STABILITY ANALYSIS OF A DETERMINISTIC MATHEMATICAL MODEL FOR TRANSMISSION DYNAMICS OF TUBERCULOSIS

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Abstract- Despite all efforts to curb and exterminate the menace of Tuberculosis (TB) epidemics on the human population, the disease still remains one of the major causes of death, with one –third of the world's population infected. In this paper, we study a deterministic mathematical model to have a better insight in the transmission dynamics of TB. The model is shown to have disease-free and endemic equilibria and their local stabilities are established using the basic reproduction number, R_o. If $R_o < 1$, the infection can be controlled and then eradicated and when $R_o > 1$, the disease will persist. Numerical simulations are performed to validate the theoretical results.

Keywords- Mathematical Model, Tuberculosis, Infectious Disease, Disease-free, Endemic, Equilibrium, Epidemics, Local Stability, Basic Reproduction Number.

I. INTRODUCTION

Tuberculosis (TB) is an air-borne infectious disease caused by *Mycobacterium tuberculosis.* The disease basically attacks the lungs (Pulmonary TB) as well as other parts of the body (Extra-pulmonary TB). Parts of affected by Extra-pulmonary TB include the central nervous system, the genital-urinary system, bones, joints and the skin.

The classical clinical features of Pulmonary TB include chronic cough, sputum production, appetite loss, weight loss, fever, night sweats and hemoptysis. Extra-pulmonary TB occurs in 10%-42% of patients, depending on the race or ethnic background, age, presence or absence of underlying disease, genotypes of the *Mycobacterium tuberculosis* strains and immune status.

Tuberculosis has slow intrinsic dynamics, the incubation period, latent period and the infectious period spam long time intervals in the order of years on average. The slow progression of TB at individual level leads to slow temporal dynamics and long-term outcomes of TB at the population level. Therefore, a mathematical model is needed to have a better insight on the dynamics of the disease.

Mathematical modeling is a powerful tool extensively used by researchers in epidemiology to have a better understanding of the transmission dynamics of infectious diseases. Several authors in [1,…,4] have studied the dynamics of TB using mathematical modeling approach with the view to investigate the role played by one or more control measure(s) in curtailing the prevalence in both developing and developed countries.

In this paper, a deterministic MSEIRS model for TB transmission dynamics is formulated and analysed rigorously with the purpose to complement the works of aforementioned authors. The rest of the paper is organized as follows. Section 2 introduces the model formulation. In Section 3, we found the equilibria also calculated the basic reproduction number. Stability of the equilibrium points was investigated in Section 4. We presented Numerical simulation results in Section 5 and finally, Section 6 contains the conclusion.

II. MODEL FORMULATION

A non-linear mathematical model for the transmission dynamics of Pulmonary TB and Extra-pulmonary TB that incorporates immunization of infants, chemotherapy, recurrent infection and treatment if formulated by sub-dividing the total human population at time, *t* denoted by *N(t)* into mutually exclusive subpopulations, namely passive immune infants *M(t)*, susceptible individuals *S(t)*, exposed individuals *E(t)*, infected individuals with Pulmonary TB *I(t)*, infected individuals with Extra-pulmonary TB *X(t)* and recovered individuals due to effective treatment *R(t).*

Thus,

$$N(t) = M(t) + S(t) + E(t) + I(t) + X(t) + R(t) \quad (1)$$

The model assumptions are as follows:

a) Death rate is not equal to birth
b) Recruited migrants are assumed susceptible
c) Vertical transmission of TB is not considered
d) The population is homogeneous and dependent on time, *t.*

Based on the above assumptions, we describe the transmission dynamics of tuberculosis by the following system of ordinary differential equations:

$$\frac{dM}{dt} = b\theta - (\mu + \emptyset)M \quad (2)$$

$$\frac{dS}{dt} = b(1-\theta) + \pi + \emptyset M + \omega R - \beta_1 SI - \mu S \quad (3)$$

$$\frac{dE}{dt} = \beta_1 SI - \beta_2 IR + r_2 I - [\mu + \sigma + k(1-r_1) + v_1]E \quad (4)$$

$$\frac{dI}{dt} = k(1-r_1)E - (r_2 + \mu + \delta_1 + v_2)I \quad (5)$$

$$\frac{dX}{dt} = \sigma E - (\mu + \delta_2 + v_3)X \quad (6)$$

$$\frac{dR}{dt} = v_1 E + v_2 I + v_3 X - \beta_2 IR - (\mu + \omega)R \quad (7)$$

By adding (2) – (7), with the aid of (1), we have

$$\frac{dN}{dt} = b + \pi - \mu N - \delta_1 I - \delta_2 X. \quad \Rightarrow \quad \frac{dN}{dt} \leq b + \pi - \mu N.$$

Then,

$$\lim_{t\to 0} sup\ N \leq \frac{b+\pi}{\mu}.$$

Hence, the feasible region of the model (2) – (7) is

$$X = \left\{M(t),\ S(t),\ E(t),\ I(t),\ X(t),\ R(t) \in \mathbb{R}_+^6 : N \leq \frac{b+\pi}{\mu}\right\},$$

and is positively invariant.

