$\frac{\beta_2 F_s(M_i + F_i)}{N_h}, \tag{2}$$

where β_2 is the transmission rate. The sub-population of infected sexually active females is increased by the quantity $\frac{\beta_2 F_s(M_i+F_i)}{N_h}$, and decreased by the quantity $\gamma_1 M_i$, where γ_1 denotes the progression rate of sexually active infected females to the recovered sub-population. Moreover, the quantities $\sigma_1 M_s$ and $\sigma_2 F_s$ increase the sub-population of sexually active male and female who are prone to acquiring HPV, where σ_1 and σ_2 denote the loss of immunity to HPV infection after recovery. The inclusion of the variables and parameters in combination with assumptions leads to the system of evolution equations that control the HPV transmission given by

$$\begin{aligned}
\dot{M}_s &= A_m - \frac{\beta_1 M_s(F_i + M_i)}{N_h} - \mu M_s + \sigma_1 M_s,\\
\dot{M}_i &= \frac{\beta_1 M_s(F_i + M_i)}{N_h} - (\mu + \gamma_o) M_s,\\
\dot{F}_s &= A_f - \frac{\beta_2 F_s(F_i + M_i)}{N_h} - \mu F_s + \sigma_2 F_s,\\
\dot{F}_i &= \frac{\beta_2 F_s(F_i + M_i)}{N_h} - \mu F_s + \sigma_2 F_s,\\
\dot{R_{mf}} &= \gamma_o M_i + \gamma_1 F_i - \mu R_{mf} - \sigma_1 M_s - \sigma_2 F_s,
\end{aligned} \tag{3}$$

under the initial conditions $M_s(t) \geq 0, M_i(t) \geq 0, F_s(t) \geq 0, F_i(t) \geq 0, R_{mf}(t) \geq 0$. Normalization of (3) such that $m_s = \frac{M_s}{N_h}, m_i = \frac{M_i}{N_h}, f_s = \frac{F_s}{N_h}, f_i = \frac{F_i}{N_h}, r_{mf} = \frac{R_{mf}}{N_h}$ leads to

$$\begin{aligned} \dot{m_s} &= A_m - \beta_1 m_s(f_i + m_i) - \mu m_s + \sigma_1 m_s, \\ \dot{m_i} &= \beta_1 m_s(f_i + m_i) - (\mu + \gamma_o) m_s, \\ \dot{f_s} &= A_f - \beta_2 f_s(f_i + m_i) - \mu f_s + \sigma_2 f_s, \\ \dot{f_s} &= \beta_2 f_s(f_i + m_i) - (\mu + \gamma_1) f_i, \\ \dot{r_{mf}} &= \gamma_o m_i + \gamma_1 f_i - \mu r_{mf} - \sigma_1 m_s - \sigma_2 f_s, \end{aligned} \tag{4}$$

under the initial conditions $m_s(t) \geq 0, m_i(t) \geq 0, f_s(t) \geq 0, f_i(t) \geq 0, r_{mf}(t) \geq 0$.

1.1. Well-Posedness and Boundedness of HPV Model System

The solutions of model system (4) with nonnegative initial conditions are bounded and remain nonnegative for time $t > 0$.

Theorem 1. *Let $m_s(t) \geq 0, m_i(t) \geq 0, f_s(t) \geq 0, f_i(t) \geq 0, r_{mf}(t) \geq 0$, then the solutions of model system (4) are positive for all $t \geq 0$. Also, the domain ζ is positively invariant such that all solutions begin and remain in ζ.*

Proof. We do not consider the fifth state equation in (4), since all the first four state equations depends on the fifth one. Add up the total human host population of bisexually active male and female individuals to obtain

$$\frac{dN_m}{dt} = A_m - \mu N_m. \tag{5}$$

Integrate both sides of (5):

$$\int_{N_m(t_o)}^{N_m} \frac{1}{A_m - \mu N_h} dN_m = \int_{t_o}^{t} dt, \tag{6}$$

and obtain

$$-\frac{1}{\mu} \ln(A_m - \mu N_m)\Big|_{N_m(t_o)}^{N_m} = t - t_o, \tag{7}$$

hence

$$-\frac{1}{\mu} \ln[(A_m - \mu N_m) - (A_m - \mu N_m(t_o))] = t - t_o, \tag{8}$$

$$\begin{aligned} \ln\Big[\frac{A_m - \mu N_m}{A_m - \mu N_m(t_o)}\Big] &= -\mu(t - t_o), \\ \Big[\frac{A_m - \mu N_m}{A_m - \mu N_m(t_o)}\Big] &= e^{-\mu(t-t_o)}, \\ (A_m - \mu N_m) &= (A_m - N_m(t_o))e^{-\mu(t-t_o)}, \\ N_m &= \frac{A_m}{\mu} - \frac{(A_m - N_m(t_o))e^{-\mu(t-t_o)}}{\mu}. \end{aligned} \tag{9}$$

