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(Dedicated to Honor Dr. R. C. Singh Chandel on His 75th Birth Anniversary Celebrations)

MODELING THE EFFECT OF ECOLOGICAL CONDITIONS IN THE HABITAT ON THE SPREAD OF TUBERCULOSIS

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Abstract

In this paper, the cumulative effect of ecological conditions in the habitat on the spread of *TB* in human population is modeled and analyzed. The total human population is divided into two classes, susceptibles and infectives where the infective class is further subdivided into latent and actively infected subclasses. It is assumed that *TB* is spread by direct contact between members of the population as well as indirectly by bacteria which are emitted by infectives in the environment, survive and get accumulated due to favorable ecological conditions in the habitat. The cumulative density of ecological factors determining conditions in the habitat is assumed to follow a population density dependent logistic model. The analysis of the model shows that as parameters governing the ecological factors in the habitat increase, the spread of *TB* increases. The same result is also found with the increase in the parameter defining the accumulation of bacteria in the habitat. It is further found that due to immigration of the population *TB* becomes more endemic. A numerical study of the model is also carried out to see the role of key parameters on the spread of tuberculosis and to support the analytical results.
2010 Mathematics Subject Classifications: 37C75, 92B05.
Keywords and phrases: Mycobacterium tuberculosis; Ecological status in the habitat; latently-infected; actively-infected.

1 Introduction

Tuberculosis (*TB*) is an infectious disease which has world-wide prevalence been declining due to vaccination and other preventive strategies [5, 19, 22], but its recent reappearance in developing countries with high burden of infection in regions of Southeast Asia have sparked renewed research in *TB*. Mycobacterium tuberculosis is the bacterium that causes most cases of tuberculosis. It is an obligate aerobe mycobacterium that divides every 16-20 hrs, extremely slow as compared to other bacteria which tend to have division times measured in minutes (for example, *E*. Coli can divide roughly every 20 min.) [13]. It is small rod like bacillus which can withstand weak disinfectants and can survive in a dry state for weeks but can only grow within a host organism [13].

Recent quantitative monitoring estimates are that over 30% of the population in developing countries is infected with *TB*, which results in approximately 2-3 million deaths each year [1, 2, 6]. Every year, 8 to 10 million new cases of tuberculosis occur and this figure is growing with the advent of *HIV* infection [21]. Socio-economic status, family size, crowding, malnutrition and limited access to health care or effective treatment also play important roles in the transmission [3, 14]. The reason for the increase in such cases in developed countries is principally immigration, poverty, living conditions, food security, etc. [12]. It is reported that eight million people develop active *TB* every year, each of which can infect between 10 and 15 people in one year just by breathing [2, 4, 20]. Overall, the mortality from tuberculosis is approximately 8%, being over 30% in the elderly cases but less than 1% in the young's [20, 23].

Humans are the natural reservoir of *TB*, which spreads from person to person by direct contact via airborne droplets [18] and indirectly from environment, by inhalation of small (1-10μ_m) droplets containing only tubercle bacilli, which are expelled during coughing, sneezing, talking or singing by a *TB* infected person [10]. *TB* also spreads indirectly by the use of contaminated utensils, contaminated dust, flowers, etc.

Mathematical models for the spread of infectious diseases have played a major role in providing deeper insight into the understanding of the transmission as well as control strategies [7, 8, 9, 11,12, 16, 17], including *HIV-TB* co-infection [15]. For example, Feng et al. [7] formulated a two strain *TB* model with an arbitrary distributed delay in the latent stage of individual infected with the drug-sensitive strain and investigated the effects of variable periods of latency on the disease dynamics. Naresh and Tripathi [15] have also modeled and studied the co-infection of *HIV* and *TB* in a variable size population.

It is noted here that in recent years the spread of infectious diseases have been modeled and analyzed by considering environmental and ecological conditions in the habitat [8, 9, 16, 17]. In particular, Singh et al. [16] have studied the

spread of carrier dependent infectious diseases by considering the effect of environmental factors which are conducive to the growth of carrier population. They have shown that the spread of the disease increases due to conducive environmental factors. They [17] have also studied the spread of malaria by taking into account environmental and ecological factors which are conducive to the growth of mosquito population. Ghosh et al. [8, 9] have studied the spread of bacteria infected diseases such as *TB* by considering environmental effect as well as by considering the effect of migration. As pointed out earlier, that in the case of *TB* the bacteria emitted from the infected persons get accumulated in the habitat as these settle down on fomites or remain suspended in the air. These bacteria then affect the suceptibles indirectly and the rate of infection depends upon the ecological conditions in the habitat. Our aim in this paper is to model and analyze the effect of accumulation of bacteria which survive due to conducive ecological factors in the habitat acting as a reservoir, on the spread of *TB*.

2 Mathematical Model

In the model presented here, the total human population, $N(t)$, is divided into three sub-populations: susceptibles, latently infected individuals and actively infected individuals with densities $S(t)$, $L(t)$, and $T(t)$ respectively. It is assumed that all susceptibles are infected by both the direct and indirect contacts with bacteria. The following system of nonlinear, ordinary differential equations is assumed to model the dynamics of the spread of *TB*,

$$
\begin{aligned}
(2.1)\quad \frac{dS}{dt} &= A - \beta S T - \lambda S B - dS + \alpha_1 T + \alpha_2 L,\\
\frac{dL}{dt} &= (1-p)\beta S T + (1-q)\lambda S B - (\sigma + d + \alpha_2)L,\\
\frac{dT}{dt} &= p\beta S T + q\lambda S B + \sigma L - (d + \alpha + \alpha_1)T,\\
\frac{dN}{dt} &= A - dN - \alpha T,\\
\frac{dB}{dt} &= sT - s_0 B + s_1 BE,\\
\frac{dE}{dt} &= \gamma E - \gamma_0 E^2 + \gamma_1 NE.
\end{aligned}
$$

