STABILITY ANALYSIS OF A SEX-STRUCTURED MODEL OF CHLAMYDIA TRACHOMATIS AND PELVIC INFLAMMATORY DISEASE (PID)

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Abstract
In this work we developed and analyzed a mathematical model of chlamydia trachomatis and Pelvic Inflammatory Disease (PID): A sex-structured approach. The model is a first order Ordinary Differential Equations, in which the human population is divided into seven mutually- exclusive compartments namely; Susceptible male individuals (S_m), Susceptible female individuals (S_f), Infected male individuals (I_m) ,Treated male individuals (T_m), Infected female individuals without Pelvic Inflammatory Disease (I_f), Treated female individuals (T_f) and female individuals infected with Pelvic Inflammatory Disease (P_f) .The equilibrium states of the model were obtained and analyzed for stability. By using Bellman and Cooke's theorem, the endemic equilibrium state was found to be stable and the criteria for stability of the disease free equilibrium state were established.

Keywords: Chlamydia Trachomatis, Pelvic Inflammatory Diseases (PID), equilibrium states, sex-structure

Introduction

Pelvic inflammatory disease or pelvic inflammatory disorder (PID) is an infection of the upper part of the female reproductive system namely the uterus fallopian tubes, and ovaries, and inside of the pelvis (Campion *et al.,* 2015*).* Chlamydia trachomatis (chlamydia) has been found in approximately 30% of all PID cases (Low et al., 2009) and is the most common bacterial sexually transmitted infection in many developed countries (WHO, 2001). Early detection and treatment of chlamydia through screening has been proposed as a strategy to prevent PID and subsequent reproductive tract morbidity in sexually active young women (Gottlieb et *al.,* 2010)

Globally about 106 million cases of chlamydia and 106 million cases of gonorrhea occurred in 2008 (WHO, 2012) .The number of cases of PID; however, is not clear. It is estimated to affect about 1.5 percent of young women yearly (Eschenbach, 2008). In the United States PID is estimated to affect about one million people yearly. Rates are highest with teenagers and first time mothers. PID causes over 100,000 women to become infertile in the US each year (CDC, 2010).

Symptoms in PID range from none to severe pains. If there are symptoms, then fever, cervical motion tenderness, lower abdominal pain, new or different discharge, painful intercourse, uterine tenderness, adnexal tenderness, or irregular menstruation may be noted (Mitchell & Prabhu, 2013).

The diagnosis is typically based on the presenting signs and symptoms. It is recommended that the disease be considered in all women of childbearing age who have lower abdominal pain. A definitive diagnosis of PID is made by finding pus involving the fallopian tubes during surgery. Ultrasound may also be useful in diagnosis (Mitchell *et al.,* 2013). Regular testing for sexually transmitted infections is encouraged for prevention (Smith *et al.,* 2007). Treatment is often started without confirmation of infection because of the serious

complications that may result from delayed treatment. Treatment depends on the infectious agent and generally involves the use of antibiotic therapy. If there is no improvement within two to three days, the patient is typically advised to seek further medical attention. Hospitalization sometimes becomes necessary if there are other complications. Treating sexual partners for possible STIs can help in treatment and prevention (CDC, 2014).

Mathematical modeling studies are a valuable tool for investigating hypothetical processes of chlamydia transmission and ascending infection. Amongst the few mathematical modeling studies with explicit descriptions of progression from chlamydia infection to PID, it has been proposed that PID develops in the first half of a chlamydia infection, in the second half, or can occur at any time during a chlamydia infection. Jacob and Catherine (2009), Dann *et al.,* (2013), and Herzog *et al.,* (2015) have all developed mathematical models of Chlamydia trachomatis and Pelvic inflammatory disease using heterogeneous population approach but none of them used a sex structured approach.

In this study, we will formulate a deterministic mathematical model for transmission dynamics of Chlamydia trachomatis and Pelvic inflammatory using a sex structured approach. The model to be developed considers a total population to be heterogeneous, non-constant and non-age structured. It should be clearly known that we are interested in investigating how susceptible male individuals can be infected via interaction with infected female individuals and vice-versa and then carry out the analysis.