Following the same procedure, addition of the bisexual female population leads to

$$N_f = \frac{A_f}{\mu_f} - \frac{(A_f - N(t_o))e^{-\mu_f(t-t_o)}}{\mu_f}. \tag{10}$$

The domain $\varsigma = \varsigma_1 \times \varsigma_2 \subset \mathrm{Re}\,{}^{2}_{+} \times \mathrm{Re}\,{}^{2}_{+}$ such that

$$\varsigma_1 = \Big[(m_s, m_i) \in \mathrm{Re}\,{}^{2}_{+} : m_s + m_i \leq \frac{A_m}{\mu}\Big] \tag{11}$$

and

$$\varsigma_2 = \Big[(f_s, f_i,) \in \mathrm{Re}\,{}^{2}_{+} : f_s + f_i \leq \frac{A_f}{\mu_f}\Big] \tag{12}$$

is positively invariant. It is enough to consider the dynamics of HPV model system (4) in ς. In this domain, the model is meaningful in the sense of HPV transmission and mathematically well-posed.

□

1.2. Steady-State Analysis

The steady-state analysis is performed on model system (4) to obtain the steady-state solutions in the absence and presence of HPV infections in the model. HPV-free steady-state solutions implies that $m_i = f_i = 0$, while it is necessary to know that the trivial steady-state does not exist as long as the recruitment terms A_m and A_f are presented. Hence, the HPV-free steady-state solutions are given by

$$E^o = (m_s, m_i, f_s, f_i, r_{mf}) = \Big(\frac{A_m}{\mu}, 0, \frac{A_f}{\mu_f}, 0, 0\Big). \tag{13}$$

Also, the HPV-endemic steady-state solutions are given by

$$\begin{gathered} E^* = (m_s^*, m_i^*, f_s^*, f_i^*) = \Big(\frac{A_m}{(m_i\beta_1 + f_i\beta_1 + \mu - \sigma_1)}, \\ \frac{-\beta_1 m_s f_i}{(m_s\beta_1 - \mu - \gamma_o)}, \frac{A_f}{(m_i\beta_2 + f_i\beta - \sigma_2 + \mu_f)}, \frac{\beta_2 f_s m_i}{(f_s\beta_2 - \gamma_1 - \mu_f)}\Big). \end{gathered} \tag{14}$$

1.3. Basic Reproduction Number of HPV Model System

Let $x = (x_1, ..., x_n)^T$ be a vector of the numbers of human individuals in each sub-population, $x_i \geq 0$, therefore the state of the model is bounded by the closed positive cone $x \in X = \mathrm{Re}\,{}_{n+}$. Assume that the sub-populations are constructed such that the first m sub-populations are associated with infected individuals. Then $X_s = \{x \in 0 | x_i = 0, i = 1, ..., m\}$, is the set of disease free steady states. The system of differential equations that control disease transmission is given on X such that

$$\dot{x} = f(x), \tag{15}$$

where the components of f are $f_i(x) = F_i(x).V_i(x)$ for $i = 1, ..., n$. Here $F_i(x)$ denotes the rate of appearance of clinical manifestations of symptoms in the i-th sub-population, while $V_i(x) = V_i^-(x) - V_i^+(x)$, where $V_i^+(x)$ is the rate of individuals moving into the i-th sub-population by all other means, and $V_i^-(x)$ is the rate of movement of individuals out of the i-th sub-population. Assume that each function is at least twice continuously differentiable in each variable. Other assumptions are stated below.

- If $x \geq 0$, then $F_i(x), V_i^+(x), V_i^-(x) \geq 0$ for $i = 1, ..., n$.
- If $x_i = 0$, then $V_i^-(x) = 0$. Therefore, if $x \in X_s$, then $V_i^-(x) = 0$ for $i = 1, ..., m$.
- $F_i(x) = 0$ if $i \geq m$.
- If $x \in X_s$, then $F_i(x) = 0$ and $V_i^+(x) = 0$ for $i = 1, ..., m$.

