MATHEMATICAL MODEL OF IMPACT OF VACCINATION AND TREATMENT STRATEGY FOR ERADICATION OF TUBERCULOSIS WITH ABSENCE OF EMIGRATION EFFECT

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Abstract: In this study, we proposed a mathematical model for the vaccination and treatment strategy to eradicate tuberculosis with absent of emigration effect, where we modified the existing model by incorporating the immigrants effect, efficacy of vaccination, treatment and new babies were considered 100% vaccinated. Existence and uniqueness of solution of the modified model was carried out and it shows that the solution exists and it is unique. The stability analysis of the disease free equilibrium shows that the disease-free equilibrium (DFE) is locally asymptotically stable. The effective reproductive number R_e was computed under different conditions. In the case where there is treatment and vaccination we found Re to be 0.2527. The results show that mycobacterium tuberculosis can be eradicated if mass vaccination and treatment actions are properly initiated and enforced. Also, Henceforth, infected emigrate should be highly discourage of leaving it residents country to ensure fast eradication of mycobacterium tuberculosis.

Keywords: Emigration, vaccination, disease, TB infection, eradication

Introduction

Tuberculosis may infect any part of the body, but most commonly occurs in the lungs (known as pulmonary tuberculosis) (Mandel *et al.*, 2010). Extra pulmonary occurs when TB develops outside the lungs.

Symptoms of TB depend on where in the body the TB bacteria grow. In the pulmonary case, the early symptoms usually include fatigue or weakness, unexplained weight loss, fever, chills, loss of appetite and night sweat (Bhunu *et al.*, 2008).

Since the symptoms are very much similar to common cold people tend to treat it as one. One may not notice any symptom of illness until the disease is quite advanced (WHO, 2010). When the infection in the lungs worsens, it may cause chest pains, bad cough that last 3 weeks or longer (WHO, 2010).

There are cases where the infection spread beyond the lungs to other parts of the body such as the bones and joints, the digestive system, the bladder and reproductive system and the nervous system. This is known as extra pulmonary TB and the symptoms will depend upon the organ involved (Golden & Vikram, 2005).

We shall now look at the symptoms of both pulmonary and extra pulmonary TB in details.

Once inhaled, the mycobacterium enters the lungs. When they reach the pulmonary alveoli, they encounter macrophages which are white blood cells that surround and digest pathogens. Sometimes, the immune system can destroy the bacteria, but if not, the bacteria begin multiplying within the macrophages. The macrophages are then used as transportation to nearby lymph nodes. Once in the lymph nodes, the bacterium can spread throughout the body (Kumar *et al.*, 2007).

Because mycobacterium is a slow-growing bacterium, the immune system, if not able to destroy, it may be able to keep it from spreading enough to cause symptoms. This is called latent tuberculosis infection and it occurs for 90% of TB infections (Skolnik, 2011). While the organism may be present in the body for years, there is only 10% chance that it will ever progress to an active infection (Arch & Claire, 2009). People with latent TB infection cannot spread TB to others. Extra pulmonary TB occurs when MTB spread beyond the lungs to affect other parts of the body. Golden and Vikram (2005), repot that in 15-20% of active cases, the infection spreads outside the respiratory organs, causing other kinds of TB. These are collectively called extra pulmonary TB. Extra pulmonary TB occurs more commonly in immunosuppressed persons and young children. In those with HIV, this occurs in more than 50% of cases (Golden & Vikram, 2005).

A partially more serious, wide spread form of TB is called disseminated TB, commonly known as military tuberculosis. Military TB makes up about 10% of extra pulmonary cases (Mandel *et al.*, 2010). In extra pulmonary TB, signs and symptoms vary, depending on the organ/part of infection.

Post exposure vaccines are those give to individuals after evidence of infection. Although these vaccines cannot prevent the initial acute infection, their purpose is to strengthen the immune surveillance to prevent reactivation of latent infection (Doherty & Andersen, 2005).

A multiphase vaccine effective both as a pre-exposure and post-exposure vaccine would be a great achievement in fighting MTB, but so far, there are none available for use. In theory, multiphase vaccine will not only inhibit the infection from becoming symptomatic, but will also prevent later activation.

Jia *et al.* (2008) investigate the impact of immigration on the transmission dynamics of tuberculosis. They too incorporated the recruitment of latent and infectious immigrants. Their analysis indicated that the disease will persist in the population if there is prevalence of TB immigrants. Their model showed that the disease never dies out and becomes endemic in the host population. The study suggests that the immigrants have a considerable influence on the overall transmission dynamics behavior of tuberculosis.

Methods

Mathematical models have played a key role in the formulation of TB control strategies and the establishment of interim goals for intervention programs. Many types of epidemic models exist. They include: the stochastic models, the deterministic (compartmental) models such as the SIR, SIS, SIRS, SEIS, SEIR, MSEIR, models, (Where S=Susceptible class; I=Infective class; M=passively immune class; E=Exposed class; and R=Recovered class).

Our model is a deterministic MSEIR type model where the population is partitioned into components or classes based on the epidemiological state of the individuals, and it is assumed that the epidemic process is deterministic.

