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Dynamical Behavior Of Tuberculosis Transmission Of A Weak And Strong Latently Immune Population

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ABSTRACT
The potency of disease transmission is hinged on contact with the infected or germs responsible for the disease and weak immunity of the uninfected person. In most cases, people with weak immunity are liable to be infected than those with strong immunity. In this paper, we formulated a tuberculosis mathematical model that in-cooperate weak immunity of latent infected and active tuberculosis to study their impact on the transmission of tuberculosis. We first, shown the properties of the model which captured that positivity of the solution and boundedness within a fixed domain. The basic reproduction number (threshold quantity) of this model was computed using next generation approach. It was proved that if this threshold quantity is less than one then the dynamics is both locally and globally stable at disease-free equilibrium points. A Lyapunov function was constructed and was used to show that the threshold quantity is greater than at the endemic equilibrium point which indicates the persistence of the diseases. The sensitivity analysis of tuberculosis was conducted with regard to all basic parameters found in the threshold quantity. Numerical simulation results agreed with analytical analysis when compared together and we show that people with weak immunity suffer most during outbreak of tuberculosis.

Keywords: *Disease, Modeling, Tuberculosis TB**,** Sensitivity analysis**,** Lyapunov function.*

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I. Introduction

The battle against epidemics is a century's effort and millions of people die due to epidemics. At one time of the other, outbreaks of epidemics occurred in various forms like plague, smallpox, HIV/AIDS, Lassa fever, COVID-19, avian flu, tuberculosis and influenza. Tuberculosis (TB) is one of the prominent and persistent epidemics known. Tuberculosis (TB) is prominently known to be caused by a bacterium known as *mycobacterium tuberculosis* (MTB) [22]. With the availability of anti-mycobacterial drugs, TB is still the leading consequence of death among infectious diseases with an estimate of over 10 million people becoming infected with TB, and about 2 million death cases globally [6]. However, the cause of morbidity, contagiousness and mortality is primarily hinged on active TB.

A condition under which an individual becomes infected with tuberculosis disease but does not show any signs or transmit the disease to others is known as latent tuberculosis infection (LTBI). Most individuals are infected with latent TB infection but do not progress to active TB. In this category of people, the *Mycobacterium tuberculosis bacteria* dormancy is inactive for life in the victim's body without causing TB disease. However, in some people the bacteria becomes active, multiplies and cause TB disease, especially for individuals with weak immune system. Even though, it is the active stage that is absolutely responsible for infection, yet people with latent TB whose immunity has been compromised promote the active stage [8, 17].

TB transmission is often caused by sputum that the tuberculosis patient spits into the environment, or the droplets discharged during coughing or sneezing. Although tuberculosis is a disease can affect several organs of its victim but majorly it occurs in the lungs [23].

Antibiotics are used to treat tuberculosis which kills bacteria responsible for the disease. The duration takes up to six months or more in treating TB. Different antibiotics are used to increase the effectiveness in order to prevent the bacteria from becoming resistant to the drugs. Active TB patients are treated using Isoniazid (INH), Rifampin (RIF), Ethambunol and Pyrazinamide [6]. In order to prevent people infected with latent tuberculosis progressing to active TB they are treated with single antibiotic. Also in a way to improve the immunity of people infected with latent TB, good hygiene, the use if chemo-prophylaxis and good diet are very necessary. The common available vaccine is Bacillus Chalmette–Guerin (BCG) and developments of others are in the process [4].

Globally, TB is one of the 10^{th} recognized killer diseases. Indonesia, China, Nigeria, Pakistan and South Africa had being identified and India as the sixth country with leading cases of TB which account for

60% dormancy in relation to world population. In 2015, an estimate of about 1 million were recorded of those infected with TB disease and 170, 000 cases of death of TB without children suffering with HIV. In this same year, it was noticed that TB contributed 35% to HIV deaths cases [2]. A population of 480 000 people are discovered to developed multi drug –resistant TB (MDR-TB) [20]. The figure shows that those infected with TB in Africa 2.7 million out of the 9.6 million [19]. Nigeria is now rated as the 3rd country apart from India and China with the highest burden of tuberculosis cases. During the Tuberculosis Day celebration in March 24th , 2023 in Nigeria, it was stated that the rate of TB prevalence is 219 for every 100,000 people as compared to an entire population over 217 million people in Nigeria. It was clearly mentioned that over 245,000 Nigerians die due to tuberculosis infection yearly and over 590,000 people with new cases of infections [1, 24].

One of the obstacles encountered in the eradication of TB globally is majorly attributed to Latent tuberculosis infection (LTBI).This is linked to people with weak immune system status. An understanding of this will be enhanced in the establishment and development of suitable mathematical model to handle and provide a solution to people with weak immunity that had been infected with latent TB.

II. Literature review

One of the exciting tools for describing the behavior of diseases is the Mathematical biology that became the fast growing field. In this field, the most current topics consist of the formulation and analysis of various mathematical models, adopting differential equation [1, 3, 7, 19, 20] or difference equations [13]. Several studies had been carried out on the transmission of TB in a given population with different techniques such as age specific [10], hard to- treat infection [6], vaccination and treatment [16] and its co-infections [2, 5, 14, 15, 18, 22]. Mehmet et al, [13], formulated a mathematical model on tuberculosis by considering two different treatment strategies which includes preventive measure on latent TB and the actual treatment of those infected with active which constituted a six compartments altogether. The region of biological interpretations of the model was studied such as the solution's positivity, existence, and uniqueness. Also, the computed the basic reproduction number for the model using the next generation approach consisted of eight parameters. It was shown that system was locally asymptotically stable (LAS) when all the eigenvalues of the dynamics were all negative and consequently $R_0 < 1$ at disease-free equilibrium points. They further, examined the endemic nature of the disease using Routh-Hurwitz stability criteria and proved that tuberculosis persisted if $R_0 > 1$at the endemic equilibrium point. The modeled ordinary differentials equations were analyzed and simulated using a fourth-order Runge-Kutta numerical method. They demonstrated that preventive measure on latent TB and treatment administered on the infected persons enhances the gradual eradication of tuberculosis.