Table 1: Parameter description and hypothetical values

S/N	Parameter	Symbol	Hypothetical value	Reference
1	Birth rate	b	0.03	[5]
2	Waning rate of vaccine	$\emptyset$	(0-1)	Estimate
3	Rate of immunizing infant	θ	(0-1)	Estimate
4	Migration rate of S(t)	π	3500	[3]
5	TB transmission rate of S(t) to become E(t)	β_1	0.99	[3]
6	TB transmission rate of R(t) to become E(t)	β_2	[0-1)	Estimate
7	Natural death rate	μ	0.04	[9]
8	Chemoprophylaxis rate of E(t)	r_1	[0-1)	Estimate
9	Slow rate to I(t) from E(t)	k	0.00013	[6]
10	Rate of effective per capita therapy	r_2	0.1828	[6]
11	TB induced death rate for I(t)	δ_1	0.2	[7]
12	TB induced death rate for X(t)	δ_2	0.3	[7]
13	Progression rate of E(t) to X(t)	δ	0.0009	[4]
14	Recovery rate of E(t)	v_1	2	[4]
15	Recovery rate of I(t)	v_2	1.5	[4]
16	Recovery rate of X(t)	v_3	1	Estimate
17	Immunization loss rate	ω	0.3	[8]

III. EQUILIBRIA AND BASIC REPRODUCTION NUMBER

3.1 Existence of Disease- free Equilibrium (DFE)

Let E_o represent the equilibrium at DFE. Thus, in the absence of infection, say $I^* = 0$, we have $E^* = X^* = R^* = 0$ from (2) - (7), $M^* = \frac{A_1}{k_1}$ and $S^* = \frac{A_1 k_1 + A_1 \emptyset}{k_1 \mu}$ from (2) - (7) respectively. Therefore, the model (2) – (7) has its DFE given by

$$E_o = (M^*, S^*, E^*, I^*, X^*, R^*) = \left(\frac{A_1}{k_1}, \frac{A_1 k_1 + A_1 \emptyset}{k_1 \mu}, 0,0,0,0\right).$$

3.2 Computation of Basic Reproduction Number

The basic reproduction number, denoted by R_o is defined as threshold parameter that represents the mean number secondary cases a typical single infective will generate in a totally naïve/susceptible population during his/her entire period of infectiveness [10]. Using the next generation approach to compute R_o, denote the new infection terms and transition term at E_o. Therefore,

$$F = \begin{bmatrix} 0 & \beta_1 S^* & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}, \qquad V = \begin{bmatrix} k_2 & -r_2 & 0 \\ -k_3 & k_4 & 0 \\ -\sigma & \sigma & k_5 \end{bmatrix}$$

Therefore,

$$R_o = \rho(FV^{-1}) = \frac{\beta_1 S^* k_3}{k_2 k_4 - k_3 r_2} = \frac{\beta_1 k_3 (A_2 k_1 + A_1 \emptyset)}{k_1 \mu (k_2 k_4 - k_3 r_2)} \quad (8)$$

where,

$A_1 = b\theta, A_2 = b(1-\theta) + \pi, k_1 = \mu + \emptyset, k_2 = \mu + \sigma + k_3 v_1,\ k_3 = k(1-r_1),\quad k_4 = r_2 + \mu + \delta_1 + v_2,$
$k_5 = \mu + \delta_2 v_3,\ k_6 = \mu + \omega.$

3.3 Existence of Endemic Equilibrium

Let E_1 denote the endemic equilibrium of (2) – (7) satisfying the following

$$M^{**} = \frac{A_1}{k_1} \quad (9)$$

$$R^{**} = \frac{L_o I^{**}}{k_3 k_5 (\beta_2 I^{**} + k_6)} \quad (12)$$

$$E^{**} = \frac{k_4 I^{**}}{k_3} \quad (10)$$

$$S^{**} = \frac{(A_2 k_1 A_1 \emptyset)(\beta_2 I^{**} + k_6) k_3 k_5 + k_1 \omega L_o I^{**}}{k_1 k_3 k_5 (\beta_2 I^{**} + k_6)(\beta_1 I^{**} + \mu)} \quad (13)$$