The modified model

We modified the work of Kalu and Inyama (2012) by incorporating immigration effect and assume 100% vaccination for the new-births. Modified model based on the

following assumptions: That the individuals that make up the population can be grouped into different compartments according to their epidemiological state, the population size in a compartment changes with time, all new-births are immunized against TB infection and enter the vaccinated class, M, and there is migration in the population. That is, there are immigrants and emigrants, and there is no vertical transmission of TB. That is, no transmission from mother to new-born, hence all new-births are previously uninfected. That the immunity conferred on individuals by vaccination wanes after some time at a given rate, the population mixes homogeneously. That infection does not confer permanent immunity on the individuals. That a susceptible individual once infected develops latent infection. Those latently infected individuals are treated and are recovered or the infection develops to active TB. That every individual can die a natural death; that all immigrants are either vaccinated and are immune or they are unvaccinated and are susceptible. Latently infected and infectious individuals are restricted from entering the population.

Model variables and parameters

The following variables and parameters shall be used in this model:

- M(t): the number of individuals who are immunized/ vaccinated against TB at time t.
- S(t): the number of susceptible individuals. That is, the individuals who can catch the disease because they have no immunity to the infectious agent so might become infected if exposed.
- L(t): the number of latently infected individuals at time t.
- I(t): the number of infectious individuals at time t.
- R(t): the number of individuals who have been treated and have recovered from the infection at time t.
- β: the rate of new-births in the population
- f: the efficacy of the vaccine in preventing initial infection.
- ϒ: Average immigration rate into the population
- K: the rate at which susceptible individuals develop latent infection
- q: the rate of expiration of vaccine (rate at which immunity wanes)
- ψ: the rate at which active TB is treated.
- ε: recovery rate of latent infection due to treatment
- α: average emigration rate
- e: efficacy of treatment in curing infected persons
- m: the rate at which latently infected become actively infected
- π: the rate at which recovered individuals become susceptible to TB again
- μ: natural mortality rate
- μ_τ: TB induced deaths
- η: Proportion of immigrants vaccinated and are immune

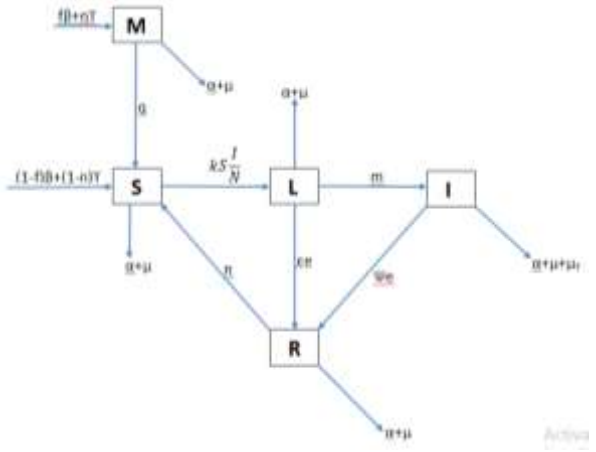

Fig. 1: Schematic presentation of the modified model

The modified model equation

This section presents the modified model equations by a system of differential equations thus:

$$\frac{dM}{dt} = f\beta + n\gamma - \alpha M - \mu M - qM$$
$$= f\beta + n\gamma - (\alpha + \mu + q)M \quad (1)$$

$$\frac{dS}{dt} = (1-f)\beta + (1-n)\gamma - \mu S - \alpha S + qM + \pi R - kS\frac{I}{N}$$
$$= (1-f)\beta + (1-n)\gamma - (\mu + \alpha)S + qM + \pi R - kS\frac{I}{N} \quad (2)$$

$$\frac{dL}{dt} = kS\frac{I}{N} - \alpha L - \mu L - mL - \varepsilon L$$
$$= kS\frac{I}{N} - (\alpha + \mu + m + \varepsilon)L \quad (3)$$

$$\frac{dI}{dt} = mL - \alpha I - \psi eI - (\mu + \mu_\tau)I$$
$$= mL - (\alpha + \psi e + \mu + \mu_\tau)I \quad (4)$$

$$\frac{dR}{dt} = \psi eI + \varepsilon L - \alpha R - \mu R - \pi R$$
$$= \psi eI + \varepsilon L - (\alpha + \mu + \pi)R \quad (5)$$

$$N(t) = M(t) + S(t) + L(t) + I(t) + R(t) \quad (6)$$

$$M(0) \geq 0, S(0) \geq 0, L(0) \geq 0, I(0) \geq 0, R(0) \geq 0$$

The system of equations (1) to (5) are the deterministic model equations which will be used to determine the existence and uniqueness of solution, the Disease-Free Equilibrium (DFE) for the disease as well as calculate the effective reproductive number R_e which determines whether the disease can be eliminated or not.

Methods of solution and analysis

Existence and uniqueness of solution

To prove the existence and uniqueness of solution of the system of equations in section 2.3, we shall use the method described by Egbetade & Ibrahim (2012).