Sulayman et al [19], designed a mathematical model on tuberculosis by incorporating public health education and treatment on those infected with the disease. The properties of the model were obtained and the basic reproduction number was also computed using next generation method. It was established that the model is locally asymptotically stable if R_0 is less than one at disease-free equilibrium and at the endemic equilibrium point the same threshold quantity is greater than one. It was found that the number of those infected with TB was minimized with public health education and those treated respectively.

Haso et al [7] studied the tuberculosis model by describing the dynamics using SEIRS compartments which was analyzed by data collected from Chiro. The value of the basic reproduction number R_0 was obtained that was described by seven parameters using next generation method and found to be less than one (0.4964) denoted as $R_0 < 1$. With this result they show that the disease (TB) with eventually die out from the community. They further used Routh – Hurwitz criterion to prove the stability of the system at disease- free equilibrium point. In order to control the spread and possibly eliminate the disease they stated that the rate of transmission must be kept below 0.4732 and $R_0 < 1$ which were deduced from sensitivity analysis of the model.

Mayowa et al, [12], investigated a six population dynamics of tuberculosis with vaccination incorporated into the dynamics. They studied the qualitative behaviors of the model with respect to the threshold quantity. The locally asymptotically stable was proved and that it exist when the effective reproduction number $R_0 < 1$ and unstable otherwise at the disease-free equilibrium point. Furthermore, endemic equilibrium point was examined and proved existence of backward bifurcation under a given conditions was discussed. They also performed numerical simulation that was shown to support the theoretical results. They found that there will massive reduction in the burden of tuberculosis when the effective contact of those with an infected TB are reduced and when more susceptible individuals were vaccinated.

Andrawus et al [3] discussed six populations with first and second treatment lines. The properties of the model were obtained and the basic reproduction number was also computed using next generation method. It was established that the model is locally asymptotically stable if R_0 is less than one at disease-free equilibrium and at the endemic equilibrium point the same threshold quantity is greater than one. It was found that first treatment when properly administered has the potential on those infected will consequently reduce those available cases for the second line treatment in the society.

Madaki et al [11] designed a four compartments model described by mathematical linear equations by incorporating a control measure which was motivated by national tuberculosis and leprosy program. They computed the threshold quantity by employing the next generation method. The local and global stabilities were proved at the disease-free equilibrium points. It was established that all the eigenvalues are all negatives hence stability holds and consequently the basic reproduction number is less than unity. They concluded that the system was locally asymptotically stable otherwise unstable. They further show that the dynamic was unstable at endemic equilibrium points if the basic reproduction number was greater than unity. The simulation of the model was made using the data they collected from general hospital Potiskum, Yobe State. The results obtained from simulations shows that the strategy by the national tuberculosis and leprosy program alone cannot completely eliminate TB from Nigeria.

Abegye S. Y and Shammah K. S. [1] formulated a mathematical model on Tuberculosis transmission with treatment that leads to a linear differential equation. The properties of the model were proved and shown to exist and has a unique solution. The threshold quantity responsible for the prediction of the elimination of the disease or endemic state of the disease was computed using next generation approach. It was shown that the system is asymptotically stable and unstable when the threshold quantity is less than unity or greater than unity at disease- free equilibrium. They conducted the sensitivity analysis of the model and show that some parameters were identified to have positive and others negative impact on the system. They also constructed a Lyapunov function in which the model was proved to be globally asymptotically stable when the threshold quantity is less or equal to unity. It was clearly shown that treatment reduces the number of those infected with TB.

Sulayman et al [20], they studied the dynamics of TB transmission model by considering re-infection scenario. They showed that the basic reproduction number R_0 predicts the behavior of TB transmission dynamics. They also proved that when $R_0 < 1$, the system is described is locally asymptotically stable and the disease goes to extinction while if $R_0 > 1$ the disease persist occurs at disease-free equilibrium and endemic equilibrium points respectively. The dynamics was showed to exhibit bifurcation in which they adopted center manifold theory technique. The results of both analytical and numerical solutions agrees with transcritical bifurcation at $R_0 = 1$. With Lyapunov function approach they examined the global stability of endemic equilibrium. From simulation results, it was showed that increase in re-infection value occurs as a result of high force of infection. They show that, re-infection among treated individuals occurs and has a significant impact on the control of TB infection.

In view of the papers reviewed above, there was no research work that considered the immunity of people infected with TB at latent state. Most papers focused on given prevention measures on latent, treatment of people the infected and vaccination of the susceptible population. Research has showed that immunity of people infected with TB at latent (either strong or weak) has an impact in the transmission of tuberculosis [8, 17]. In this study, we formulated a new model that addressed the impact of a latent person's immunity on the tuberculosis model and considered other measures on the TB active infected people. The paper is aimed at providing a solution to those infected with TB bacteria at latent stage that has weak immune system. The analytical and numerical analysis of the model shall be discussed and compared.

III. Methodology

In order to study the tuberculosis disease appropriately, the compartmental technique which represent populations of both non-infected and infected individuals was used to design the model that leads to a system of differential equations. These systems were analyzed both analytical and numerical by these phenomena. The odes were used to obtain the threshold quantity for tuberculosis and the two equilibrium points. The local and global stabilities were also considered.

Model Formulation

Model assumption

i. It is assumed that entry into the susceptible population is by migration and birth.
ii. It is considered that those populations with weak immunity are likely to contact tuberculosis and those with strong immunity dented by L_w and L_s respectively.
iii. We assume that those ng that migrate to from susceptible class to strong latently immune returned to susceptible class again.
iv. In this model it considered that the force of infection is apply to those with weak immune latently infected individuals.
v. The latently strong tuberculosis (TB) infected individuals does not show TB symptoms and cannot transfer the bacteria to others but die naturally with it if they did not contact active.

vi. The latently weak tuberculosis (TB) infected individuals does not show TB symptoms and cannot transfer the bacteria to others but the bacteria can become active after some time.

Model description

In this new TB mathematical model, the entire population is subdivided into five populations at time t, shown as follows; $S(t)$ represent susceptible population, $L_s(t)$ those with strong immunity but latently infected, $L_w(t)$ those with weak immunity but latently infected, $I(t)$ represent active TB, shows symptoms and are infectious and $R(t)$ recovered population from all infected classes. The active TB population is the only infectious population and other populations becomes infected when they come in contact with the infected active class are the of λ. The influx of people into susceptible of birth or immigration increases the susceptible population at the rate of Λ and all population die naturally are the rate of μ. The susceptible population progress to latently strong immune population are the rate of α_1 and returns are the rate of α_2. The weak and strong latently immune TB becomes infected with active TB are the rate of τ_1 and τ_2 and they recovers at the rate of γ_1 and γ_2 respectively. The death due to active Tb is denoted by δ_T and they recovers at rate of ω. Figure 1 demonstrate the schematic diagram of tuberculosis and the meaning of the parameters were described in Table 1.

