



A Nonlinear Mathematical model for Asthma: Effect of Environmental Pollution

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Abstract

In this paper, we explore a nonlinear mathematical model to study the spread of asthma due to inhaled pollutants from industry as well as tobacco smoke from smokers in a variable size population. The model is analyzed using stability theory of differential equations and computer simulation. It is shown that with an increase in the level of air pollutants concentration, the asthmatic (diseased) population increases. It is also shown that along with pollutants present in the environment, smoking (active or passive) also helps in the spread of asthma. Moreover, with the increase in the rate of interaction between susceptibles and smokers, the persistence of the spread of asthma is higher. A numerical study of the model is also performed to see the role of certain key parameters on the spread of asthma and to support the analytical results.

Keywords: pollutants, smokers, asthma, stability, Liapunov function, computer simulation

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1 Introduction

Asthma is a chronic disease of the respiratory system in which the airways occasionally constricts, becomes inflamed and is lined with excessive amount of mucus, often in response to one or more triggers as allergens, pollutants released into the environment and workplace exposures. In susceptible individuals, this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night or the early morning. During very severe attacks, asthma sufferers can turn blue due to lack of oxygen and can experience chest pain or even loss of consciousness.

Studies reveal that not only air pollutants like di-isocyanates, hexachloroplatinates, etc., can cause asthma but also tobacco smoke causes asthma [4,7]. It is well known that smoking can harm our body in many ways but it is very harmful to the lungs. It leads to decreased lung function making lungs susceptible to asthma triggers. Cigarette smoke contains high concentration of irritants such as formaldehyde, acrolein, ammonia and nitrogen oxides. Pulmonary damage results not only from mainstream smoke (that inhaled by the smoker) but also from sidestream smoke, the visible smoke that comes from the tip of a burning cigarette and is inhaled involuntarily by nonsmokers who are nearby. Therefore, when a person inhales tobacco smoke whether for personal smoking or passive smoke, these irritating substances can set off an asthma attack [8]. The environmental tobacco smoke (ETS) can both induce and exacerbate asthma. The largest impact of exposure to ETS can be seen in children and their respiratory system. Children of all ages who live in a home with smokers are 63% more likely to have asthma because their lungs are still developing [6,8]. About 15 million children are regularly exposed to secondhand smoke and upto 1 million children with asthma become more severe after exposure to secondhand smoke [6]. Also the pollutants emitted in the environment like particulates of vanadium and nickel from oil

refineries and power stations, cocktails of heavy metals from SLF burning cement, brick and lime works and dust from open cast coal mining and coal fired cement and other works play significant roles in the cause of asthma [2, 3, 7, 9].

Thus, due to continuous exposure to air pollutants, a susceptible population becomes asthmatic. The literature on the mathematical modeling of the study of asthma is scant. For example, Ghosh [4] presented a model to study the effect of environmental pollutants on the spread of asthma. It is noted that continuous exposure to smoking plays a very significant role in the development and spread of asthma. This very important aspect, by considering a separate class of smokers, has been accounted for in our model.

In view of the above, we have proposed a nonlinear mathematical model to study the effect of environmental pollutants on the spread of asthma in presence of smokers that are mainly responsible to pollute the otherwise pollution free environment. The model is analyzed using stability theory of nonlinear differential equations. A numerical study is also performed to see the role of key parameters on the spread of asthma.

2 Mathematical Model

For model building, we have subdivided the total population $N(t)$ into four compartments namely, susceptibles $S(t)$, exposed $E(t)$, diseased class (asthmatic class) $I(t)$ and smokers class $C(t)$, $P(t)$ is the cumulative concentration of pollutants present in the environment. It is assumed that the susceptible population becomes asthmatic by continuous exposure to air pollutants such as di-isocyanates, hexachloroplatinates, etc. and by interaction with smokers in two steps. First it moves from the susceptible class to exposed class with transmission coefficient γ and β due to interaction of susceptibles with pollutants present in the environment and smokers respectively. Further, from exposed class, it moves to

diseased class due to continuous exposure with pollutants and smokers with transmission coefficient λ_1 and λ_2 respectively.

In view of the above assumptions and considerations, and by using simple mass action interaction, a mathematical model is proposed as follows:

$$\frac{dS}{dt} = \Lambda - \mu S - \gamma SP - \beta SC \quad (1)$$

$$\frac{dE}{dt} = \gamma SP + \beta SC - \lambda_1 EP - \lambda_2 EC - \mu E \quad (2)$$

$$\frac{dI}{dt} = \lambda_1 EP + \lambda_2 EC + \theta_1 C + \theta_2 CP - \alpha I - \mu I \quad (3)$$

$$\frac{dC}{dt} = Q - \theta_1 C - \theta_2 CP - \theta C - \mu C \quad (4)$$

$$\frac{dP}{dt} = A(N) - \tau P + qC \quad (5)$$

with $S(0) = S_0 > 0, E(0) = E_0 > 0, I(0) = I_0 > 0, C(0) = C_0 > 0, P(0) = P_0 > 0$.

Since $N(t) = S(t) + E(t) + I(t) + C(t)$, therefore, we can write the equation governing the total population $N(t)$ as,

$$\frac{dN}{dt} = \Lambda + Q - \mu N - \alpha I - \theta C \quad (6)$$

Here Λ is the constant recruitment rate of susceptibles in the population under consideration, μ is the natural mortality rate taken to be same in all the classes. It is assumed that higher the number of smokers, higher is the pollutants concentration, especially in the household regions, which provides a conducive environment to induce the asthmatic conditions. Q is the constant inflow rate of

smokers i.e. the rate at which new members become smoker, θ_1 is the rate at which smokers become infected and join the infective class, θ_2 is the transmission coefficient due to exposure of smokers with environmental pollutants and θ is the rate at which smokers quit smoking. $A(N)$ is the rate of emission of pollutants into the environment which is, in general, population dependent but in the subsequent analysis we assume it to be a constant A , τ is the natural depletion rate coefficient of environmental pollutants and q is the rate at which smokers emit fumes (inhale and exhale smoke from cigarettes, cigars, pipes, etc.) which in turn increases the concentration level of pollutants in the environment. α is the disease induced death rate. It is assumed that all the dependent variables and parameters of the model are non-negative.