Model Formulation

Mathematical model to study the dynamics of Chlamydia Trachomatis and Pelvic Inflammatory Disease using Sex-Structured Approach is presented in this section. The model divides the population into seven mutually-exclusive compartments namely; Susceptible male (S_m), Infected male (I_m), Treated male individuals (T_m), Susceptible female (S_f), Infected female (I_f), Treated female individuals (T_f) and Infected female with PID (P_f). This can be shown as a flow diagram in which the circles represent the different compartments and the arrows represent the transition between the compartments.

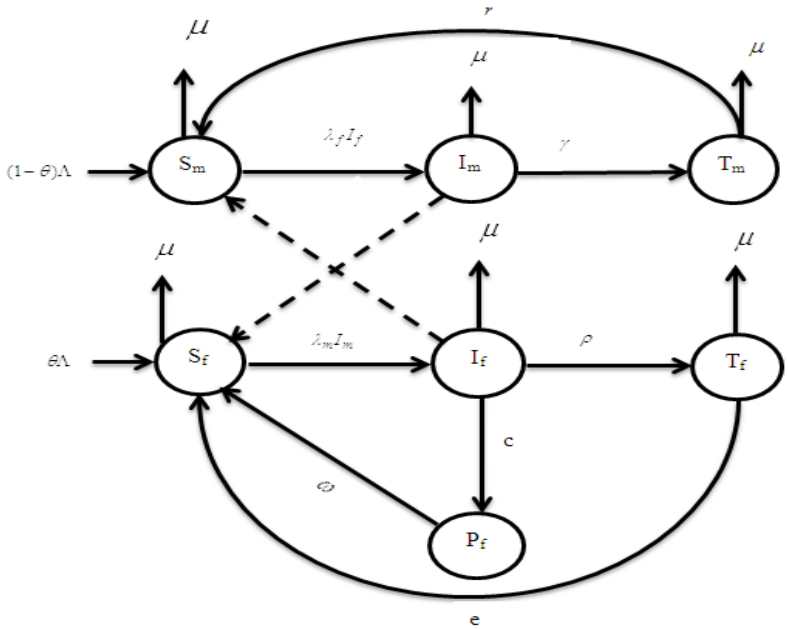

Fig. 1: A schematic description of the model

Basic Assumptions are:

(i) Susceptible male individuals can be infected via interaction with infected female individuals
(ii) Susceptible female individuals can be infected via interaction with infected male individuals
(iii) Infected female individuals can only develop PID if there is lack of treatment
(iv) Homosexual interaction was not considered.

To describe this mathematically, we have the following differential equations;

$$\frac{dS_m}{dt} = (1-\theta)\Lambda + rT_m - (\lambda_f I_f + \mu)S_m \quad (1)$$

$$\frac{dS_f}{dt} = \theta\Lambda + eT_f + \omega P_f - (\lambda_m I_m + \mu)S_f \quad (2)$$

$$\frac{dI_m}{dt} = \lambda_f I_f S_m - (\mu+\gamma)I_m \quad (3)$$

$$\frac{dT_m}{dt} = \gamma I_m - (\mu+r)T_m \quad (4)$$

$$\frac{dI_f}{dt} = \lambda_m S_f I_m - (\mu+\rho+c)I_f \quad (5)$$

$$\frac{dT_f}{dt} = \rho I_f - (\mu+e)T_f \quad (6)$$

$$\frac{dP_f}{dt} = cI_f - (\mu+\omega)P_f \quad (7)$$

where

S_m	Susceptible male
S_f	Susceptible female
I_m	Infected male
T_m	Treated male
I_f	Infected female
T_f	Treated female
P_f	Infected female with PID
Λ	Constant recruitment rate
μ	Natural death rate
γ	Recovery rate for infected male
ρ	Recovery rate for infected female without PID
ω	The rate at which infected individuals with PID move to the susceptible class
e	The rate which treated female move to susceptible class
c	rate at which infected female develop PID

Model Analysis

Positivity of Solution

Theorem 1: Let the initial data be

$$\left\{S_m(0)>0, S_f(0)>0, \left(I_m^{(0)}, T_m^{(0)}, I_f{}^0, T_f^{(0)}, P_f^{(0)} \geq 0\right)\right\} \in D$$

Then the solution set $\left\{S_m, S_f, I_m, T_m, I_f, T_f, P_f\right\}(t)$ of the system of equations (1) to (7) is positive for all t>0.