The ordinary differential equations of the new tuberculosis model are obtained following the assumptions and the diagram is giving as:

$$\frac{dS}{dt} = \Lambda + \alpha_2 L_s - \lambda S - (\mu + \alpha_1)S \quad (1)$$

$$\frac{dL_s}{dt} = \alpha_1 S - (\mu + \alpha_2 + \tau_2 + \gamma_2)L_s \quad (2)$$

$$\frac{dL_w}{dt} = \lambda S - (\mu + \tau_1 + \gamma_1)L_w \quad (3)$$

$$\frac{dI}{dt} = \tau_1 L_w + \tau_2 L_s - (\mu + \delta_T + \omega)I \quad (4)$$

$$\frac{dR}{dt} = \gamma_1 L_w + \gamma_2 L_s + \omega I - \mu R \quad (5)$$

where $\lambda = \frac{\beta}{N}(L_w + I)$

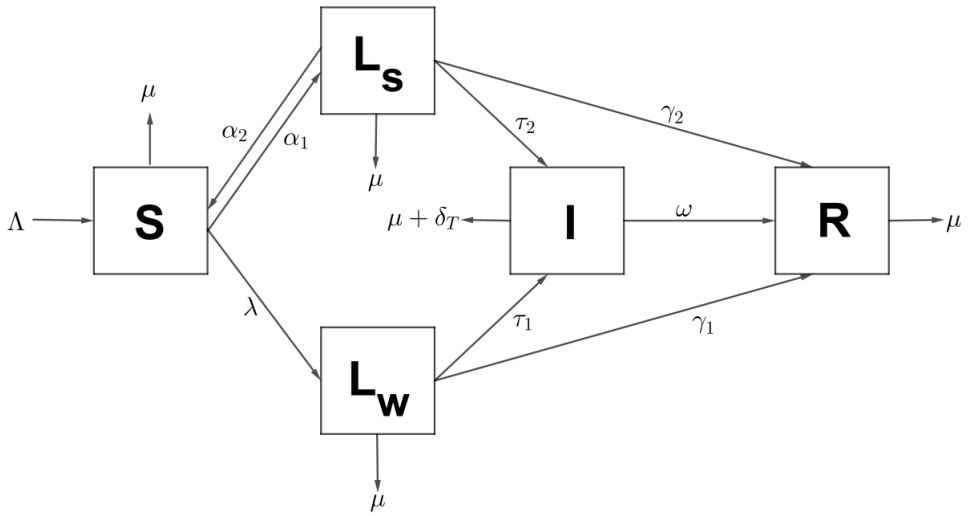


Figure 1: The schematic diagram of a Tuberculosis transmission.

Table 1. The parameters description of Tuberculosis

Parameters	Descriptions
Λ	Recruitment rate of human population
μ	Natural deaths rate
α_1	The rate at which susceptible progress to strong latently infected TB
α_2	The rate at which strong latently infected TB progress to susceptible
τ_1, τ_2	Rate at which weak and strong latently immune becomes infected active TB
γ_1, γ_2	Rate of recovery of weak and strong latently immune infected TB
ω	Rate of recovery of active TB
β	Probability of contact rate
δ_T	Rate of death due to disease

The basic properties of Tuberculosis model

The meaningfulness of dynamics (1 – 5) portray that all the variables are non – negative for time (t). We show that, for all $t \geq 0$ the solution of system (1 – 5) will possess positive initial data which will remain positive.

Positivity and boundedness of Tuberculosis model solution

Theroem 1. Consider $S(0), L_s(0), L_w(0), I(0)$ and $R(0)$ be non – negative with initial conditions, then it follows that the solutions $(S(t),\ L_s(t), L_w(t), I(t), R(t)\ )$ of the tuberculosis are positive for all $t > 0$.

Proof. Consider equation 1 first given as;

$\frac{dS}{dt} = \Lambda + \alpha_2 L_s - \lambda S - (\mu + \alpha_1)S,$ it follows that

$$\frac{dS}{dt} \geq -(\mu + \alpha_1 + \lambda)S \qquad (6)$$

Now solving equation (6) by separating the variable approach of integration and applying the initial condition with respective to t, we have

$$S(t) \geq S_0 e^{-(\mu + \alpha_1 + \lambda)t} > 0 \qquad (7)$$

Adopting the same procedure, equations (2 – 5) becomes

$$L_s(t) \geq L_s(0) e^{-(\mu + \alpha_2 + \tau_2 + \gamma_2)t} \qquad (8)$$

$$L_w(t) \geq L_w(0) e^{-(\mu + \tau_1 + \gamma_1)t} \qquad (8)$$

$$I(t) \geq I(0) e^{-(\mu + \delta_T + \omega)t} \qquad (9)$$

$$R(t) \geq R(0) e^{-\mu t} \qquad (10)$$

It is very obvious that equations (6 – 10) has a positive solution for all $t > 0$. From this result, it follows that this model from equations (1 – 5) is significantly epidemiological and mathematically well- posed within the domain Ω.

Invariant Region.

In order to ascertain that the solution of this model is bounded it becomes very necessary to use invariant region to determine it.

Theroem 2. The closed region $\Omega = \{S, L_s, L_w, I,\ R) \in \mathbb{R}_+^5 : N \leq \frac{\Lambda}{\mu}\}$ is considered positive invariant set for the tuberculosis model.

Proof: Taking the sum of the entire population as N, from equation (1 - 5), we have

$$\frac{dN}{dt} = \Lambda - \mu N - \delta_T I \qquad (11)$$

In the absence of tuberculosis, death due to tuberculosis δ_T equals zero, hence equation (11) becomes

$$\frac{dN}{dt} \leq \Lambda - \mu N \qquad (12)$$

Integrating equation (12) with initial condition, then we have

$$\Lambda - \mu N(t) \geq (\Lambda - \mu N(0)) e^{-\mu t} \qquad (13)$$

Applying limit as $t \to \infty$ on equation (13), we obtain

$$N(t) \leq \frac{\Lambda}{\mu} \qquad (14)$$

It implies that all the state variables with its given initial conditions for this population is given by

$$\Omega = \{S, L_s, L_w, I,\ R) \in \mathbb{R}_+^5 : N \leq \frac{\Lambda}{\mu} \qquad (15)$$

This equation gives the set of feasible solution for the dynamics (1 – 5) which are contained in it, hence we conclude that the system is mathematically and epidemiologically well-posed within Ω [21].