Consider the system of equations below

$$\left.\begin{aligned} x_1' &= f_1(t, x_1, x_2, \dots, x_n),\ x_1(t_0) = x_{10} \\ x_2' &= f_2(t, x_1, x_2, \dots, x_n),\ x_2(t_0) = x_{20} \\ &\vdots \\ x_n' &= f_n(t, x_1, x_2, \dots, x_n),\ x_n(t_0) = x_{n0} \end{aligned}\right\} \quad (7)$$

We may write (3.31) in compact form as

$$x' = f(t, x), x(t_0) = x_0 \quad (8)$$

Theorem 1:

Let D denotes the region $|t - t_0| \leq a, ||x - x_0|| \leq b, x = (x_1, x_2 \dots, x_n)$ (9)

Suppose that $f(t, x)$ satisfies the Lipschitz condition $\|f(t, x_1) - f(t, x_2)\| \leq k\|x_1 - x_2\|$, where the pairs $(t, x_1), (t, x_2) \in D$, k is a positive constant. Then, there is

a constant $\delta > 0$ such that there exist a unique continuous vector solution $\underline{x}(t)$ of the system (7) in the interval $|t - t_0| \leq \delta$.

It is important to note that Lipschitz condition is satisfied by the requirement that $\frac{\partial f_i}{\partial x_j}$, $i, j = 1,2,\ldots,n$ are continuous and bounded in D.

Equilibrium and stability analysis for the existing model

We shall use the formulation of Disease Free Equilibrium (DFE) and stability analysis presented in Ayodeji (2016) to find the DFE for the formulated model and carryout stability analysis.

Consider the equation (7).

Definition 1: An equilibrium solution or fixed point, or steady-state solution of the system (7) is a constant solution x of the equation (Ayodeji, 2016).

At the equilibrium point, the derivatives in the equations (1) to (5) are equal to zero. That is, $M' = S' = L' = I' = R' = 0$. In the absence of any infections (DFE), $L = I = 0$.

To determine the stability of the model, we shall evaluate the DFE of the system.

***Theorem 2*:** Suppose that x^* is an equilibrium solution of (7), i.e. $f(x^*) = 0$, then

- $x^*$is locally asymptotically stable (LAS) if all the eigenvalues of J_{x^*} have negative real parts.
- If at least one eigenvalue has positive real part then x^* is unstable. The eigenvalues are the roots of the characteristic equation of the Jacobian matrix, J, where $J = \left[\frac{\partial f_i}{\partial x_j}\right], i, j = 1, 2, \ldots, n.$

Results

The modified model was considered in details by carrying out the existence and stability analysis of the disease-free equilibrium (DFE) state and determines the basic reproductive number R_0 for the formulated model.

Existence and uniqueness of solution

We shall prove the existence and uniqueness of solution or otherwise of model equations (1) to (5) using the formulation of Egbetade & Ibrahim (2012). Specifically, we shall use **Theorem 1.** Proof:

Let

$$f_1 = f\beta + n\gamma - (\alpha + \mu + q)M$$
$$f_2 = (1-f)\beta + (1-n)\gamma - (\mu + \alpha)S + qM + \pi R - kS\frac{I}{N}$$
$$f_3 = kS\frac{I}{N} - (\alpha + \mu + m + \varepsilon e)L$$
$$f_4 = mL - (\alpha + \psi e + \mu + \mu_\tau)I$$
$$f_5 = \psi eI + \varepsilon eL - (\alpha + \mu + \pi)R.$$

It suffices to show that $\frac{\partial f_i}{\partial x_j}$, $i, j = 1,2,\ldots,n$ are continuous and bounded in the region D defined by equation (3.33).

Consider the partial derivatives below:

$$\left|\frac{\partial f_1}{\partial M}\right| = |-(\alpha+\mu+q)| < \infty$$
$$\left|\frac{\partial f_1}{\partial S}\right| = \left|\frac{\partial f_1}{\partial L}\right| = \left|\frac{\partial f_1}{\partial I}\right| = \left|\frac{\partial f_1}{\partial R}\right| = 0 < \infty$$
$$\left|\frac{\partial f_2}{\partial M}\right| = |q| < \infty$$
$$\left|\frac{\partial f_2}{\partial S}\right| = \left|-(\alpha+\mu) - k\frac{I}{N}\right| < \infty$$
$$\left|\frac{\partial f_2}{\partial L}\right| = 0 < \infty$$
$$\left|\frac{\partial f_2}{\partial I}\right| = |\pi| < \infty$$
$$\left|\frac{\partial f_2}{\partial R}\right| = |-kS| < \infty$$
$$\left|\frac{\partial f_3}{\partial M}\right| = \left|\frac{\partial f_3}{\partial R}\right| = 0 < \infty$$
$$\left|\frac{\partial f_3}{\partial S}\right| = \left|k\frac{I}{N}\right| < \infty$$
$$\left|\frac{\partial f_3}{\partial I}\right| = |kS| < \infty$$
$$\left|\frac{\partial f_3}{\partial L}\right| = |-(\alpha+\mu+m+\varepsilon e)| < \infty$$
$$\left|\frac{\partial f_4}{\partial M}\right| = \left|\frac{\partial f_4}{\partial R}\right| = \left|\frac{\partial f_4}{\partial S}\right| = 0 < \infty$$
$$\left|\frac{\partial f_4}{\partial L}\right| = |m| < \infty$$
$$\left|\frac{\partial f_4}{\partial I}\right| = |-(\alpha+\psi e+\mu+\mu_T)| < \infty$$
$$\left|\frac{\partial f_5}{\partial M}\right| = \left|\frac{\partial f_5}{\partial S}\right| = 0 < \infty$$
$$\left|\frac{\partial f_5}{\partial L}\right| = |\varepsilon e| < \infty$$
$$\left|\frac{\partial f_5}{\partial I}\right| = |\psi e| < \infty$$
$$\left|\frac{\partial f_5}{\partial R}\right| = |-(\alpha+\mu+\pi)| < \infty$$

Clearly, all these partial derivatives are continuous and bounded. Hence by **Theorem 1** there exists a unique solution of the model equation (1)-(5) in the region D.