Note that the first two points together with the assumption on smoothness of the functions involved guarantee that the non-negative cone $(x_i \geq 0, i = 1, ..., n)$ is forward invariant and there exists a unique non-negative solution for each non-negative initial condition. Therefore, from model system (4),

$$F = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\beta_1 A_m}{\mu} & 0 & \frac{\beta_1 A_m}{\mu} & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\beta_2 A_f}{\mu} & 0 & \frac{\beta_2 A_f}{\mu} & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}, \quad V = \begin{bmatrix} \sigma_1 + \mu & 0 & 0 & 0 & 0 \\ 0 & \mu + \gamma_o & 0 & 0 & 0 \\ 0 & 0 & \sigma_2 + \mu_f & 0 & 0 \\ 0 & 0 & 0 & \mu_f + \gamma_1 & 0 \\ \sigma_1 & \gamma_o & \sigma_2 & \gamma_1 & \mu \end{bmatrix}, \quad (16)$$

such that

$$V^{-1} = \begin{bmatrix} (\sigma_1 + \mu)^{-1} & 0 & 0 & 0 & 0 \\ 0 & (\mu + \gamma_o)^{-1} & 0 & 0 & 0 \\ 0 & 0 & (\sigma_2 + \mu_f)^{-1} & 0 & 0 \\ 0 & 0 & 0 & (\mu_f + \gamma_1)^{-1} & 0 \\ -\frac{\sigma_1}{(\sigma_1+\mu)\mu} & -\frac{\gamma_o}{(\mu+\gamma_o)\mu} & -\frac{\sigma_2}{(\sigma_2+\mu_f)\mu} & -\frac{\gamma_1}{(\mu_f+\gamma_1)\mu} & \mu^{-1} \end{bmatrix} \quad (17)$$

and

$$FV^{-1} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\beta_1 A_m}{(\mu+\gamma_o)\mu} & 0 & \frac{\beta_1 A_m}{(\mu+\gamma_o)\mu} & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\beta_2 A_f}{(\mu_f+\gamma_1)\mu} & 0 & \frac{\beta_2 A_f}{(\mu_f+\gamma_1)\mu} & 0 \\ 0 & -\frac{\gamma_o \beta_1 A_m}{(\mu+\gamma_o)\mu^2} - \frac{\gamma_1 \beta_2 A_f}{(\mu_f+\gamma_1)\mu^2} & 0 & -\frac{\gamma_o \beta_1 A_m}{(\mu+\gamma_o)\mu^2} - \frac{\gamma_1 \beta_2 A_f}{(\mu_f+\gamma_1)\mu^2} & 0 \end{bmatrix}. \quad (18)$$

The largest eigenvalue of (18) is the basic reproduction number of model system (4) given by

$$R_*(FV^{-1}) = \frac{\gamma_o \beta_1 A_m / \gamma_1 \beta_2 A_f}{((\mu + \gamma_o)\mu^2)((\mu_f + \gamma_1)\mu^2)}. \quad (19)$$

2. Stability Analysis of HPV Model System

Theorem 2. *Let $\bar{0}$ be a critical point of $\bar{x} = f(\bar{x})$, L_y be positive definite function on the neighborhood U of $\bar{0}$.*

- *If* $\dot{L_y} \leq 0$ *for* $\bar{x} \in U - \{\bar{0}\} \Longrightarrow \bar{0}$ *is stable.*
- *If* $\dot{L_y} < 0$ *for* $\bar{x} \in U - \{\bar{0}\} \Longrightarrow \bar{0}$ *is asymptotically stable.*
- *If* $\dot{L_y} > 0$ *for* $\bar{x} \in U - \{\bar{0}\} \Longrightarrow \bar{0}$ *is unstable.*

L_y *is a Lyapunov function if* L_y *is positive definite and* $\dot{L_y} \leq 0$.

Theorem 3. *Let* L_y *be a* $C^1(R^n)$ *real valued function,* $U = \{\bar{x} \in \mathrm{Re}^{\,n} | L_y(\bar{x}) < k\}, k \in \mathrm{Re}$, *and* $\dot{L_y}(\bar{x}) \leq 0$. *If* P *is the largest invariant set in* $D = \left\{\bar{x} \in L_y | \dot{L_y}(\bar{x}) = 0\right\}$, *then the solution trajectories begin in* L_y *and remain there, for all time* $t > 0$.

2.1. Local Stability Analysis of HPV-Free Steady-State Solutions

Theorem 4. *The HPV-free steady-state of model system* (4) *is locally asymptotically stable whenever* $R_* < 1$.

Proof. The Jacobian matrix of model system (4) at HPV-free steady-state solutions (13) is given by

$$\begin{bmatrix} -\mu+\sigma_1 & -\frac{\beta_1 A_m}{\mu} & 0 & -\frac{\beta_1 A_m}{\mu} \\ 0 & -\mu-\gamma_o & 0 & \frac{\beta_1 A_m}{\mu} \\ 0 & -\frac{\beta_2 A_f}{\mu_f} & -\mu+\sigma_2 & -\frac{\beta_2 A_f}{\mu_f} \\ 0 & \frac{\beta_2 A_f}{\mu_f} & 0 & -\mu+\gamma_1 \end{bmatrix}. \tag{20}$$

