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Between Host Model for Cervical Cancer Incorporating Diagnosis

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Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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Abstract

In this paper a mathematical model describing a between host cervical cancer infection incorporating diagnosis was formulated and analysed. The qualitative analysis of model showed that the infection dynamics can best be described by the threshold value R_{0B}, in which for the value of $R_{0B} < 1$ the infection free equilibrium is globally asymptotically stable. This implies that we do not expect the disease outbreak for life. Thus, the disease will die out of the population. The endemic states are shown to exist provided that the reproduction number is greater than unity $R_{0B} > 1$. By use of Routh-Hurwitz criterion and suitable Lyapunov functions, the endemic states are shown to be locally and globally asymptotically stable respectively. This implies that disease transmission levels can be kept quite low or manageable with minimal deaths at the peak times of the re-occurrences. The numerical results show that the disease related mortality is eradicated if diagnosis is done at an early stage hence late diagnosis increases the risk of cervical cancer infection among the infected individuals.

Keywords: Diffusion; human papilloma virus; reproduction number; stability analysis.

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1 Introduction

Cervical cancer has attracted more attention due to its social economic ramifications and its complex behavior. Even with the introduction of routine screening programs and vaccination, the cervical cancer prevalence remains high especially in Sub-saharan Africa. However, in the early stages if diagnosed it can be cured and prevented. Cervical cancer is mainly due to the infections of Human papilloma Virus (HPV) though the risk due to the various HPV types has been given little attention. Over one hundred dissimilar strains of HPV being identified and classified with HPV types 16, 18, 31 and 45 been classified as "high-risk". Approximately 85 percentage cancer of the cervix are reported to be as a result of these four strains alone [1]. There is no treatment for HPV but in most cases it disappears naturally. However, with persistent infections the high risk strains may become chronic and shed HPV virions.

Females whose immune system is normal may take 15 to 20 years to develop to cervical cancer. However, those with weak immune systems such as those with HIV/AIDs may take only 5 to 10 years to develop the disease. There is a high likelihood of people living with Human Immunodeficiency Virus (HIV) to be infected with HPV and which progresses to cancer [1]. Other factors that speed up the danger of developing to cervical cancer beside them having High-risk Human papilloma Virus include Immune system suppression, HIV infection, tobacco smoking, overweight, history of a family with cancer of the cervix, Past or current Chlamydia infection, prolonged use of oral contraceptives and Poverty.

The stage of diagnosis is also a factor. When detected early, and attended to effectively, cervical cancer is a form of cancer that can be successfully managed. However, appropriate treatment and palliative care can handle late stage diagnosed cancers. Public health problem like cervical cancer can be eliminated if a comprehensive approach to prevention, screening and treatment is done [2, 3, 4].

Mathematical models have been used to describe Human Papilloma virus infection that lead to cervical cancer and their intervention strategies by many researchers. A mathematical model to explore the transmission dynamics of human papilloma virus (HPV) was formulated by [5]. In their model, infected individuals can recover with a limited immunity that results in a lower probability of being infected again.

Cancer research is vital as the prognosis of cancer enables clinical applications for patients. A new approach that applies an ensemble approach to machine learning models for the automatic diagnosis of cervical cancer was demonstrated by [6]. Ansley et al [7] examined a monogamy as a risk factor for non vaccination and explored how risk perception may influence this association. Results showed that women in monogamous relationships had a lower average sexually transmitted disease (STD) risk perception compared to women who were single and dating $(p < 0.0001)$.

The World Health Assembly adopted the global strategy to accelerate the elimination of cervical cancer as a public health problem. The definition of elimination of cervical cancer has been set up as a country by reaching the threshold of less than 4 cases of cervical cancer per 100 000 women per year. To reach this threshold by the end of 21st century, WHO has set up the 90-70-90 targets to be reached by 2030 and to be maintained. WHO has developed guidance and tools on how to prevent and control cervical cancer through vaccination, screening, treatment and management of invasive cancer. WHO works with countries and partners to develop and implement comprehensive programmes in line with the global strategy. The Global strategy towards eliminating cervical cancer as a public health problem, adopted by the World Health Assembly in 2020, recommends a comprehensive approach to cervical cancer prevention and control [4].