$$X^{**} = \frac{\sigma k_4 I^{**}}{k_3 k_5} \quad (11)$$

$$G_2^{**} = \frac{k_2 k_4}{k_3} \quad (14)$$

Thus, by algebraic manipulations on (9) – (14) at endemic equilibrium, we obtain

$$A(I^{**})^2 + BI^{**} + C = 0, \quad (15)$$

where,

$A = \beta_1 \beta_2 k_1 [k_5 (k_2 k_4 - r_2 k_3) - L_o]$,

$B = k_1 k_5 [k_2 k_4][\beta_2 \mu + \beta_6 - L_o k_1 (\beta_2 \mu + \beta_1 \omega) - \beta_1 \beta_2 k_3 k_5 (A_2 k_1) + A_1 \emptyset]$

$C = \mu k_1 k_5 k_6 [k_2 k_4 - r_2 k_3][1 - R_o]$

$L_o = v_1 k_4 k_5 + v_2 k_3 k_5 + v_3 \sigma k_4$

$G_2^{**} = \beta_1 S^{**} + \beta_2 R^{**} + r_2$.

It is instructive to note that $A > 0$ since $k_5 (k_2 k_4 - r_2 k_3) - L_o > 0$. Thus, (15) will have a unique positive root whenever $R_o > 1$, hence the following result is established.

Lemma The model (2) – (7) has a unique positive (endemic) equilibrium whenever $R_o > 1$.

IV. LOCAL STABILITY OF THE EQUILIBRIA

4.1 Local Stability at DFE

Theorem Whenever $R_o < 1$, the disease-free equilibrium $E_{o,}$ is locally asymptotically stable and unstable when $R_o > 1$.

Proof

The variational matrix of the model (2) – (7) at E_o is given as

$$J(E_0) = \begin{bmatrix} -k_1 & 0 & 0 & 0 & 0 & 0 \\ \phi & -\mu & 0 & -\beta_1 S^* & 0 & \omega \\ 0 & 0 & -k_2 & \beta_1 S^* + r_2 & 0 & 0 \\ 0 & 0 & k_3 & -k_4 & 0 & 0 \\ 0 & 0 & \sigma & 0 & -k_5 & 0 \\ 0 & 0 & v_1 & v_2 & v_3 & -k_6 \end{bmatrix}$$

The characteristic equation of $J(E_o)$ is obtained as

$$(\lambda + k_1)(\lambda + \mu)(\lambda + k_6)(\lambda + k_5)[\lambda^2 + a_o \tau + a_1] = 0, \quad (16)$$

where,

$a_o = k_2 + k_4, \quad a_1 = (k_2 k_4 - r_2 k_3)(1 - R_o)$.

To establish that all eigenvalues of (16) are negative, we note that $a_o > 0$ and $a_1 > 0$ when $R_o < 1$. Thus, by Routh-Hurtwiz criterion, the quadratic polynomial will have negative roots. Since all eigenvalues are negative whenever $R_o < 1$, then the proof is complete.

4.2 Local Stability at Endemic Equilibrium

Theorem Whenever $R_o > 1$ and $\beta_1 = \beta_2$, the endemic equilibrium E_1, is asymptotically stable and unstable otherwise.

Proof

The Jacobian matrix of (2) – (7) evaluated at E_1 is given as

$$J(E_1) = \begin{bmatrix} -k_1 & 0 & 0 & 0 & 0 & 0 \\ \phi & -G^{**} & 0 & -\beta_1 S^{**} & 0 & \omega \\ 0 & \beta_1 I^{**} & -k_2 & G_2^{**} & 0 & \beta_2 I^{**} \\ 0 & 0 & k_3 & -k_4 & 0 & 0 \\ 0 & 0 & \sigma & 0 & -k_5 & 0 \\ 0 & 0 & v_1 & v_3 - \beta_2 R^{**} & v_3 & -G_3^{**} \end{bmatrix}.$$

By elementary row transformation with tedious supplications, we have

$$J(E_1) = \begin{bmatrix} -k_1 & 0 & 0 & 0 & 0 & 0 \\ 0 & -G^{**} & 0 & -\beta_1 S^{**} & 0 & \omega \\ 0 & 0 & -k_2 & -D_1^{**} & 0 & D_2 I^{**} \\ 0 & 0 & 0 & -J_1^{**} & 0 & D_3 I^{**} \\ 0 & 0 & \sigma & 0 & -k_5 & D_4 I^{**} \\ 0 & 0 & 0 & 0 & 0 & -J_2^{**} \end{bmatrix}$$

where,

$G_1 = \beta_1 I^{**} + \mu, \quad G_2 = \beta_2 I^{**} + k_6, \quad J_1 = \frac{k_3 \beta_1^2 S^{**} I^{**}}{k_2 G_1^{**}}, \quad J_2 = \frac{k_3 k_5 G_3^{**} \beta_1^2 S^{**} I^{**} - k_3 k_5 k_6 R^{**} (\beta_1 G_1^{**} + B_{1\omega})}{k_3 k_5 \beta_1^2 S^{**} I^{**}}$.