Existence and stability of disease-free equilibrium state of the modified model

The researcher investigates for the existence and stability of the DFE state of the modified model.

Equilibrium solution

Let $E(M, S, L, I, R)$ be the equilibrium point of the system described by the equations (1) to (5). At the equilibrium state we have:

$$\frac{dM}{dt} = \frac{dS}{dt} = \frac{dL}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = 0$$

That is,

$$f\beta + n\gamma - (\alpha + \mu + q)M = 0 \quad (10)$$
$$(1-f)\beta + (1-n)\gamma - (\mu+\alpha)S + qM + \pi R - kS\tfrac{I}{N} = 0 \quad (11)$$
$$kS\frac{I}{N} - (\alpha + \mu + m + \varepsilon)L = 0 \quad (12)$$
$$mL - (\alpha + \psi e + \mu + \mu_\tau)I = 0 \quad (13)$$
$$\psi eI + \varepsilon L - (\alpha + \mu + \pi)R = 0 \quad (14)$$

In order to obtain the disease-free equilibrium state, we solve the system of equations (10) to (14) simultaneously.

Existence of trivial equilibrium state

Let $E_0(M_0, S_0, L_0, I_0, R_0)$ be the trivial equilibrium state for the model. That is, when $M = S = L = I = R = 0$. so that$E_0(M_0, S_0, L_0, I_0, R_0) = (0,0,0,0,0)$. But no such equilibrium exists for the model since the population cannot go extinct so long as new babies are born into the population and there is migration into the population. In other words, so long as the recruitment terms $f\beta$ and $(1-f)\beta$ are not both zero and also $\eta\gamma$ and $(1-\eta)\gamma$ cannot be both zero, the population will never go extinct; and so $E_0(M_0, S_0, L_0, I_0, R_0) \neq (0,0,0,0,0)$.

The disease-free equilibrium state

The disease-free equilibrium state is the state of total eradication of the disease. Let $E^0(M^0, S^0, L^0, I^0, R^0)$ be the

DFE state for the model. For disease-free equilibrium state, the disease states of the model must be zero. That is, the infectious class, I and the latently infected class, L must be zero. Mathematically, for the DFE state $L^0 = I^0 = 0$.

Now, substituting $L^0 = I^0 = 0$ into the system of equations (10) to (14) we obtain the following:

From (10),

$f\beta + n\gamma - (\alpha + \mu + q)M = 0$

$\Rightarrow \quad (\alpha + \mu + q)M = f\beta + n\gamma$

$\Rightarrow \quad M = \frac{f\beta + n\gamma}{\alpha + \mu + q}$,

That is,

$M^0 = \frac{f\beta + n\gamma}{\alpha + \mu + q}$ (15a)

From ((11),

$(1-f)\beta + (1-n)\gamma - (\mu + \alpha)S + qM + \pi R - kS\frac{I}{N} = 0$

For $I = 0$, we have:

$(1-f)\beta + (1-n)\gamma - (\mu + \alpha)S + qM + \pi R = 0$ (15b)

But $M^0 = \frac{f\beta + n\gamma}{\alpha + \mu + q}$, substituting into (15b) yields:

$(1-f)\beta + (1-n)\gamma - (\mu + \alpha)S + \frac{q(f\beta + n\gamma)}{\alpha + \mu + q} + \pi R = 0$ (16a)

From (12),

$kS\frac{I}{N} - (\alpha + \mu + m + \varepsilon e)L = 0$

For $I = L = 0$, the equation vanishes.

Similarly, equation (13) vanishes on substituting $I = L = 0$, since it depends entirely on I and L only.

From equation (14),

$\psi eI + \varepsilon eL - (\alpha + \mu + \pi)R = 0$

$\Rightarrow \quad 0 + 0 - (\alpha + \mu + \pi)R = 0$ (since I=L=0)

$\Rightarrow \quad (\alpha + \mu + \pi)R = 0$ (16b)

Either $\alpha + \mu + \pi = 0$ Or $R = 0$

But $\alpha + \mu + \pi$ cannot be zero since α, μ, π are positive constants. i.e. $(\alpha + \mu + \pi) \neq 0$

$\Rightarrow \quad$ For (16b) to be true, then necessarily, $R = 0$.

Therefore, $R^0 = 0$ (17)

If $R = 0$, equation (16a) becomes

$(1-f)\beta + (1-n)\gamma - (\mu + \alpha)S + \frac{q(f\beta + n\gamma)}{\alpha + \mu + q} + \pi(0) = 0$

$\Rightarrow \quad S = \frac{\{(1-f)\beta + (1-n)\gamma\}(\alpha + \mu + q) + q(f\beta + n\gamma)}{(\alpha + \mu)(\alpha + \mu + q)}$

$\Rightarrow \quad S^0 = \frac{q(\beta + \gamma) + (\alpha + \mu)\{(1-f)\beta + (1-\eta)\gamma\}}{(\alpha + \mu)(\alpha + \mu + q)}$ (18)

Therefore, the DFE state for the model is

$E_0(M_0, S_0, L_0, I_0, R_0)$

$= (\frac{f\beta + n\gamma}{\alpha + \mu + q}, \frac{q(\beta + \gamma) + (\alpha + \mu)\{(1-f)\beta + (1-\eta)\gamma\}}{(\alpha + \mu)(\alpha + \mu + q)}, 0, 0, 0)$

Stability analysis of the disease- free equilibrium state

To determine the stability or otherwise of the disease-free equilibrium state E^0, we examine the behavior of the model equations near this equilibrium solution. Here we examine the condition(s) that must be met for the disease-free equilibrium state to be stable. In other words, we determine the conditions that must be met if the disease is to be totally eradicated from the population.