Between host models are epidemiological models of cervical cancer infections. These models classify individuals in the population as either infected or susceptible. Infected individuals may transmit Human Papilloma Virus which causes cervical cancer to susceptible hosts(susceptible infectious epidemic model) mainly through sexual contact. Research has established that transmission dynamics of cervical cancer in the population(between host) is dependent on the individuals' immune viral dynamics [8].

2 The Model

A model in which the total human population at any time t denoted by N is formulated. The model is subdivided into classes, $S(t)$ the class of individuals susceptible to cervical cancer infection. Recruitment into susceptible class is done at a rate Λ. The class $I_h(t)$ consists of individuals who are infected with higher risk Human papilloma virus, this infection occurs at the rate λ. Most HPV infected Individuals recover from the infection at a rate α and slide back to the $S(t)$ class, ρ is the rate of progression to the cervical cancer $C(t)$ class due to persistence of the HPV infection. Mortality occurs among cervical cancer patients at the rate ν while natural death is assumed to occur in all classes at the rate μ.

The force of infection is given by

$$\lambda = \frac{\kappa\tau I_h}{N} \tag{1}$$

Where κ is the transmission rate of Human Papilloma Virus while τ is the effective contact rate with HPV infected individuals. This part of study sought to investigate the effect of diagnosis on the between host transmission dynamics of cervical cancer infection. Let π denote the diagnostic term where $0 \leq \pi$. The modified force of infection for cervical cancer is:

$$\lambda = \frac{\kappa\tau\pi I_h}{N} \tag{2}$$

From the above definitions, the resulting diagram for the model is given below.

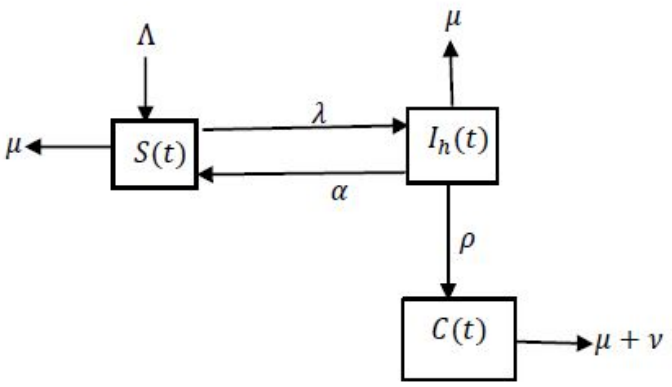

Fig. 1. Between - Host Model flow diagram

The dynamics described can be represented mathematically as:

$$\begin{aligned} \dot{S}(t) &= \Lambda + \alpha I_h(t) - (\lambda + \mu)S(t) \\ \dot{I_h}(t) &= \lambda S(t) - \{\alpha + \rho + \mu\}I_h(t) \\ \dot{C}(t) &= \rho I_h(t) - (\nu + \mu)C(t) \end{aligned} \tag{3}$$

3 Model Analysis

The basic reproduction number R_{0B} is defined as the average number of secondary infections produced by one infectious individual over the course of their infectious period in a purely uninfected susceptible population. The

basic reproduction number, R_{0B}, for model (1) was computed using the next generation matrix method as used in [9, 10].

$$R_{0B} = \frac{\pi\kappa\tau}{\mu+\alpha+\rho} \tag{4}$$

4 Disease-free Equilibrium Point (DFE)

The disease-free equilibrium point, denoted by E_{oB} is a steady-state solution for which there is no disease or infection in the population [11] . To obtain the disease-free equilibrium point we set the normalized model system (1) equal to zero. Since there are no infections in the human populations, we set $I_h(t) = C(t) = 0$. This implies that $E_{0B} = \{S(t), I_h(t), C(t)\} = (\frac{\Lambda}{\mu}, 0, 0)$