2.1 Boundedness of Solutions

Continuity of right hand side of system (1)-(6) and its derivative imply that the model is well posed for $N > 0$ [5]. The invariant region where solution exists is obtained as follows:

$$\frac{\Lambda + Q}{(\alpha + \mu + \theta)} \leq \liminf N(t) \leq \limsup N(t) \leq \frac{\Lambda + Q}{\mu} \quad (\text{as } t \rightarrow \infty)$$

since $N(t) > 0$ for all $t \geq 0$. Therefore, from eq.(6), $N(t)$ cannot blow up to infinity in finite time and consequently, the model system is dissipative (solutions are bounded). Hence, the solution exist globally for all $t > 0$ in the invariant and compact set,

$$\Omega = \left\{ (N, E, I, C, P) \in R_+^5 : 0 < N \leq \frac{\Lambda + Q}{\mu} + \varepsilon, 0 \leq E \leq \bar{E}, 0 \leq I \leq \bar{I}, 0 \leq C \leq \bar{C}, P \leq \bar{P} \right\} \quad (7)$$

which gives a region of attraction for any arbitrary small $\varepsilon > 0$.

Here,
$$\bar{E} = \frac{(\Lambda + Q)(\gamma\bar{P} + \beta\bar{C})}{\mu(\lambda_1\bar{P} + \lambda_2\bar{C} + \mu)}, \quad \bar{I} = \frac{(\lambda_1\bar{P} + \lambda_2\bar{C})\bar{E} + (\theta_1 + \theta_2\bar{P})\bar{C}}{(\alpha + \mu)},$$

$$\bar{C} = \frac{Q}{\theta_1 + \theta + \mu} \quad \text{and} \quad \bar{P} = \frac{A + q\bar{C}}{\tau}$$

As $N(t)$ tends to zero, $S(t)$, $E(t)$, $I(t)$ and $C(t)$ also tend to zero. Hence, each of these subpopulations tends to zero as $N(t)$ does. It is, therefore, natural to interpret these terms as zero at $N(t) = 0$.

2.2 Positivity of Solutions

Let the initial data be $N(0) = N_0 > 0$, $E(0) = E_0 \geq 0$, $I(0) = I_0 \geq 0$, $P(0) = P_0 \geq 0$ and $C(0) = C_0 \geq 0$ for all $t \geq 0$. Then, the solution $[S(t), E(t), I(t), C(t), P(t)]$ of the model remain positive for all time $t \geq 0$.

From eq.(3) we get $I'(t) \geq -(\alpha + \mu)I(t)$ and applying a theorem on differential inequalities [1] we obtain, $I(t) \geq c_1 e^{-(\alpha + \mu)t}$

Here c_1 is a constant of integration. A similar reasoning for the remaining equations shows that they are always positive in Ω for $t > 0$.

We assume that at $t = 0$, $N(t)$, $E(t)$, $I(t)$, $C(t)$ and $P(t)$ are all non-negative and that $N(0) > 0$. We notice that

$$\frac{\Lambda + Q}{(\alpha + \mu + \theta)} \leq \liminf N(t) \leq \limsup N(t) \leq \frac{\Lambda + Q}{\mu}, \text{ this implies that } S(t)$$

> 0 for all t .

3. Equilibrium and Stability Analysis

In this section, we present the existence of model equilibrium and its local and nonlinear asymptotic stability analysis.

3.1 Equilibrium of the Model

For equilibrium analysis, we study the reduced system, since $N(t) = S(t) + E(t) + I(t) + C(t)$, of the model system(1)-(6) as follows,

$$\frac{dN}{dt} = \Lambda + Q - \mu N - \alpha I - \theta C \tag{8}$$

$$\frac{dE}{dt} = \gamma(N - E - I - C)P + \beta(N - E - I - C)C - \lambda_1 EP - \lambda_2 EC - \mu E \tag{9}$$

$$\frac{dI}{dt} = \lambda_1 EP + \lambda_2 EC + \theta_1 C + \theta_2 CP - \alpha I - \mu I \tag{10}$$

$$\frac{dC}{dt} = Q - \theta_1 C - \theta_2 CP - \theta C - \mu C \tag{11}$$

$$\frac{dP}{dt} = A - \tau P + qC \tag{12}$$

The model (8)-(12) has only one non-negative equilibrium $W^* (N^*, E^*, I^*, C^*, P^*)$ where N^*, E^*, I^*, C^* and P^* are positive solutions of the following system of algebraic equations,

$$\Lambda + Q - \mu N - \alpha I - \theta C = 0 \tag{13}$$

$$\gamma(N - E - I - C)P + \beta(N - E - I - C)C - \lambda_1 EP - \lambda_2 EC - \mu E = 0 \quad (14)$$

$$\lambda_1 EP + \lambda_2 EC + \theta_1 C + \theta_2 CP - \alpha I - \mu I = 0 \quad (15)$$

$$Q - \theta_1 C - \theta_2 CP - \theta C - \mu C = 0 \quad (16)$$

$$A - \tau P + qC = 0 \quad (17)$$

From eq. (17) we get,

$$P = \frac{A + qC}{\tau} \quad (18)$$

From eq. (16) we obtain,

$$\frac{\theta_2 q}{\tau} C^2 + (\theta_1 + \theta + \mu + \theta_2 \frac{A}{\tau}) C - Q = 0 \quad (19)$$

This equation has two roots of C (say C_1 and C_2), which are given as follows,

$$C_1 = \frac{-\left(\theta_1 + \theta + \mu + \theta_2 \frac{A}{\tau}\right) - \sqrt{\left(\theta_1 + \theta + \mu + \theta_2 \frac{A}{\tau}\right)^2 + \frac{4Q\theta_2 q}{\tau}}}{(2\theta_2 q / \tau)} < 0 \text{ and}$$

$$C_2 = \frac{-\left(\theta_1 + \theta + \mu + \theta_2 \frac{A}{\tau}\right) + \sqrt{\left(\theta_1 + \theta + \mu + \theta_2 \frac{A}{\tau}\right)^2 + \frac{4Q\theta_2 q}{\tau}}}{(2\theta_2 q / \tau)} > 0$$

Here $C_1 < 0$ which is biologically irrelevant and not feasible in positive non-trivial equilibrium, therefore, we use positive value of C i.e. C_2 .