Recall that the system of equations in this model at equilibrium state is:

$f\beta + n\gamma - (\alpha + \mu + q)V = 0$

$(1-f)\beta + (1-n)\gamma - (\mu + \alpha)S + qV + \pi R - kS\frac{I}{N} = 0$

$kS\frac{I}{N} - (\alpha + \mu + m + \varepsilon)L = 0$

$mL - (\alpha + \psi e + \mu + \mu_\tau)I = 0$

$\psi eI + \varepsilon L - (\alpha + \mu + \pi)R = 0$

We now linearize the system of equations, to get the Jacobian matrix, J as;

$$J = \begin{bmatrix} -(\alpha + \mu + q) & 0 & 0 & 0 & 0 \\ q & -(\alpha + \mu) - k\frac{I}{N} & 0 & -kS & \pi \\ 0 & kI & -(\alpha + \mu + m + \varepsilon) & kS & 0 \\ 0 & 0 & m & -(\alpha + \psi e + \mu + \mu_\tau) & 0 \\ 0 & 0 & \varepsilon & \psi e & -(\alpha + \mu + \pi)R \end{bmatrix}$$

At the disease-free equilibrium

$E^0(M^0, S^0, L^0, I^0, R^0) = (\frac{f\beta + n\gamma}{\alpha + \mu + q}, \frac{q(\beta + \gamma) + (\alpha + \mu)\{(1-f)\beta + (1-\eta)\gamma\}}{(\alpha + \mu)(\alpha + \mu + q)}, 0, 0, 0)$,

The Jacobian Matrix (4.21) becomes

$$J_{E^0} = \begin{bmatrix} -(\alpha + \mu + q) & 0 & 0 & 0 & 0 \\ q & -(\alpha + \mu) & 0 & \frac{-k\{q(\beta + \gamma) + (\alpha + \mu)[(1-f)\beta + (1-\eta)\gamma]\}}{(\alpha + \mu)(\alpha + \mu + q)} & \pi \\ 0 & 0 & -(\alpha + \mu + m + \varepsilon) & \frac{k\{q(\beta + \gamma) + (\alpha + \mu)[(1-f)\beta + (1-\eta)\gamma]\}}{(\alpha + \mu)(\alpha + \mu + q)} & 0 \\ 0 & 0 & m & -(\alpha + \psi e + \mu + \mu_T) & 0 \\ 0 & 0 & \varepsilon & \psi e & 0 \end{bmatrix}$$

Where the quantity $\frac{q(\beta+\gamma)+(\alpha+\mu)[(1-f)\beta+(1-\eta)\gamma]}{(\alpha+\mu)(\alpha+\mu+q)} = s^o$

The Eigen values are calculated from the characteristics equation $|J_{E^o} - \lambda I| = 0$ where I is a 5×5 identity matrix. That is,

$$|J_{E^o} - \lambda I| = \begin{vmatrix} -(\alpha+\mu+q)-\lambda & 0 & 0 & 0 & 0 \\ q & -(\alpha+\mu)-\lambda & 0 & -ks^o & \pi \\ 0 & 0 & -(\alpha+\mu+m+\varepsilon)-\lambda & ks^o & 0 \\ 0 & 0 & m & -(\alpha+\psi e+\mu+\mu_\tau)-\lambda & 0 \\ 0 & 0 & \varepsilon & \psi e & -(\alpha+\mu+\pi)-\lambda \end{vmatrix} = 0$$

For simplicity of appearance and computational advantage, we let $c = \alpha + \mu$. Then we obtain the following

$$|J_{E^o} - \lambda I| = (-(c+q)-\lambda)\begin{vmatrix} -c-\lambda & 0 & -ks^o & \pi \\ 0 & -(c+m+\varepsilon)-\lambda & ks^o & 0 \\ 0 & m & -(c+\psi e+\mu_\tau)-\lambda & 0 \\ 0 & \varepsilon & \psi e & -(c+\pi)-\lambda \end{vmatrix} = 0$$

$$= (-(c+q)-\lambda)(-c-\lambda)\begin{vmatrix} -(c+m+\varepsilon)-\lambda & ks^o & 0 \\ m & -(c+\psi e+\mu_\tau)-\lambda & 0 \\ \varepsilon & \psi e & -(c+\pi)-\lambda \end{vmatrix} = 0$$

$$= (-(c+q)-\lambda)(-c-\lambda)(-(c+\pi)-\lambda)\begin{vmatrix} -(c+m+\varepsilon)-\lambda & ks^o \\ m & -(c+\psi e+\mu_\tau)-\lambda \end{vmatrix} = 0 \qquad (19)$$