Proof:

From the first equation (1)

$$\frac{dS_m}{dt} = (1-\theta)\Lambda + rT_m - \left(\lambda_f I_f + \mu\right)S_m \geq -\left(\lambda_f I_f + \mu\right)S_m \quad (8)$$

$$\frac{dS_m}{dt} \geq -(\lambda_f I_f + \mu)S_m \quad (9)$$

Separating the variables we have

$$\frac{dS_m}{S_m} \geq -(\lambda_f I_f + \mu)dt \quad (10)$$

Integrating we have

$$InS_m \geq -(\lambda_m I_m + \lambda_f I_f + \mu)t + c \quad (11)$$

$$S_m(t) = e^{-(\lambda_f I_f + \mu)t + c} \quad (12)$$

$$S_m(t) \geq Ke^{-(\lambda_f I_f + \mu)t} \quad (13)$$

Where $k = e^c$

Using the initial condition $t = 0 \Rightarrow S_m(0) \geq K$ (14)

Therefore, $S_m(t) \geq S_m(0)e^{-(\lambda_f I_f + \mu)t} \geq 0$ (15)

From equation (2)

$$\frac{dS_f}{dt} = \theta\Lambda + eT_f + \omega P_f - (\lambda_m I_m + \mu)S_f \geq -(\lambda_m I_m + \mu)S_f \quad (16)$$

$$\frac{dS_f}{dt} \geq -(\lambda_m I_m + \mu)S_f \quad (17)$$

Separating the variables

$$\frac{dS_f}{S_f} \geq -(\lambda_m I_m + \mu)dt \quad (18)$$

Integrating we have;

$$InS_f \geq -(\lambda_m I_m + \mu)t + c \quad (19)$$

$$S_f(t) = e^{-(\lambda_m I_m + \mu)t + c} \quad (20)$$

$$S_f(t) \geq ke^{-(\lambda_m I_m + \mu)t} \quad (21)$$

Using the initial condition $t = 0 \Rightarrow S_f(0) \geq K$

Therefore, $S_f(t) \geq S_f(0)e^{-(\lambda_m I_m + \mu)t} \geq 0$ (22)

Similarly, it can be verified that the rest of the equations are positive for all $t > 0$ since $e^{\omega} > 0$

For all $\omega \in R$

Equilibrium Points

At equilibrium point $\frac{dS_m}{dt}=\frac{dS_f}{dt}=\frac{I_m}{dt}=\frac{T_m}{dt}=\frac{I_f}{dt}=\frac{T_f}{dt}=\frac{dP_I}{dt}=0$

Now, let $S_m=x_1, S_f=x_2, I_m=x_3, T_m=x_4, I_f=x_5, T_f=x_6 \text{ and } P_f=x_7$

Disease Free Equilibrium (DFE)

The equilibrium state with no infection is called the disease free equilibrium state which is given below.

$$\begin{pmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \\ x_5 \\ x_6 \\ x_7 \end{pmatrix} = \begin{pmatrix} \frac{(1-\theta)\Lambda}{\mu} \\ \frac{\theta\Lambda}{\mu} \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

Stability Analysis

Stability Analysis of Disease Free Equilibrium State

The Jacobian matrix at disease free equilibrium is:

$$J(\frac{(1-\theta)\Lambda}{\mu},\frac{\theta\Lambda}{\mu},0,0,0,0,0) = \begin{vmatrix} -\mu & 0 & 0 & r & -\lambda_f\frac{(1-\theta)\Lambda}{\mu} & 0 & 0 \\ 0 & -\mu & -\lambda_m\frac{\theta\Lambda}{\mu} & 0 & 0 & e & \omega \\ 0 & 0 & -(\mu+\gamma) & 0 & \lambda_f\frac{(1-\theta)\Lambda}{\mu} & 0 & 0 \\ 0 & 0 & \gamma & -(\mu+r) & 0 & 0 & 0 \\ 0 & 0 & \lambda_m\frac{\theta\Lambda}{\mu} & 0 & -(\mu+\rho+c) & 0 & 0 \\ 0 & 0 & 0 & 0 & \rho & -(\mu+e) & 0 \\ 0 & 0 & 0 & 0 & c & 0 & -(\mu+\omega) \end{vmatrix}$$