From eq. (13) we have,

$$N = \frac{1}{\mu} [\Lambda + Q - \theta C_2 - aI] \quad (20)$$

From eq. (15) we get,

$$I = \frac{1}{(\alpha + \mu)} \left[\left\{ \lambda_1 \left(\frac{A + qC_2}{\tau} \right) + \lambda_2 C_2 \right\} E + \theta_1 C_2 + \theta_2 C_2 \left(\frac{A + qC_2}{\tau} \right) \right] \quad (21)$$

From eq. (14) we obtain,

$$I = \frac{l \left[\frac{1}{\mu} (\Lambda + Q - \theta C_2) - E - C_2 \right] - \left[\lambda_1 \frac{(A + qC_2)}{\tau} + \lambda_2 C_2 + \mu \right] E}{l \left(\frac{\alpha}{\mu} + 1 \right)} \quad (22)$$

where $l = \gamma \left(\frac{A + qC_2}{\tau} \right) + \beta C_2 > 0$

From eq. (21) we note,

(i) $I = \frac{C_2}{(\alpha + \mu)} \left[\theta_1 + \theta_2 \left(\frac{A + qC_2}{\tau} \right) \right] = I_1$ (say) > 0 as $E = 0$

(ii) $E \rightarrow \infty$ as $I \rightarrow \infty$

(iii) $\frac{dE}{dI} = \frac{(\alpha + \mu)}{\lambda_1 \left(\frac{A + qC_2}{\tau} \right) + \lambda_2 C_2} > 0$

From eq. (22) we note,

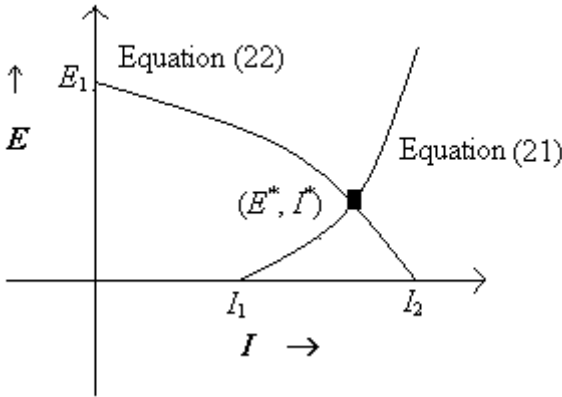
$$(i) E = l \frac{\frac{1}{\mu}(\Lambda + Q - \theta C_2) - C_2}{\lambda_1 \left(\frac{A + qC_2}{\tau} \right) + \lambda_2 C_2 + \mu + l} = E_1(\text{say}) > 0 \text{ if } \frac{\Lambda + Q}{\mu} > \left(1 + \frac{\theta}{\mu} \right) C_2 \text{ as}$$

$$I = 0$$

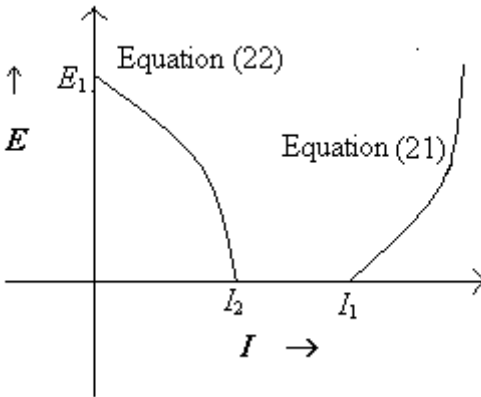
$$(ii) I = \frac{\frac{1}{\mu}(\Lambda + Q - \theta C_2) - C_2}{\left(1 + \frac{\alpha}{\mu} \right)} = I_2(\text{say}) > 0 \text{ if } \frac{\Lambda + Q}{\mu} > \left(1 + \frac{\theta}{\mu} \right) C_2 \text{ as } E = 0$$

$$(iii) \frac{dE}{dI} = \frac{-l \left(1 + \frac{\alpha}{\mu} \right)}{\lambda_1 \left(\frac{A + qC_2}{\tau} \right) + \lambda_2 C_2 + \mu + l} < 0$$

Thus, we get positive values of E and I (say E^* and I^* respectively) if the following condition $\frac{\Lambda + Q}{\mu} > \left(1 + \frac{\theta}{\mu} \right) C_2$ and $I_1 < I_2$ are satisfied (see Figs. 1a, 1b),



(a)



(b)

Figure 1. Intersection of two isoclines (21) and (22) to determine existence of W^* (a) when $I_1 < I_2$ (b) when $I_1 > I_2$

To study the local and nonlinear (global) asymptotic stability behavior of the equilibrium, we propose the following theorems.

Theorem 1. The equilibrium W^* is locally asymptotically stable provided the

condition $\begin{vmatrix} a_4 & 1 & 0 & 0 \\ a_2 & a_3 & a_4 & 1 \\ 0 & a_1 & a_2 & a_3 \\ 0 & 0 & 0 & a_1 \end{vmatrix} > 0$ is satisfied.

(See Appendix A for proof)

Theorem 2. Let the following inequalities hold in Ω ,

$$\frac{9\alpha^2(\lambda_1 P^* + \lambda_2 C^*)}{4\mu(\alpha + \mu)} < \frac{4\mu[(\lambda_1 + \gamma)P^* + (\lambda_2 + \beta)C^* + \mu]}{9(\gamma P^* + \beta C^*)}$$

(23)

then W^* is nonlinearly (globally) asymptotically stable.

(See Appendix B for proof)

Remarks:

(1) It is noted that the system (8)-(12) is bounded by the same system when $\alpha = 0$, which implies that the solution of (8)-(12) is bounded by the solution of the latter. If $\alpha = 0$, the system is globally stable without any condition. Hence we speculate that the nontrivial equilibrium of system (8)-(12) may be globally stable as given in the theorem.

(2) If λ_1 and λ_2 tends to zero in inequality (23), it is automatically satisfied. This implies that the continuous exposure to environmental pollutants and smokers has destabilizing effect on the system.

(3) If γ and β tends to zero in inequality (23), then the possibility of satisfying the condition increases. This implies that these parameters have destabilizing effect on the system.

4. Numerical Analysis

It is noted here that our main aim is to show, through a nonlinear model and its qualitative analysis, the effects of pollutants present in the environment and smokers on the spread of asthma in the population. It is, therefore, desirable that we must show the existence of equilibrium values of variables of the model as well as the feasibility of stability conditions numerically for a set of parameters.

We study the model (8-12) numerically to see the effects of various parameters on the spread of the disease by Runge-Kutta fourth order method using the following set of parameter values given in Table 1*.

Table 1.

Parameter description	Symbol	Parameter value
Recruitment rate of susceptibles	Λ	100
Interaction of susceptibles with smokers	β	0.0002
Interaction of susceptibles with pollutants	γ	0.0003
Natural death rate	μ	$1/70 = 0.014$
Disease induced death rate	α	$1/55 = 0.018$
Recruitment rate of smokers	Q	60
Rate at which smokers quit smoking	θ	0.002

Cumulative density of pollutants	A	10
Rate at which pollution increase due to smoker's smoke	q	0.00001
Depletion rate of environmental discharge as environment cleans	τ	0.01
Interaction of exposed persons with pollutants	λ_1	0.0001
Interaction of exposed persons with smokers	λ_2	0.00015
Rate at which smokers become infected	θ_1	0.0002
Rate at which smokers came into the contact of pollution	θ_2	0.00025

**Actual parameter values are not known to authors.*

The equilibrium values of different variables in W^* are computed as follows,

$$N^* = 5634.98, E^* = 650.11, I^* = 4481.09, C^* = 225.35, P^* = 1000.23,$$

The eigen values of the matrix corresponding to equilibrium W^* are obtained as follows,

$$-0.03200000000, -0.1478245471, -0.3591369540, -0.2662541383, -0.01000219847$$

Since all the eigen values corresponding to W^* are negative, therefore, W^* is locally asymptotically stable. It has been checked that for the above set of parameters, the local as well as nonlinear stability conditions are satisfied.