Disease-free Equilibrium

In absence of tuberculosis disease, the tuberculosis- free equilibrium which indicate the critical points of the system (1 – 5). By setting the equations (1 – 5) to zero and solving them at $I(t) = 0$, we obtained

$$E_0 = (S^0, I_s^0, L_w^0, I^0, R^0) \qquad (16)$$

where $S^0 = \frac{\Lambda}{\mu + \alpha_1}$.

The tuberculosis free equilibrium points are steady state condition in which tuberculosis does not exist. Consequently the latently weak, strong immune and actively infected populations are considered to absence which implies $L_s = L_w = I = 0$, then solving for S^* to gets $S^* = \frac{\Lambda}{\mu + \alpha_1}$ and the tuberculosis disease free equilibrium, $E_0 = (S^*, L_s^*, L_w^*, I^*, R^*) = (\frac{\Lambda}{\mu + \alpha_1}, 0,0,0,0)$. From the linear stability of the disease-free equilibrium using the next generation approach of the above model, the basic reproduction number is obtained by $R_0^T = \rho(FV^{-1})$, where ρ denote the spectral radius of the matrix for the next generation. Considering two matrices $\mathcal{F}_i$ and $\mathcal{V}_i$ which denote the rate of new infection progressing into the compartment i and the rate of transfer out of the compartment i respectively. It follows that $\mathcal{F}_i$ and $\mathcal{V}_i$ are ;

$$\mathcal{F}_i = \begin{pmatrix} \lambda S \\ 0 \end{pmatrix} \text{ and } \mathcal{V}_i = \begin{pmatrix} \mathrm{CL_w} \\ \mathrm{DI} - \tau_1 \mathrm{L_w} - \tau_2 \mathrm{L_s} \end{pmatrix}$$

where $A = \mu + \alpha_1, \mathrm{B} = \mu + \alpha_2 + \tau_2 + \gamma_2$, $C = \mu + \tau_1 + \gamma_1$ and $D = \mu + \delta_T + \omega$ from system (1 – 5).

Hence, $\mathrm{F} = \begin{pmatrix} \frac{\beta S_0}{N_0} & \frac{\beta S_0}{N_0} \\ 0 & 0 \end{pmatrix}$ and , $\mathrm{V} = \begin{pmatrix} \mathrm{C} & 0 \\ -\tau_1 & \mathrm{D} \end{pmatrix}$ It follows that , $\mathrm{V}^{-1} = \begin{pmatrix} \frac{1}{\mathrm{C}} & 0 \\ \frac{\tau_1}{\mathrm{CD}} & \frac{1}{\mathrm{D}} \end{pmatrix}$ and

$$\mathrm{FV}^{-1} = \begin{pmatrix} \frac{\beta S_0}{N_0}\left(\frac{D+\tau_1}{CD}\right) & \frac{\beta S_0}{N_0 D} \\ 0 & 0 \end{pmatrix} \qquad (17)$$

Using equation (17), the basic reproduction number $R_0^T = \rho(FV^{-1})$ which is obtained by the expression $|FV^1 - \lambda| = 0$ given as

$$|FV^1 - \lambda| = \begin{vmatrix} \frac{\beta S_0}{N_0}\left(\frac{D+\tau_1}{CD}\right) - \lambda & \frac{\beta S_0}{N_0 D} \\ 0 & -\lambda \end{vmatrix} = 0 \qquad (18)$$

Therefore, the largest eigenvalue from equation (18) is given as :

$$R_0^T = \beta \frac{\mu(\mu + \delta_T + \omega + \tau_1)}{(\mu+\alpha_1)(\mu+\tau_1+\gamma_1)(\mu+\delta_T+\omega)} \qquad (19)$$

The threshold quantity shown inn equation (19), determine the disease transmission potential of Tuberculosis governs by seven parameters. This number describes the new infection that occurs by the presence of a single infectious person in a completely susceptible population.

Local stability of Tuberculosis disease- free Equilibrium

Theorem 3. The Tuberculosis disease-free equilibrium point of the dynamic (1 – 5) is considered locally asymptotically stable in Ω if $R_0^T < 1$.

Proof: Using linearization method the Jacobian matrix of the system (1 – 5) is computed as follows:

$$J_{E_0} = \begin{pmatrix} -(A+\lambda) & \alpha_2 & -\frac{\beta S_0}{N_0} & -\frac{\beta S_0}{N_0} & 0 \\ \alpha_1 & -B & 0 & 0 & 0 \\ \lambda & 0 & \frac{\beta S_0}{N_0} - C & \frac{\beta S_0}{N_0} & 0 \\ 0 & \tau_2 & \tau_1 & -D & 0 \\ 0 & \gamma_2 & \gamma_1 & \omega & -\mu \end{pmatrix} \qquad (20)$$

We further compute the Jacobian matrix (20) at disease-free equilibrium, gives

$$J_{E_0} = \begin{pmatrix} -A & \alpha_2 & -\frac{\beta\mu}{\mu+\alpha_1} & -\frac{\beta\mu}{\mu+\alpha_1} & 0 \\ \alpha_1 & -B & 0 & 0 & 0 \\ 0 & 0 & \frac{\beta\mu}{\mu+\alpha_1} - C & \frac{\beta\mu}{\mu+\alpha_1} & 0 \\ 0 & \tau_2 & \tau_1 & -D & 0 \\ 0 & \gamma_2 & \gamma_1 & \omega & -\mu \end{pmatrix} \qquad (21)$$

Adopting the method used by [21], the first two eigenvalues of Jacobian matrix (21) are $\lambda_1 = -A$ and $\lambda_2 = -\mu$ and consequently matrix (21) reduces to a 3×3 matrix shown below;

$$\begin{vmatrix} -B & 0 & 0 \\ 0 & \frac{\beta\mu}{\mu+\alpha_1} - C & \frac{\beta\mu}{\mu+\alpha_1} \\ \tau_2 & \tau_1 & -D \end{vmatrix} \qquad (22)$$