The characteristic equation

$$J(A-I\lambda)=\begin{vmatrix} -\mu-\lambda & 0 & 0 & r & -\lambda f\frac{(1-\theta)\Lambda}{\mu} & 0 & 0 \\ 0 & -\mu-\lambda & -\lambda_m\frac{\theta\Lambda}{\mu} & 0 & 0 & e & \omega \\ 0 & 0 & -(\mu+\gamma)-\lambda & 0 & \lambda f\frac{(1-\theta)\Lambda}{\mu} & 0 & 0 \\ 0 & 0 & \gamma & -(\mu+r)-\lambda & 0 & 0 & 0 \\ 0 & 0 & \lambda_m\frac{\theta\Lambda}{\mu} & 0 & -(\mu+\rho+c)-\lambda & 0 & 0 \\ 0 & 0 & 0 & 0 & \rho & -(\mu+e)-\lambda & 0 \\ 0 & 0 & 0 & 0 & c & 0 & -(\mu+\omega)-\lambda \end{vmatrix}$$

The determinant gives;

$$(-\mu-\lambda)(-\mu-\lambda)(-(\mu+\gamma)-\lambda)(-(\mu+r)-\lambda)(-(\mu+\rho+c)-\lambda)(-(\mu+e)-\lambda)(-(\mu+\omega)-\lambda)=0 \quad (23)$$

Either

$$(-\mu-\lambda)\,or\,(-\mu-\lambda)or(-(\mu+\gamma)-\lambda)or(-(\mu+r)-\lambda)or(-(\mu+\rho+c)-\lambda)or(-(\mu+e)-\lambda)or(-(\mu+\omega)-\lambda)=0 \quad (24)$$

Therefore;

$$\lambda_1=-\mu,\lambda_2=-\mu,\ \lambda_3=-(\mu+\gamma),\lambda_4=-(\mu+r),\lambda_5=-(\mu+\rho+c),\ \lambda_6=-(\mu+e),\lambda_7=-(\mu+\omega) \quad (25)$$

From (25)

$\lambda_1,\lambda_2,\lambda_3,\lambda_4,\lambda_5\,\lambda_6,\lambda_7<0$

Hence, the DFE is stable

Stability Analysis of Endemic Equilibrium State

$$J(A-I\lambda)=\begin{vmatrix} -A_1-\lambda & 0 & 0 & r & -A_2 & 0 & 0 \\ 0 & -A_3-\lambda & -A_4 & 0 & 0 & e & \omega \\ A_5 & 0 & -A_6-\lambda & 0 & A_7 & 0 & 0 \\ 0 & 0 & \gamma & -A_8-\lambda & 0 & 0 & 0 \\ 0 & A_9 & A_{10} & 0 & -A_{11}-\lambda & 0 & 0 \\ 0 & 0 & 0 & 0 & \rho & -A_{12}-\lambda & 0 \\ 0 & 0 & 0 & 0 & c & 0 & -A_{13}-\lambda \end{vmatrix}$$

The determinant

$$(-A_1-\lambda)(-A_3-\lambda)(-A_6-\lambda)(-A_8-\lambda)(-A_{11}-\lambda)(-A_{12}-\lambda)(-A_{13}-\lambda)=0 \quad (26)$$

Where

$A_1=\lambda_f I_f+\mu$, $A_2=\lambda_f S_m$, $A_3=\lambda_m I_m+\mu$, $A_4=\lambda_m S_f$, $A_5=\lambda_f I_f$, $A_6=\mu+\gamma$, $A_7=\lambda_{,f} S_m$

$A_8=(\mu+r)$, $A_9=\lambda_m I_m$, $A_{10}=\lambda_m S_f$, $A_{11}=\mu+\rho+c$, $A_{12}=\mu+e$, $A_{13}=\mu+\omega$

Next we shall use the idea of Bellman and Cook (1963) to (26) to establish the stability or otherwise of the model.

Lemma 1 (Bellman and Cooke (1963)): Let $H(Z)=P(z,e^z)$ where $p(z,w)$ a polynomial with principal term.