Using MAPLE the phase plane diagrams of $N-I$ and $E-I$ have been drawn in figs.(2-3) showing the nonlinear behavior of W^* with respect to these parameters.

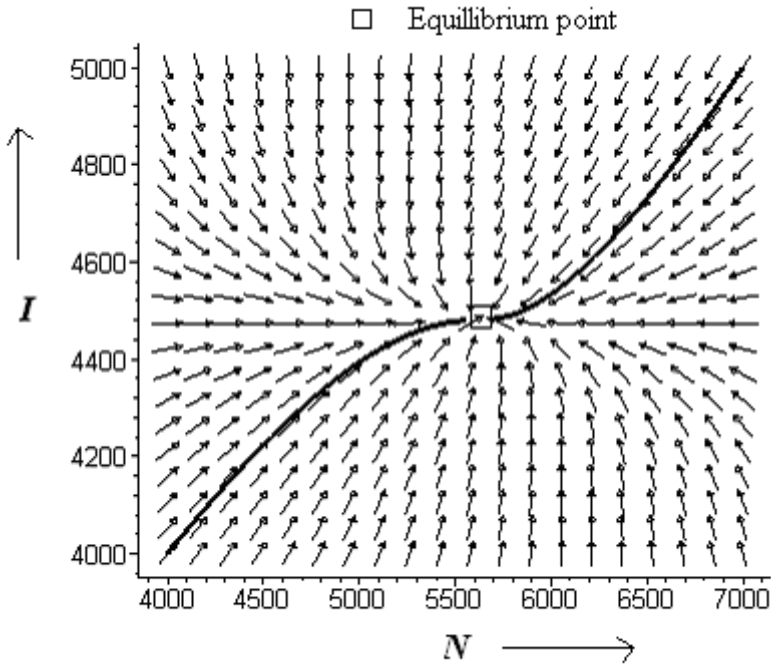


Figure 2. Variation of population N with infectives I

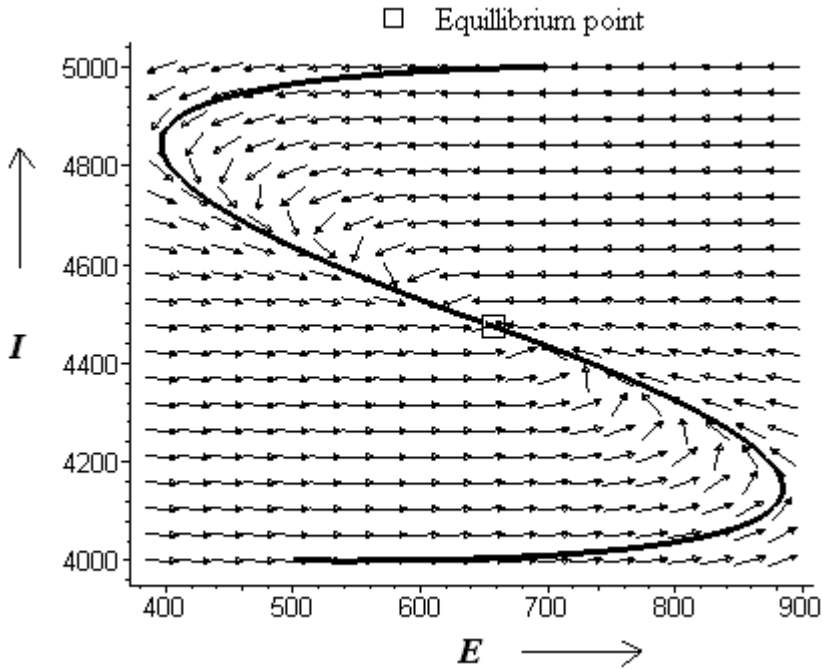


Figure 3. Variation of exposed persons E with asthmatic infectives I

In figs.(4-5), the asthmatic population against time is plotted for different values of interaction rates β and γ of susceptibles with smokers and pollutants respectively. From these figures, we note that as the interaction between susceptibles-smokers and susceptibles-pollutants increases, asthmatic population also increases. Figs. (6-7) depict the variation of asthmatic population with time for different values of interaction rate λ_1 and λ_2 of exposed individuals with pollutants and smokers respectively. It is seen that as the contact rate of exposed individual with pollutants and smokers increases, it further leads to increase the number of asthmatic population. Thus, it is concluded that if the continuous exposure of exposed individuals to environmental pollutants and smokers is restricted, the number of asthmatic population can be kept under control. In fig.(8), we have explicitly shown the effect of increase of pollutants on the asthmatic population and it is found that when cumulative concentration of pollutants increases, the asthmatic population also increases. In fig.(9), the

variation of asthmatic population is shown with time for different values of constant inflow rate of smokers. It is seen that as the recruitment rate of smokers increases, the smoker population increases continuously which, in turn, increases the asthmatic population. Fig.(10) depicts the role of θ , the rate at which smokers quit smoking, on asthmatic population. It is observed that as θ increases, the smokers population decreases. This decrease in smokers population results in decreasing the asthmatic population. Thus, if many people stay away from smoking the development and spread of the disease can be slowed down. Fig. (11) shows the role of θ_1 , the rate at which smokers become infected. It is noted that as θ_1 increases, the higher number of smokers join the asthmatic class and increase the asthmatic population. Fig. (12) depicts the role of θ_2 , the transmission coefficient due to exposure of smokers with environmental pollutants. It is seen that as θ_2 increases, the higher number of smokers came in the contact with environmental pollutants and hence the asthmatic population increases.