The appropriate characteristics equation from equation (22) is in the form;

$$(-B-\lambda)\left[\left(\frac{\beta\mu}{\mu+\alpha_1} - C - \lambda\right)(-D-\lambda) - \frac{\beta\mu}{\mu+\alpha_1}\right] = 0 \qquad (23)$$

It then follows from equation (23) that the third eigenvalue is $\lambda_3 = -B$ hence it had been shown that

$$\begin{cases} \lambda_1 = -A < 0 \\ \lambda_2 = -\mu < 0 \\ \lambda_3 = -B < 0 \end{cases} \qquad (24)$$

Therefore the remaining characteristics equation can be represented in the form:

$\lambda^2 + a_1\lambda + a_2 = 0$ (25)

where $a_1 = C + D$ and $a_2 = CD - \frac{\beta\mu\ (\mathrm{D} + \tau_1)}{\mu + \alpha_1} = 1 - \frac{\beta\mu\ (\mathrm{D} + \tau_1)}{(\mu + \alpha_1)\mathrm{CD}}$

$= 1 - R_0^T$ (26)

Now, applying the Routh-Hurwitz criteria [21] to equation (26), this equation possesses real root which are strictly negative if $a_1 > 0$ and $a_2 > 0$. For the fact that a_1 is the sum of positive parameters, it is observed that $a_1 > 0$ and $a_2 = 1 - R_0^T$. Also for $a_2 > 0$ enhances the satisfaction of the equation for $1 - R_0^T$ must be positive this implies that $R_0^T < 1$. Since it had been shown that $R_0^T < 1$, it follows that the system (1 – 5) is locally asymptotically stable in Ω at disease-free equilibrium point.

Globally stability of Tuberculosis at disease-free equilibrium point

Theorem 4. If $R_0^T < 1$, it follows that the tuberculosis disease equilibrium point of the model (1 – 5) is said to be globally asymptotically stable in Ω.

Proof: We construct a suitable Lyapunov function as used in [21] defined as

$\mathrm{L} = \frac{(\mu + \delta_\mathrm{T} + \omega + \tau_1)}{\mathrm{CD}}\mathrm{L_w} + \frac{1}{\mathrm{D}}\mathrm{I} - \frac{1}{2}\frac{1}{\mathrm{D}}(\tau_1\mathrm{L_w^2} + \tau_2\mathrm{L_s^2}) + \frac{1}{2}\frac{(\mu + \delta_\mathrm{T} + \omega + \tau_1)}{\mathrm{D}}\mathrm{L_w^2}$ (27)

as the tuberculosis disease-free equilibrium is an open neighoond in Ω. The functions $\mathrm{L_w}(\mathrm{t})$ and $\mathrm{I}(\mathrm{t})$ are continuous Lyapunov differentiable functions L and $\mathrm{L} > 0$ for all $(\mathrm{L_w}, \mathrm{I}) \in \Omega$ for as much as $\mathrm{L} = 0$ at disease-free equilibrium point. Therefore, by differentiating equation (27), we have

$$\frac{\mathrm{dL}}{\mathrm{dt}} = \frac{(\mu + \delta_\mathrm{T} + \omega + \tau_1)}{\mathrm{CD}}\frac{\mathrm{dL_w}}{\mathrm{dt}} + \frac{1}{\mathrm{D}}\frac{\mathrm{dI}}{\mathrm{dt}} - \frac{1}{\mathrm{D}}(\tau_1\mathrm{L_w} + \tau_2\mathrm{L_s}) + \frac{(\mu + \delta_\mathrm{T} + \omega + \tau_1)}{\mathrm{D}}\mathrm{L_w}$$

$$= \frac{(\mu + \delta_\mathrm{T} + \omega + \tau_1)}{\mathrm{CD}}[\lambda\mathrm{S} - \mathrm{CL_w}] + \frac{1}{\mathrm{D}}[\tau_1\mathrm{L_w} + \tau_2\mathrm{L_s} - \mathrm{DI}] - \frac{1}{\mathrm{D}}(\tau_1\mathrm{L_w} + \tau_2\mathrm{L_s}) + \frac{(\mu + \delta_\mathrm{T} + \omega + \tau_1)}{\mathrm{D}}\mathrm{L_w}$$

The above equation can be simplified further at disease-free equilibrium point and it gives

$$= \left[\beta\frac{\mu(\mu + \delta_\mathrm{T} + \omega + \tau_1)}{\mathrm{ACD}} - 1\right]\mathrm{I} + \beta\frac{\mu(\mu + \delta_\mathrm{T} + \omega + \tau_1)}{\mathrm{ACD}}\mathrm{L_w}$$

$$= [R_0^T - 1]\mathrm{I} + \beta\frac{\mu(\mu + \delta_\mathrm{T} + \omega + \tau_1)}{\mathrm{ACD}}\mathrm{L_w}$$

Therefore,

$\frac{\mathrm{dL}}{\mathrm{dt}} \leq [R_0^T - 1]\mathrm{I}$ (28)

Hence for $\frac{\mathrm{dL}}{\mathrm{dt}} \leq 0$ implies that $R_0^T - 1 \leq 0$ and furthermore, $\frac{\mathrm{dL}}{\mathrm{dt}} < 0$ if $R_0^T < 1$ and $\frac{\mathrm{dL}}{\mathrm{dt}} = 0$ occurs if and only $\mathrm{I}(\mathrm{t}) = 0$. It then follows that the set $E_0 = \left(\frac{\Lambda}{\mu + \alpha_1}, 0,0,0,0\right)$ possesses the largest compact invariant set in $(\mathrm{L_w}, \mathrm{I}) \in \Omega$ and that ends the prove.