Here A is the immigration rate of susceptible β and λ are the transmission coefficients for susceptibles due to person to person contact with infectives and by inhalation of bacteria from environment respectively; $p > 0$ and $q > 0$ are the fraction of infected individuals who develop active *TB* soon after initial infection; σ is the rate of progression of latently infected individuals to active *TB*; d is the natural death rate and is the death rate due to *TB* infection. The parameters and are the therapeutic treatment rate of actively infected and latently infected individuals respectively. The second last differential equation represents change in bacterial population $B(t)$ in the environment. Since bacteria of *TB* grows only in the host (human) body and it only survives in the environment, therefore, no growth term is taken into consideration. In the environment, growth in the density of bacterial population is all due to number of bacteria released from actively infected *TB* patients and also because of accumulation due to conducive ecological conditions in the habitat. The parameter s is the rate of release of bacteria from the actively infected individuals, s_0 is their decay coefficient due to natural factors or control measures and s_1 is the rate of accumulation of bacteria population due to conducive ecological factors in the habitat; $E(t)$ is the cumulative density of ecological factors governing the condition in the habitat which is conducive to the accumulation of bacteria population; γ is the growth rate of cumulative density of ecological factors in the habitat, $\frac{\gamma}{\gamma_0}$ is the carrying capacity of the habitat, γ_1 is the interaction coefficient with respect to total human population.

In the following lines, we analyze the model (2.1) using stability theory of differential equations. We need the bounds of dependent variables involved in the model. For this, we give the region of attraction in the form of following lemma, stated without proof.

***Lemma* 2.1** *The region of attraction for the system* (2.1) *is given by,*

$$(2.2)\quad \Omega = \{(L, T, N, B, E) : 0 \le A/d,\ 0 \le T \le N \le A/d,\ 0 \le B \le B_m,\ 0 \le E \le E_m\}$$

which attracts all solutions initiating in the positive octant,

$$(2.3)\quad \textit{where, } B_m = \left[\frac{s\gamma_0 A/d}{s_0\gamma_0 - s_1(\gamma + \gamma_1 A/d)}\right] \textit{ and } E_m = \frac{\gamma + \gamma_1 A/d}{\gamma_0}.$$

3 Equilibrium Analysis

It is sufficient to consider the reduced system of model system (2.1) (since $S + L + T = N$), as follows,

$$
\begin{aligned}
(3.1)\quad \frac{dL}{dt} &= (1-p)\beta(N-L-T)T + (1-q)\lambda(N-L-T)B - (\sigma+d+\alpha_2)L,\\
\frac{dT}{dt} &= p\beta(N-L-T)T + q\lambda(N-L-T)B - \sigma L - (d+\alpha+\alpha_1)T,\\
\frac{dN}{dt} &= A - dN - \alpha T,\\
\frac{dB}{dt} &= sT - s_0 B + s_1 BE,\\
\frac{dE}{dt} &= \gamma E - \gamma_0 E^2 + \gamma_1 NE.
\end{aligned}
$$

The equilibrium analysis of the model system (3.1) has been carried out and the results are given as follows:

There exist following four nonnegative equilibria of the model system (3.1),

(I) Disease free equilibrium $W_0\left(0, 0, \frac{A}{d}, 0, 0\right)$.

This equilibrium exists without any condition. It explains that if the bacterial population is absent, due to non-conducive ecological conditions in the habitat and the TB infected individuals are not present, the disease would not persist and population remains at its equilibrium A/d.

(II) The equilibrium $W_1\left(0, 0, \frac{A}{d}, 0, E_m\right)$.

This equilibrium also exists without any condition in the absence of disease and bacterial population. However, in that case the population remains at its equilibrium A/d and the ecological status of the habitat is maintained at the level E_m.

(III) The equilibrium $W_2(\bar{L}, \bar{T}, \bar{N}, \bar{B}, 0)$

In this case the disease would still persist due to release of bacteria from the infected individuals even if the bacteria population is not accumulated further as it does not depend on the ecological conditions in the habitat. The explicit equilibrium values of different variables are given as follows,

$$
(3.2)\quad \bar{T} = \frac{\{\beta s_0[\sigma + p(d+\alpha_2)] + s\lambda[\sigma + q(d+\alpha_2)]\}A - (d+\alpha+\alpha_1)(\sigma+d+\alpha_2)s_0 d}{(\alpha+d)\{\beta s_0[\sigma + p(d+\alpha_2)] + s\lambda[\sigma + q(d+\alpha_2)]\} + d(d+\alpha+\alpha_1)[\beta s_0(1-p) + \lambda s(1-q)]},
$$

$$
(3.3)\quad \bar{L} = \frac{[(1-p)s_0\beta + (1-q)\lambda s][A - (\alpha+d)T]T}{d[(1-p)s_0\beta\bar{T} + (1-q)\lambda s\bar{T} + s_0(\sigma+d+\alpha_2)]},
$$

$$
(3.4)\quad \bar{N} = \frac{A - \alpha\bar{T}}{d}, \bar{B} = \frac{s\bar{T}}{s_0}, \text{ as } \bar{T} < \frac{A}{\alpha},
$$

provided that $p\beta\frac{A}{d} > (d + \alpha + \alpha_1)$.