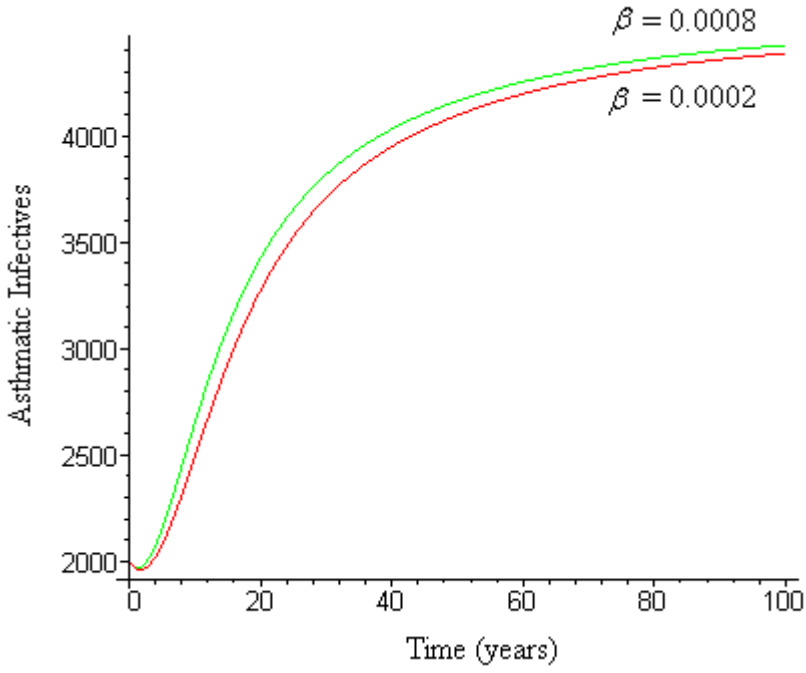


Figure 4. Variation of asthmatic population I with time for different values of interaction rate β

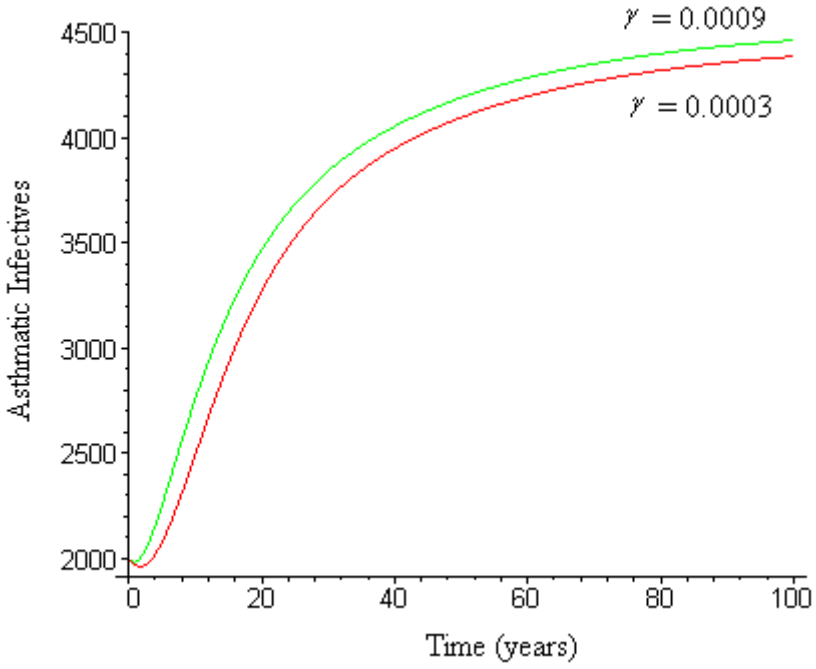


Figure 5. Variation of asthmatic infectives I with time for different values of interaction rate γ

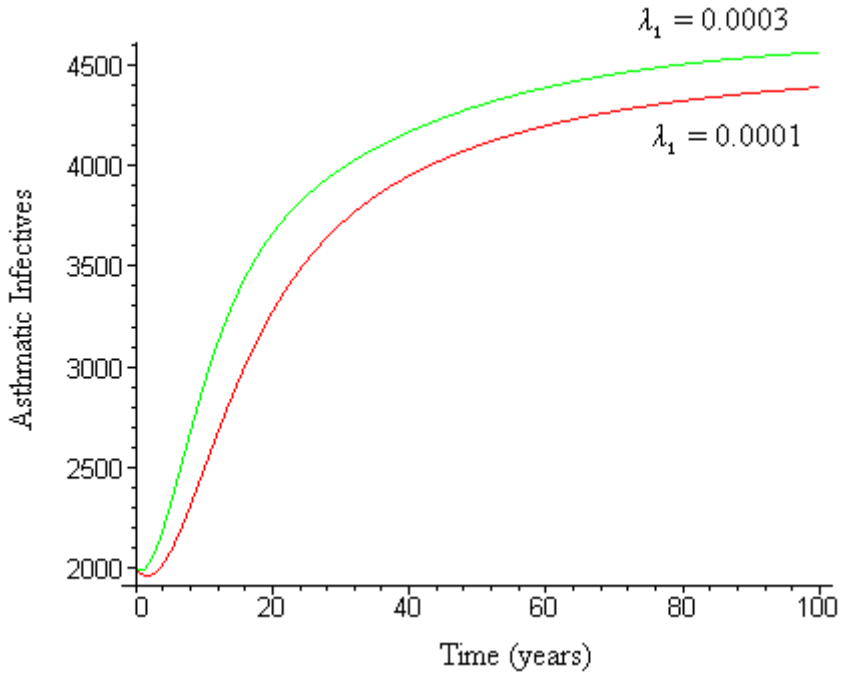


Figure 6. Variation of asthmatic infectives I with time for different values of interaction rate λ_1

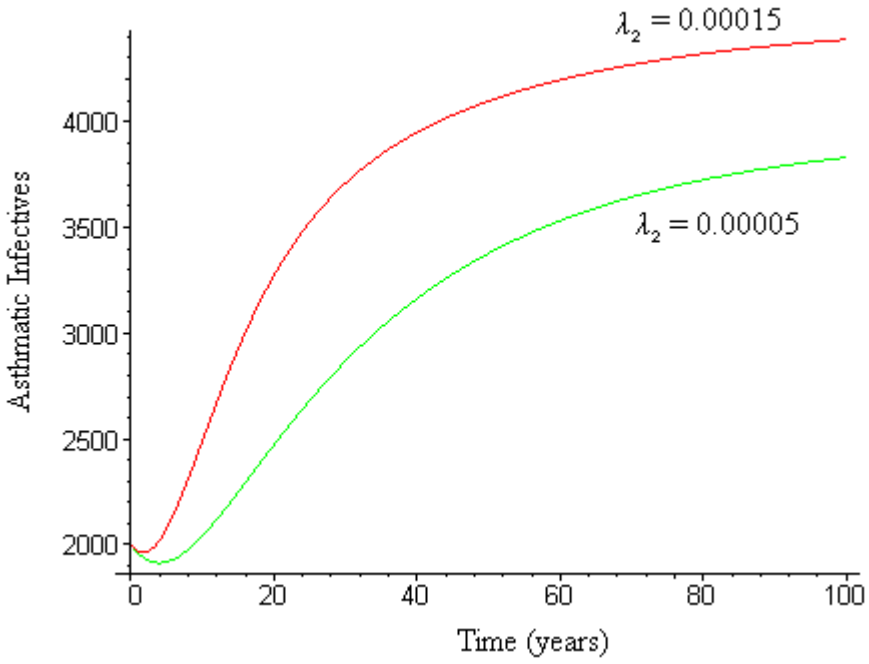


Figure 7. Variation of asthmatic infectives I with time for different values of interaction rate λ_2