4.1 Local stability of disease-free Equilibrium point

The model in Equation (1) has disease free equilibrium (DFE) given by

$$E_{0B} = (S_0, I_{h0}, C_0) = (\frac{\Lambda}{\mu}, 0, 0) \tag{5}$$

Theorem 4.1. *If $R_{0B} < 1$, then $E_{0B} = (\frac{\Lambda}{\mu}, 0, 0)$ is an equilibrium state in Ω and is Locally asymptotically stable otherwise unstable*

Proof. The Jacobian matrix of Equation (1) is given by

$$J_1 = \begin{pmatrix} -(\mu + \frac{\tau\pi\kappa I_h}{N}) & \alpha - \frac{\tau\pi\kappa S}{N} & 0 \\ \frac{\tau\pi\kappa I_h}{N} & \frac{\tau\pi\kappa S}{N} - (\alpha+\rho+\mu) & 0 \\ 0 & \rho & -(\mu+\nu) \end{pmatrix} \tag{6}$$

To evaluate the stability of the Jacobi matrix at DFE, we compute the eigenvalues of of Equation (6)

$$J_1 = \begin{pmatrix} -\mu-\lambda & \alpha - \tau\pi\kappa & 0 \\ 0 & (\alpha+\rho+\mu)(R_{0B}-1) - \lambda & 0 \\ 0 & \rho & -(\mu+\nu)-\lambda \end{pmatrix} = 0 \tag{7}$$

We analyse the reduced matrix

$$J_1 = (-\mu-\lambda)\begin{pmatrix} (\alpha+\rho+\mu)(R_{0B}-1) - \lambda & 0 \\ \rho & -(\mu+\nu)-\lambda \end{pmatrix} = 0 \tag{8}$$

This simplifies to

$$(-\mu-\lambda-\lambda)((\alpha+\rho+\mu)(R_{0B}-1)-\lambda)(-\mu-\nu-\lambda) = 0 \tag{9}$$

Using Routh-Hurwitz criterion [12], the eigenvalues obtained are;
$\lambda_1 = -\mu$
$\lambda_2 = (\alpha+\rho+\mu)(R_{0B}-1)$ and
$\lambda_3 = -(\mu+\nu)$

which have negative real parts provided that $R_{0B} < 1$ and the determinant upon calculation using mathematica is given by

$$(-\mu-\nu)\mu(R_{0B}-1)(\alpha+\rho+\mu)$$

which is positive provided that $R_{0B} < 1$. Therefore, by Routh-Hurwitz criterion [12], the disease-free equilibrium $E_{0B} = (S(t), I_h(t), C(t)) = (\frac{\Lambda}{\mu}, 0, 0,)$ is locally asymptotically stable. Given a small initial infective population each infected individual in the entire period of infectivity will produce less than one infected individual on average if $R_{0B} < 1$. This shows that the disease will die out of the population when $R_{0B} < 1$. □

4.2 Global stability of disease-free Equilibrium point

For global stability of the DFE, the technique by Castillo [13] is used. There are two conditions that if met guarantee the global asymptotic stability of the disease free state. Equation (1) may be written in the form

$$\frac{dX}{dt} = H(X,Z),$$
$$\frac{dZ}{dt} = G(X,Z), G(X,0) = 0 \tag{10}$$

where $X = \{S(t)\}$ with $X \in \mathbb{R}^1$ denoting the number of uninfected compartments and $Z \in \mathbb{R}^2$ where $Z = (I_h(t), C(t))$ denotes the number of infected individuals. $E_{0B} = (\frac{\Lambda}{\mu}, 0, 0)$ denotes the disease free equilibrium point of this system where

$X^* = \frac{\Lambda}{\mu}$

Conditions below must be met to guarantee a local asymptotic stability:

$\frac{dX}{dt} = H(X,0), X^*$ is globally asymptotically stable (GAS)

$$G(X,Z) = PZ - \hat{G}(X,Z), \hat{G}(X,Z) \geq 0 for (X,Z) \in \Omega \tag{11}$$

Where $P = D_z G(X^*, 0)$ is an M-matrix (the off-diagonal elements of P are non-negative) and Ω is the region where the model makes medical sense.

Theorem 4.2. *If system* (10) *satisfies conditions* (11)*, then the fixed point* $E_{0B} = (X^*, 0, 0)$ *is a globally asymptotically stable equilibrium provided that* $R_{0B} < 1$ *and the assumptions in* (11) *are satisfied.*

Proof. Consider
$H(X,O) = \Lambda - \mu S$ and $G(X,Z) = PZ - \hat{G}(X,Z)$

Where $P = \begin{pmatrix} -(\alpha+\rho+\mu) & 0 \\ \rho & -(\mu+\nu) \end{pmatrix}$

And
$$G(X,Z) = \begin{pmatrix} \hat{G}_1(X,Z) \\ \hat{G}_2(X,Z) \end{pmatrix} = \begin{pmatrix} -\pi\kappa\tau I_t(h) \\ 0 \end{pmatrix}$$

Considering the Jacobian matrix, and replacing $S(t) = \frac{\Lambda}{\mu}$, $I_h(t) = 0$ $C(t) = 0$, we obtain $\hat{G}_1(X,Z) = 0$ and so the conditions in (11) are met so E_{0B} is globally asymptotically stable when $R_{0B} < 1$. Epidemiologically, any perturbation of the model by the introduction of infectives shows that the model solutions will converge to the DFE whenever $R_{0B} < 1$. Thus, the epidemic will die out of the population.

□

5 Existence of Endemic Equilibrium

At the Endemic equilibrium point, we have persistence of infection thus at least one of the infected classes is greater than zero. The positive endemic equilibrium of model (1) is denoted by

$$E_{eB}(S^*(t), I_h^*(t), C^*(t)). \tag{12}$$

Theorem 5.1. *Human Papilloma virus and cervical cancer infections exist and persist in the population where* $I_h^* > 0$ *and* $C^* > 0$ *whenever* $R_{0B} > 1$

Proof. Using mathematica software, the endemic states were given as

$$I_h^*(t) = \frac{\Lambda}{(\mu+\rho)R_{0B}}(R_{0B}-1)$$
$$C^*(t) = \frac{\Lambda\rho}{R_{0B}(\mu+\nu)(\mu+\rho)}(R_{0B}-1) \tag{13}$$

From Equation (13), $I_h^*(t) > 0$ and $C^*(t) > 0$ when $R_{0B} > 1$. This shows that if $R_{0B} > 1$, then each HPV infected individual in the entire infection period having contact with susceptible individual will produce more than one infected individuals and this leads to the disease invading the susceptible population. □

5.1 Local stability of endemic equilibrium point

Theorem 5.2. *If $R_{0B} > 1$, then the endemic equilibrium $E_{eB}(S^*(t), I_h^*(t), C^*(t))$, is locally asymptotically stable*

Proof. The Jacobian of Equation (1) at endemic state is given by

$$J_e = \begin{pmatrix} -\mu - \frac{\tau\pi\kappa I_h^*}{N} & \alpha - \frac{\tau\pi\kappa S^*}{N} & 0 \\ \frac{\tau\pi\kappa I_h^*}{N} & \frac{\tau\pi\kappa S^*}{N} - (\alpha+\rho+\mu) & 0 \\ 0 & \rho & -(\mu+\nu) \end{pmatrix} \tag{14}$$

On substituting $(S^*(t), I_h^*(t), C^*(t))$, Equation (14) becomes

$$J_e = \begin{pmatrix} -\mu - \frac{\tau\pi\kappa\Lambda(R_{0B}-1)}{R_{0B}(\mu+\rho)N} & \alpha - (\alpha+\rho+\mu) & 0 \\ \frac{\tau\pi\kappa\Lambda(R_{0B}-1)}{R_{0B}(\mu+\rho)N} & 0 & 0 \\ 0 & \rho & -(\mu+\nu) \end{pmatrix} \tag{15}$$

Using Routh-Hurwitz criterion [12], the characteristic equation of (15) has one of the eigenvalues given by $\lambda_1 = -\mu - \nu < 0$. The remaining eigenvalues can be determined by expressing (15) as a 2 by 2 block matrix M defined by

$$J_e = \begin{pmatrix} -\mu - \frac{\tau\pi\kappa\Lambda(R_{0B}-1)}{R_{0B}(\mu+\rho)N} & \alpha - (\alpha+\rho+\mu) \\ \frac{\tau\pi\kappa\Lambda(R_{0B}-1)}{R_{0B}(\mu+\rho)N} & 0 \end{pmatrix} \tag{16}$$

If $R_{0B} > 1$, then the trace of matrix J_e is negative and the determinant will given by

$$\frac{\tau\pi\kappa\Lambda(R_{0B}-1)}{R_{0B}(\mu+\rho)N}(\alpha+\rho+\mu) - \frac{\alpha\tau\pi\kappa\Lambda(R_{0B}-1)}{R_{0B}(\mu+\rho)N} \tag{17}$$

From equation (17), if $R_{0B} > 1$ and $\frac{\tau\pi\kappa\Lambda(R_{0B}-1)}{R_{0B}(\mu+\rho)N}(\alpha+\rho+\mu) > \frac{\alpha\tau\pi\kappa\Lambda(R_{0B}-1)}{R_{0B}(\mu+\rho)N}$, then the $DetM > 0$. This implies that the Routh-Hurwitz criterion holds and thus the endemic Equilibrium (E_{eB}) of model (1) is locally asymptotically stable otherwise unstable.

□

5.2 Global stability of endemic equilibrium point

The global stability of the equilibrium is obtained by means of Lyapunov's direct method and LaSalle's invariance principle De Leon [14].

Theorem 5.3. *The endemic equilibrium E_{eB} of model (1) is globally asymptotically stable in Ω whenever $R_{0B} > 1$.*

Proof. Consider the non-linear Lyapunov function
$V : (S(t), I_h(t), C(t)) \in \Omega \subset \mathbb{R}^3_+ : S(t), I_h(t), C(t) > 0$

defined as

$$V = S - S^* \ln S + I_h - I_h^* \ln I_h + C - C^* \ln C \tag{18}$$

where V is in the interior of the region Ω. E_{eB} is the global minimum of V on Ω and $V : \{S(t), I_h(t), C(t)\} = 0$. Differentiating V with respect to time gives

$$\frac{dV}{dt} = \dot{V} = \dot{S}(1 - \frac{S^*}{S}) + \dot{I}_h(1 - \frac{I_h^*}{I_h}) + \dot{C}(1 - \frac{C^*}{C}) \tag{19}$$

Replacing $\dot{S}, \dot{I}_h, \dot{C}$ from equation (1) in equation (19) we obtain

$\dot{V} = [\Lambda + \alpha I_h(t) - (\frac{\kappa\tau\pi I_h}{N} + \mu)S](1 - \frac{S^*}{S}) + [\frac{\kappa\tau\pi I_h}{N}S - \{\alpha + \rho + \mu\}I_h(t)](1 - \frac{I_h^*}{I_h}) +$
$[\rho I_h(t) - (\nu + \mu)C(t)](1 - \frac{C^*}{C})$

At boundary $N \leq \frac{\Lambda}{\mu}$, we let $N = \frac{\Lambda}{\mu}$

$$\dot{V} = [\Lambda + \alpha I_h(t) - (\frac{\mu\kappa\tau\pi I_h}{\Lambda} + \mu)S](1 - \frac{S^*}{S}) + [\frac{\mu\kappa\tau\pi I_h}{\Lambda}S - \{\alpha + \rho + \mu\}I_h(t)](1 - \frac{I_h^*}{I_h}) + [\rho I_h(t) - (\nu + \mu)C(t)](1 - \frac{C^*}{C})$$

At steady state the following results from model (1) were obtained

$$\begin{aligned} \Lambda &= (\frac{\mu\kappa\tau\pi I_h}{\Lambda} + \mu)S(t) - \alpha I_h(t) \\ \frac{\mu\kappa\tau\pi I_h}{\Lambda}S(t) &= \{\alpha + \rho + \mu\}I_h(t) \\ \rho I_h(t) &= (\nu + \mu)C(t) \end{aligned} \tag{20}$$