(IV) The endemic equilibrium, $W_3(L^*, T^*, N^*, B^*, E^*,)$

The endemic equilibrium W_3 is given by the solution of following algebraic equations and a quadratic equation, obtained from (3.1),

$$
(3.5)\quad N = \frac{A - \alpha T}{d},
$$

$$
(3.6)\quad E = \frac{\gamma d + \gamma_1(A - \alpha T)}{d\gamma_0},
$$

$$
(3.7)\quad B = \frac{ds\gamma_0 T}{ds_0\gamma_0 - s_1[\gamma d + \gamma_1(A - \alpha T)]},
$$

$$
(3.8)\quad L = \frac{[(1-p)\beta T + (1-q)\lambda B][A - (\alpha+d)T]}{d[(1-p)\beta T + (1-q)\lambda B + (\sigma+d+\alpha_2)]},
$$

$$
(3.9)\quad aT^2 + bT - c = 0,
$$

where

$$a = \beta s_1\gamma_1\alpha\{(1-p)[d^2(d+\alpha+\alpha_1)+\sigma(\alpha+d)]+(\alpha+d)(\sigma+d+\alpha_2)\},$$
$$b = \alpha_2(\alpha+d)p\beta[ds_0\gamma_0 - s_1(\gamma d+\gamma_1 A)] + (\alpha+d)(\alpha_2+d)\{dsq\lambda\gamma_0 - \beta s_1\gamma_1\alpha A[\sigma+p(\alpha_2+d)]\}$$
$$+\sigma(\alpha+d)\{\beta[ds_0\gamma_0 - s_1(\gamma d+\gamma_1 A)] + ds\lambda\gamma_0\} + \alpha_1 d(1-p)\beta[ds_0\gamma_0 - s_1(\gamma d+\gamma_1 A)]$$
$$+d(d+\alpha+\alpha_1)[(1-q)s\lambda\gamma_0 + s_1\gamma_1\alpha(\sigma+d+\alpha_2)],$$
$$c = [ds_0\gamma_0 - s_1(\gamma d+\gamma_1 A)]\{\beta A[\sigma+p(\alpha_2+d)] - d(d+\alpha+\alpha_1)(\sigma+d+\alpha_2)\} + ds\lambda\gamma_0 A[\sigma+q(\alpha_2+d)].$$

There exists unique positive root of eq.(3.9) is given as $T^* = \frac{-b+\sqrt{b^2+4ac}}{2a}$ if $p\beta\frac{A}{d} > (d+\alpha+\alpha_1)$and $s_0 > s_1E_m$. Substituting the value of T^* in eqs. (3.5-3.8), we can compute the value of L^*, N^*, B^* and E^*.

4 Stability Analysis

Now, we analyze the stability of each of the equilibrium W_0, W_1, W_2 and W_3.

***Theorem* 4.1** *The equilibrium W_0, W_1 and W_2 are unstable and the endemic equilibrium W_3 is locally asymptotically stable provided the following conditions are satisfied,*

(4.1) $\alpha\gamma_1^2E^* < \frac{2}{3}d(p\beta T^* + q\lambda B^*)$,

(4.2) $q^2\lambda^2(N^*-L^*-T^*)^2 < \frac{1}{5}(s_0-s_1E^*)^2\xi_1 \min.\left\{\frac{\gamma_0^2E^*}{2s_1^2B^{*2}},\ \frac{\xi_1}{5s^2}\right\}$,

(4.3) $(p\beta T^* + q\lambda B^* - \sigma)^2 < \xi_1\xi_2^2 \min.\left\{\frac{\xi_1}{5\xi_3^2}, \frac{d(p\beta T^*+q\lambda B^*)}{3\alpha[(1-p)\beta T^*+(1-q)\lambda B^*]^2}, \frac{k_3(s_0-s_1E^*)}{4(1-q)^2\lambda^2(N^*-L^*-T^*)^2}\right\}$

where,

$$\xi_1 = \left[p\beta T^* + q\lambda(N^*-L^*)\tfrac{B^*}{T^*} + \sigma\tfrac{L^*}{T^*}\right],\quad \xi_2 = \left[(1-p)\beta(N^*-T^*)\tfrac{T^*}{L^*} + (1-q)\lambda(N^*-T^*)\tfrac{B^*}{L^*}\right],$$
$$\xi_3 = [(1-p)\beta(N^*-L^*-T^*) - (1-p)\beta T^* - (1-q)\lambda B^*].$$

Proof. See ***Appendix*-I**

***Theorem* 4.2** *The endemic equilibrium W_3 is nonlinearly asymptotically stable in the region Ω provided the following inequalities are satisfied:*

(4.4) $\alpha\, q^2\lambda^2B_m^2 < \frac{1}{3}d\, p^2\beta^2T^{*2}$,

(4.5) $s\, q\lambda(N^*-L^*)^2 < \frac{1}{3}p\beta(s_0-s_1E^*)T^{*2}$,

(4.6) $\alpha\, q\lambda\, \gamma_1^2s_1^2B_m^2 < \frac{4}{9}\gamma_0^2\, s\, p\beta\, d(s_0-s_1E^*)$,

(4.7) $(p\beta T^* + q\lambda B_{\max} - \sigma)^2 < \frac{1}{4}p\beta(\sigma+d+\alpha_2)^2T^{*2}$,

$$\min.\left\{\frac{p\beta}{4\xi_4^2}, \frac{p\beta\, d}{3\alpha\left[(1-p)\beta A/d + (1-q)\lambda B_{\max}\right]^2}, \frac{q\lambda(s_0-s_1E^*)}{3s(1-q)^2\lambda^2(N^*-L^*-T^*)^2}\right\},$$

where $\xi_4 = \left[(1-p)\beta\frac{A}{d} + (1-q)\lambda B_{\max} - (1-p)\beta(N^*-L^*-T^*)\right]$.