From equation (4.12),

Either $(-(c+q)-\lambda)(-c-\lambda)(-(c+\pi)-\lambda) = 0$ (20)

or

$$\begin{vmatrix} -(c+m+\varepsilon)-\lambda & ks^o \\ m & -(c+\psi e+\mu_\tau)-\lambda \end{vmatrix} = 0 \qquad (21)$$

Let A$= \begin{pmatrix} -(c+m+\varepsilon) & ks^o \\ m & -(c+\psi e+\mu_\tau) \end{pmatrix}$

From equation (12)

$$\left.\begin{aligned} \lambda_1 &= -(c+q) \\ \lambda_2 &= -c \\ \lambda_3 &= -(c+\pi) \end{aligned}\right\} \qquad (22)$$

From equation (22), we see that the first three (3) Eigen values λ_1, λ_2 *and* λ_3 are all negative.

Using ***theorem 2,*** we see that the DFE of this model will be asymptotically stable if the remaining Eigen values, λ_4 *and* λ_5 are also negative.

Now, we consider equation (13). For local asymptotic stability (LAS) of the DFE, we require the remaining two eigenvalues λ_4 *and* λ_5 to be negative.

Theorem 3

Let A be an $n \times n$ matrix. Then:

i. The matrix A has n eigenvalues (including each according to its multiplicity).
ii. The sum of the n eigenvalues of A is the same as the trace of A.
iii. The product of the n eigenvalues of A is equal to the determinant of A.

Using t***heorem 3***, we shall prove that λ_4 *and* λ_5 are both negative or otherwise.

$$Trace(A) = -(c+m+\varepsilon) - (c+\psi e+\mu_\tau) \qquad (23a)$$

$$Det(A) = (c+m+\varepsilon)(c+\psi e+\mu_\tau) - kms^o \qquad (23b)$$

If λ_4 *and* λ_5 are both negative, then we have

$\lambda_4 + \lambda_5 < 0$, it implies that $Trace(A) < 0$

i.e. $-(c+m+\varepsilon) - (c+\psi e+\mu_\tau) < 0$

It is clear that $Trace(A) < 0$ since all the parameters are positive constant.

Also, $\lambda_4 . \lambda_5 > 0$, it implies that $Det(A) > 0$

i.e. $(c+m+\varepsilon)(c+\psi e+\mu_\tau) - kms^o > 0$

$$\Rightarrow \quad kms^o < (c+m+\varepsilon)(c+\psi e+\mu_\tau) \qquad (24)$$

Dividing both sides of inequality (24) by $(c+m+\varepsilon)(c+\psi e+\mu_\tau)$ yields:

$$\frac{kms^o}{(c+m+\varepsilon)(c+\psi e+\mu_\tau)} < 1, \quad \text{where } c = \alpha+\mu \qquad (25)$$

The inequality (24) determines the threshold under which the disease can be eliminated or brought under control. It is the necessary and sufficient condition for the disease free equilibrium of the model to be stable.

The effective reproduction number, R_e

We determine the basic reproduction number, R_e for the model equations (10) to (14). This will be calculated using the next generation matrix method as described by Hefferman *et al.* (2005).

Consider the next generation matrix G, which is made up of two parts: F and V^{-1}, **where:**

$$F = \left[\frac{\partial F_i(E^o)}{\partial x_j}\right]$$

And

$$V = \left[\frac{\partial V_i(E^o)}{\partial x_j}\right]$$

The F_i's are the new infections while the V_i's shows the transfer of infections from one compartment to another. Here E^o is the disease-free equilibrium state. The basic reproduction number is the dominant Eigen value of the matrix G.

In this model, there are two disease states i.e. the latent class, L and the infectious class, I.

Recall that

$$\frac{dL}{dt} = kS\frac{I}{N} - (\alpha + \mu + m + \varepsilon)L$$

$$\frac{dI}{dt} = mL - (\alpha + \psi e + \mu + \mu_\tau)I$$

The vector F_x, of the rates of new infections in compartments L and I is given by;

$$F_x = \begin{bmatrix} kS\dfrac{I}{N} \\ 0 \end{bmatrix}$$

Also the remaining transfer terms in compartments L and I is given by

$$V_x = \begin{bmatrix} ((\alpha + \mu + m + \varepsilon)L \\ (\alpha + \psi e + \mu + \mu_\tau)I - mL \end{bmatrix}$$

Now we compute the matrix of partial derivatives of F_x at the disease-free equilibrium state $E^o = (V^o, S^o, 0,0,0,)$. Thus,

$$F_x(E^o) = \begin{pmatrix} 0 & kS^o \\ 0 & 0 \end{pmatrix}$$ Where$s^o = \frac{q(\beta+\gamma)+(\alpha+\mu)\{(1-f)\beta+(1-\eta)\gamma\}}{(\alpha+\mu)(\alpha+\mu+q)}$

And the matrix of the partial derivatives of V_x at the disease-free equilibrium state $E^o = (V^o, S^o, 0,0,0,)$ is:

$$V_x(E^o) = \begin{pmatrix} \alpha + \mu + m + \varepsilon & 0 \\ -m & \alpha + \psi e + \mu + \mu_\tau \end{pmatrix}$$

R_0 is the dominant Eigen value of the next generation matrix G.

$G = F_x(E^o)V_x^{-1}$.