Thus we have

$\dot{V} = [(\frac{\mu\kappa\tau\pi I_h}{\Lambda}S(t) + \mu S(t) - \alpha I_h(t) + \alpha I_h(t) - (\frac{\mu\kappa\tau\pi I_h}{\Lambda}S(t) + \mu S](1 - \frac{S^*}{S}) + [\frac{\mu\kappa\tau\pi I_h}{\Lambda}S - \{\alpha + \rho + \mu\}I_h(t)](1 - \frac{I_h^*}{I_h}) + [\rho I_h(t) - (\nu + \mu)C(t)](1 - \frac{C^*}{C})$

$= \{\frac{\mu\kappa\tau\pi I_h^* S^*}{\Lambda} + \mu S^* - \alpha I_h^*\}(2 - \frac{S}{S^*} - \frac{S^*}{S}) + \frac{\mu\kappa\tau\pi I_h^* S^*}{\Lambda}(1 - \frac{S}{S^*}\frac{I_h^*}{I_h}) + \rho I_h^*(1 - \frac{I_h}{I_h^*}\frac{C^*}{C})$

At $S = S^*, I_h = I_h^*, C = C^*$ and from the property that the geometric mean is less than or equal to the arithmetic mean, the inequality $\dot{V} \leq 0$ holds iff $(S(t), I_h(t), C(t))$ takes the equilibrium values $S^*(t), I_h^*(t), C^*(t)$. Thus, by LaSalle's invariance principle [14], the endemic equilibrium E_{eB} is globally asymptotically stable.

Epidemiologically, any perturbation of the model by the introduction of infectives shows that the model solutions will converge to the E_{eB} whenever $R_{oB} > 1$. This implies that the disease transmission levels can be kept quite low or manageable with minimal deaths at the peak times of the re-occurrence

□

If DFE and EE are locally and globally asymptotically stable, then all the epidemiological situation different from the given stable equilibria $t \to 0$ evolve to the equilibrium points. This is significant to epidemiologists, as the conditions required for stability of the model when $R_{oB} < 1$, will provide a basis for the necessary indicators to be controlled in the reduction of the transmission of Human papilloma virus.

6 Sensitivity Analysis

Sensitivity analysis of R_{0B} with respect to the model parameters is carried out in order to determine the effect of diagnosis in the control and management of cervical cancer infection [15]. To perform sensitivity analysis, the normalised forward sensitivity index also known as elasticity [16] was used. The normalised forward sensitivity index of the reproduction number R_{0B} in Equation (4) with respect to diagnostic parameter π is given by;

$$\Gamma_{\pi}^{R_{0B}} = \frac{\partial R_{0B}}{\partial \pi} \times \frac{\pi}{R_{0B}} = 1 \tag{21}$$

This implies that, the late the diagnosis the higher the rate of infection thus, late diagnosis increases the risk of cervical cancer infection among the infected individuals.

7 Numerical Simulation

Numerical simulations were carried out to graphically illustrate the between host dynamics of cervical cancer. To do this, some parameter values were used as indicated in Table (1).

Table 1. Parameter values used in simulation of model (1)

Parameter	description	Value	Source
S(t)	Susceptible individuals	3000	Estimate
$I_h(t)$	HPV infected individuals	500	Estimate
C(t)	Cervical cancer infected individuals	100	Estimate
Λ	Recruitment rate	149 per year	[17]
κ	transmission rate of	0.31 per year	[2, 3]
τ	Contact rate with HPV infective	0.80 per year	[3, 18]
μ	Natural mortality rate	0.05393 per year	[3]
ν	Cervical cancer related death rate	0.61325 per year	[17]
α	Recovery rate of HPV infection	0.70 per year	[3]
ρ	Rate of progression to Cervical cancer	0.1271 per year	[3, 18, 19]
π	diagnostic term	$0 \leq \pi$	Estimate

Based on the initial conditions and parameter values in table (1), where diagnosis is considered after $\pi = 0.1$ of a year, one year, 10 years and 30 years, the following graphs were obtained;
The Susceptible class rises sharply before reducing and remaining constant while the infected and cervical cancer classes reduces sharply to zero. The reason why the susceptible are rising is because much of Human Papilloma Virus (HPV) clears on its own and thus individuals recover and slide back to Susceptible class, those who progress to cervical cancer are diagnosed at 0.1 years, treated, recover and slide back to the susceptible class.

The Susceptible class rises before reducing and remaining constant, infected class reduces to zero while the cervical cancer class reduces slowly to zero. The reason why the susceptible are rising is because much of Human Papilloma Virus (HPV) clears on its own and thus individuals slide back to Susceptible class, those who progress to cervical cancer are diagnosed at 1 year, treated, recover and slide back to the susceptible class. This explains why the cervical cancer class is reducing slowly.

At early diagnosis of cervical cancer as shown by Fig. (2) and Fig. (3), the growth of Susceptibles is bounded and converges to $S(t) \leq \frac{\Lambda}{\mu}$ as the infected classes decrease to zero. This decline can be attributed to the recovery of the infected individuals thus, sliding back to the susceptible class. As discussed earlier in chapter one, much HPV clears on its own and the small percentage which progresses to cervical cancer will be diagnosed

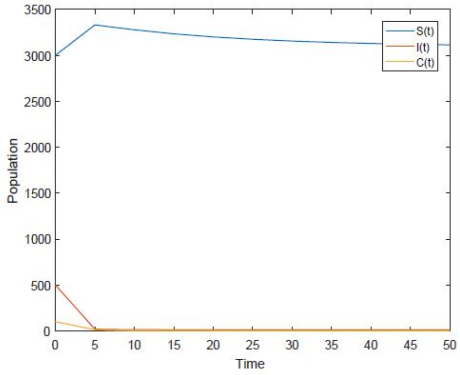

Fig. 2. Graph trajectory of $S(t), I_h(t)$ and $C(t)$ at early diagnosis of cervical cancer for $\pi = 0.1$ with $R_{0B} = 0.02682854$.

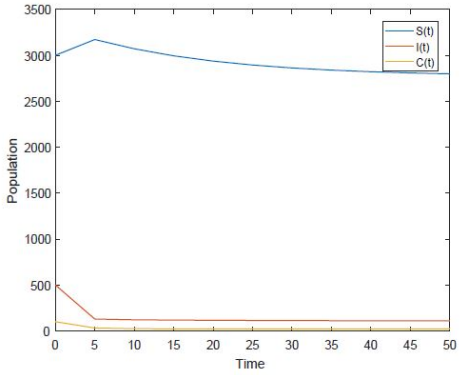

Fig. 3. Graph trajectory of $S(t), I_h(t)$ and $C(t)$ at early diagnosis of cervical cancer for $\pi = 1$ with $R_{0B} = 0.2814887$.

and treated. Early diagnosis of cervical cancer plays a major role in accelerating the decline of the infected classes as opposed to late diagnosis and this increases the susceptible individuals since recovery of the infection is experienced. This shows that the population grows normally with only natural mortality influencing the population growth.

It can be noted that, for some values of diagnosis (π), e.g 35 days (0.1 years) and one year, the corresponding values of R_{0B} are $R_{0B} = 0.02682854$ and $R_{0B} = 0.2814887$ and thus $R_{0B} < 1$. This clearly shows that the Disease Free Equilibrium (DFE) is locally and globally asymptotically stable which is in agreement with the mathematical analysis at the Disease Free Equilibrium E_{0B}.

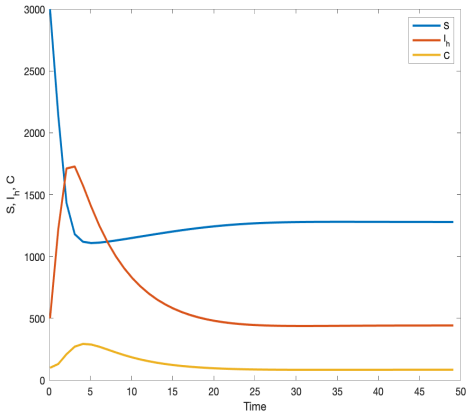

Fig. 4. Graph trajectory of $S(t), I_h(t)$ and $C(t)$ at late diagnosis of cervical cancer for $\pi = 10$ with $R_{0B} = 2.814887$.

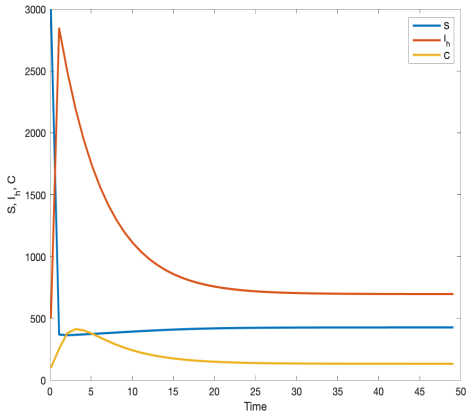

Fig. 5. Graph trajectory of $S(t), I_h(t)$ and $C(t)$ at late diagnosis of cervical cancer for $\pi = 30$ with $R_{0B} = 8.44466$.

The Susceptible class reduces even to a point where the infected individuals are more. Infected class rises before reducing and remaining constant while the cervical cancer class rises before reducing and remaining constant. The virus exist and persist in the population and this explains why the susceptible individuals are reducing as

infected individuals are increasing. Many individuals are progressing to cervical cancer and this explains why the cervical cancer class is rising.

The Susceptible class reduces even to a point where the cervical cancer class is higher, Infected class rises sharply before reducing and remaining constant while the cervical cancer class rises before reducing and remaining constant. The virus exist and persist at the population and this explains why the susceptible individuals are reducing as infected individuals are increasing. Many individuals are progressing to cervical cancer and dying due to the cervical cancer infection and this explains why the cervical cancer class is rising.

Late diagnosis of cervical cancer is more difficult to eliminate from the host population and is the main causes of the disease related deaths worldwide. This is one of the main concerns in developing countries. Late diagnosis as shown in Fig. (4) and Fig. (5), results in reduction in the number of $S(t)$ individuals to almost half before remaining constant. On the other hand, the infected classes begin with an increase to a point where $I_h(t)$ is higher than the susceptible individuals and then decrease before remaining constant. The reduction in susceptible $S(t)$ individuals is an indication that more individuals are channeling to $I_h(t)$ class. The decline in $I_h(t)$ class can be attributed to the progression of the infected individuals into the cervical cancer $C(t)$ class. The increase in the number of individuals with cervical cancer is as a result of the development of new strains that are difficult to eradicate and this confirms that late diagnosis results in high number of cervical cancer individuals leading to high disease related mortality rate.

It can be observed, that late diagnosis (i.e $\pi = 10$ years, and $\pi = 30$ years) corresponds to $R_{0B} = 2.814887$ and $R_{0B} = 8.44466$ and thus $R_{0B} > 1$. This means that the Endemic Equilibrium (EE) is globally asymptotically stable implying disease persistence in the population. This is in agreement with the mathematical analysis at the Endemic Equilibrium E_{eB}.

8 Conclusion

Analysis of the results showed that the disease free equilibrium point for Equation (1) is locally and globally asymptotically stable when $R_{0B} < 1$. This implies that we do not expect the disease outbreak for life. Thus, the disease will die out of the population. The endemic states are shown to exist provided that the reproduction number is greater than unity. By use of Routh-Hurwitz criterion and suitable Lyapunov functions, the endemic states are shown to be locally and globally asymptotically stable respectively. This implies that disease transmission levels can be kept quite low or manageable with minimal deaths at the peak times of the re-occurrences.

From the numerical simulation, the disease related mortality is eradicated if diagnosis is done at an early stage hence late diagnosis increases the risk of cervical cancer infection among the infected individuals. Early diagnosis of cervical cancer is considered one of the most promising interventions against cervical cancer infected individuals as experiments from various groups have reported its significant effectiveness.

Despite the advocacy for screening and vaccination, new incident HPV infections continues to be a problem. Thus, the importance of combined prevention strategies to the transmission of high risk HPV which is the main Cause of cervical cancer. Additionally, early diagnosis is perceived to yield better results in the reduction of cervical cancer mortality rate.

Competing Interests

Author has declared that no competing interests exist.

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