Proof. See ***Appendix*-II**.

***Remark* 4.1** *As the growth rate of cumulative density of ecological factors conducive to the accumulation of bacterial population due to human population activities tends to zero i.e., $\gamma_1 \to 0$, inequalities* (4.1) *and* (4.4) *are automatically satisfied. This implies that the ecological factors conducive to the accumulation of bacterial population have a destabilizing effect on the system. If the rate of accumulation of bacteria due to conducive ecological conditions is very small i.e., $s \to 0$ then inequalities* (4.2) *and* (4.5) *are satisfied.*

The above theorems imply that under appropriate conditions, if the density of bacteria due to conducive ecological conditions increases, then the number of latently-infected and actively-infected individuals increases leading to fast spread of TB. However, the effect of immigration is to make TB more endemic.

5 Numerical Simulation

In this section, we conduct simulation analysis of the model (3.1) to study its dynamical behavior and to prove the feasibility of local and nonlinear stability conditions of the model system. The numerical simulation of the system (3.1) is done by MAPLE 7.0 using the parameters values [8, 9, 11, 15] given below:

***Table* 5.1:** Parameter values

Parameters	**Symbol**	**Parameter value**
recruitment rate of susceptible	A	500
transmission coefficient (by infectives)	β	0.0005
transmission coefficient (through bacteria)	λ	0.0003
recovery rate of latently-infected TB patient	α_1	0.012
recovery rate of actively-infected TB class	α_2	0.01
natural death rate	d	0.15
disease-induced death rate	α	0.2
rate with which latently-infected goes to actively-infected TB class	σ	0.02
rate of release of bacteria from TB patients	s	1
accumulation of bacteria due to ecology	s_1	0.0001
decay rate of bacteria in the environment	s_0	0.3
growth rate of ecological status in the habitat	γ	25
growth rate of ecological status due to human activities	γ_1	0.002
depletion rate of ecological status	γ_0	0.1
fraction of infected individuals (by infectives) who develop active TB soon after initial infection	p	0.45
fraction of infected individuals (by bacteria population) who develop active TB soon after initial infection	q	0.6

The equilibrium values for the model system (3.1) are computed as follows:
N^* =2300.799543, L^* = 1153.414779, T^* = 774.4003430, B^* =2863.923531, E^* = 296.0159909.
The eigen values of variational matrix corresponding to the endemic equilibrium for the model system (3.1) are

$$-1.353015784, -0.1854221833, -0.3408624139, -0.2455538488, -29.601599.$$

Since all the eigen values are negative which implies that the endemic equilibrium W3 is locally asymptotically stable.

The results of numerical simulation are displayed graphically in ***Figs.* 5.1-5.11.** ***Fig.* 5.1** shows that the system (3.1) is nonlinearly asymptotically stable in T-N plane. All the trajectories starting from different initial starts reaches to equilibrium point.

(i) $L(0) = 1500$, $T(0) = 600$, $N(0) = 3000$, $B(0) = 2863$, $E(0) = 296$.
(ii) $L(0) = 1000$, $T(0) = 1000$, $N(0) = 3000$, $B(0) = 2863$, $E(0) = 296$.
(iii) $L(0) = 400$, $T(0) = 400$, $N(0) = 1000$, $B(0) = 2863$, $E(0) = 296$.
(iv) $L(0) = 200$, $T(0) = 1000$, $N(0) = 1400$, $B(0) = 2863$, $E(0) = 296$.

In ***Figs.* 5.2 - 5.3**, the variation of density of bacteria population and the actively-infected *TB* population with time is shown respectively for different values of accumulation rates (s_1) of bacteria due to conducive ecological status of the habitat. It is found that as the accumulation rate of bacteria increases, bacteria population also increases which results in increasing the spread of tuberculosis. Thus ecological conditions conducive to the accumulation of bacterial population help in spreading the tuberculosis infection. In ***Figs.* 5.4 - 5.5**, we show the variation of bacterial population density and actively-infected *TB* population with time for different values of rate of release of bacteria from actively-infected population. From these figures, we infer that as the rate of emission of bacteria, (s) from actively-infected *TB* population increases, the accumulation of the bacterial population in the habitat also increases due to conducive ecological conditions. These bacteria when comes in contact with susceptibles through contaminated clothes, utensils, etc., further increases the spread of tuberculosis which ultimately results in rise in the actively infected *TB* population. ***Figs.* 5.6** and **5.7** depict the role of decay coefficients (s_0) of bacteria on the variation of bacteria population density and actively-infected *TB* population. When there is a rise in the decay coefficient due to natural factors or control measures, the density of bacteria population decreases significantly and

consequently the actively infected *TB* population declines. This decline in actively-infected population does not seem to be much significant. It seems, it is due to the fact that disease spreads not only through bacteria but also through direct interaction of susceptibles with actively-infected *TB* individuals. It is, therefore, speculated that not only the accumulation of bacteria be curbed using effective control mechanism but the direct interaction of susceptibles with actively-infected *TB* population be also restricted.

***Figs.* 5.8 - 5.9**, show that as the growth rate of cumulative density of ecological factors in the habitat (γ) conducive to the accumulation of bacteria increases, there is a significant increase in the density of bacteria population. This, in turn, increases the number of actively-infected *TB* individuals. Thus, if the density of ecological factors is higher, the spread of tuberculosis is faster due to significant increase in bacterial population in a conducive environment. Also, as the growth of ecological status making the environment conducive to bacteria population due to human population activities (γ_1) increases, the density of bacteria population increases resulting in the spread of tuberculosis, see ***Figs.* 5.10 - 5.11**. Thus, the human population related factors responsible for making the ecological conditions favourable for the accumulation of bacterial population further increases the load of tuberculosis.

Finally, from the above discussion, we infer that the spread of tuberculosis not only depends upon the interaction of susceptibles with actively-infected population but also depends upon the interaction of susceptibles with bacteria population. Moreover, the ecological status of the surroundings plays a vital role in the accumulation of *Mycobacterium Tuberculosis*. It may be possible to curb the spread of tuberculosis if the bacterial population is diminished by way of providing hyegenic environment in the habitat and restricting the interaction of *TB* patients with the susceptible population.

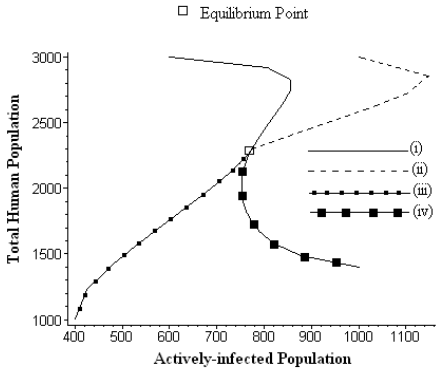

***Figure* 5.1:** Variation of total human population with actively-infected population

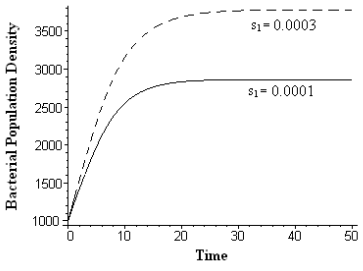

***Figure* 5.2:** Variation of bacterial population density with time for different values of s_1

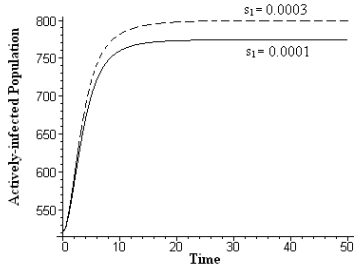

***Figure* 5.3:** Variation of actively-infected population with time for different values of s_1

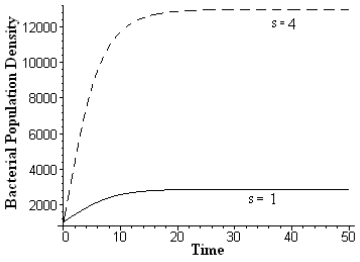

***Figure* 5.4:** Variation of bacterial population density with time for different values of s

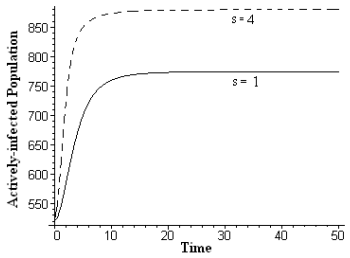

***Figure* 5.5:** Variation of actively-infected population with time for different values of s

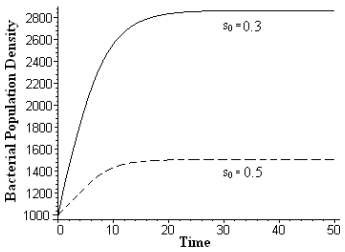

***Figure* 5.6:** Variation of bacterial population density with time for different values of s_0

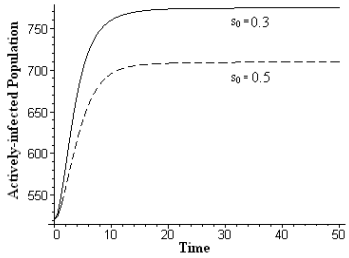

***Figure* 5.7:** Variation of actively-infected population with time for different values of s_0

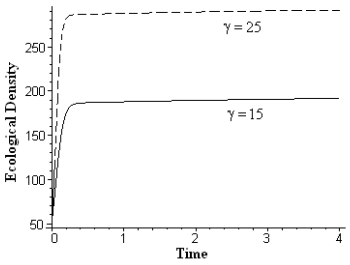

***Figure* 5.8:** Variation of ecological density with time for different values of γ

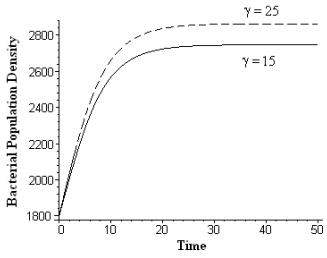

***Figure* 5.9:** Variation of bacterial population density with time for different values of γ

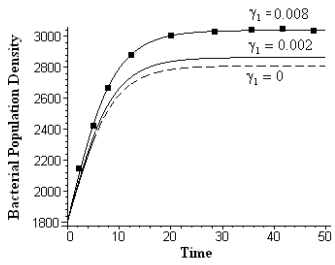

***Figure* 5.10:** Variation of bacterial population density with time for different values of γ_1

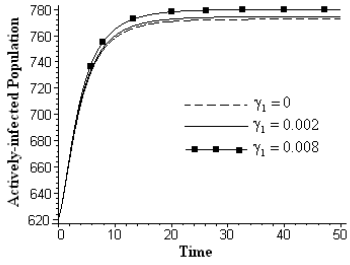

***Figure* 5.11:** Variation of actively-infected population with time for different values of γ_1

6 Conclusion

In this paper, a two stage SIS model for Tuberculosis, caused by *Mycobacterium Tuberculosis* is proposed and analyzed with constant migration of human population. The cumulative density of ecological factors in the habitat is assumed to be governed by a logistic model which is population density dependent. The endemic equilibrium is shown to be

locally and nonlinearly stable under certain conditions. Our analysis shows that the spread of tuberculosis not only depends upon the interaction of susceptibles with actively-infected population but also depends upon the interaction of susceptibles with bacteria population accumulated in the habitat. The ecological status of the habitat plays a vital role in the accumulation of *Mycobacterium Tuberculosis*. It is shown that the cumulative effect of ecological factors is to increase the spread of the disease. Thus, an effective control mechanism must be undertaken to curb the accumulation of bacteria in the environment and the direct interaction of susceptibles with actively-infected population be restricted.