Endemic Equilibrium Point

The endemic equilibrium point is the steady state solution in which the disease persist and affect a given population represented be $E_1 = (S^*, L_s^*, L_w^*, I^*, R^*)$. Considering equation (1 – 5), equating them to zero and solving the models gives the following endemic equilibrium points;

$S^* = \frac{\Lambda B}{B(\lambda^* + A) - \alpha_1\alpha_2}$ (29)

$L_s^* = \frac{\alpha_1}{B}S^*$ (30)

$L_w^* = \frac{\lambda^*}{C}S^*$ (31)

$I^* = \left(\frac{\tau_1\lambda^*}{CD} + \frac{\alpha_1\tau_2}{BD}\right)S^*$ (32)

$R^* = \left[\frac{\lambda^*(\gamma_1 D + \tau_1\omega)}{CD\mu} + \frac{\alpha_1(\gamma_2 D + \tau_1)}{BD\mu}\right]S^*$ (33)

Substituting equations (29 – 33) into equation (34) and (35) we then obtained a quadratics equations in terms of lambda

$\lambda = \frac{\beta}{N}(L_w + I)$ (34)

$N^* = S^* + L_s^* + L_w^* + I^* + R^*$ (35)

We then obtained a quadratics equation in the form:

$a_1\lambda^2 + a_2\lambda + a_3 = 0$ (36)

where

$a_1 = \frac{\mu(D + \tau_1) + \gamma_1 D + \tau_1\omega}{CD\mu}$, $a_2 = \frac{\alpha_1(D\mu + BD\mu + \gamma_1 D + \tau_1)}{CD\mu} + R_0^T - 1$ and $a_3 = -\beta\frac{\alpha_1\gamma_1}{BD}$

Globally Stability of Endemic Equilibrium

Theorem 5. If $R_0^T > 1$, then the endemic equilibrium point of model (1 – 5) is said to be globally asymptotically stable.

Proof. Let us construct a Lyapunov function denoted by L and defined as,

$$L = \frac{1}{2}[(S - S^*) + (L_s - L_s^*) + (L_w - L_w^*) + (I - I^*) + (R - R^*)]^2 \quad (37)$$

Taking the partial derivative of equation (37) with respective to time (t), corresponding to equation (1 – 5) is stated below as;

$$\frac{dL}{dt} = [(S - S^*) + (L_s - L_s^*) + (L_w - L_w^*) + (I - I^*) + (R - R^*)]\frac{d}{dt}[S + L_s + L_w + I + R]$$

$$= [(S - S^*) + (L_s - L_s^*) + (L_w - L_w^*) + (I - I^*) + (R - R^*)]\frac{dN}{dt} \quad (38)$$

It had been shown from equation (12), that

$$\frac{dN}{dt} = \frac{d}{dt}[S + L_s + L_w + I + R] \leq \Lambda - \mu N \quad (39)$$

Then inserting equation (39) in (38) to have

$$\frac{dL}{dt} = [(S - S^*) + (L_s - L_s^*) + (L_w - L_w^*) + (I - I^*) + (R - R^*)][\Lambda - \mu N],$$

$$\frac{dL}{dt} \leq \left[\boldsymbol{N} - \frac{\Lambda}{\mu}\right][\Lambda - \mu N] \quad (40)$$

Further simplifying and rearranging equation 40, the following result gives

$$\frac{dL}{dt} \leq -\frac{1}{\mu}[\Lambda - \mu N]^2 \text{ ‘} \quad (41)$$

It follows that $\frac{\mathbf{d}}{\mathbf{dt}}(\boldsymbol{S}, \boldsymbol{L_s}, \boldsymbol{L_s}, \boldsymbol{I}, \boldsymbol{R}) \leq \mathbf{0}$ and $\frac{\mathrm{dL}}{\mathrm{dt}} = \mathbf{0}$, which is possible only $S^* = S, L_s^* = L_s, L_w^* = L_w$, $I^* = I$ and $R^* = R$. Then the largest positive invariant set in $\left\{(S^*, L_s^*, L_w^*, I^*, R^*) \in \Omega : \frac{\mathrm{dL}}{\mathrm{dt}} = 0\right\}$ which ia singleton set. It is therefore, obvious that E_1 is globally asymptotically stable in the set Ω as found in Lasalle's invariant [21].

IV. Sensitivity Analysis

In this section, we considered the sensitivity analysis of the parameters of model (1 – 5) that has either positive or negative impact on the behavior of the basic reproduction number of the tuberculosis disease as the parameter values are varied. Sensitivity analysis as seen in [1], helps to ascertain parameters that increases or decreases the value of basic reproduction number and consequently suggests suitable intervention strategies in the control of tuberculosis.

Definition 1: The normalized forward sensitivity index of R_0^T can be differentiable with respective to a specific parameter χ is defined as [1, 21]

$$S_\chi^{R_0^T} = \frac{\partial R_0^T}{\partial \chi} \times \frac{\chi}{R_0^T} \quad (42)$$

It follows that the sensitivity index of R_0^T with respect to β is given as

$$S_\beta^{R_0^T} = \frac{\partial R_0^T}{\partial \beta} \times \frac{\beta}{R_0^T} \quad (43)$$

$$= 1 > 0$$

Applying the same procedure for the other parameters with respect to R_0^T, the values are shown in table 2.

Table 2. Parameters values and sources

Parameters	symbol	Sensitivity index
β		+1.00
μ		+0.50
δ_T		- 0.10
α_1		- 0.60
τ_1		- 0.02
γ_1		- 0.70
ω		- 0.03

It follows from table 2 that the sensitivity index $S_\beta^{R_0^T}, S_\mu^{R_0^T} > 0$ and the $S_{\delta_T}^{R_0^T}, S_{\alpha_1}^{R_0^T}, S_{\gamma_1}^{R_0^T}, S_{\tau_1}^{R_0^T}, S_\omega^{R_0^T} < 0$. It can be seen that the rate of contact and natural death both has a positive impact on tuberculosis transmission. This implies that as this value increases, more and more people become infected with active TB. Hence, to control active TB infection people, the value of the contact rate should be reduced below 0. Similarly, natural death rate should be reduced to zero which can be enhanced by improving the standard of living of Nigerian.