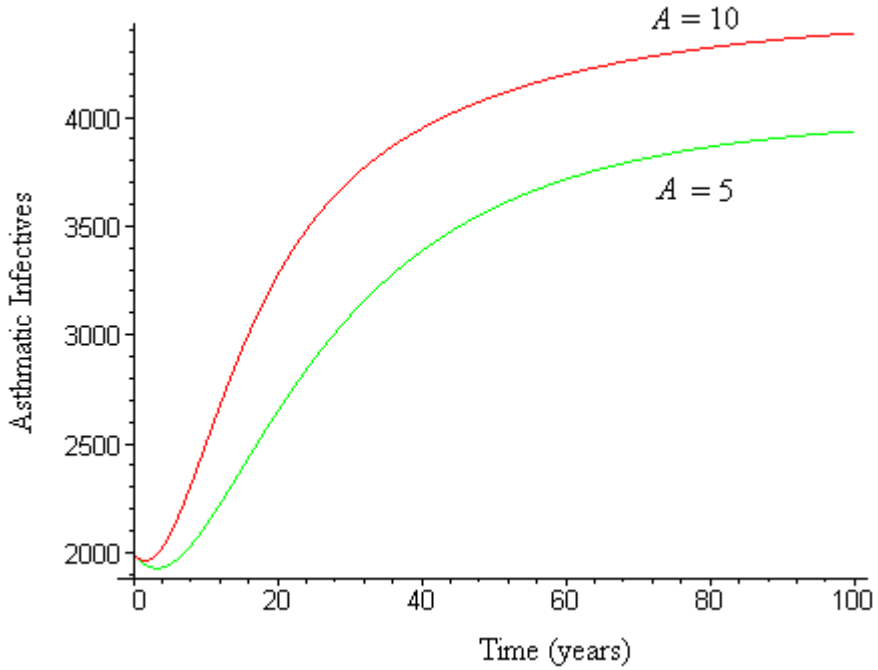


Figure 8. Variation of asthmatic infectives I with time for different values of cumulative density of pollutants A

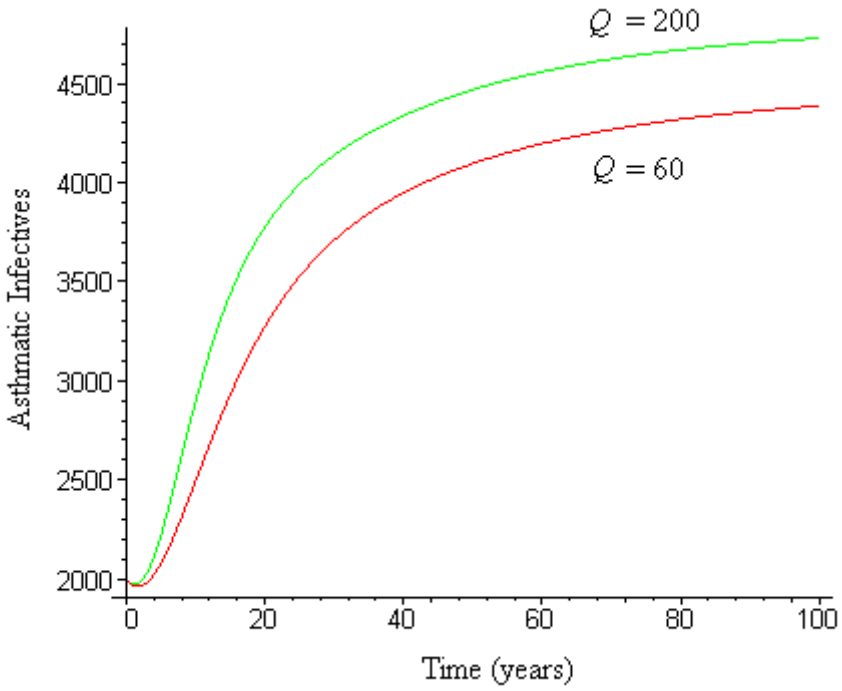


Figure 9. Variation of asthmatic infectives I with time for different values of recruitment rate Q of smokers

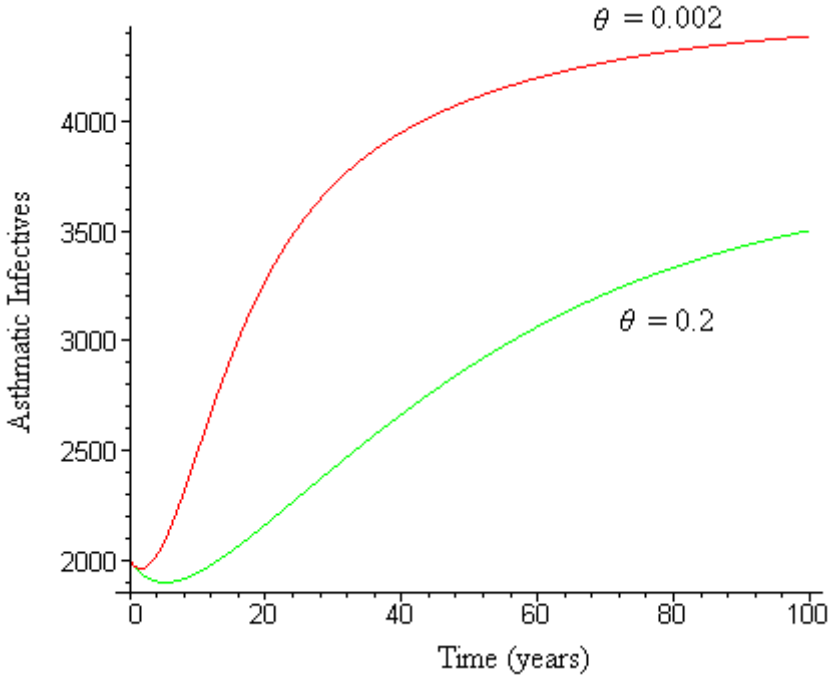


Figure 10. Variation of asthmatic infectives I with time for different values of θ , the rate by which smokers quit smoking

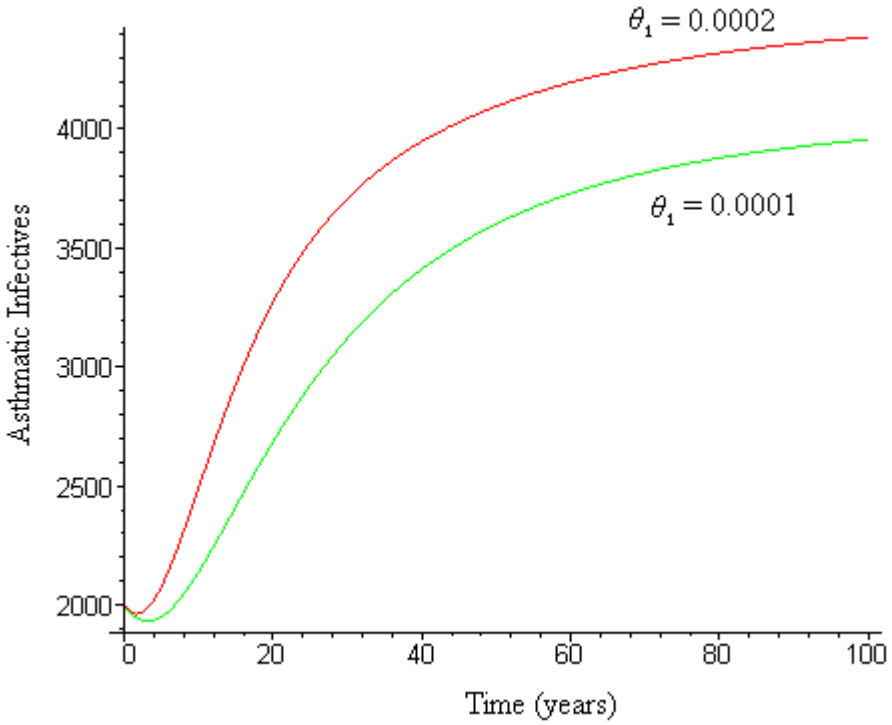


Figure 11. Variation of asthmatic infectives I with time for different values of θ_1 , the rate by which smokers become infected

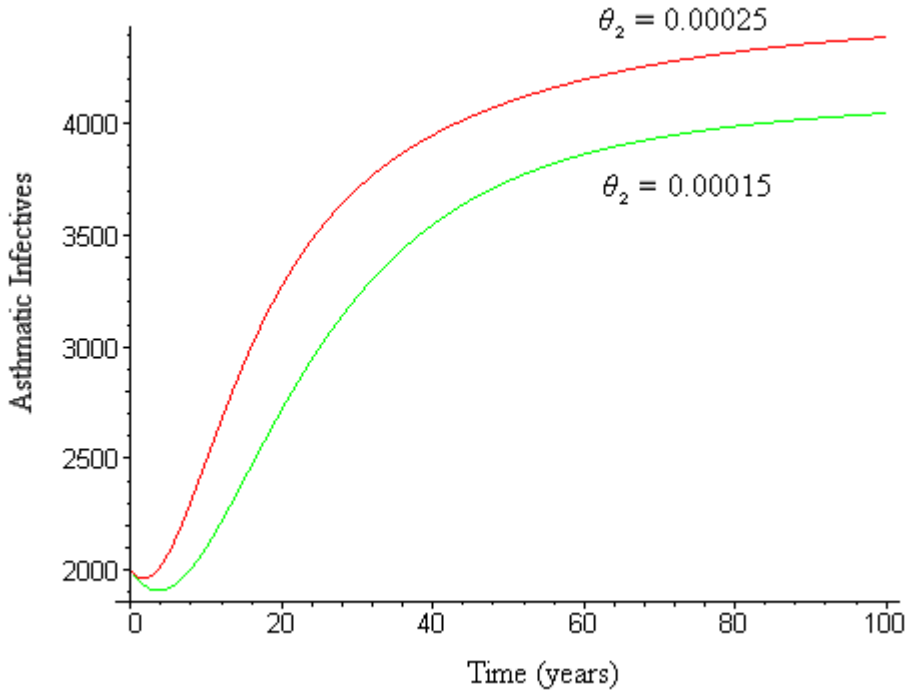


Figure 12. Variation of asthmatic infectives I with time for different values of θ_2 , the transmission coefficient due to exposure of smokers with pollutants

5. Conclusion

We have proposed and analyzed a nonlinear mathematical model for the spread of asthma in a variable size population by taking into account the effects of pollutants emitting continuously in the environment and constant inflow of smokers. It is assumed that susceptibles become asthmatic when they are continuously exposed to smoking (active or passive) or when they enter into polluted environment and inhale the pollutants from the atmosphere. The model system exhibits only one non-negative equilibrium which is nonlinearly

asymptotically stable under certain conditions. It has been shown qualitatively and numerically that when pollutants are emitted at a constant rate into the environment and smokers are recruited constantly into the population, the asthma disease persistence is higher. This is due to the fact that as the interaction rate of susceptibles with pollutants and with smokers increases, the asthmatic population increases. Hence, the spread of asthma can be slowed down if inflow of smokers is restricted into the population and the rate of release of pollutants is controlled in the environment.

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APPENDIX A

Proof of Theorem 1. The variational matrix of the model system (8)-(12) corresponding to equilibrium W^* is given by,

$$M(W^*) = \begin{bmatrix} -\mu & 0 & -\alpha & 0 & 0 \\ n & -l & -n & -n+m & r \\ 0 & \lambda_1 P^* + \lambda_2 C^* & -(\alpha + \mu) & \theta_1 + \lambda_2 E^* + \theta_2 P^* & \lambda_1 E^* + \theta_2 C^* \\ 0 & 0 & 0 & -(\theta_1 + \theta + \mu + \theta_2 P^*) & -\theta_2 C^* \\ 0 & 0 & 0 & q & -\tau \end{bmatrix}$$

where

$$n = \gamma P^* + \beta C^*,$$

$$l = \gamma P^* + \beta C^* + \lambda_1 P^* + \lambda_2 C^* + \mu,$$

$$r = \gamma(N^* - E^* - I^* - C^*) - \lambda_1 E^*,$$

$$m = \beta(N^* - E^* - I^* - C^*).$$

The characteristic equation corresponding to the matrix $M(W^*)$ is given by

$$f(\lambda) = (\lambda^5 + a_4 \lambda^4 + a_3 \lambda^3 + a_2 \lambda^2 + a_1 \lambda + a_0) = 0$$

where

$$a_4 = l + \alpha + \theta_1 + \theta_2 P^* + \theta + 3\mu + \tau > 0$$

$$a_3 = l(\alpha + \mu) + n(\lambda_1 P^* + \lambda_2 C^*) + q\theta_2 C^* + (\tau + \mu)(\theta_1 + \theta_2 P^* + \theta + \mu) + \mu(l + \alpha + \tau + \mu) > 0$$

$$a_2 = l\mu(\alpha + \mu) + n(\lambda_1 P^* + \lambda_2 C^*)(\alpha + \mu) + (l + \alpha + 2\mu)[\tau(\theta_1 + \theta_2 P^* + \theta + \mu) + q\theta_2 C^*] \\ + [n(\lambda_1 P^* + \lambda_2 C^*) + l(\alpha + \mu)](\theta_1 + \theta_2 P^* + \theta + \mu + \tau) > 0$$

$$a_1 = [l(\alpha + \mu) + \mu(l + \alpha + \mu) + n(\lambda_1 P^* + \lambda_2 C^*)][\tau(\theta_1 + \theta_2 P^* + \theta + \mu) + q\theta_2 C^*] \\ + (\theta_1 + \theta_2 P^* + \theta + \mu + \tau)[\mu l(\alpha + \mu) + \mu n(\lambda_1 P^* + \lambda_2 C^*)] \\ + n\alpha(\theta_1 + \theta_2 P^* + \theta + \mu + \tau)(\lambda_1 P^* + \lambda_2 C^*) > 0$$

$$a_0 = [l\mu(\alpha + \mu) + n(\alpha + \mu)(\lambda_1 P^* + \lambda_2 C^*)][\tau(\theta_1 + \theta_2 P^* + \theta + \mu) + q\theta_2 C^*] + n\alpha\tau^2(\lambda_1 P^* + \lambda_2 C^*) > 0$$

It is noted that $a_i > 0$ ($i = 0, 1, \dots, 4$), $a_4 a_3 > a_2$ and $a_2(a_4 a_3 - a_2) - a_4^2 a_1 > 0$ are satisfied. Thus,

by Routh Hurwitz criteria, this equilibrium is locally asymptotically stable if

$$\begin{vmatrix} a_4 & 1 & 0 & 0 \\ a_2 & a_3 & a_4 & 1 \\ 0 & a_1 & a_2 & a_3 \\ 0 & 0 & 0 & a_1 \end{vmatrix} > 0.$$

APPENDIX B

Proof of Theorem 2. We consider the following positive definite function about W^* ,

$$V = \frac{1}{2} \left[(N - N^*)^2 + k_1(E - E^*)^2 + k_2(I - I^*)^2 + k_3(C - C^*)^2 + k_4(P - P^*)^2 \right]$$

where the constants k_i ($i = 1, 2, \dots, 4$) can be chosen suitably.

The derivative of V w. r. t. 't' is given as,

$$\dot{V} = \dot{N}(N - N^*) + k_1\dot{E}(E - E^*) + k_2\dot{I}(I - I^*) + k_3\dot{C}(C - C^*) + k_4\dot{P}(P - P^*)$$

$$\dot{V} = -\mu(N - N^*)^2 - k_1[(\lambda_1 + \gamma)P^* + (\lambda_2 + \beta)C^* + \mu](E - E^*)^2 - k_2(\alpha + \mu)(I - I^*)^2$$

$$- k_3(\theta_1 + \theta_2P + \theta + \mu)(C - C^*)^2 - k_4\tau(P - P^*)^2 - \alpha(N - N^*)(I - I^*)$$

$$+ k_1(\gamma P^* + \beta C^*)(N - N^*)(E - E^*) - \theta(N - N^*)(C - C^*)$$

$$+ [k_2(\lambda_1 P^* + \lambda_2 C^*) - k_1(\gamma P^* + \beta C^*)](E - E^*)(I - I^*)$$

$$+ k_1\beta(N - E - I - C)(E - E^*)(C - C^*) - k_1(\gamma P^* + \beta C^* + \lambda_2 E)(E - E^*)(C - C^*)$$

$$+ k_1\gamma(N - E - I - C)(E - E^*)(P - P^*) - k_1(\lambda_1 E)(E - E^*)(P - P^*)$$

$$+ k_2\gamma(\theta_1 + \theta_2 P^* + \lambda_2 E)(I - I^*)(C - C^*) + k_2(\lambda_1 E + \theta_2 C)(I - I^*)(P - P^*)$$

$$+(k_4q - k_3\theta_2C^*)(C - C^*)(P - P^*)$$

where the constants $k_i > 0$ (for $i = 1, 2, 3, 4$) have been chosen as,

$$\frac{9\alpha^2(\lambda_1P^* + \lambda_2C^*)}{4\mu(\alpha + \mu)(\gamma P^* + \beta C^*)} < k_1 < \frac{4\mu[(\lambda_1 + \gamma)P^* + (\lambda_2 + \beta)C^* + \mu]}{9(\gamma P^* + \beta C^*)^2},$$

$$k_2 = \frac{\gamma P^* + \beta C^*}{\lambda_1 P^* + \lambda_2 C^*} k_1,$$

$$k_4 = \frac{\theta_2 C^*}{q} k_3 \text{ and } k_3 > \max\{\sigma, \omega, \chi, \zeta, \zeta\}$$

Here $\sigma = \frac{9\theta^2}{4\mu(\theta_1 + \theta + \mu)}$, $\omega = \frac{9(\gamma P^* + \beta C^*)(\theta_1 + \theta_2 P^* + \lambda_2 \bar{E})^2}{4(\lambda_1 P^* + \lambda_2 C^*)(\alpha + \mu)(\theta_1 + \theta + \mu)} k_1$

$$\chi = \frac{3(\gamma P^* + \beta C^*)(\lambda_2 \bar{E} + \theta_2 \bar{C})q}{2(\lambda_1 P^* + \lambda_2 C^*)(\alpha + \mu)\tau\theta_2 C^*} k_1,$$

$$\zeta = \frac{9k_1}{[(\lambda_1 + \gamma)P^* + (\lambda_2 + \beta)C^* + \mu](\theta_1 + \theta + \mu)} \max\{\beta_2 \bar{N}^2, (\gamma P^* + \beta C^* + \lambda_2 \bar{E})^2\}$$

and $\zeta = \frac{3qk_1}{[(\lambda_1 + \gamma)P^* + (\lambda_2 + \beta)C^* + \mu]\tau\theta_2 C^*} \max\{\gamma^2 \bar{N}^2, \lambda_1^2 \bar{E}^2\}$

Using the above, the stability condition can be obtained as stated in the theorem.

Hence \dot{V} will be negative definite showing that V is a Liapunov function with respect to W^* whose domain contains Ω , proving the theorem.