The characteristics polynomial of (20) is given by

$$A_4\lambda^4 + A_3\lambda^3 + A_2\lambda^2 + A_1\lambda + A_0. \tag{21}$$

Let $G_1 = -\mu+\sigma_1, G_2 = -\mu-\gamma_o, G_3 = -\mu+\sigma_2, G_4 = -\mu+\gamma_1$, where

$$\begin{aligned} A_4 &= 1, \\ A_3 &= G_1 + G_2 + G_3 + G_4, \\ A_2 &= (G_1+G_2)(G_3+G_4) + G_1G_2 + G_3G_4, \\ A_1 &= (G_1+G_2)G_3G_4 + (G_3+G_4)G_1G_2, \\ A_0 &= G_1G_2G_3G_4 - R_*. \end{aligned} \tag{22}$$

Also, the determinant of (20) is given by

$$\frac{(\mu-\sigma_2)\left(\mu^3\mu_f - \mu_f(\gamma_1-\gamma_o)\mu^2 - \mu\gamma_1\gamma_o\mu_f - \beta_2A_f\beta_1A_m\right)(\mu-\sigma_1)}{\mu_f\mu} > 0,$$

while the trace

$$-4\mu + \sigma_1\gamma_o + \sigma_2 + \gamma_1 < 0.$$

The Routh–Hurwitz criteria states that all roots of characteristics polynomial (20) have negative real parts if and only if the coefficients A_i are positive and the Hurwitz matrices $H_i > 0$ for $i = 0, 1, 2, 3, 4$. From (22), it is easy to see that $A_1 > 0, A_2 > 0, A_3 > 0, A_4 > 0$,

since all G_i are positive. Moreover, if $R_* < 1$, then $A_0 > 0$. Construction of the positive Hurwitz matrices yields

$$H_1 = A_3 > 0, \quad H_2 = \begin{vmatrix} A_1 & A_4 \\ A_1 & A_2 \end{vmatrix} > 0,$$
$$H_3 = \begin{vmatrix} A_3 & A_4 & 0 \\ A_1 & A_2 & A_3 \\ 0 & A_0 & A_1 \end{vmatrix} > 0, \quad H_4 = \begin{vmatrix} A_3 & A_4 & 0 & 0 \\ A_1 & A_2 & A_3 & A_4 \\ 0 & A_0 & A_1 & A_2 \\ 0 & 0 & 0 & A_0 \end{vmatrix} > 0. \tag{23}$$

Therefore, all the eigenvalues of the Jacobian matrix $J(E^o)(20)$ have negative real parts if $R_* < 1$, this implies that the HPV-free steady-state is locally asymptotically stable. Moreover, if $R_* > 1$, then $A_0 < 0$. Applying the Descartes' rule of signs, we see that there is only one sign change in A_4, A_3, A_2, A_1, A_0, involving the coefficients of (20), which implies that there exists the unique eigenvalue with positive real part. Hence the HPV-free steady-state is unstable.

□

2.2. Global Stability Analysis of HPV-Free Steady-State Solutions

Theorem 5. *The HPV-free steady-state* (13) *of model system* (4) *is globally asymptotically stable whenever* $R_* < 1$.

Proof. Let $\{L_y : Q_+ \to \mathrm{Re}\,, \|Q_+ = \{(m_s, m_i, f_s, f_i) \in Q | m_s > 0, m_i > 0, f_s > 0, f_i > 0\}\}$, then

$$L_y(m_s, m_i, f_s, f_i) = L_y(m_i,\ f_i), \tag{24}$$

such that

$$\dot{L_y}(m_i, f_i) = \beta_1 m_s(f_i + m_i) - (\mu + \gamma_o)m_i + \beta_2 f_s(f_i + m_i) - (\mu + \gamma_1)f_i, \tag{25}$$

and

$$(\gamma_o + \mu)[R_* m_s - 1]m_i + (\gamma_1 + \mu_f)[R_* f_s - 1]f_i \leq 0 \tag{26}$$

for $R_* \leq 1$. Note that $R_* < 1 : \dot{L_y} = 0 \Leftrightarrow m_i = 0$ and $f_i = 0$, and $R_* = 1 : \dot{L_y} = 0 \Leftrightarrow m_s = 1$ and $f_s = 1$. It can be observed that all trajectories in Q_+ approach the HPV-free steady-state solutions E^o (13). Since the vector on the right hand side of model system (4) points to the interior of Q. Hence, the HPV-free steady-state of model system (4) is globally asymptotically stable.

□

2.3. Global Stability of HPV-Endemic Steady-State Solutions

Theorem 6. *If* $R_* > 1$, *then the unique HPV-endemic steady-state solution* E^* *of model system* (14) *is globally asymptotically stable in the interior of* ς.

