Communications on Applied Nonlinear Analysis
ISSN: 1074-133X
Vol 31 No. 3s (2024)

Exploring Tuberculosis: A Theoretical Framework for Infection Regulation and Eradication

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Article History:

Received: *12-04-2024*

Revised: *30-05-2024*

Accepted: *18-06-2024*

Abstract

In this paper we explored the study of tuberculosis, throughout human history, tuberculosis (TB) has been a persistent challenge due to its severe consequences for society. It is an infectious disease transmitted by Mycobacterium tuberculosis (MT),more than 150 million years ago, it wasthought to have originated from the genus Mycobacterium. Our theoretical framework presents methods for regulating and eradicating tuberculosis infections. This has led to the compartmentalization of the model population and the analytical solution of the ensuing model equations. To validate the outcomes of the theoretical approach, a numerical simulation has been deployed. This model carried out six compartment stage, susceptible, latent for a short time period and latent for long time period, infected in hospital, random infectedat public placeand the recovered class. In this model we examined Disease free equilibrium points (DFEP), Basic reproduction numberR_0. Positive boundaries solution is used to describe the infection at particular stage. If R_0<1, the DFE is locally asymptotically stable, using Jacobian matrix weexplored the negative Eigen values.Lyapunovfunction is used to examined the global stability of endemic equilibrium. We used Carrying out a simulation using random data in a selected region,using random values in MATLAB, to simulate the result of the model.

Keywords: Tuberculosis, Equilibrium points, Basic Reproduction Number, Stability analysis, Jacobian matrix, Lyapunov function.

1. INTRODUCTION

A comprehensive history of tuberculosis covers every detail, from the disease's origins to the discovery of treatments and vaccination techniques, with the objective reducing and controlling its effects. The expressions "White Plague," "phthisis," and "consumption" have been all used to describe tuberculosis over history. The majority of researchers agree that earlier, earliest species

within the same genus, Mycobacterium, are the causes of the causative agent, Mycobacterium tuberculosis, that causes these diseases [1-4].

The complex of Mycobacterium tuberculosis has proven that a pathogen particular to human beings witnessed a population shortage and was the complex's latest common ancestor. According to an investigation of mycobacterial interspersed recurrent units, the bottleneck in growth has been dated to approximate 40,000 years. This period corresponds to the era shortly after Homo sapiens left Africa [5-8]. The Mycobacterium bov is lineage was also dated by the analysis of mycobacterial interspersed repetitive units to have begun to disperse about 6,000 years. which may have something to do with early farming and domestication of livestock. Due to Mycobacterium tuberculosis (MT), which generally persists over life and causes tubercles to emerge in different areas of the body, tuberculosis (TB) is an infectious disease that is highly contagious. With over 2 billion cases of TB each year and over 70,000 years of survival, MT has extremely ancient origins. Nearly a third of the human population worldwide is at increased risk of developing an active infection as bearers of the TB bacillus. Furthermore, there are 10 million new cases of TB each year [9-10].Over the centuries, tuberculosis (TB) has been linked to a high death rate. At present, as the second-most prevalent infectious disease after HIV roughly 1.4 million deaths are attributed to TB.Neolithic remains of humans contain research on bacterial infections. A 500,000-year-old Homo erectus fossil fuel has also supposedly been determined to have tuberculosis-like inflammation; nevertheless, this conclusion is debatable. The scriptures of the Vedas contain the earliest mentions of tuberculosis in non-European civilization. The disease is referred to as yaksma in the Rigveda, which dates back to 1500 BC [11-14].It is referred to as balasa in the Atharvaveda. This is the first consideration of scrofula found in the Atharvaveda. Around 600 BC, the book Sushruta Samhita was composed. It recommends breast milk as well as different meat products, alcoholic beverages, and rest to treat the illness. Those impacted have been urged to relocate to higher altitudes by the Yajurveda. Benjamin Marten suggested in anew theory of the consumption more particularly of Phthisis or The Consumption of the Pulmonary Arteries in 1720 that animalcule or very tiny microorganisms that are able to survive in an entirely novel body, had been the source of tuberculosis (similar to the ones that were identified by Anton van Leeuwenhoek in 1695[15-18]. Robert Koch had to wait an additional 162 years to prove the theory's reliability after it was categorically rejected. The initial medical description of tuberculosis meningitis was given by Robert Why in 1768 and the vertebral lesions that bear the name of Percivall Pott, an English surgeon, were first described in 1779. The percussion technique for diagnosing tuberculosis was created in 1761 by the Austrian physician Leopold Auen Brugger. It was discovered again in 1797 by Jean-Nicolas Corv is art of France. Corv is art found it informative and transformed into French so that the academic community was able to read it. Tuberculosis (TB) developed into an epidemic throughout Europe in the 18th and 19th centuries, with a seasonal pattern [19-21]. As many as 900 people died from tuberculosis (TB) for every 100,000 people in the western part of Europe in the 18th century, which includes cities like Hamburg, the Swedish city of Stockholm and the city of London. The mortality rate in North America was similar. Mortality data in the United Kingdom indicate that the epidemic of tuberculosis may have peaked around 1750[22].

Tuberculosis was one of the most serious medical problems facing the UK at the start of the 20th century. In 1901,royal authority was established. The commission of inquiry was design to examine

the connection between humans and animals with tuberculosis. The purpose of this study was to determine whether animal and human tuberculosis are the same illnesses and whether infections in humans and animals are possible. The Commission subsequently changed its name to the UK's Medical Research Council in 1919.The type of bacteria Streptomyces griseus is the source of streptomycin and was discovered in 1944 by Albert Schatz, Elizabeth Bugieand Selman Waksman. The first antibiotic that proved effective against Mycobacterium tuberculosis was streptomycin. The majority of individuals agree that this discovery marked the commencement of the modern era of tuberculosis. Streptomycin was used in conjunction with para-amino salicylic acid, which was discovered in 1946, to prevent the growth of resistance to different versions of the medication.which significantly enhanced outcomes for patients. The true revolution commenced a few years later, in 1952, when a drug called the first oral mycobactericidal medication, was developed. Rifampin's implementation in the 1970s sped up the healing process and, up until the 1980s, substantially reduced the number of tuberculosis cases [23-32].

In 2022, 10.6 million new cases of infectious tuberculosis (TB) are expected to occur countrywide. Six million men 34,000,000 women (about twice the population of New York)and 12,000,000 children (about twice the population of Arizona) in every generation and region have TBYet, TB can be controlled and protected. Multidrug-resistant TB, or MDR-TB, is still a public health problem and an imminent security threat. In 2021,almost one in three people who have drug-resistant TB will receive therapy. The identification and treatment of tuberculosis has been estimated to have prevented 74 million hospitalizations between 2000 and 2021. It requires a spending plan of $13 billion (about $40 per person in the US) (about $40 per person in the US) (about $40 per person in the US) annually, the leading cause of mortality worldwide [33-35].

The WHO launched the "End TB" campaign in 2014, with the goal of 80% fewer TBcases and 90% fewer TB-related deaths by 2030. The target numberof 206calls for a 20% decrease in TB incidence and 35% decrease in TB deaths by 2020. In 2020, however, the global incidence per population decreased by only 9%, while the European and African regions decreased it 19% and 16%, respectively. The total number of deaths decreased by only 14%, falling short of the 2020 target of 35% reductions; however, certain regions saw greater progress, with Europe and Africa seeing reductions of 31% and 19%, respectively. Accordingly, 2020 saw a failure to meet targets for funding, treatment, and prevention. In 2020,only 6.3 million people started getting TB preventatives; this is less than the suggested number of 30 million. In 2010, India contributed to the largest number of tuberculosis cases worldwide, partly because of inadequate disease treatment in both private and public healthcare networks. Programs such as the Revised National Tuberculosis Control Program aim to lower the prevalence of tuberculosis (TB) among patients receiving healthcare from the government [36-38].

2. MODEL OF THE PARAMETER

S : Rate of Susceptible population

E_1 : Latent period short term to become high risk of infectious population

E_2 : Latent period for long term become low risk of infectious population

I_1 : Rate of Infected at hospital stage of population

I_2 : Rate of randomly Infectious population at publicplace

R : Rate of Recovered population

π : Recruitment rate of TB

γ : Susceptible people get to early latent infection

β :The rate at which susceptible individual will move to long latent class of infection (E_2)

μ : Natural death rate of TB

σ :Progression rate of active tuberculosis from (E_1)class to(I_1)

δ : The rate at which susceptible individual will move to long latent class of infectious stage

ξ :The progression rate of Latent period of long-term people become low risk of infectious at the rate of (E_2)

get cure and again reinfected in public placeat the rate of I_2class.

θ : The rate of long latent people gets infection in early latent class

ω :The rate at which infective class of people get cure and move to recovered class

ϑ : The rate of early latent people gets long term

α :The progression rate of the long latent period of (E_2) population move to recovered class (R).

MODEL FORMULATION

The proposed model is developed from the idea of the basic $SE_1E_2I_1I_2R$compartment model. Here we have classified thetotal population (N) into six compartments: the Susceptible (S), the short latent period (E_1) which consists of apopulation which has high risk to become infectious by TB, the long latent period (E_2), which has low risk to become infectious by TB, the infective at hospital (I_1), infective at public(I_2) and the recovered compartment (R). We used reproduction number R_0, We examined disease free equilibrium and endemic equilibrium points, we used Jacobian matrix to find out the negative eigen values, if $R_0 < 1$ the disease-free equilibrium is locally asymptotically stable.We construct with a positive magnitude of time $'t'$ for all the six regions and we demonstrated feasible region Ω, we explored uniform boundaries condition for all stages. