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Mathematical Model for Co-infection of HPV with Cervical Cancer and HIV with AIDS Diseases

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Abstract: In this paper a deterministic mathematical model for co-infection of HPV with Cervical Cancer and HIV/AIDS diseases has been formulated and rigorously analyzed. Both local and global stability of the disease free equilibrium and endemic of the model was established using basic reproduction number. The results show that in HPV only model, HIV only model and HPV-HIV co-infection model if the basic reproduction is less than one then the solution converges to the disease free steady state and the disease free equilibrium is locally asymptotically stable. The endemic states are considered to exist when the basic reproduction number for each disease is greater than one. Sensitivity analysis of the model was performed on the key parameters to find out their relative significance and potential impact on the transmission dynamics of HPV and HIV separately. Numerical simulations indicate the effect of varying the contact rate parameters on single disease and the co-infection dynamics. As we increase contact rates, the infections increases.

Keywords*: Co-infection, HPV, HIV/AIDS, Cervical Cancer, Stability Analysis, Sensitivity*.

I. INTRODUCTION

Epidemiology of HPV: Human Papilloma Virus (HPV) is the name of a group of viruses that includes more than 100 different types and also more than 40 of these viruses are the most common and sexually transmit in the world. HPV types 16, 18, 31 and 45 are referred to as "high-risk'' and causes approximately 85% of cervical cancers [1]. Most of the HPV infections are asymptomatic and can feed away without treatment over the course of a few years. For instance, about 70% of HPV infections fed away within a year and 90% within two years. However, in some people infection can persist for many years and can cause warts or low risk genotype of HPV, while other types lead to different kinds of cancers or high risk genotype of HPV including cervical cancer [2-3]. HPV is transmitted via skin-to-skin contact during sexual intercourse and less commonly through other forms of non-penetrative genital contact. Statistics show that there are 18.1 million new cases, 9.6 million cancer related deaths, and 43.8 million people living with cancer in 2018. The number of new cases is expected to rise from 18 million to 22 million by 2030 and the number of global cancer deaths is projected to increase by 45% by 2030 [4].

Epidemiology of HIV/AIDS: Human Immunodeficiency Virus (HIV) is the causative agent of Acquired Immunodeficiency Syndrome (AIDS). It is a disease that causes progressive failure of the immune system. HIV is an RNA retrovirus. That is, to enter a cell, HIV translates its RNA to DNA with a viral enzyme called reverse transcriptase [5]. HIV is transmitted primarily via unprotected sexual intercourse, contaminated blood transfusions, hypodermic needles, and from mother to child during pregnancy, delivery, or breastfeeding. There is no cure or vaccine to AIDS. However, antiretroviral (ART) treatment improves health, pro-longs life, and substantially reduces the risk of HIV transmission. More than 90% of adults in sub-Saharan Africa acquire HIV infection from unprotected sexual intercourse with infected partners [6].

Globally, new HIV infections among young women aged 15–24 years were reduced by 25% between 2010 and 2018.The annual number of deaths from AIDS-related illness among people living with HIV globally has fallen from a peak of 1.7 million in 2004 to 770 000 in 2018. The global decline in deaths has largely been driven by progress in eastern and southern Africa, which is home to 54% of the world's people living with HIV. AIDS-related mortality in the region declined by 44% from 2010 to 2018.The annual number of new infections since 2010 has declined from 2.1 million to 1.7 million in 2018 [7].

Co-infection of HPV and HIV/AIDS: Co-infection is more than one disease co-existing within a single host. HPV and HIV/AIDS are among the diseases that contaminate a large number of individuals worldwide. This paper explains the rate

of co-infection of HPV and HIV/AIDS on the effect of transmission. People with a weakened immune system such as those with HIV/AIDS are susceptible to diseases such as HPV. HPV-HIV is the co-infection of two diseases responsible for loss of many lives. The individuals with CD4+T-cells less than 200 *cells/mm*^{3} are vulnerable to acquire HPV. The patient with the co-infection is observed to have some of the symptoms including dry cough, weakness and difficulty in breathing [8]. If the body immune system is strong, HPV infection can be fought off. For HIV/AIDS victims, the sexually transmitted diseases are the ones causing very serious sickness and if not treated they cause death as well [9]. HIV/AIDS weakens or destroys body immune system giving room for other sexually transmitted diseases to easily attack the body. HPVis the most common sexually transmitted disease affecting individuals with HIV. Some of the symptoms of the co-infection include weight loss, breathlessness andgeneral body weakness [8]. When an individual is co-infected with HPV and HIV atacute and clinical latency stages is called the initial stage. The final stage of the co-infection of HIV and HPV involves AIDS and Cervical cancer.

HPV is the most sexually transmitted disease observed in people with HIV/AIDS. HPV itself cannot be treated, the cellular changes that come from any HPV infection can be treated. For examples, genital warts, cervical, anal, and genital cancers can be treated if the infection is diagnosed during the early stage of development. If not cured, it is the one common sexually transmitted disease causing the increased death rates of people with HIV/AIDS. This paper develops and analyses the mathematical model of HIV/AIDS and HPV co-infection.

Survey of Modeling: The mathematical model is used as a tool for better understanding of the co-infection dynamics, studying the approximations, and effects of the parameters and predicting the behaviour of the problem in a specific period of time as well as showing the connectivity of theories and observations using the system of equations with state variables and parameters [10]. Parameters are the constants incorporated into the equations to express the fundamental quantities such as birth rates, transmission rates, recovery rates and death rates [11].

A lot of scholars developed a mathematical model to illustrate the dynamics of the disease that helped them to suggest disease control mechanism and also described the dynamics of the co-infection with other infectious diseases. Some of them are [12-14] proposed mathematical models that played important roles in predicting appropriate control strategies and ranking their cost-effectiveness strategies in justifying the disease. Also, Geomira et al. [15] Modelling Co-dynamics of Cervical Cancer and HIV Disease. Their model had a total number of ten compartments and it was found that if the basic reproduction number of HPV becomes very small approaching zero, there is no new HPV infection which reduces the rate of AIDS progression. In this paper we modify the model developed by Geomira et al.[15], by adding the asymptomatic compartment.

II. Basic Assumption and Model Formulation

The total sexually active population at time t, denoted by $N(t)$ is sub-divided into thirteen mutually-exclusive compartments, namely susceptible individuals, which are capable of becoming infected $S(t)$, individuals who are exposed to HIV $E_h(t)$, individuals who are exposed to HPV $E_p(t)$, individuals who are exposed to both HIV and HPV $E_{hp}(t)$, asymptomatic to HIV but show no symptoms of the disease $A_h(t)$, asymptomatic to HPV but show no symptoms of the disease $A_p(t)$, asymptomatic to both HIV and HPV but show no symptoms of the disease $A_{hp}(t)$, infected individuals with clinical symptoms of HIV $I_h(t)$, infected individuals with clinical symptoms of HPV $I_p(t)$, infected individuals with clinical symptoms of both HIV and HPV $I_{hp}(t)$, individuals having AIDS $A(t)$, individuals having Cervical cancer $C(t)$, individuals having both AIDS and Cervical cancer $AC(t)$.The total population at time t is given by

$$N(t) = S(t) + E_h(t) + E_p(t) + E_{hp}(t) + A_h(t) + A_p(t) + A_{hP}(t) + I_h(t) + I_p(t) + I_{hp}(t) + A(t) + C(t) + AC(t) \quad (1)$$

Here, a mathematical model of the Human Papilloma Virus and Human Immunodeficiency Virus is constructed based on the following assumptions:

The susceptible population is increased by the recruitment of individuals (assumed susceptible) into the population at a rate Π.

Susceptible individuals acquire HIV infection with infection force of

$$\lambda_h = [\beta_h q_h(\gamma_1 A_h + \gamma_2 I_h)]/[N]$$

Here β_h is a transmission rate of HIV infection, q_h is a mean number of contacts and infectivity rates of HIV infection are γ_1 and $\gamma_2$with $\gamma_2 > \gamma_1$.

Similarly, susceptible individuals acquire HPV infection with infection force of

$$\lambda_p = \left[\beta_p q_p(\gamma_3 A_p + \gamma_4 I_p)\right]/[N]$$

Here β_p is a transmission rate of HPV infection, q_p is a mean number of contacts and infectivity rates of HPV infection are γ_3 and γ_4 with $\gamma_4 > \gamma_3$.

Finally susceptible individuals acquire both HIV and HPV infection with infection force of

$$\lambda_{hp} = \left[\beta_{hp} q_{hp}(\gamma_5 A_{hp} + \gamma_6 I_{hp})\right]/[N]$$

Here β_{hp} is a transmission rate of HIV and HPV infection, q_{hp} is a mean number of contacts and infectivity rates of multiple infections are γ_5 and γ_6 with $\gamma_6 > \gamma_5$. Individuals in class E_h, E_p and E_{hp} progress to the symptomatic individuals I_h, I_p and I_{hp} with probability p, q and e respectively. Individuals in class E_h, E_p and E_{hp} progress to the asymptomatic individuals A_h, A_p and A_{hp} with probability $(1-p)$, $(1-q)$ and $(1-e)$ respectively.

Individuals in E_h and E_p compartments move to E_{hp} with rate θ_1 and θ_2 respectively. Individuals in class A_h and $A_p$may asymptomatic to both infection A_{hp} with a rate θ_3 and θ_4 respectively. Individuals in class I_h and $I_p$may symptomatic to both infection I_{hp} with a rate θ_5 and θ_6 respectively. Individuals in class A_h, A_p and A_{hp} after having a symptom of HIV, HPV, and HIV-HPV move to class A, C and AC with rate ω_1, ω_2 and ω_3 respectively.

Individuals in class I_h, I_p and I_{hp} compartments may develop AIDS, Cervical cancer and co-infection of AIDS and cervical cancer with the progression rates α_1, α_2 and α_3 respectively. Finally, individuals in A and C may develop co-infection of HIV-HPV $(AC)$with rates ε_1 and ε_2 respectively. All individuals have natural mortality rate μ. The variables and parameters used in this model are introduced in Table 1 and 2. Their notations and descriptions are also included.

Table 1. Notation and description of model Variables

Variable	Description
$\mathrm{N(t)}$	The total population at time t
$\mathrm{S(t)}$	Susceptible Individuals
$\mathrm{E_h(t)}$	Individuals who are exposed to HIV
$\mathrm{E_p(t)}$	Individuals who are exposed to HPV
$\mathrm{E_{hp}(t)}$	Individuals who are exposed to HIV and HPV
$\mathrm{A_h(t)}$	Individuals asymptomatic with HIV
$\mathrm{A_p(t)}$	Individuals asymptomatic with HPV
$\mathrm{A_{hp}(t)}$	Individuals asymptomatic with HIV and HPV
$\mathrm{I_h(t)}$	Individuals infected with HIV
$\mathrm{I_p(t)}$	Individuals infected with HPV
$\mathrm{I_{hp}(t)}$	Individuals infected with HIV and HPV
$\mathrm{C(t)}$	Individuals having Cervical Cancer
$\mathrm{A(t)}$	Individuals having AIDS
$\mathrm{AC(t)}$	Individuals having Cervical Cancer and AIDS

Table 2. Notation and Description of model parameter

Parameter	Description
Π	Recruitment rate of human.
$\beta_h, \beta_p, \beta_{hp}$	Transmission rate of HIV, HPV and HIV-HPV
$q_h,\ q_p,\ q_{hp}$	Contact rate of HIV, HPV and HIV-HPV
γ_1 and γ_2	Infectivity rate of HIV
γ_3 and γ_4	Infectivity rate of HPV
γ_5 and γ_6	Infectivity rate of multiple infections
p	Probability of E_h joining to I_h
q	Probability of E_p joining to I_p
e	Probability of E_{hp} joining to I_{hp}
θ_1 and θ_2	Transfer rate between (E_h, E_p) to E_{hp}
θ_3 and θ_4	Transfer rate between (A_h, A_p) to A_{hp}
θ_5 and θ_6	Transfer rate between $(I_h,\ I_p)$ to I_{hp}
ω_1, ω_2 and ω_3	Progression rate from $(A_h,\ A_p,\ A_{hp})$ to (A, C, AC).
α_1, α_2 and α_3	Progression rate from $(I_h,\ I_p,\ I_{hp})$ to (A, C, AC).
ε_1 and ε_2	Progression rate from (A, C) to (AC).
μ	Natural death rate.

Taking into account of the above consideration, we then have the following transfer diagram of the model in figure 1.

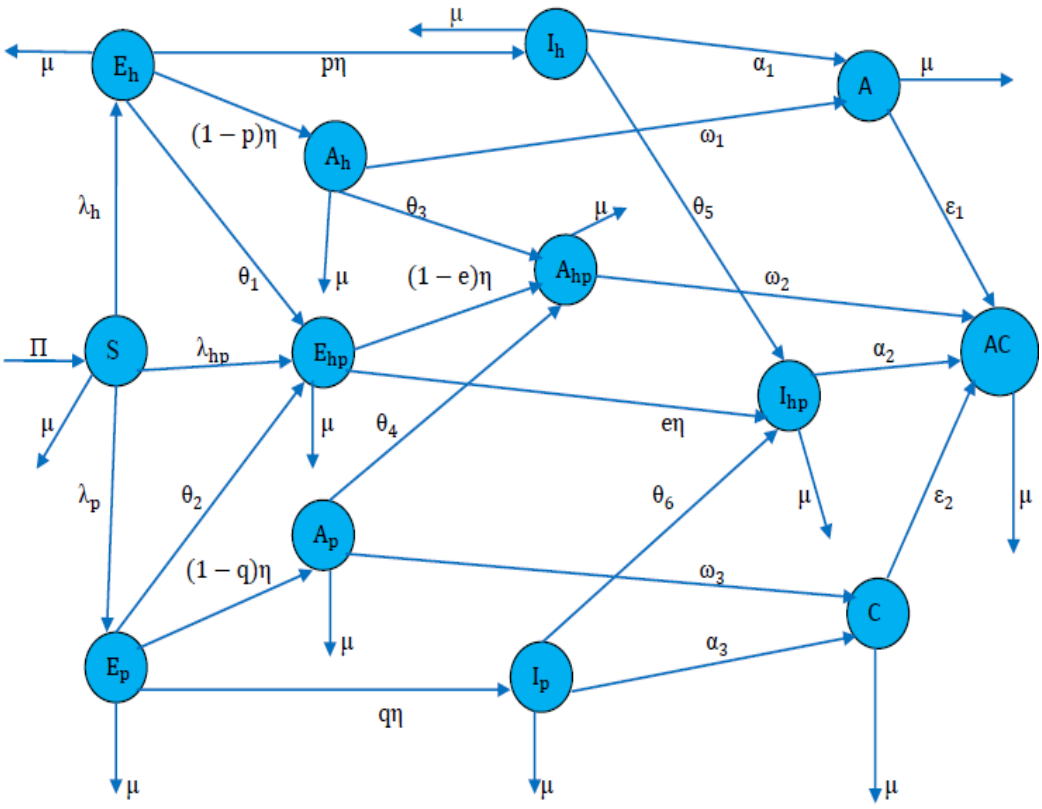

Figure 1. Schematic diagram of the model

Based on the model assumptions, the notations of variables and parameters and the schematic diagram, the model equations are formulated and given as follows:

$$
\begin{aligned}
dS/dt &= \Pi - (\lambda_h + \lambda_p + \lambda_{hp})S - \mu S \\
dE_h/dt &= \lambda_h S - (\eta + \theta_1 + \mu)E_h \\
dE_p/dt &= \lambda_p S - (\eta + \theta_2 + \mu)E_p \\
dE_{hp}/dt &= \lambda_{hp} S + \theta_1 E_h + \theta_2 E_p - (\eta + \mu)E_{hp} \\
dA_h/dt &= (1-p)\eta E_h - (\omega_1 + \theta_3 + \mu)A_h \\
dA_p/dt &= (1-q)\eta E_p - (\omega_3 + \theta_4 + \mu)A_p \\
dA_{hp}/dt &= (1-e)\eta E_{hp} + \theta_3 A_h + \theta_4 A_p - (\omega_2 + \mu)A_{hp} \quad (2) \\
dI_h/dt &= p\eta E_h - (\alpha_1 + \theta_5 + \mu)I_h \\
dI_p/dt &= q\eta E_p - (\alpha_3 + \theta_6 + \mu)I_p \\
dI_{hp}/dt &= e\eta E_{hp} + \theta_5 I_h + \theta_6 I_p - (\alpha_2 + \mu)I_{hp} \\
dA/dt &= \alpha_1 I_h + \omega_1 A_h - (\varepsilon_1 + \mu)A \\
dC/dt &= \alpha_3 I_p + \omega_3 A_p - (\varepsilon_2 + \mu)C \\
dAC/dt &= \alpha_2 I_{hp} + \omega_2 A_{hp} + \varepsilon_1 A + \varepsilon_2 C - \mu AC
\end{aligned}
$$

Here

$$
\lambda_h = [\beta_h q_h(\gamma_1 A_h + \gamma_2 I_h)]/[N]
$$

$$
\lambda_p = \left[\beta_p q_p(\gamma_3 A_p + \gamma_4 I_p)\right]/[N] \quad (3)
$$

$$
\lambda_{hp} = \left[\beta_{hp} q_{hp}(\gamma_5 A_{hp} + \gamma_6 I_{hp})\right]/[N]
$$

With initial condition $S(0) = S_0,\ E_h(0) = E_{h0},\ E_p(0) = E_{p0}, E_{hp}(0) = E_{hp0},\ A_h(0) = A_{h0},\ A_p(0) = A_{p0},\ A_{hp}(0) = A_{hp0},\ I_h(0) = I_{h0},\ I_p(0) = I_{p0},\ I_{hp}(0) = I_{hp0},\ A(0) = A_0,\ C(0) = C_0,\ AC(0) = AC_0$.

III. HIV/AIDS ONLY MODEL

Here HIV/AIDS only model is obtained from model equation (2) by setting $E_p = E_{hp} = A_p = A_{hp} = I_p = I_{hp} = C = AC = \lambda_p = \lambda_{hp} = 0$.Then we obtain;

$$
\begin{aligned}
dS/dt &= \Pi - (\lambda_h)S - \mu S \\
dE_h/dt &= \lambda_h S - (\eta + \mu)E_h \\
dA_h/dt &= (1-p)\eta E_h - (\omega_1 + \mu)A_h \quad (4) \\
dI_h/dt &= p\eta E_h - (\alpha_1 + \mu)I_h \\
dA/dt &= \alpha_1 I_h + \omega_1 A_h - \mu A
\end{aligned}
$$

A. Invariant region

In this section we obtain a region in which the solution of model equation (4) is bounded. For this model the total population $N_1 = S + E_h + A_h + I_h + A$.Then, after differentiating N_1 with respect to time and substituting the expression for $dS/dt,\ dE_h/dt,\ dA_h/dt, dI_h/dt, dA/dt$ from equation (4) we obtain;

$$
\begin{aligned}
dN_1/dt &= \Pi - \mu N_1 \\
dN_1/dt + \mu N_1 &\leq \Pi \quad (5)
\end{aligned}
$$

After, solving equation (5) and equating it as time tends to infinity, we got $\Omega_1 = \{S,\ E_h,\ A_h,\ I_h,\ A \in \mathbb{R}_+^5 : 0 \leq N_1 \leq [\Pi/\mu]\}$. Therefore, all the solution set of model equation (4) is bounded in Ω_1.

B. Positivity of the solution

In this section, we show all the solution of the model equation (4) remain positive for future time if their respective initial values are positive.

Theorem 1. *If* $S_0 > 0,\ E_{h0} > 0,\ A_{h0} > 0,\ I_{h0} > 0,\ A_0 > 0$ *then all the solution set* $(S(t),\ E_h(t),\ A_h(t),\ I_h(t),\ A(t))$ *are positive for future time.*

Proof. Positivity is verified separately for each of the model equation (4).

The model equation (4) given by $dS/dt = \Pi - (\lambda_h)S - \mu S$ can be expressed without loss of generality, after eliminating the positive terms Π which are appearing on the right hand side, as an inequality as $dS/dt \geq -[\lambda_h + \mu]S$. Using variables separable method and on applying integration, the solution of the foregoing differentially inequality can be obtained as $S(t) \geq e^{-\mu t - \int \lambda_h dt}$. Recall that an exponential function is always non–negative irrespective of the sign of the exponent, i.e., the exponential function $e^{-\mu t - \int \lambda_h dt}$ is a non-negative quantity. Hence, it can be concluded that $S(t) \geq 0$ for all $t \geq 0$. Similarly, it can be shown that $E_h(t) \geq 0,\ A_h(t) \geq 0,\ I_h(t) \geq 0$ and $A(t) \geq 0$ for all $t \geq 0$.

C. Local Stability of the Disease-free Equilibrium (DFE)

The disease free equilibrium of model equation (4) is obtained by equating all equations of the model equation to zero and then letting $E_h = A_h = I_h = A = 0$. Then we obtain;

$$\epsilon_{\mathrm{h}} = \{(\Pi/\mu),\quad 0,\quad 0,\quad 0,\quad 0\}$$

The linear stability of the DFE,$\epsilon_{0\mathrm{h}}$, can be established using the next generation operator method in Van den Driessche and Watmouth [16] on the system (4). The matrices F (for the new infection terms) and V (of the transition terms) are given, respectively by,

$$F = \begin{bmatrix} 0 & \beta_h q_h \gamma_1 & \beta_h q_h \gamma_2 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \text{ and}$$

$$V = \begin{bmatrix} a & 0 & 0 & 0 \\ -(1-p)\eta & b & 0 & 0 \\ -p\eta & 0 & c & 0 \\ 0 & -\omega_1 & -\alpha_1 & \mu \end{bmatrix}$$

The associated reproduction number, denoted by $\Re_h$ is then given by

$$\Re_h = [\beta_h q_h \eta((1-p)\gamma_1 c + \gamma_2 bp)]/[abc]$$

Where $a = \eta + \mu$, $b = \omega_1 + \mu$ and $c = \alpha_1 + \mu$.

Further using Theorem 2 in Van den Driessche and Watmouth [16], the following result is established. The DFE is locally asymptotically stable if $\Re_h < 1$ and unstable is$\Re_h > 1$.

D. Existence of Endemic Equilibrium

Lemma 1. *The HIV only model has a unique endemic equilibrium if and only if* $\Re_h > 1$.

Proof. Let the endemic equilibrium point of the model equation (4) be denoted by,

$$\varepsilon_h^* = (S_h^*,\quad E_h^*,\quad A_h^*,\quad I_h^*,\quad A^*)$$

and consider the force of infection

$$\lambda_h^* = [\beta_h q_h(\gamma_1 A_h^* + \gamma_2 I_h^*)]/[N] \qquad (6)$$

Solving the equations in system (4) by setting the right hand sides of equations in (4) to zero, gives,

$$\begin{aligned} S_h^* &= [\Pi]/[\lambda_h^* + \mu] \\ E_h^* &= [\lambda_h^* \Pi]/[(\lambda_h^* + \mu)a] \\ A_h^* &= [(1-\mathrm{p})\eta\Pi\lambda_h^*]/[(\lambda_h^* + \mu)ab] \qquad (7) \\ I_h^* &= [\lambda_h^* \mathrm{p}\eta\Pi]/[(\lambda_h^* + \mu)ac] \end{aligned}$$

$$A^* = [[\lambda_h^* \eta\Pi]/[\mu(\lambda_h^* \mathrm{p}\eta + \mu)a]]\big[[\alpha_1 p/c] + [\omega_1(1-p)/b]\big]$$

Substituting (7) in equation (6) gives

$$\lambda_h^* = \begin{bmatrix} \beta_h q_h(\gamma_1[[(1-\mathrm{p})\eta\Pi\lambda_h^*]/[(\lambda_h^* + \mu)ab]] \\ +\gamma_2[[\lambda_h^* \mathrm{p}\eta\Pi]/[ac]]) \end{bmatrix}/[N]$$

$$a(\lambda_h^*)^2 + \mu a\lambda_h^* - \beta_h q_h \mu\eta[[\gamma_1(1-p)c + p\gamma_2 b]/[bc]]\lambda_h^* = 0$$

$$a(\lambda_h^*)^2 + \mu a[1 - \Re_h]\lambda_h^* = 0$$

Hence, the HIV force of infection, λ_h^*, satisfies the following polynomial

$$p(\lambda_h^*) = (\lambda_h^*)^2 + D\lambda_h^* = 0$$

Where $D = \mu[1 - \Re_h]$

Clearly, $D \geq 0$ whenever $\Re_h < 1$ so that $\lambda_h^* = -1/D \leq 0$. Therefore the model has no endemic equilibrium whenever $\Re_h < 1$. The above result suggests the impossibility of backward bifurcation in the HIV model, since no endemic equilibrium exists when $\Re_h < 1$.

IV. HPV ONLY MODEL

Here HPV only model is obtained from model equation (2) by setting $E_h = E_{hp} = A_h = A_{hp} = I_h = I_{hp} = A = AC = \lambda_h = \lambda_{hp} = 0$. Then we obtain;

$$\begin{aligned} dS/dt &= \Pi - (\lambda_p)S - \mu S \\ dE_p/dt &= \lambda_p S - (\eta + \mu)E_p \\ dA_p/dt &= (1-q)\eta E_p - (\omega_3 + \mu)A_p \qquad (8) \\ dI_p/dt &= q\eta E_p - (\alpha_3 + \mu)I_p \\ dC/dt &= \alpha_3 I_p + \omega_3 A_p - \mu C \end{aligned}$$

A. *Invariant region*

In this section we obtain a region in which the solution of model equation (8) is bounded. For this model the total population $N_2 = S + E_p + A_p + I_p + C$. Then, after differentiating N_2 with respect to time and substituting the expression for dS/dt, dE_p/dt, dA_p/dt, dI_p/dt, dC/dt from equation (8) we obtain;

$$dN_2/dt = \Pi - \mu N_2$$
$$dN_2/dt + \mu N_2 \leq \Pi \qquad (9)$$

After, solving equation (9) and equating it as time tends to infinity, we got $\Omega_2 = \{S,\ E_p,\ A_p,\ I_p,\ A \in \mathbb{R}_+^5 : 0 \leq N_2 \leq [\Pi/\mu]\}$. Therefore, all the solution set of model equation (8) is bounded in Ω_2.

B. *Positivity of the solution*

In this section, we show all the solution of the model equation (8) remain positive for future time if their respective initial values are positive.

Theorem 2. *If* $S_0 > 0,\ E_{p0} > 0,\ A_{p0} > 0,\ I_{p0} > 0,\ C_0 > 0$ *then all the solution set* $(S(t),\ E_p(t),\ A_p(t),\ I_p(t),\ C(t))$ *are positive for future time.*

Proof. Positivity is verified separately for each of the model equation (8).

The model equation (8) given by $dS/dt = dS/dt = \Pi - (\lambda_p)S - \mu S$ can be expressed without loss of generality, after eliminating the positive terms Π which are appearing on the right hand side, as an inequality as $dS/dt \geq -[\lambda_p + \mu]S$. Using variables separable method and on applying integration, the solution of the foregoing differentially inequality can be obtained as $S(t) \geq e^{-\mu t - \int \lambda_p dt}$ Recall that an exponential function is always non–negative irrespective of the sign of the exponent, i.e., the exponential function $e^{-\mu t - \int \lambda_p dt}$ is a non-negative quantity. Hence, it can be concluded that $S(t) \geq 0$ for all $t \geq 0$. Similarly, it can be shown that $E_p(t) \geq 0,\ A_p(t) \geq 0,\ I_p(t) \geq 0$ and $C(t) \geq 0$ for all $t \geq 0$.

C. *Local Stability of the Disease-free Equilibrium (DFE)*

The disease free equilibrium of model equation (8) is obtained by equating all equations of the model equation to zero and then letting $E_p = A_p = I_p = C = 0$. Then we obtain;

$$\varepsilon_p = \{(\Pi/\mu),\quad 0,\quad 0,\quad 0,\quad 0\}$$

The linear stability of the DFE,ε_p, can be established using the next generation operator method in Van den Driessche and Watmouth [16] on the system (8). The matrices F (for the new infection terms) and V (of the transition terms) are given, respectively by,

$$F = \begin{bmatrix} 0 & \beta_p q_p \gamma_3 & \beta_p q_p \gamma_4 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \text{ and}$$

$$V = \begin{bmatrix} a & 0 & 0 & 0 \\ -(1-q)\eta & d & 0 & 0 \\ -q\eta & 0 & e & 0 \\ 0 & -\omega_3 & -\alpha_3 & \mu \end{bmatrix}$$

The associated reproduction number, denoted by $\Re_p$ is then given by

$$\Re_p = [\beta_p q_p \eta((1-q)\gamma_3 e + \gamma_4 dq)]/[ade]$$

Where $a = \eta + \mu,\ \ d = \omega_3 + \mu$ and $e = \alpha_3 + \mu$.

Further using Theorem 2 in Van den Driessche and Watmouth [16], the following result is established. The DFE is locally asymptotically stable if $\Re_p < 1$ and unstable is $\Re_p > 1$.

D. *Existence of Endemic Equilibrium*

Lemma 2. *The HPV only model has a unique endemic equilibrium if and only if* $\Re_p > 1$.

Proof. Let the endemic equilibrium point of the model equation (8) be denoted by,

$$\varepsilon_p^* = (S_p^*,\quad E_p^*,\quad A_p^*,\quad I_p^*,\quad C^*)$$

and consider the force of infection

$$\lambda_p^* = [\beta_p q_p(\gamma_3 A_p^* + \gamma_4 I_p^*)]/[N] \qquad (10)$$

Solving the equations in system (10) by setting the right hand sides of equations equal to zero, gives,

$$S_p^* = [\Pi]/[\lambda_p^* + \mu]$$
$$E_p^* = [\lambda_p^* \Pi]/[(\lambda_p^* + \mu)a]$$
$$A_p^* = [(1-\mathrm{q})\eta\Pi\lambda_p^*]/[(\lambda_p^* + \mu)ad] \qquad (11)$$

$I_p^* = [\lambda_p^* q\eta\Pi]/[(\lambda_p^* + \mu)ae]$ $C^* = [[\lambda_p^*\eta\Pi]/[\mu(\lambda_p^* q\eta + \mu)a]][[\alpha_3 q/e] + [\omega_3(1-q)/d]]$

Substituting (11) in equation (10) gives

$$\lambda_p^* = \begin{bmatrix}\beta_p q_p(\gamma_3[[(1-q)\eta\Pi\lambda_p^*]/[(\lambda_p^* + \mu)ad]] \\ +\gamma_4[[\lambda_p^* q\eta\Pi]/[ae]])\end{bmatrix}/[N]$$

$$a(\lambda_p^*)^2 + \mu a\lambda_p^* - \beta_p q_p \mu\eta[[\gamma_3(1-q)e + q\gamma_4 d]/[de]]\lambda_p^* = 0$$

$$a(\lambda_p^*)^2 + \mu a[1 - \Re_p]\lambda_p^* = 0$$

Hence, the HPV force of infection, λ_p^*, satisfies the following polynomial

$$p(\lambda_p^*) = (\lambda_p^*)^2 + Q\lambda_p^* = 0$$

Where $Q = \mu[1 - \Re_p]$

Clearly, $Q \geq 0$ whenever $\Re_p < 1$ so that $\lambda_p^* = -1/Q \leq 0$. Therefore the model has no endemic equilibrium whenever $\Re_p < 1$. The above result suggests the impossibility of backward bifurcation in the HPV model, since no endemic equilibrium exists when $\Re_p < 1$.

V. HPV-HIV CO-INFECTION MODEL

A. *Positivity and Boundedness.*

Here we assume that all parameters are positive because they represent the population of human beings. Then the model lies in $\mathbb{R}_+^{13}$ where $S > 0,\ E_p > 0,\ E_h > 0,\ E_{hp} > 0,\ A_h > 0,\ A_p > 0,\ A_{hp} > 0,\ I_h > 0,\ I_p > 0,\ I_{hp} > 0,\ A > 0,\ C > 0,\ AC > 0$. Since the initial values of the model are positive, we have to prove that the solutions are all positive and bounded.

Theorem 3. *The solutions of the system in* $\mathbb{R}_+^{13}$ *for* $t \geq 0$ *are positively bounded if the initial values are positive.*

Proof. Let $N(t)$ represent the whole population at time t,

$N = S + E_h + E_p + E_{hp} + A_h + A_p + A_{hp} + I_h + I_p + I_{hp} + A + C + AC.$

Then, after differentiating N with respect to time and substituting the expression for $dS/dt,\ dE_h/dt,\ dE_p/dt, dE_{hp}/dt, dA_h/dt, dA_p/dt, dA_{hp}/dt, dI_h/dt$ $, dI_p/dt, dI_{hp}/dt,\ dA/dt,\ dC/dt,\ dAC/dt$ from equation (2) we obtain;

$$dN/dt = \Pi - \mu N$$

After, solving equation $dN/dt + \mu N \leq \Pi$and equating it as time tends to infinity, we got $\Omega = \{S,\ E_h,\ E_p,\ E_{hp},\ A_h,\ A_p,\ A_{hp},\ I_h,\ I_p,\ I_{hp},\ A,\ C,\ AC \in \mathbb{R}_+^{13}: 0 \leq N \leq [\Pi/\mu]\}$. Hence, all the solution set of model equation (2) are positive and bounded in Ω.