Proof. Define the Lyapunov function $L_y : \{(m_s, m_i, f_s, f_i) \in \varsigma : m_s, m_i, f_s, f_i\} \Rightarrow \mathfrak{R}^4_+$ so that

$$L_y = \left(m_s - m_s^* - m_s^* \ln \frac{m_s}{m_s^*}\right) + \left(m_i - m_i^* - m_i^* \ln \frac{m_i}{m_i^*}\right) + \left(f_s - f_s^* - f_s^* \ln \frac{f_s}{f_s^*}\right) + \left(f_i - f_i^* - f_i^* \ln \frac{f_i}{f_i^*}\right)$$

differentiating L_y with model system (4) leads to

$$\dot{L}_y = \Big(1 - \frac{m_s^*}{m_s}\Big)\dot{m}_s + \Big(1 - \frac{m_i^*}{m_i}\Big)\dot{m}_i + \Big(1 - \frac{f_s^*}{f_s}\Big)\dot{f}_s + \Big(1 - \frac{f_i}{f_i}\Big)\dot{f}_i. \tag{27}$$

Lyapunov function (27) is continuous and positive definite for $m_s, m_i, f_s, f_i > 0$. It can be shown that $L_y(m_s, m_i, f_s, f_i) = 0$ at the HPV-endemic steady-state E^*, where the global minimum of $L_y(m_s, m_i, f_s, f_i)$ takes place at E^* of (14). At equilibrium, model system (4) yields

$$\begin{aligned} A_m &= \beta_1 m_s^*(f_i^* + m_i^*) + \mu m_s^* - \sigma_1 m_s^*, \\ (\mu + \gamma_o) &= \frac{\beta_1 m_s^*(f_i^* + m_i^*)}{m_i^*}, \\ A_f &= \beta_2 f_s^*(f_i^* + m_i^*) + \mu_f f_s^* - \sigma_2 f_s^*, \\ (\mu_f + \gamma_1) &= \frac{\beta_2 f_s^*(f_i^* + m_i^*)}{f_i^*}. \end{aligned} \tag{28}$$

Then the time derivative of $L_y(m_s, f_s, m_i, f_i)$ along the solutions of (27) is given by

$$\begin{aligned} \dot{L}_y = \Big(1 - \tfrac{m_s^*}{m_s}\Big)(A_m - \beta_1 m_s(f_i + m_i) - \mu m_s + \sigma_1) + \\ + \Big(1 - \tfrac{m_i^*}{m_i}\Big)(\beta_1 m_s(f_i + m_i) - (\mu + \gamma_o)m_s) + \Big(1 - \tfrac{f_s^*}{f_s}\Big)(A_f - \beta_2 f_s(f_i + m_i) - \\ - \mu f_s + \sigma_2 f_s) + \Big(1 - \tfrac{f_i}{f_i}\Big)(\beta_1 f_s(f_i + m_i) - (\mu + \gamma_1)f_i) + \sigma_1 m_s. \end{aligned} \tag{29}$$

Substituting (28) into (29), after further rearrangement and simplification we have

$$\begin{aligned} \left(1 - \frac{m_s^*}{m_s}\right)\dot{m}_s = (\sigma_1 - \mu)m_s^*\left(2 - \frac{m_s}{m_s^*} - \frac{m_s^*}{m_s}\right) + \\ + (m_s - m_s^*)\left[\left(\frac{m_s f_i}{m_s} + \frac{m_i m_s}{m_s} - \frac{m_s^* f_s^*}{m_s} - \frac{m_s^* m_s^*}{m_s}\right)\right] \end{aligned} \tag{30}$$

and

$$\left(1 - \frac{m_i^*}{m_i}\right)\dot{m}_i = (m_i - m_i^*)\Big[\beta_1\Big[\frac{m_s f_i}{m_i^*} + \frac{m_s m_i}{m_i^*} - \frac{m_s^* f_i^*}{m_i^* m_s^*} - \frac{m_s^* m_i^*}{m_i^* m_s^*}\Big]\Big]. \tag{31}$$

Also,

$$\begin{aligned} \left(1 - \frac{f_s^*}{f_s}\right)\dot{f}_s = (\sigma_2 - \mu)f_s^*\left(2 - \frac{f_s}{f_s^*} - \frac{f_s^*}{f_s}\right) + \\ + (f_s - f_s^*)\left[\left(\frac{f_s m_i}{f_s} + \frac{f_i f_s}{f_s} - \frac{f_s^* m_i^*}{f_s} - \frac{f_s^* f_s^*}{f_s}\right)\right] \end{aligned} \tag{32}$$

and

$$\left(1 - \frac{f_i^*}{f_i}\right)\dot{f}_i = (f_i - f_i^*)\Big[\beta_2\Big[\frac{f_s m_i}{f_i^* f_i} + \frac{f_s f_i}{f_i^* f_i} - \frac{f_s^* m_i^*}{f_i^* f_i} - \frac{f_s^* f_i^*}{f_i^* f_i}\Big]\Big]. \tag{33}$$

It is obvious that $\left(2 - \frac{m_s}{m_s^*} - \frac{m_s^*}{m_s}\right) \leq 0$ and $\left(2 - \frac{f_s}{f_s^*} - \frac{f_s^*}{f_s}\right) \leq 0$. Therefore, the largest compact invariant set in $\Big\{(m_s, m_i, f_s, f_i) \in \varsigma : \dot{L}_y(m_s, m_i, f_s, f_i) = 0\Big\}$ is the singleton set E^* of (14). By the Barbashin–Krasovskii–LaSalle principle [5], E^* is globally asymptotically stable in the interior of ς.

□

3. Numerical Simulations

The numerical simulations were carried out using the in-built fourth order Runge–Kutta method in MAPLE 18 computational software. Table gives the values of parameters obtained in the cited literature which are involved in the computation/simulation.

Also, Fig. 1 shows behavior of the sub-population of sexually active males who are prone to acquiring HPV overtime in the absence of health intervention strategies.

Fig. 2 describes behavior of sexually active males infected with HPV. As time increases, the sharp rise depicts that infected male individuals rise in the community in the absence of health intervention strategies. Fig. 3 displays behavior of the sub-population of sexually active females who are prone to acquiring HPV overtime in the absence of health intervention strategies. Fig. 4 shows behavior of sexually active females who are directly infected with HPV. Medical strategies should be adopted in order to minimize infection in this sub-population.

Table

Variables and Parameter Values of Model System (4)

Parameter	Values	Source
m_s	0,50	[13]
m_i	0,20	[13]
f_s	0,45	[11]
f_i	0,20	[11]
A_m	0,13	[9]
A_f	0,02	[9]
β_1	0,28	[9]
μ	0,12	[9]
σ_1	0,123	[9]
σ_2	0,142	[9]
β_2	0,011	[9]
γ_o	0,11	[9]
γ_1	0,000136	[9]

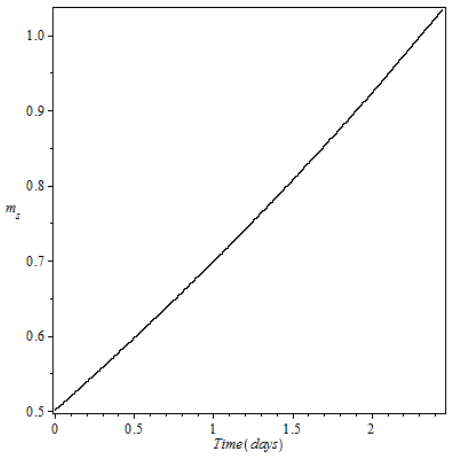

Fig. 1. Graph of sexually active males who are prone to acquiring HPV

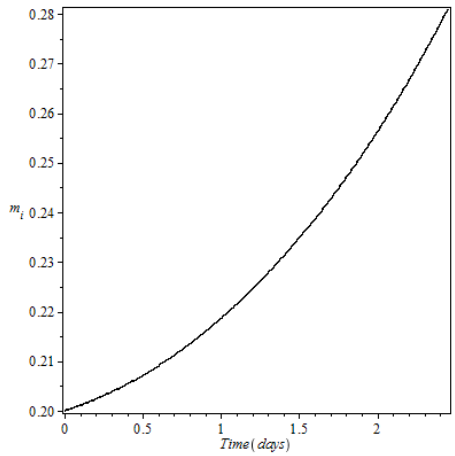

Fig. 2. Graph of sexually active males infected with HPV

In turn, Fig. 5 describes variation of the parameter σ_2 (0,900 – 0,930). As time increases, sexually active female individuals lose their immunity. Fig. 6 depicts behavior of the parameter β_1 (0,2 – 0,6). As time increases, effective infectious contact increases when there are no health intervention policies to stop HPV spread. Fig. 7 describes variation of the parameter σ_1 (0,89 – 0,93). As time increases, sexually active male individuals lose their immunity. Also, Fig. 8 depicts variation of the recovery rate γ_o (0,49 – 0,53). As time increases, sexually active infected males recover with compliance to health intervention strategies.

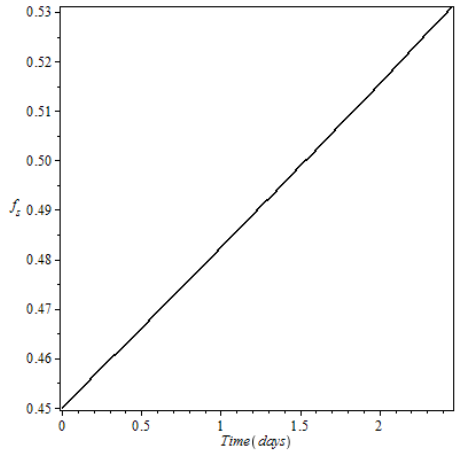

Fig. 3. Graph of sexually active infected females who are prone to acquiring HPV

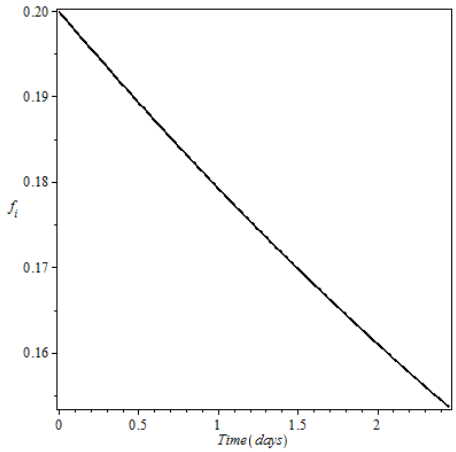

Fig. 4. Graph of sexually active females infected with HPV

Fig. 9 describes variation of A_f (0,4 – 0,6). As time increases, more sexually active males are recruited into host community of bisexuals. Fig. 10 describes the rate at which sexually active male individuals are recruited into the host population varying A_m (0,48 – 0,53) as time increases. Moreover, the effective infectious contact rate is displayed by varying β_2 (0,48 – 0,53) in Fig. 11, which shows that more individuals become infected as time increases.

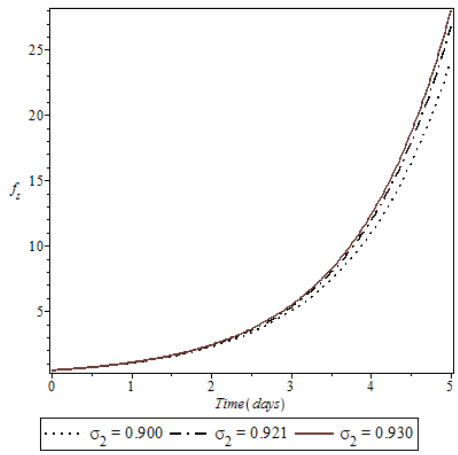

Fig. 5. Graph of variation of σ_2 (0,900 – 0,930) as time increases

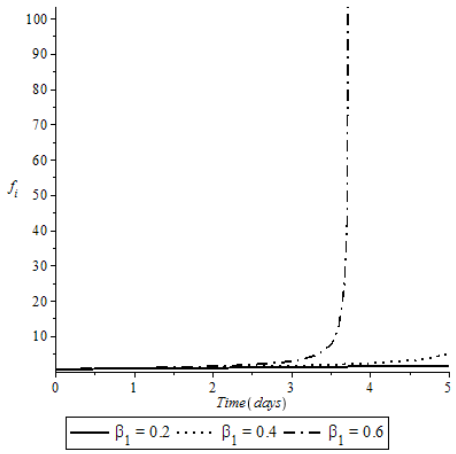

Fig. 6. Graph of variation of β_1 (0,2 – 0,6) as time increases

Finally, Fig. 12 depicts variation of γ_1 (0,4 – 0,6). The gradual decline shows that more sexually active infected females recover from HPV in active compliance to health intervention strategies.

Conclusion and Recommendations

The deterministic model of HPV transmission in a bisexually active human host population is considered. The model is analyzed in a feasible domain and shown to be positive, well-posed and realistic in the sense of HPV transmission. The basic reproduction number R_* is obtained and the stability of the model's steady-state solutions at the HPV-