Suppose $H(iy), y\in R,$ is divided into its real and imaginary parts,

$$H(z) = F(y) + iG(y) \quad (27)$$

If all zeros of $H(z)$ have negative real parts, then the zeros of $F(y) and G(y)$ are real, Simple and alternate and

$G'(0)F(0) - G(0)F'(0) > 0$ for all $y \in R$. (28)

Now let (26) take the form

$$H(\lambda) = (-A_1 - \lambda)(-A_3 - \lambda)(-A_6 - \lambda)(-A_8 - \lambda)(-A_{11} - \lambda)(-A_{12} - \lambda)(-A_{13} - \lambda) \quad (29)$$

Expanding and rearranging in ascending powers of λ we have

$$\begin{aligned}
H(\lambda) &= -\lambda^7 + (A_1 + A_3 + A_6 + A_8 + A_{11} + A_{12} + A_{13})\lambda^6 \\
&+(-A_1A_3 + (-A_1 - A_3)A_6 - (A_1 + A_3 + A_6)A_8 + \\
&(-A_1 - A_3 - A_6 - A_8)A_{11} - (A_1 + A_3 + A_6 + A_8 + A_{11})A_{12} \\
&+(-A_1 - A_3 - A_6 - A_8 - A_{11} - A_{12})A_{13})\lambda^5 + (A_1A_3A_6 \\
&-(-A_1A_3 + (A_1 - A_3)A_6)A_8 + (A_1A_3 - (-A_1 - A_3)A_6 + \\
&(A_1 + A_3 + A_6)A_8)A_{11} - (-A_1A_3 + (-A_1 - A_3)A_6 - \\
&(A_1 + A_3 + A_6)A_8 + (-A_1 - A_3 - A_6 - A_8)A_{11})A_{12} \\
&+(A_1A_3 - (-A_1 - A_3)A_6 + (A_1 + A_3 + A_6)A_8 - (-A_1 - \\
&A_3 - A_6 - A_8)A_{11} + (A_1 + A_3 + A_6 + A_8 + A_{11})A_{12}) \\
&A_{13})\lambda^4 + (-A_1A_3A_6A_8 + (-A_1A_3A_6 + (-A_1A_3 + (-A_1 \\
&-A_3)A_6)A_8 + (A_1A_3 - (-A_1 - A_3)A_6)A_8)A_{11} - (A_1A_3A_6 \\
&-(-A_1A_3 + (-A_1 - A_3)A_6)A_8 + (A_1A_3 - (-A_1 - A_3)A_6 + \\
&(A_1 + A_3 + A_6)A_8)A_{11})A_{12} + (-A_1A_3A_6 + (-A_1A_3 + (A_1 - \\
&A_3)A_6)A_8 - (A_1A_3 - (-A_1 - A_3)A_6 + (A_1 + A_3 + A_6)A_8)A_{11} + \\
&(-A_1A_3 - (-A_1 - A_3)A_6 - (A_1 + A_3 + A_6)A_8) + (-A_1 - A_3 \\
&-A_6 - A_8)A_{11})A_{12})A_{13}\lambda^3 + (A_1A_3A_6A_8A_{11} - (-(A_1A_3A_6)A_8) \\
&+(-A_1A_3A_6 + (-A_1A_3 + (-A_1 - A_3)A_6)A_8)A_{11})A_{12} \\
&+(A_1A_3A_6A_8 - (-A_1A_3A_6 + (-A_1A_3 + (-A_1 - A_3)A_6)A_8)A_{11} \\
&+(A_1A_3A_6(-A_1A_3 - (-A_1 - A_3)A_6)A_8) + (A_1A_3 - (-A_1 - A_3)A_6 \\
&+(A_1 + A_3 + A_6)A_8)A_{11})A_{12})A_{13})\lambda^2 + (-A_1A_3A_6A_8A_{11} \\
&+(-A_1A_3A_6A_8A_{11} + (-A_1A_3A_6A_8 + (-A_1A_3A_6) \\
&(-A_1A_3 + (-A_1 - A_3)A_6)A_8)A_{12})A_{13}\lambda + A_1A_3A_6A_8A_{11}A_{12}A_{13}
\end{aligned} \quad (30)$$

Now set $\lambda = iw$ in (30) and then apply the result of Bellman and Cook (1963)