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Appendix – I

***Proof of Theorem* 4.1.**
The variational matrix M_0 of model (3.1) corresponding to equilibrium W_0 is given by,

$$M_0 = \begin{bmatrix} -(\sigma+d+\alpha_2) & \frac{(1-p)\beta A}{d} & 0 & \frac{(1-q)\lambda A}{d} & 0 \\ \sigma & \frac{p\beta A}{d} - (d+\alpha+\alpha_1) & 0 & \frac{q\lambda A}{d} & 0 \\ 0 & -\alpha & -d & 0 & 0 \\ 0 & s & 0 & -\left(s_0 - \frac{s_1(\gamma+\gamma_1 A/d)}{\gamma_0}\right) & s_1 \\ 0 & 0 & 0 & 0 & \left(\gamma + \frac{\gamma_1 A}{d}\right) \end{bmatrix}.$$

The fifth eigenvalue of M_0 is positive, as all the model parameters are nonnegative. Therefore, disease free equilibrium W_0 is unstable.
The variational matrix M_1 of model (3.1) corresponding to equilibrium W_1 is given by,

$$M_1 = \begin{bmatrix} -(\sigma+d+\alpha_2) & \frac{(1-p)\beta A}{d} & 0 & \frac{(1-q)\lambda A}{d} & 0 \\ \sigma & \frac{p\beta A}{d} & 0 & \frac{q\lambda A}{d} & 0 \\ 0 & -\alpha & -d & 0 & 0 \\ 0 & s & 0 & -\left(s_0 - \frac{s_1(\gamma+\gamma_1 A/d)}{\gamma_0}\right) & s_1 \\ 0 & 0 & \frac{\gamma_1(\gamma+\gamma_1 A/d)}{\gamma_0} & 0 & -\left(\gamma + \frac{\gamma_1 A}{d}\right) \end{bmatrix}.$$

The characteristic polynomial corresponding to above matrix is given by,

$$(d+\psi)(\sigma+d+\alpha_2+\psi)(\gamma+\gamma_1 A/d+\psi)(\psi^2+h_1\psi+h_2) = 0,$$

where $h_1 = \left(s_0 - \frac{s_1(\gamma+\gamma_1 A/d)}{\gamma_0} - \frac{p\beta A}{d}\right)$,

$$h_2 = -spq\beta\lambda\frac{A^2}{d^2} \quad < \quad 0..$$

Using Routh-Hurwitz criteria as $h_2 < 0$, therefore, disease free equilibrium W_1 is unstable.
The variational matrix M_2 of model (3.1) corresponding to equilibrium W_2 is given by,

$$M_2 = \begin{bmatrix} m_{11} & m_{12} & (1-p)\beta\bar{T} + (1-q)\lambda\bar{B} & (1-q)\lambda(\bar{N}-\bar{L}-\bar{T}) & 0 \\ \sigma - p\beta\bar{T} - q\lambda\bar{B} & m_{22} & p\beta\bar{T} + q\lambda\bar{B} & q\lambda(\bar{N}-\bar{L}-\bar{T}) & 0 \\ 0 & -\alpha & -d & 0 & 0 \\ 0 & s & 0 & -s_0 & s_1 \\ 0 & 0 & 0 & 0 & (\gamma+\gamma_1\bar{N}) \end{bmatrix}.$$

where, $m_{11} = -(1-p)\beta(\bar{N}-\bar{T})\frac{\bar{T}}{\bar{L}} - (1-q)\lambda(\bar{N}-\bar{T})\frac{\bar{B}}{\bar{L}}$,
$m_{12} = (1-p)\beta(\bar{N}-\bar{L}-\bar{T}) - (1-p)\beta\bar{T} - (1-q)\lambda\bar{B}$ and $m_{22} = -p\beta\bar{T} - q\lambda(\bar{N}-\bar{L})\frac{\bar{B}}{\bar{T}} - \sigma\frac{\bar{L}}{\bar{T}}$.
This equilibrium is also unstable as fifth eigen value is always positive.
To establish the local stability of endemic equilibrium W_3, we consider the following positive definite function,
$U_1 = \frac{1}{2}(k_0 l^2 + k_1 t^2 + k_2 n^2 + k_3 b^2 + k_4 e^2)$,
where $ki(i = 0, 1, 2, 3, 4)$ are positive constants to be chosen appropriately and l, t, n, b and e are small perturbations about W_3, defined as follows
$L = L^*+ l$, $T = T^*+ t$, $N = N^*+ n$, $B = B^*+ b$ and $E = E^*+ e$.
Differentiating above equation, with respect to 't' and using the linearized system of model equations (3.1) corresponding to W_3, we get,

$$\frac{dU_1}{dt} = -k_0\left[(1-p)\beta(N^*-T^*)\frac{T^*}{L^*} + (1-q)\lambda(N^*-T^*)\frac{B^*}{L^*}\right]l^2 - k_1\left[p\beta T^* + q\lambda(N^*-L^*)\frac{B^*}{T^*} + \sigma\frac{L^*}{T^*}\right]t^2 - k_2 dn^2 - k_3(s_0 - s_1E^*)b^2 - k_4\gamma_0 E^* e^2 + k_0[(1-p)\beta(N^*-L^*-T^*) - (1-p)\beta T^* - (1-q)\lambda B^*]\,lt$$
$$+k_0[(1-p)\beta T^* + (1-q)\lambda B^*]\ \ln + k_0(1-q)\lambda(N^*-L^*-T^*)\,lb + k_1(\sigma - p\beta T^* - q\lambda B^*)\,lt$$
$$+[k_1(p\beta T^* + q\lambda B^*) - k_2\alpha\,]nt + k_1 q\lambda(N^*-L^*-T^*)bt + k_3 s\,tb + k_3 s_1 B^* be + k_4\gamma E^* ne$$