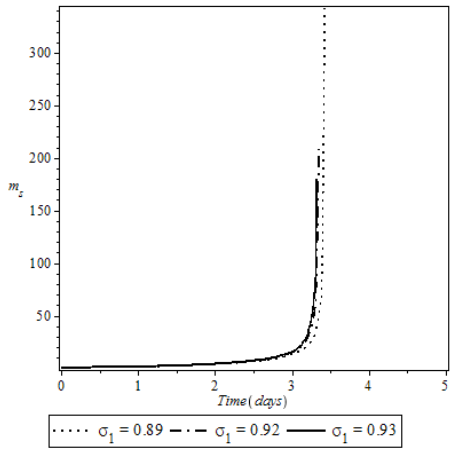

Fig. 7. Graph of variation of σ_1 (0,89 – 0,93) as time increases

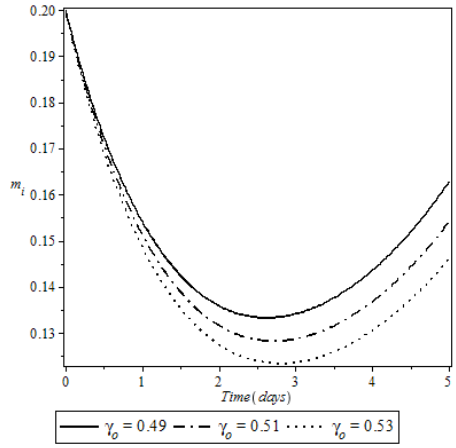

Fig. 8. Graph of variation of γ_o (0,49 – 0,53) as time increases

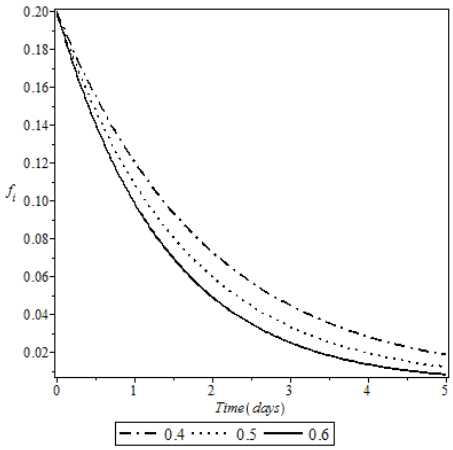

Fig. 9. Graph of variation of A_f (0,4–0,6) as time increases

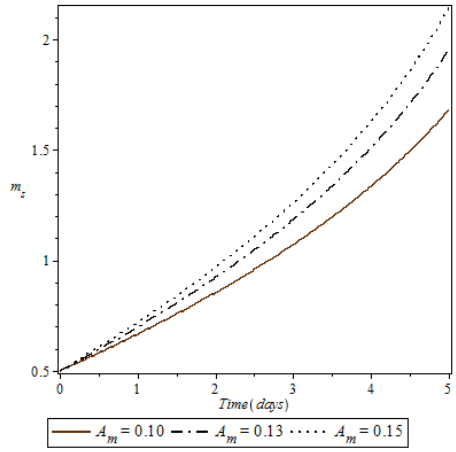

Fig. 10. Graph of variation of A_m (0,48–0,53) as time increases

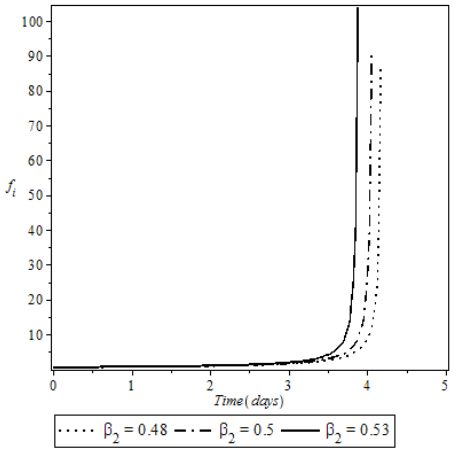

Fig. 11. Graph of the variation of β_2 (0,48–0,53) as time increases

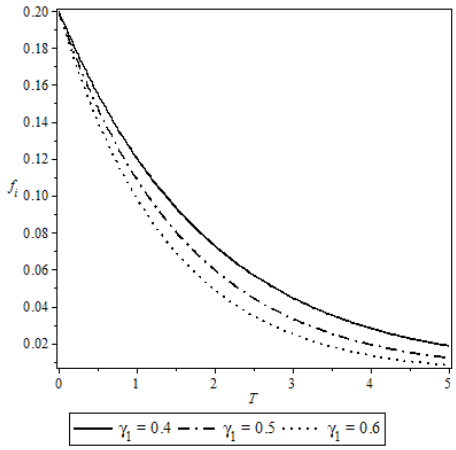

Fig. 12. Graph of variation of γ_1 (0,4–0,6) as time increases

free and endemic is investigated locally and globally. It was shown that if $R_* < 1$, then the HPV-free steady-state is locally and globally asymptotically stable. Also, if $R_* > 1$, then the HPV-endemic steady-state is globally stable. Further, we intend to consider the impact of optimal control strategies and cost effective analysis involving HPV transmission.

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Received September 20, 2019

УДК 57:51-76 **DOI: 10.14529/mmp200207**

МОДЕЛИРОВАНИЕ ВИРУСНОЙ ПЕРЕДАЧИ ПАПИЛЛОМЫ ЧЕЛОВЕКА

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В этой статье сформулирована математическая модель, описывающая динамику передачи вируса папилломы человека (ВПЧ) в бисексуально активном сообществе носителей. Комплексные математические методы были использованы для качественного и количественного анализа модели. Локальная и глобальная устойчивость равновесий модели была проанализирована, и показано, что если R_* меньше единицы, то модель локально и глобально асимптотически устойчива в статических состояниях, свободных от ВПЧ. Также, если R_* больше единицы, ВПЧ-эндемичное статическое состояние является глобально асимптотически устойчивым. Было проведено численное моделирование и представлены графические иллюстрации.

Ключевые слова: ВПЧ; базовый репродуктивный номер; локальная устойчивость; глобальная устойчивость.

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Поступила в редакцию 20 сентября 2019 г.