B. *Local Stability of Disease Free Equilibrium*

The HPV-HIV model equation (2) has a DFE, obtained by setting the right hand sides of the equations in the model to zero, given by,

$$\varepsilon_{hp} = \{(\Pi/\mu),\ 0,\ 0,\ 0,\ 0,\ 0,\ 0,\ 0,\ 0,\ 0,\ 0,\ 0,\ 0\}$$

The linear stability of ε_{hp} can be established using the next generation operator method in Driessche and Watmough [16] on the system (2). It follows that the reproduction number of the HPV-HIV model equation (2), denoted by $\Re_{hp}$, is given by,

$$\Re_{hp} = \max\{\Re_h, \Re_p\}$$

Where

$$\Re_h = [\beta_h q_h \eta((1-p)\gamma_1 c + \gamma_2 bp)]/[abc]$$
$$\Re_p = [\beta_p q_p \eta((1-q)\gamma_3 e + \gamma_4 dq)]/[ade]$$

Theorem 4. *The disease free equilibrium point* ε_{hp} *is locally asymptotically stable whenever* $\Re_{hp} < 1$ *and unstable otherwise.*

Proof. To proof this theorem first we obtained the Jacobian matrix of the model equation (2) at the disease free equilibrium ε_{hp} and is given by;

$$J(\varepsilon_{hp}) = \begin{bmatrix} -\mu & 0 & 0 & 0 & -\beta_h q_h \gamma_1 & -\beta_p q_p \gamma_3 & -\beta_{hp} q_{hp} \gamma_5 & -\beta_h q_h \gamma_2 & -\beta_p q_p \gamma_4 & -\beta_{hp} q_{hp} \gamma_6 & 0 & 0 & 0 \\ 0 & -k_1 & 0 & 0 & \beta_h q_h \gamma_1 & 0 & 0 & \beta_h q_h \gamma_2 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -k_2 & 0 & 0 & \beta_p q_p \gamma_3 & 0 & 0 & \beta_p q_p \gamma_4 & 0 & 0 & 0 & 0 \\ 0 & \theta_1 & \theta_2 & -a & 0 & 0 & \beta_{hp} q_{hp} \gamma_5 & 0 & 0 & \beta_{hp} q_{hp} \gamma_6 & 0 & 0 & 0 \\ 0 & (1-p)\eta & 0 & 0 & -k_3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & (1-q)\eta & 0 & 0 & -k_4 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & (1-e)\eta & \theta_3 & \theta_4 & -k_5 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & p\eta & 0 & 0 & 0 & 0 & 0 & -k_6 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & q\eta & 0 & 0 & 0 & 0 & 0 & -k_7 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & e\eta & 0 & 0 & 0 & \theta_5 & \theta_6 & -k_8 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \omega_1 & 0 & 0 & \alpha_1 & 0 & 0 & -k_9 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \omega_3 & 0 & 0 & \alpha_3 & 0 & 0 & -k_{10} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \omega_2 & 0 & 0 & \alpha_2 & \varepsilon_1 & \varepsilon_2 & -\mu \end{bmatrix}$$

One has

$$trace\, J(\varepsilon_{hp}) = -[k_1 + k_2 + k_3 + k_4 + k_5 + k_6 + k_7 + k_8 + k_9 + k_{10} + a + 2\mu] < 0$$

and

$$det\, J(\varepsilon_{hp}) = k_9 k_{10} \mu^2 [k_6 \beta_h q_h \gamma_1 \eta(1-p) + k_3 p\eta \beta_h q_h \gamma_2 - k_1 k_3 k_6] \Big[k_7 k_8 \Big[[-k_2 k_4 \eta((1-e)+a) - \beta_p q_p \gamma_3 \eta(1-q)][\beta_{hp} q_{hp} \gamma_5 - k_5][k_3 k_4 k_8 \beta_p q_p \gamma_4 q\eta][\beta_{hp} q_{hp} \gamma_5 p\eta \beta_h q_h \gamma_2 (1-e) + a k_5 - k_1 k_6][-k_6 \beta_h q_h \gamma_1 \eta(1-p)(a + (1-e)\eta)]\Big] + k_4 k_5 p\eta \beta_{hp} q_{hp} \gamma_5 e\eta \beta_p q_p \gamma_4 \Big[1 + [k_7 \beta_p q_p \gamma_3 \eta(1-q) - k_2 k_4 k_7][k_3 p\eta \beta_h q_h \gamma_2 - \eta(1-p) - k_3]\Big]\Big] > 0,$$

when $\mathfrak{R}_{hp} < 1$.

We have just proved that the disease free equilibrium ε_{hp} of model equation (2) is locally asymptotically stable if $\mathfrak{R}_{hp} < 1$ and unstable if $\mathfrak{R}_{hp} > 1$.

C. Global Stability of Disease Free Equilibrium

To investigate the global stability of disease free equilibrium we used technique implemented by Castillo-Chavez and Song [17]. First the model equation (2) can be re-written as

$$dX/dt = F(X, Z)$$
$$dZ/dt = G(X, Z), \quad G(X, 0) = 0$$

Where, X stands for the uninfected population, that is $X = (S)$ and Z also stands for the infected population, that is $Z = (E_h,\ E_p,\ E_{hp},\ A_h,\ A_p,\ A_{hp},\ I_h,\ I_p,\ I_{hp},\ C,\ A,\ AC)$. The disease free equilibrium point of the model is denoted by $U = (X^*, 0)$. The point $U = (X^*, 0)$ to be globally asymptotically stable equilibrium for the model provided that $\mathfrak{R}_{hp} < 1$ and the following conditions must be met:

(H_1). For $dX/dt = F(X, 0)$, $X^*$is globally asymptotically stable.

(H_2). $G(X, Z) = AZ - \tilde{G}(X, Z)$, $\tilde{G}(X, Z) \geq 0$ for $(X, Z) \in \Omega$.

Where $A = D_Z G(U, 0)$ is a Metzler matrix (the off diagonal elements of A are non-negative) and G is the region where the model make biologically sense.

If the model (2) met the above two criteria then the following theorem holds.

Theorem 5. *The point $U = (X^*, 0)$ is globally asymptotically stable equilibrium provided that $\mathfrak{R}_0 < 1$ and the condition (H_1) and $(H_2)$are satisfied.*

Proof. From system (2) we can get $F(X, Z)$ and $G(X, Z)$;

$$dX/dt = F(X, Z) = \left[\Pi - \left(\lambda_h + \lambda_p + \lambda_{hp} + \mu\right)S\right] \quad \text{and}$$

$$dZ/dt = G(X, Z) = \begin{bmatrix} \lambda_h S - k_1 E_h \\ \lambda_p S - k_2 E_p \\ \lambda_{hp} S + \theta_1 E_h + \theta_2 E_p - a E_{hp} \\ (1-p)\eta E_h - k_3 A_h \\ (1-q)\eta E_p - k_4 A_p \\ (1-e)\eta E_{hp} + \theta_3 A_h + \theta_4 A_p - k_5 A_{hp} \\ p\eta E_h - k_6 I_h \\ q\eta E_p - k_7 I_p \\ e\eta E_{hp} + \theta_5 I_h + \theta_6 I_p - k_8 I_{hp} \\ \alpha_1 I_h + \omega_1 A_h - k_9 A \\ \alpha_3 I_p + \omega_3 A_p - k_{10} C \\ \alpha_2 I_{hp} + \omega_2 A_{hp} + \varepsilon_1 A + \varepsilon_2 C - \mu AC \end{bmatrix}$$

Consider the reduced system

$$\frac{dX}{dt}_{|Z=0} = [\Pi - \mu S] \qquad (12)$$

From (12), it is obvious that $X^* = [(\Pi/\mu)]$ is the global asymptotic point. This can be verified from the solution, namely $S = [\Pi/\mu] + [S(0) - (\Pi/\mu)]e^{-\mu t}$. As $t \to \infty$, the solution $(S) \to [\Pi/\mu]$, implying that the global convergence of (12) in Ω.