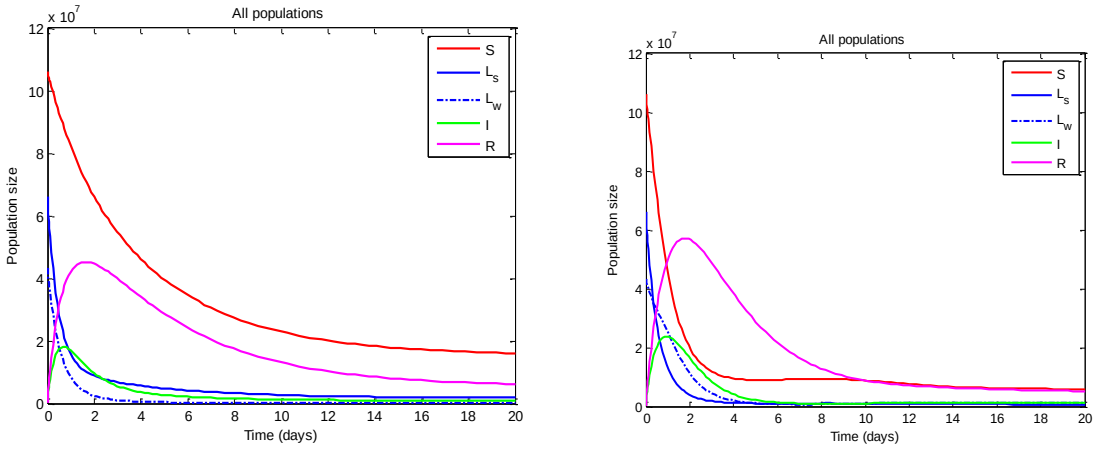
The parameters has negative influence and the implication is that increasing these values would result in reducing the population of those infected with TB.

V. Numerical simulation

In this section, the study aim at verifying some of the analytical results obtained above from model (1 – 5) and compares this result with the numerical results. This is achieved by using the values of the parameter obtained from literatures as well as assumptions made from simulation behavior of the model. The simulation is done using MATLAB ODE solver. The initial conditions for the population $N = 2.17 \times 10^8, S = 1.06 \times 10^8, I = 5.9 \times 10^5$, $R = 3.5 \times 10^5$ were obtained from [24] and $L_s = 6.6 \times 10^7$ and $L_w = 4.34 \times 10^7$ were estimated. The values of the parameters used for the simulation of the model (1 – 5) are given in table 3 shown below.

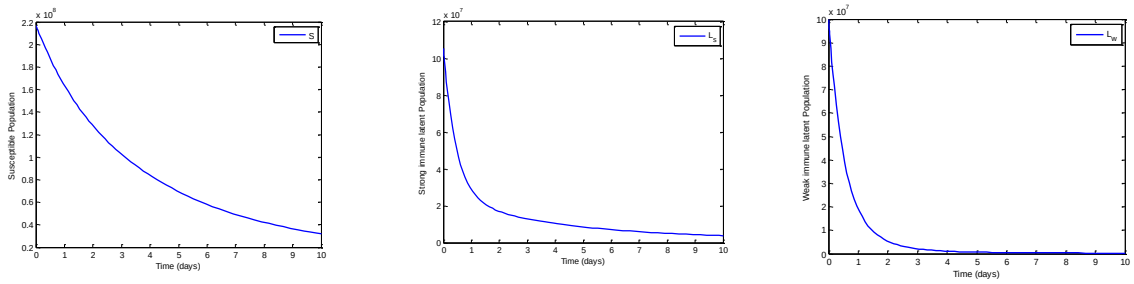
Table 3. Parameters values and sources

Parameters	Values	Sources
Λ	[500 – 3587400]	Estimate, [1]
μ	0.17937	[1]
β	0.398181	[1]
δ_T	0. 570776	[1]
α_1	0.26	Estimated
α_2	0.42	Estimated
τ_1	0. 13	[4, 24]
τ_2	0.513	[4, 24]
γ_1	0.74	[4, 5]
γ_2	0.98	[4, 24]
ω	0.35	[24]



(a) (b)

Figure1. The solution curve of model (1 – 5) illustrating the stability of tuberculosis disease-free equilibrium points for $R_0^T = 0.173 < 1$ and $R_0^T = 1.11 > 1$ with parameters values shown in table 3.



(a) (b) (c)

Figure 2. Illustrate the dynamics of (a) Susceptible population , (b) strong immune latent population, (c) weak immune latent population , (d) infected population, (e) Recovered population. The parameter values as shown in Table (3) and the values of the variables as mentioned above.

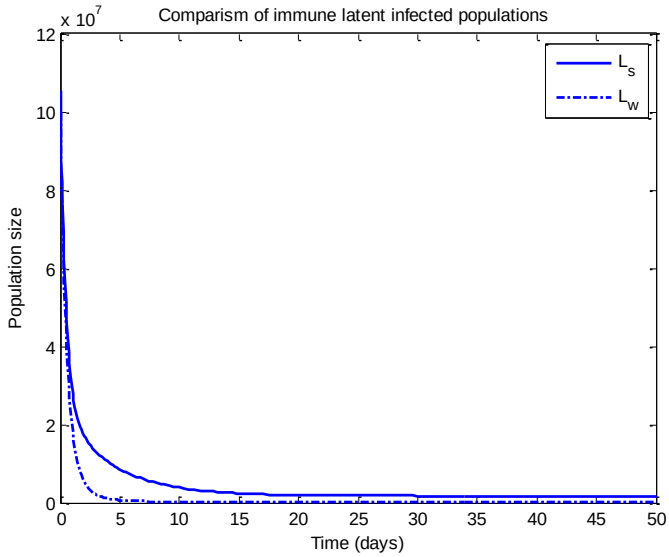


Figure 3. Illustrate the simulation of strong and weak immune latent peoples with parameter values as shown in table 3.