It is obvious that $\lambda_i < 0 \; \forall \; i = 1, \ldots, 5$. To show that $\lambda_6 = -J_2 < 0$, we substitute (14) in J_2 to get

$$J_2 = \frac{G_3^{**k} k_5 \beta_1 I^{**} (k_2 k_4 - r_2 k_3) - G_3^{**} k_5 \beta_1 \beta_2 k_3 R^{**} I^{**} - k_3 k_5 k_6 R^{**} (\beta_2 G^{**} + \beta_1 \omega)}{k_3 k_5 \beta_1^2 S^{**} I^{**}}.$$

We note that $G_3^{**} = G_1^{**} + \omega$ when $\beta_1 = \beta_2$, hence

$$J_2 = \frac{G_3^{**k} k_5 \beta_1 I^{**} (k_2 k_4 - r_2 k_3) - G_3^{**} k_5 \beta_1 k_3 R^{**} (\beta_1 I^{**} + k_6)}{k_3 k_5 \beta_1^2 S^{**} I^{**}}.$$

Substituting (12) for $\beta_1 = \beta_2$, we get

$$J_2 = \frac{G_2 \beta_1 I [k_5 (k_2 k_4 - r_2 k_3) - L_o]}{k_3 k_5 \beta_1^2 S^{**} I^{**}} > 0.$$

Thus, $\lambda_6 < 0$ when $\beta_1 = \beta_2$ which completes the proof.

V. NUMERICAL SIMULATION

In this section, we present some numerical simulations for the set of parameter presented in Table 1, in order to study the dynamical behavior of the model (2) – (7) and authenticate the above analytical findings.

Table 2: Effect of R_o on the number of TB cases at steady states

ϕ	θ	r_1	R_o	$E^{**}+I^{**}+X^{**}$	*Remarks*
0.8	0.4	0	2.8695	56703	E_1 stable (no eradication)
0.8	0.4	0.2	2.2956	49124	E_1 stable (no eradication)
0.4	0.6	0.4	1.7218	36489	E_1 stable (no eradication)
0.4	0.6	0.6	1.1478	11213	E_1 stable (no eradication)
0.2	0.8	0.6	1.1478	11212	E_1 stable (no eradication)
0.2	0.8	0.8	0.5739	0	E_o stable (disease eradication)

Note: Table 2 is generated by varying ϕ, θ and r_1 with $\beta_2 = 0.99$ and all other parameter values on Table 1

Table 3: Effect of β_2 on R_O and TB prevalence

β_2	R_o	$E^{**}+I^{**}+X^{**}$
0.1	1.1478	1813
0.2	1.1478	2030
0.3	1.1478	2305
0.4	1.1478	2660
0.5	1.1478	3137
0.6	1.1478	3799
0.7	1.1478	4762
0.8	1.1478	6213
0.9	1.1478	8418
1.0	1.1478	40433

Note: Table 3 is generated by varying β_2 with $\phi = 0.2, \theta = 0.8, r_1 = 0.6$ and all other parameter values in Table 1.

5.1 Discussion of Results

The above tabulated results clearly reveal that, as the total population of TB infectives increase, R_o also increases provided the transmission rate coefficient of recurrent infection R_2 is kept fixed/constant. Furthermore, increase in chemoprophylaxis rate will reduce R_o thus reducing TB burden. Similarly, changes in the transmission coefficient of recurrent infection β_2 do not affect R_o, but influences TB prevalence.

CONCLUSION

An MSEIXRS deterministic model for the transmission dynamics of Pulmonary and Extra-pulmonary tuberculosis disease is developed and rigorously analyzed in the presence of immunization, chemoprophylaxis, recurrent infection and treatment. The main findings of the study are as follows:

1. The model (2) – (7) has a locally –asymptotically stable disease-free equilibrium whenever $R_o < 1$.
2. The model (2) – (7) has a unique endemic equilibrium whenever $R_o > 1$.
3. The chemoprophylaxis rate reduces the reproductive number hence affecting the quantitative behavior of TB and helps to decrease TB prevalence.
4. R_o is independent of the transmission coefficient of recurrent infection β_2, but more promote (when β_2 increases) or curtail (when β_2 decreases) TB prevalence.

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