From the equation for infected compartments in the model we have:

$$A = \begin{bmatrix} -k_1 & 0 & 0 & \beta_h q_h \gamma_1 & 0 & 0 & \beta_h q_h \gamma_2 & 0 & 0 & 0 & 0 & 0 \\ 0 & -k_2 & 0 & 0 & \beta_p q_p \gamma_3 & 0 & 0 & \beta_p q_p \gamma_4 & 0 & 0 & 0 & 0 \\ \theta_1 & \theta_2 & -a & 0 & 0 & \beta_{hp} q_{hp} \gamma_5 & 0 & 0 & \beta_{hp} q_{hp} \gamma_6 & 0 & 0 & 0 \\ (1-p)\eta & 0 & 0 & -k_3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & (1-q)\eta & 0 & 0 & -k_4 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & (1-e)\eta & \theta_3 & \theta_4 & -k_5 & 0 & 0 & 0 & 0 & 0 & 0 \\ p\eta & 0 & 0 & 0 & 0 & 0 & -k_6 & 0 & 0 & 0 & 0 & 0 \\ 0 & q\eta & 0 & 0 & 0 & 0 & 0 & -k_7 & 0 & 0 & 0 & 0 \\ 0 & 0 & e\eta & 0 & 0 & 0 & \theta_5 & \theta_6 & -k_8 & 0 & 0 & 0 \\ 0 & 0 & 0 & \omega_1 & 0 & 0 & \alpha_1 & 0 & 0 & -k_9 & 0 & 0 \\ 0 & 0 & 0 & 0 & \omega_3 & 0 & 0 & \alpha_3 & 0 & 0 & -k_{10} & 0 \\ 0 & 0 & 0 & 0 & 0 & \omega_2 & 0 & 0 & \alpha_2 & \varepsilon_1 & \varepsilon_2 & -\mu \end{bmatrix}$$

Since A is Metzler matrix, i.e. all off diagonal elements are nonnegative. Then, $G(X,Z)$ can be written as, $G(X,Z) = AZ - \tilde{G}(X,Z)$,

where

$$\tilde{G}(X,Z) = \begin{bmatrix} \beta_h q_h(\gamma_1 \mathrm{A_h} + \gamma_2 \mathrm{I_h})(1 - [\mathrm{S/N}]) \\ \beta_p q_p(\gamma_3 \mathrm{A_p} + \gamma_4 \mathrm{I_p})(1 - [\mathrm{S/N}]) \\ \beta_h q_h(\gamma_5 \mathrm{A_{hp}} + \gamma_6 \mathrm{I_{hp}})(1 - [\mathrm{S/N}]) \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ \varepsilon_1 A + \varepsilon_2 C \end{bmatrix} = \begin{bmatrix} \tilde{G}_1(X,Z) \\ \tilde{G}_2(X,Z) \\ \tilde{G}_3(X,Z) \\ \tilde{G}_4(X,Z) \\ \tilde{G}_5(X,Z) \\ \tilde{G}_6(X,Z) \\ \tilde{G}_7(X,Z) \\ \tilde{G}_8(X,Z) \\ \tilde{G}_9(X,Z) \\ \tilde{G}_{10}(X,Z) \\ \tilde{G}_{11}(X,Z) \\ \tilde{G}_{12}(X,Z) \end{bmatrix}$$

It follows that $\widetilde{G_1}(X,Z) = \tilde{G}_2(X,Z) = \tilde{G}_3(X,Z) = \geq$, $\tilde{G}_{12}(X,Z) \geq 0$, $\tilde{G}_4(X,Z) = \tilde{G}_5(X,Z) = \tilde{G}_6(X,Z) = \tilde{G}_7(X,Z) = \tilde{G}_8(X,Z) = \tilde{G}_9(X,Z) = \tilde{G}_{10}(X,Z) = \tilde{G}_{11}(X,Z) = 0$.

Thus, $\tilde{G}(X,Z) \geq 0$. Conditions (H_1) and (H_2) are satisfied and we conclude that U is globally asymptotically stable for $\Re_{hp} < 1$.

D. ***Endemic Equilibrium Point***

The endemic equilibrium point is obtained through the assumption that $dS/dt = dE_h/dt = dE_p/dt = dE_{hp}/dt = dA_h/dt = dA_p/dt = dA_{hp}/dt = dI_h/dt = dI_p/dt = dI_{hp}/dt = dA/dt = dC/dt = dAC/dt = 0$. Then we obtain,

$$S^* = [\Pi]/\left[\lambda_h^* + \lambda_p^* + \lambda_{hp}^* + \mu\right]$$

$$E_h^* = [\lambda_h^* \Pi]/[(\lambda_h^* + \mu)a]$$

$$E_p^* = \left[\lambda_p^* \Pi\right]/\left[(\lambda_p^* + \mu)a\right]$$

$$E_{hp}^* = \left[\lambda_{hp}^* S^* + \theta_1 E_h^* + \theta_2 E_p^*\right]/[a]$$

$$A_h^* = [(1 - \mathrm{p})\eta \Pi \lambda_h^*]/[(\lambda_h^* + \mu)ab]$$

$$A_p^* = \left[(1 - \mathrm{q})\eta \Pi \lambda_p^*\right]/\left[(\lambda_p^* + \mu)ad\right]$$

$$A_{hp}^* = \left[(1 - \mathrm{e})\eta E_{hp}^* + \theta_3 A_h^* + \theta_4 A_p^*\right]/[k_5]$$

$$I_h^* = [\lambda_h^* \mathrm{p}\eta \Pi]/[(\lambda_h^* + \mu)ac]$$

$$I_p^* = \left[\lambda_p^* \mathrm{q}\eta \Pi\right]/\left[(\lambda_p^* + \mu)ae\right]$$

$$I_{hp}^* = \left[\mathrm{e}\eta E_{hp}^* + \theta_5 I_h^* + \theta_6 I_p^*\right]/[k_8]$$

$$A^* = [[\lambda_h^* \eta \Pi]/[\mu(\lambda_h^* \mathrm{p}\eta + \mu)a]] \begin{bmatrix} [\alpha_1 p/c] \\ +[\omega_1(1-p)/b] \end{bmatrix}$$
$$C^* = [[\lambda_p^* \eta \Pi]/[\mu(\lambda_p^* \mathrm{q}\eta + \mu)a]] \begin{bmatrix} [\alpha_3 q/e] \\ +[\omega_3(1-q)/d] \end{bmatrix}$$
$$(AC)^* = [\alpha_2 I_{hp}^* + \omega_2 A_{hp}^* + \varepsilon_1 A^* + \varepsilon_2 C^*]/[\mu]$$

After substituting the variables we see that the endemic equilibrium point is very long and complicated. We have therefore decided to use numerical simulation of the co-infection dynamics considering when $\Re_{hp} < 1$ and $\Re_{hp} > 1$.

E. Impact of HIV on HPV Dynamics.

Since the reproduction number for the co-infection is indicated in terms of two reproduction numbers with respect to the two diseases, we have to analyse the co-infection by considering the impact of one disease on the other.To describe the impact of HIV on HPV dynamics and vice versa, we express $\Re_h$in terms of $\Re_p$. Since,

$$\Re_p = [\beta_p q_p \eta((1-q)\gamma_3 e + \gamma_4 dq)]/[(\eta + \mu)de]$$

We express the parameter independent of both diseases as the subject. In this study we make μ the subject and after few manipulations we obtain,

$$\mu = \left[[\beta_p q_p \eta((1-q)\gamma_3 e + \gamma_4 dq)] - \eta \Re_p de\right]/[\Re_p de]$$

Then substituting the expression for μ in $\Re_h$ give,

$$\Re_h = [\beta_h q_h \eta((1-p)\gamma_1 c + \gamma_2 bp)]\Re_p de/[\beta_p q_p \eta((1-q)\gamma_3 e + \gamma_4 dq)]bc$$

To investigate the impact of the two diseases each other, obtaining the partial derivative of $\Re_h$with respect to $\Re_p$we get,

$$\partial \Re_h / \partial \Re_p = de[\beta_h q_h \eta((1-p)\gamma_1 c + \gamma_2 bp)]/[\beta_p q_p \eta((1-q)\gamma_3 e + \gamma_4 dq)]bc \quad (13)$$

If equation (13) is positive, implies that an increase in HIV cases results in an increase of HPV infections in the community, when Equation (13) equals to zero means that HIV has no impact on HPV infection and when Equation (13) is negative implies that HIV has a negative impact on HPV infections.