Using the software, Mapple, we have:

$$V_x^{-1} = \begin{pmatrix} \dfrac{1}{\alpha + \mu + m + \varepsilon} & 0 \\ \dfrac{m}{(\alpha + \mu + m + \varepsilon)(\alpha + \psi e + \mu + \mu_\tau)} & \dfrac{1}{\alpha + \psi e + \mu + \mu_\tau} \end{pmatrix}$$

So that

$$G = \begin{pmatrix} 0 & kS^o \\ 0 & 0 \end{pmatrix} \times \begin{pmatrix} \dfrac{1}{\alpha + \mu + m + \varepsilon} & 0 \\ \dfrac{m}{(\alpha + \mu + m + \varepsilon)(\alpha + \psi e + \mu + \mu_\tau)} & \dfrac{1}{\alpha + \psi e + \mu + \mu_\tau} \end{pmatrix}$$

$$G = \begin{pmatrix} \dfrac{kmS^o}{(\alpha + \mu + m + \varepsilon)(\alpha + \psi e + \mu + \mu_\tau)} & \dfrac{kS^o}{\alpha + \psi e + \mu + \mu_\tau} \\ 0 & 0 \end{pmatrix}$$

By definition, R_o is the dominant or the leading Eigen value of G. So,

$$R_e = \frac{kmS^o}{(\alpha + \mu + m + \varepsilon)(\alpha + \psi e + \mu + \mu_\tau)}$$

But $S^o = \frac{q(\beta+\gamma)+(\alpha+\mu)\{(1-f)\beta+(1-\eta)\gamma\}}{(\alpha+\mu)(\alpha+\mu+q)}$

Therefore,

$$R_e = \frac{kmq(\beta + \gamma) + km(\alpha + \mu)\{(1 - f)\beta + (1 - \eta)\gamma\}}{(\alpha + \mu + m + \varepsilon)(\alpha + \psi e + \mu + \mu_\tau)(\alpha + \mu)(\alpha + \mu + q)}$$

We now use the parameter values presented in **Table 1** to find the numerical value of R_e which determines whether the disease can be eliminated or not.

Let $R_e = \frac{Num}{Den}$

Where $Num = kmq(\beta + \gamma) + km(\alpha + \mu)\{(1 - f)\beta + (1 - \eta)\gamma\}$

And $Den = (\alpha + \mu + m + \varepsilon)(\alpha + \psi e + \mu + \mu_\tau)(\alpha + \mu)(\alpha + \mu + q)$

So that,

$$Num = \{0.238 * 0.13 * 0.37 * (0.0369 + 0.0049)\} + \{0.238 * 0.13 * (0.0051 + 0.0124) * \big((0.05 * 0.0369) + (0.86 * 0.0049)\big)\}$$
$$= 4.817986856 \times 10^{-4}$$

$$Den = \{0.0049 + 0.0124 + 0.13 + (0.7 * 0.8)\} * \{0.0049 + 00124 + (0.55 * 0.8) + 0.024\} * \{0.0049 + 0.0124\} * \{0.0049 + 0.0124 + 0.37\}$$
$$= 2.280536106 \times 10^{-3}$$

$$\therefore R_e = \frac{4.817986856 \times 10^{-4}}{2.280536106 \times 10^{-3}}$$
$$= 0.2112.$$

Table 1 gives the values of R_e under different conditions.

Table 1: Computed effective reproductive number, (R_e) and basic reproductive number, (R_0) of the modified model

Population	R_e: Treatment and vaccination	R_e: Treatment but No Vaccination	R_e: Vaccination but No Treatment	R_0: Without Vaccination and without Treatment
Absence of Emigrant	0.2527	0.2599	19.5637	20.1216

Table 2: ***Model parameters and their interpretations***

S/N	Parameter	Symbol	Value (per year)	Source
01	The rate of new births	β	0.0369	Nigerian Demographic Profile (2018)
02	The rate of Latent infection	k	0.2380	Egbetade & Ibrahim (2014)
03	The rate of Expiration of vaccine	q	0.3700	Egbetade & Ibrahim (2014)
04	Treatment rate for active TB	ψ	0.5500	Nadhirah BT A. H. (2013
05	Treatment rate of latent TB	ε	0.7000	Nadhirah BT A. H. (2013)
06	The rate at which latent becomes infectious	m	0.1300	Nadhirah BT A. H. (2013)
07	The natural mortality rate	μ	0.0124	Nigerian Demographic Profile (2018)
08	TB induced death	μ_τ	0.0240	Nadhirah BT A. H. (2013)
09	Efficacy of vaccine	f	0.9500	Egbetade & Ibrahim (2014)
10	Efficacy of treatment	e	0.8000	Assumed
11	The rate at which recovered become Susceptible	π	0.0001	Nadhirah BT A. H. (2013)
12	Average Immigration rate	γ	0.0049	
13	Average Emigration rate	α	0.0051	
14	Proportion of vaccinated immigrants	η	0.1400	Egbetade & Ibrahim (2014)

Initial conditions are taken as follows:
S(0)=11 000, L(0)=3 500, I(0)=500, R(0)=0 (Nadhirah, 2013)

Graphical simulation

In this section, the numerical simulations for the model systems under different conditions are presented. This we shall achieve by using the parameter values given in Table 1 and Table 2.