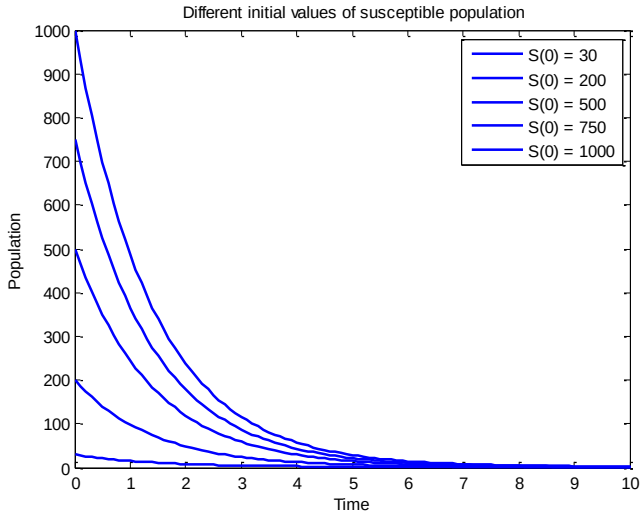
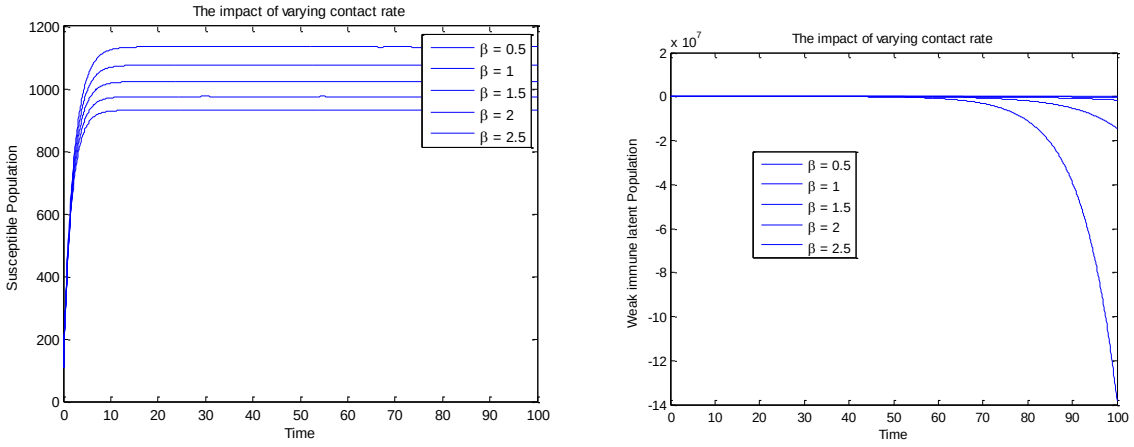


Figure 4.Draw of varying susceptible population at different initial conditions



(a) **(b)**

Figure 5. Impacts of contact rate on susceptible and infected population

VI. DISCUSSION

Figure 1 (a) shows the solution plot of the tuberculosis model for the values of parameters used in the caption. The basic reproduction number obtained was $\boldsymbol{R_0^T = 0.172 < 1,}$ which suggested that the dynamics is asymptotically stable at disease-free equilibrium point and consequently shows absence of endemic equilibrium point at this instance. This absence of endemic equilibrium point is shown as the plot of susceptible pollution was drawn, the solution curve converges when different initial conditions were used in figure 4 at disease-free equilibrium point. Figure 1 (b) displayed the time series of the curve of tuberculosis model in which the basic reproduction number is greater than unity ($\boldsymbol{R_0^T = 1.11 > 1}$). From our findings in section 3, it has been pointed out that the system is unstable at disease-free equilibrium but stable at stable at endemic equilibrium point. It follows then, that both the analytical and numerical simulation analysis agrees with each other.

The plots in figure 2 was conducted to investigate the behavior of tuberculosis model when there no interventions. In the absence of intervention, the susceptible population decreases in figure 2(a). The transition of individuals is faster in the strong immune population than the susceptible class and seen to lead to a decrease in the weak immune latent population in figure 2(c). In figure 2(d) as more individuals progresses to infected class since there is no control measure, this increases the population of the infected class at a start but consequently decline because of lack of treatment. In figure 2(d), it is expected that the population should collapses without any increase. But it increases because of the influx of people with strong immunity that was able to resist the disease. However, at a long run the recovered population decreases because they were not completely free from the disease.

Figure 3, compares the the immnue latent populations to examine which of the populations goes to extinction faster. It is observed that at day 5, those with weak immune latent infection goes to extinction while the strong immune latent population survives beyond 50 days. When the time span was extended beyond 50 days, this same population when beyond 500 days. In fact, it is evidently clear that people with strong immune system has the ability to resist diseases and better chances of survival than those with weak immune system as shown in [8,17].

Figure 4, is the simulation of the susceptible population solution curve that shows that the poulation converges to its disease-free equilibrium point. This implies that tuberculosis can be eradicated in the community at this point.

In Figure 5, shows the effects of tuberculosis contact rate on the susceptible and infected populations as it was varied from 0.5 to 2.5. It is observed from Fig. 5a that the numbers of people in susceptible class continue to increase until it remains constant. This means that, as the tuberculosis spread due contact between susceptible and those infected. There is an increase in the number of those infected with the disease that consequently result in the decrease of susceptible population or remain constant. This phenomenal becomes possible in the presence of intervention like public health care, vaccination and development of immunity which can lead to stabilization or decrease in the rate of new infections that leads to the population of the susceptible remaining constant [Fig. 5b displayed both a constant and a decreasing phase as the contact rate was varied respectively. The constant phase occurred when the number of those infected balances with the number of those recovering from tuberculosis. The decreasing phase in the number of the infected tuberculosis population over a given suggested positive impact made to for the eradication of the disease through vaccination, treatment and prevention measures adopted.

VII. CONCLUSION

The purpose of this paper was to investigate the impact of latent immune infected TB population on the transmission of TB in Nigeria and the world at large. The value of R_0^T was computed using the next generation technique, this derived value has eleven parameters which related to the five compartments discussed. From the expression of R_0^T, it follows that two parameters has positive impact on the transmission of TB namely: the contact rate and natural death rate. This result was observed from the computation of the sensitivity index showed on table 3 and other parameters have negative impact. The stability of the model were analyzed both at disease-free equilibrium and at endemic equilibrium points. It was proved that the system is locally asymptotically stable if $R_0^T < 1$ and unstable if $R_0^T > 1$. The global stability was proved using Lyapunov function in which the existence and uniqueness of the EEP was established and shown to exist if $R_0^T > 1$. It was observed that both the analytical and numerical simulation results agreed with each other. Furthermore, it was shown that at the absence of intervention all the populations goes to extinction. Therefore, the need of prevention measure, treatment and vaccination can not be over-emphasized in the eradication of tuberculosis in Nigeria. Also, it was that people with weak immunity suffer most during outbreak of tuberculosis.

FUTURE RESEARCH

The model had discussed some peculiarity in relation to the transmission of TB in Nigeria with more emphasis on immune latent TB infection. However, this paper can be extended further to address some aspects, like the cost analysis using optimal control, and adopted by incorporating prevention measure, treatment and vaccination measures. These will assist the stakeholder on the cost to embarked on the project of eradicating TB in Nigeria.

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