VI. SENSITIVITY ANALYSIS

In this section we perform the sensitivity analysis of the reproductive number. Sensitivity analysis tells us how important each parameter is to disease transmission. Such information is crucial not only for experimental design, but also to data assimilation and reduction of complex nonlinear models. Sensitivity analysis is commonly used to determine the robustness of model predictions to parameter values, since there are usually errors in data collection and presumed parameter values. It is used to discover parameters that have a high impact on basic reproduction number and should be targeted by intervention strategies. Following Eshetu and Koya [18], we present the normalized forward sensitivity indices of $\Re_p$ and $\Re_h$with respect to our model parameter values $\beta_p = 0.45,\ q_p = 0.03,\ q = 0.1286,\ \gamma_4 = 1.051,\ \gamma_3 = 1.016,\ \eta = 1.124,\ \mu = 0.02,\ \omega_3 = 1.1152,\ \alpha_3 = 0.011$ and$\beta_h = 0.55,\ q_h = 0.04,\ p = 0.1,\ \gamma_2 = 1.051,\ \gamma_1 = 1.016,\ \eta = 1.124,\ \mu = 0.02,\ \omega_1 = 1.0054,\ \alpha_3 = 0.016$ respectively.

A. Sensitivity Analysis for $\Re_p$

The explicit expression of $\Re_p$is given by:

$$\Re_p = \beta_p q_p \eta[\gamma_3(1-q)(\alpha_3 + \mu) + \gamma_4 q(\omega_3 + \mu)]/[(\eta + \mu)(\omega_3 + \mu)(\alpha_3 + \mu)]$$

Since $\Re_p$ depends only on nine parameters, we derive an analytical expression for its sensitivity to each parameter using the normalized forward sensitivity index as follows in Table 3 [19].The sensitivity indices of the basic reproductive number with respect to main parameters are arranged orderly in Table 3. The parameters are arranged from the most sensitive one to the least sensitive one. Those parameters that have positive indices i.e. $\beta_p,\ q_p,\ q,\ \gamma_4,\ \gamma_3$ and η show that they have great impact on expanding the disease in the community if their values are increasing. Due to the reason that the basic reproduction number increases as their values increase, it means that the average number of secondary cases of infection increases in the community. Furthermore, those parameters in which their sensitivity indices are negative i.e. $\mu,\ \omega_3$ and $\alpha_3$have an influence of minimizing the burden of the disease in the community as their values increase while the others are left constant. And also as their values increase, the basic reproduction number decreases, which leads to minimizing then endemicity of the disease in the community.

B. Sensitivity Analysis for $\Re_h$

The explicit expression of $\Re_h$is given by:

$\Re_h = \beta_h q_h \eta[\gamma_1(1-q)(\alpha_1 + \mu) + \gamma_2 q(\omega_1 + \mu)]/[(\eta + \mu)(\omega_1 + \mu)(\alpha_1 + \mu)]$Since $\Re_h$ depends only on nine parameters, we derive an analytical expression for its sensitivity to each parameter using the normalized forward sensitivity index as follows in Table 4 [19].The sensitivity indices of the basic reproductive number with respect to main parameters are arranged orderly in Table 4. The parameters are arranged from the most sensitive one to the least sensitive one. Those parameters that have positive indices i.e. $\beta_h,\ q_h,\ p,\ \gamma_2,\ \gamma_1$ and ηshow that they have great impact on

expanding the disease in the community if their values are increasing. Due to the reason that the basic reproduction number increases as their values increase, it means that the average number of secondary cases of infection increases in the community. Furthermore, those parameters in which their sensitivity indices are negative i.e. μ, $\omega_1$and $\alpha_1$have an influence of minimizing the burden of the disease in the community as their values increase while the others are left constant. And also as their values increase, the basic reproduction number decreases, which leads to minimizing then endemicity of the disease in the community.

T**able** 3. Sensitivity index and indices Table for $\Re_p$.

Parameter Symbol	**Sensitivity index**	**Sensitivity indices**
β_p	$\Upsilon_{\beta_p}^{\Re_p} = [\partial\Re_p/\beta_p] \times [\beta_p/\Re_p]$	1
q_p	$\Upsilon_{q_p}^{\Re_p} = [\partial\Re_p/q_p] \times [q_p/\Re_p]$	1
q	$\Upsilon_{q}^{\Re_p} = [\partial\Re_p/q] \times [q/\Re_p]$	0.0994
γ_4	$\Upsilon_{\gamma_4}^{\Re_p} = [\partial\Re_p/\gamma_4] \times [\gamma_4/\Re_p]$	0.090
γ_3	$\Upsilon_{\gamma_3}^{\Re_p} = [\partial\Re_p/\gamma_3] \times [\gamma_3/\Re_p]$	0.0629
η	$\Upsilon_{\eta}^{\Re_p} = [\partial\Re_p/\eta] \times [\eta/\Re_p]$	0.0088
μ	$\Upsilon_{\mu}^{\Re_p} = [\partial\Re_p/\mu] \times [\mu/\Re_p]$	-0.0258
ω_3	$\Upsilon_{\omega_3}^{\Re_p} = [\partial\Re_p/\omega_3][\omega_3/\Re_p]$	-0.4076
α_3	$\Upsilon_{\alpha_3}^{\Re_p} = [\partial\Re_p/\alpha_3] \times [\alpha_3/\Re_p]$	-0.4823

Table 4: Sensitivity index and indices Table for $\Re_h$.

Parameter Symbol	Sensitivity index	Sensitivity indices
β_h	$\Upsilon_{\beta_h}^{\Re_0} = [\partial\Re_h/\beta_h] \times [\beta_h/\Re_h]$	1
q_h	$\Upsilon_{q_h}^{\Re_0} = [\partial\Re_h/q_h] \times [q_h/\Re_h]$	1
p	$\Upsilon_{p}^{\Re_0} = [\partial\Re_h/p] \times [p/\Re_h]$	0.0994
γ_2	$\Upsilon_{\gamma_2}^{\Re_0} = [\partial\Re_h/\gamma_2] \times [\gamma_2/\Re_h]$	0.090
γ_1	$\Upsilon_{\gamma_1}^{\Re_0} = [\partial\Re_h/\gamma_1] \times [\gamma_1/\Re_h]$	0.0629
η	$\Upsilon_{\eta}^{\Re_0} = [\partial\Re_h/\eta] \times [\eta/\Re_h]$	0.0088
μ	$\Upsilon_{\mu}^{\Re_0} = [\partial\Re_h/\mu] \times [\mu/\Re_h]$	-0.0258
ω_1	$\Upsilon_{\omega_1}^{\Re_0} = [\partial\Re_h/\omega_1] \times [\omega_1/\Re_h]$	-0.4076
α_1	$\Upsilon_{\alpha_1}^{\Re_0} = [\partial\Re_h/\alpha_1] \times [\alpha_1/\Re_h]$	-0.4823

VII. NUMERICAL SIMULATION

In this section, numerical simulation study of model equations (2), (4) and (8) are carried out using the software DE Discover 2.6.4 and MATLAB R2015b with ODE45 solver. To conduct the study, a set of physically meaningful values are assigned to the model parameters. These values are either taken from literature or assumed on the basis of reality. Using the parameter values given in Table 5 and the initial conditions $S(0) = 200$, $E_h(0) = 170, E_p(0) = 160$, $E_{hp}(0) = 150, A_h(0) = 180$, $A_p(0) = 175, A_{hp}(0) = 170, I_h(0) = 150, I_p(0) = 140$, $I_{hp}(0) = 120$, $A(0) = 60$, $C(0) = 50$, $AC(0) = 40$ in the model equations (2), (4) and (8) a simulation study is conducted and the results are given in the following Figures.