Now set $\lambda = iw$ in (30) and resolving into real and imaginary parts we have

$$H(i\omega) = F(\omega) + iG(\omega) \quad (31)$$

$$F(\omega) = -(A_1 + A_3 + A_6 + A_8 + A_{11} + A_{12} + A_{13})(\omega)^6 + (A_1A_3A_6 - (-A_1A_3 + (A_1 - A_3)A_6)A_8 + (A_1A_3 - (-A_1 - A_3)A_6 + (A_1 + A_3 + A_6)A_8)A_{11} - (-A_1A_3 + (-A_1 - A_3)A_6 - (A_1 + A_3 + A_6)A_8 + (-A_1 - A_3 - A_6 - A_8)A_{11})A_{12} + (A_1A_3 - (-A_1 - A_3)A_6 + (A_1 + A_3 + A_6)A_8 - (-A_1 - A_3 - A_6 - A_8)A_{11} + (A_1 + A_3 + A_6 + A_8 + A_{11})A_{12})A_{13})(\omega)^4 - (A_1A_3A_6A_8A_{11} - (-(A_1A_3A_6)A_8) + (-A_1A_3A_6 + (-A_1A_3 + (-A_1 - A_3)A_6)A_8)A_{11})A_{12} + (A_1A_3A_6A_8 - (-A_1A_3A_6 + (-A_1A_3 + (-A_1 - A_3)A_6)A_8)A_{11} + (A_1A_3A_6(-A_1A_3 - (-A_1 - A_3)A_6)A_8) + (A_1A_3 - (-A_1 - A_3)A_6 + (A_1 + A_3 + A_6)A_8)A_{11})A_{12})A_{13})(\omega)^2 + A_1A_3A_6A_8A_{11}A_{12}A_{13} \quad (32)$$

$$G(\omega) = \omega^7 + (-A_1A_3 + (-A_1 - A_3)A_6 - (A_1 + A_3 + A_6)A_8 + (-A_1 - A_3 - A_6 - A_8)A_{11} - (A_1 + A_3 + A_6 + A_8 + A_{11})A_{12} + (-A_1 - A_3 - A_6 - A_8 - A_{11} - A_{12})A_{13})(\omega)^5 - (-A_1A_3A_6A_8 + (-A_1A_3A_6 + (-A_1A_3 + (-A_1 - A_3)A_6)A_8 + (A_1A_3 - (-A_1 - A_3)A_6)A_8)A_{11} - (A_1A_3A_6 - (-A_1A_3 + (-A_1 - A_3)A_6)A_8 + (A_1A_3 - (-A_1 - A_3)A_6 + (A_1 + A_3 + A_6)A_8)A_{11})A_{12} + (-A_1A_3A_6 + (-A_1A_3 + (A_1 - A_3)A_6)A_8 - (A_1A_3 - (-A_1 - A_3)A_6 + (A_1 + A_3 + A_6)A_8)A_{11} + (-A_1A_3 - (-A_1 - A_3)A_6 - (A_1 + A_3 + A_6)A_8) + (-A_1 - A_3 - A_6 - A_8)A_{11})A_{12})A_{13}(\omega)^3 + (-A_1A_3A_6A_8A_{11} + (-A_1A_3A_6A_8A_{11} + (-A_1A_3A_6A_8 + (-A_1A_3A_6)(-A_1A_3 + (-A_1 - A_3)A_6)A_8)A_{12})A_{13}(\omega) \quad (33)$$

Differentiating (32) and (33) with respect to w and putting $w = 0$

$$F'(0) = 0$$

$$G'(\omega) = (-A_1A_3A_6A_8A_{11} + (-A_1A_3A_6A_8A_{11} + (-A_1A_3A_6A_8 + (-A_1A_3A_6)(-A_1A_3 + (-A_1 - A_3)A_6)A_8)A_{12})A_{13} \quad (34)$$

Setting $w = 0$ (32) and (33)

$$F(0) = A_1A_3A_6A_8A_{11}A_{12}A_{13} \quad (35)$$

$$G(0) = 0 \quad (36)$$

Since $F'(0) = 0, G(0) = 0, F(0) \neq 0 and G' \neq 0$

Hence $F(0)G'(0) - F'(0)G(0) > 0$

Therefore, the endemic equilibrium state is stable.

Conclusion

In this study, we have formulated a deterministic mathematical model for transmission dynamics of Chlamydia trachomatis and Pelvic inflammatory using a sex structured approach. Based on the findings of this research, it could be seen that the Disease Free Equilibrium State (DFE) of the model is stable since all the eigen-values are less than zero and the analysis of the Endemic Equilibrium State (EE) indicated that it is stable since it satisfies the condition of Bellman and Cook $F(0)G'(0) - F'(0)G(0) > 0$. These results are in conformity with results of other authors.

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