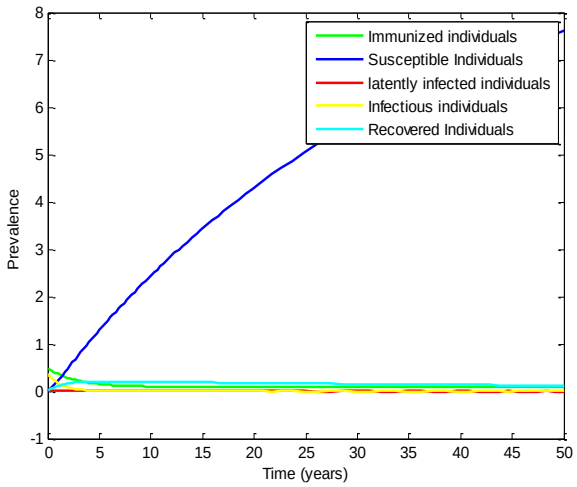

Fig. 1: Graph showing the prevalence of each class in the presence of vaccination and treatment

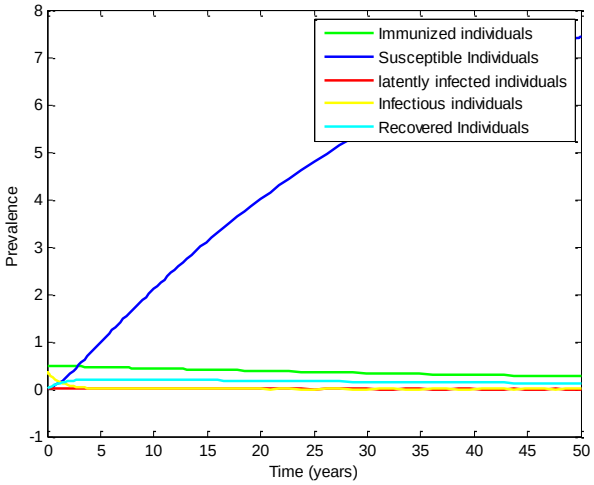

Fig. 2: Graph showing the prevalence of each class in the presence of treatment and absence of vaccination

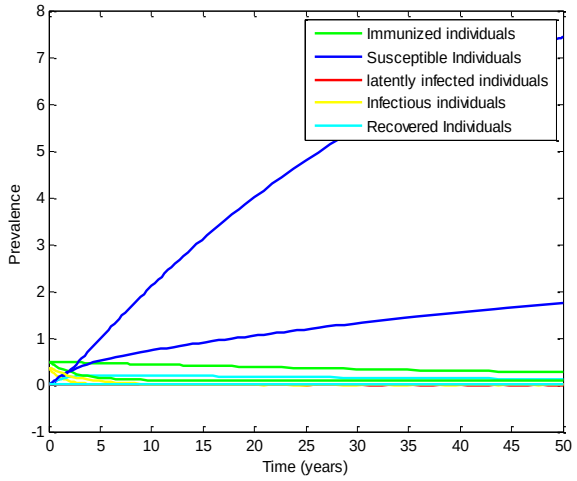

Fig. 3: Graph showing the prevalence of each class in the presence of vaccination and absence of treatment

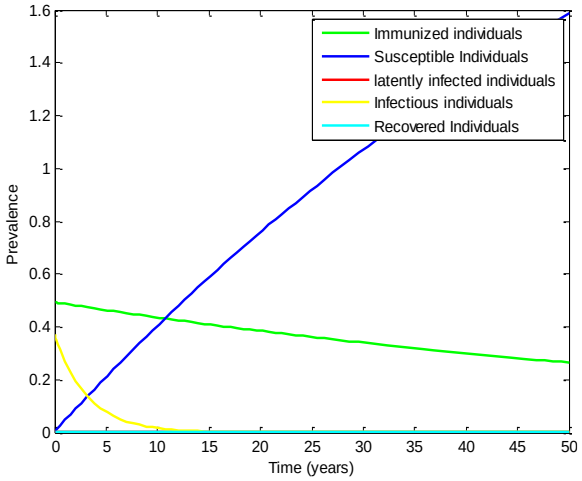

Fig. 4: Graph showing the prevalence of each class in the absence of vaccination and treatment

Discussion and Conclusion

We put forward a mathematical model for predicting eradication of Tuberculosis in the course of vaccination treatment strategy with not present of emigration effect. It was assumed that the participants into population are new-births and immigration. We examine the existence and uniqueness of the solution of the model and it was establish that the solution exist and unique. Stability analysis was carried out and it was found that the modified model is stable since term β (rate of new births) cannot be zero. Also, the disease free equilibrium is locally asymptotically stable since DFE<1. Furthermore, effective reproduction number (R_e) was found to be, when there is treatment and vaccination=0.2527, when there is treatment and no vaccination=0.2599, when there is vaccination and no treatment =19.5637 and basic reproduction number (R_0) was found to be 20.1216 as shown in Table 1. In Fig. 2, when there is treatment and no vaccination, the disease is eradicated slowly. While Fig. 3, when there is vaccine and no treatment the latently infected individuals increase and disease eradicate very slowly. Furthermore, in figure 4, in absence of emigration the recovered individual increases and the disease eradicate faster without treatment and vaccination. Henceforth, infected emigrate should be highly discourage of leaving it residents country.

Conflict of Interest

Authors declare that there is no conflict of interest.

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