Table 5: Parameter values used in simulations

e	**Value**	**Source**
Π	0.004	[1]
λ_h	0.00197	assumed
λ_p	0.002	assumed
λ_{hp}	0.0018	assumed
μ	0.02	[1]
α_1	0.016	assumed
α_2	0.017	assumed

α_3	0.011	assumed
p	0.067	assumed
q	0.067	assumed
e	0.067	assumed
θ_1	0.003	assumed
θ_2	0.003	assumed
θ_3	0.003	assumed
θ_4	0.003	assumed
θ_5	0.003	assumed
θ_6	0.003	assumed
ω_1	0.054	assumed
ω_2	0.064	assumed
ω_3	0.039	assumed
ε_1	0.001	assumed
ε_2	0.001	assumed
η	0.0024	assumed

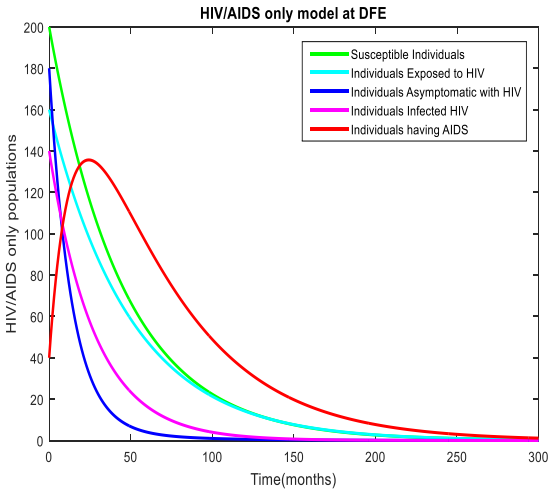

Figure 2. HIV/AIDS Dynamics.

In figure 2 we observe that all the solutions converge towards the equilibrium point. This was obtained when $\Re_h < 1$. At disease free equilibrium point, all infection solutions converge to zero while the susceptible individuals decreases and then remains constant. Susceptible individuals remain constant AIDS cannot be cured. This indicates that the disease free equilibrium point is locally asymptotically stable.

Figure 3 show that all the solutions converge towards the equilibrium point. This was obtained when $\Re_p < 1$. At disease free equilibrium point, all infection solutions converge to zero while the susceptible individuals decreases and then remains constant. Susceptible individuals remain constant Cervical cancer cannot be cured. This indicates that the disease free equilibrium point is locally asymptotically stable.

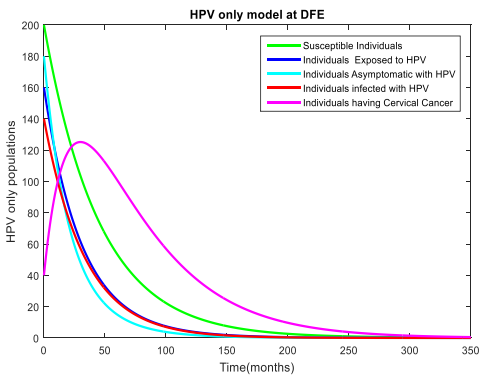

Figure 3. HPV Dynamics.

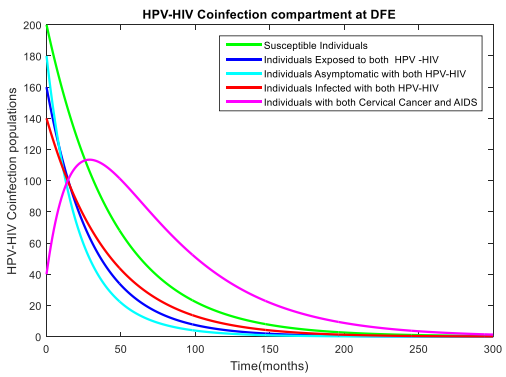

Figure 4: HPV-HIV Dynamics.

Figure 4 show that all the solutions converge towards the equilibrium point. At disease free equilibrium point, all infection solutions converge to zero while the susceptible individuals decreases and then remains constant. Susceptible individuals remain constant AIDS with Cervical cancer cannot be cured. This indicates that the disease free equilibrium point is locally asymptotically stable.

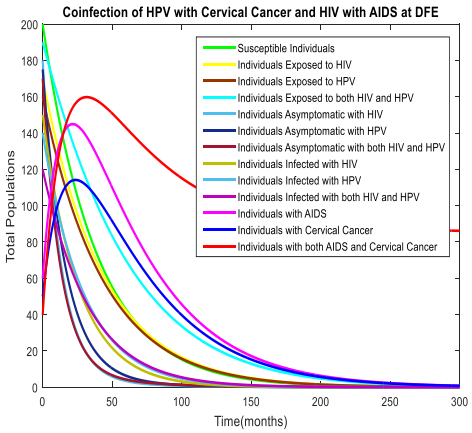

Figure 5: Co-infection of HPV with Cervical and HIV with AIDS Dynamics

In figure 5 we observe that all the solutions converge towards the equilibrium point. At disease free equilibrium point, all infection solutions converge to zero while the susceptible individuals decreases and then remains constant. Susceptible individuals remain constant AIDS, Cervical Cancer and AIDS with Cervical cancer cannot be cured. This indicates that the disease free equilibrium point is locally asymptotically stable.

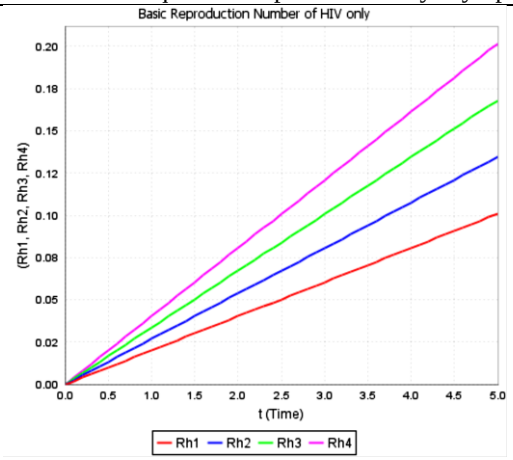

Figure 6: Effect of varying the contact rate β_h on $\Re_h$.

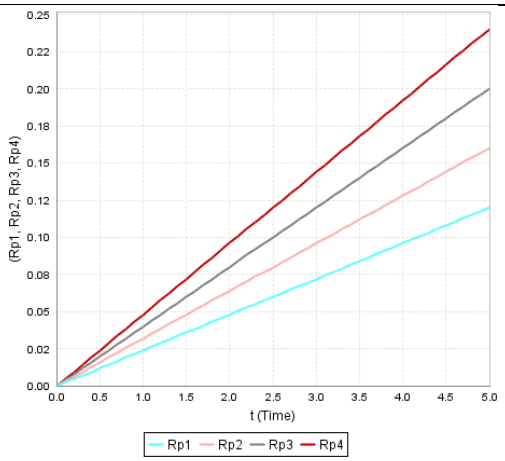

Figure 7: Effect of varying the contact rate β_p on $\Re_p$.

Figure 6 show that $\Re_4 > \Re_3 > \Re_2 > \Re_1$, indicating that contact rate has an effect on reducing the reproduction number. An increase in level of contact rate among individuals in a community has an effect on reducing the prevalence of HIV/AIDS the disease.

Figure 7 show that$\Re_4 > \Re_3 > \Re_2 > \Re_1$, indicating that contact rate has an effect on reducing the reproduction number. An increase in level of contact rate among individuals in a community has an effect on reducing the prevalence of HPV and Cervical Cancer the disease.

VIII. Discussions and Conclusions

In this paper, we formulated and analyzed a deterministic model for the transmission dynamics of HPV with Cervical Cancer and HIV with AIDS co-infection. The qualitative analysis of the model shows that there exists a domain where the model is epidemiologically and mathematically well-posed. The equilibria points of the model are obtained and their local as well as global stability conditions are established. The stability analysis of the model was investigated using the threshold parameter that governs the disease transmission. The HPV only model has a locally-stable disease free equilibrium whenever the associated reproduction number is less than unity. Also, the model has a unique endemic equilibrium whenever $\Re_p > 1$. The HIV only model also has a locally-stable disease free equilibrium whenever the associated reproduction number is less than unity. It also has a unique endemic equilibrium when-ever $\Re_h > 1$.The HPV–

HIV co-infection model has a locally-stable disease free equilibrium whenever the associated reproduction number is less than unity. We found from the analysis of the impact of HIV on HPV that HPV infection increases the risk of HIV; similarly, HIV infection increases the risk for HPV. Sensitivity analysis of the reproduction number suggested that increasing the rate of contact has high impact on the transmission of the diseases. Furthermore, analysis of the reproduction number through simulation shows that the reproduction number can be reduced to very low levels by decreasing contact rate. Therefore these findings conclude that using different treatment would be a very effective way for reducing the disease from community.

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