For $\frac{dU_1}{dt}$ to be negative definite, the following conditions must be satisfied,

(i) $k_0[(1-p)\beta(N^*-L^*-T^*) - (1-p)\beta T^* - (1-q)\lambda B^*]^2 <$
$\frac{1}{5}k_1\left[(1-p)\beta(N^*-T^*)\frac{T^*}{L^*} + (1-q)\lambda(N^*-T^*)\frac{B^*}{L^*}\right]\left[p\beta T^* + q\lambda(N^*-L^*)\frac{B^*}{T^*} + \sigma\frac{L^*}{T^*}\right]$

(ii) $k_1(\sigma - p\beta T^* q\lambda B^*)^2 < \frac{1}{5}k_0\left[(1-p)\beta(N^*-T^*)\frac{T^*}{L^*} + (1-q)\lambda(N^*-T^*)\frac{B^*}{L^*}\right]\left[p\beta T^* + q\lambda(N^*-L^*)\frac{B^*}{T^*} + \sigma\frac{L^*}{T^*}\right]$

(iii) $k_0[(1-p)\beta T^* + (1-q)\lambda B^*]^2 < \frac{1}{3}k_2 d\left[(1-p)\beta(N^*-T^*)\frac{T^*}{L^*} + (1-q)\lambda(N^*-T^*)\frac{B^*}{L^*}\right]$

(iv) $k_0(1-q)^2\lambda^2(N^*-L^*-T^*)^2 < \frac{1}{4}k_3(s_0-s_1E^*)\left[(1-p)\beta(N^*-T^*)\frac{T^*}{L^*}+(1-q)\lambda(N^*-T^*)\frac{B^*}{L^*}\right]$
(v) $[k_1(p\beta T^*+q\lambda B^*)-k_2\alpha]^2 < \frac{4}{15}k_1k_2d\left[p\beta T^*+q\lambda(N^*-L^*)\frac{B^*}{T^*}+\sigma\frac{L^*}{T^*}\right]$
(vi) $k_1q^2\lambda^2(N^*-L^*-T^*)^2 < \frac{1}{5}k_3(s_0-s_1E^*)\left[p\beta T^*+q\lambda(N^*-L^*)\frac{B^*}{T^*}+\sigma\frac{L^*}{T^*}\right]$
(vii) $k_3s^2 < \frac{1}{5}k_1(s_0-s_1E^*)\left[p\beta T^*+q\lambda(N^*-L^*)\frac{B^*}{T^*}+\sigma\frac{L^*}{T^*}\right]$
(viii) $k_3s_1^2B^{*2} < \frac{1}{2}k_4\gamma_0E^*(s_0-s_1E^*)$
(ix) $k_4\gamma_1^2E^{*2} < \frac{2}{3}k_2d\gamma_0E^*$
After choosing $k_1 = 1, k_2 = \frac{p\beta T^*+q\lambda B^*}{\alpha}$ and $k_4 = \gamma_0$, we can choose k_0 and k_3 such that

$$\frac{q^2\lambda^2(N^*-L^*-T^*)^2}{(s_0-s_1E^*)\xi_1} < k_3 < \frac{1}{5}(s_0-s_1E^*)\min.\left\{\frac{\gamma_0^2E^*}{2s_1^2B^{*2}},\ \frac{\xi_1}{5s^2}\right\}$$

$$\frac{(p\beta T^*+q\lambda B^*-\sigma)^2}{\xi_1\xi_2} < k_0 < \xi_2\min.\left\{\frac{\xi_1}{5\xi_3^2}, \frac{d(p\beta T^*+q\lambda B^*)}{3\alpha[(1-p)\beta T^*+(1-q)\lambda B^*]^2}, \frac{k_3(s_0-s_1E^*)}{4(1-q)^2\lambda^2(N^*-L^*-T^*)^2}\right\}\alpha\gamma_1^2E^* < \frac{2}{3}d(p\beta T^*+q\lambda B^*)$$

Hence, we obtain the conditions as stated in the ***Theorem* 4.1**.
Thus, dU_1/dt is a negative definite under the conditions (4.1), (4.2) and (4.3) as stated in the ***Theorem* 4.1**, showing that W_3 is locally asymptotically stable.

Appendix – II

***Proof of Theorem* 4.2**
Consider the following positive definite function, corresponding to the model system (3.1) about W_3,

$$U_2 = \frac{k_0}{2}(L-L^*)^2+\frac{k_1}{2}\left(T-T^*-T^*\ln\frac{T}{T^*}\right)+\frac{k_2}{2}(N-N^*)^2+\frac{k_3}{2}(B-B^*)^2+\frac{k_4}{2}\left(E-E^*-E^*\ln\frac{E}{E^*}\right),$$

where the coefficients k_0, k_1, k_2, k_3 and k_4 can be chosen appropriately.
Differentiating the above equation with respect to 't' and using (3.1), we get,
$\frac{dU_2}{dt} = -k_0[(1-p)\beta T+(1-q)\lambda B](L-L^*)^2-k_1\left[\frac{q\lambda B(N-L)+\sigma L}{TT^*}\right](T-T^*)^2$
$-k_0(\sigma+d+\alpha_2)(L-L^*)^2-k_1p\beta(T-T^*)^2-k_2d(N-N^*)^2-k_3(s_0-s_1E^*)(B-B^*)^2-k_4\gamma_0(E-E^*)^2+k_0\{(1-p)\beta(N^*-L^*-T^*)-(1-p)\beta T-(1-q)\lambda B\}(L-L^*)(T-T^*)+k_1\left(\frac{\sigma}{T^*}-\frac{q\lambda B}{T^*}-p\beta\right)(L-L^*)(T-T^*)+k_0[(1-p)\beta T+(1-q)\lambda B](L-L^*)(N-N^*)+k_0(1-q)\lambda(N^*-L^*-T^*)(L-L^*)(B-B^*)$
$+\left[k_1\left(p\beta+\frac{q\lambda B}{T^*}\right)-k_2\alpha\right](T-T^*)(N-N^*)+k_1\frac{q\lambda(N^*-L^*-T^*)}{T^*}(T-T^*)(B-B^*)+k_3s(T-T^*)(B-B^*)+k_3s_1B(B-B^*)(E-E^*)+k_4\gamma_1(E-E^*)(N-N^*)$.
Assuming $k_1 = 1$, $k_2 = \frac{p\beta}{\alpha}$ and $k_3 = \frac{q\lambda}{s}$, the above equation reduces to the form,
$\frac{dU_2}{dt} = -k_0[(1-p)\beta T+(1-q)\lambda B](L-L^*)^2-\left[\frac{q\lambda B(N-L)+\sigma L}{TT^*}\right](T-T^*)^2$
$-k_0(\sigma+d+\alpha_2)(L-L^*)^2-p\beta(T-T^*)^2-\frac{p\beta d}{\alpha}(N-N^*)^2-\frac{q\lambda(s_0-s_1E^*)}{s}(B-B^*)^2-k_4\gamma_0(E-E^*)^2$
$+k_0\{(1-p)\beta(N^*-L^*-T^*)-(1-p)\beta T-(1-q)\lambda B\}(L-L^*)(T-T^*)+\left(\frac{\sigma}{T^*}-\frac{q\lambda B}{T^*}-p\beta\right)(L-L^*)(T-T^*)$ For dU_2/dt
$+k_0[(1-p)\beta T+(1-q)\lambda B](L-L^*)(N-N^*)+k_0(1-q)\lambda(N^*-L^*-T^*)(L-L^*)(B-B^*)$
$+\frac{q\lambda B}{T^*}(T-T^*)(N-N^*)+\frac{q\lambda(N^*-L^*)}{T^*}(T-T^*)(B-B^*)+\frac{qs_1\lambda B}{s}(B-B^*)(E-E^*)+k_4\gamma_1(E-E^*)(N-N^*)$.
to be negative definite, the following conditions must be satisfied,
(i) $k_0[(1-p)\beta(N^*-L^*-T^*)-(1-p)\beta T-(1-q)\lambda B]^2 < \frac{1}{4}p\beta(\sigma+d+\alpha_2)$,
(ii) $\left(\frac{\sigma-p\beta T^*-q\lambda B}{T^*}\right)^2 < \frac{1}{4}k_0p\beta(\sigma+d+\alpha_2)$,
(iii) $k_0[(1-p)\beta T+(1-q)\lambda B]^2 < \frac{1}{3}\frac{p\beta d}{\alpha}(\sigma+d+\alpha_2)$,
(iv) $k_0(1-q)^2\lambda^2(N^*-L^*-T^*)^2 < \frac{q\lambda(s_0-s_1E^*)(\sigma+d+\alpha_2)}{3s}$,
(v) $\frac{q^2\lambda^2B^2}{T^{*2}} < \frac{p^2\beta^2d}{3\alpha}$,
(vi) $\frac{q^2\lambda^2(N^*-L^*)^2}{T^{*2}} < \frac{pq\beta\lambda(s_0-s_1E^*)}{3s}$,
(vii) $\frac{q\lambda s_1^2B^2}{s} < \frac{2}{3}k_4\gamma_0(s_0-s_1E^*)$,
(ix) $k_4\gamma_1^2 < \frac{2}{3}\frac{p\beta d\gamma_0}{\alpha}$.
Now choosing k_0 and k_4 such that,

$$\frac{4(p\beta T^*+q\lambda B_{\max}-\sigma)^2}{p\beta(\sigma+d+\alpha_2)T^{*2}} < k_0 < (\sigma+d+\alpha_2,)$$

$$\min . \left\{ \frac{p\beta}{4\xi_4^2}, \frac{p\beta\, d}{3\alpha\left[(1-p)\beta A/d + (1-q)\lambda B_{\max}\right]^2}, \frac{q\lambda(s_0 - s_1E^*)}{3s(1-q)^2\lambda^2(N^* - L^* - T^*)^2} \right\}$$

$$\frac{3q\lambda\, s_1^2 B_m^2}{2\, s\, \gamma_0(s_0 - s_1E^*)} < k_4 < \frac{2\gamma_0 p\beta\, d}{3\alpha\gamma_1^2},$$

$$\alpha\, q^2\lambda^2 B_m^2 < \frac{1}{3} d\, p^2\beta^2 T^{*2},$$

$$s\, q\lambda(N^* - L^*)^2 < \frac{1}{3} p\beta(s_0 - s_1E^*)T^{*2}.$$

Hence, we obtain the conditions as stated in the ***Theorem* 4.2**. Thus, $\frac{dU_2}{dt}$ is a negative definite under the conditions (4.4 - 4.7) as given in the statement of the theorem, showing that W_3 is nonlinearly asymptotically stable inside the region Ω.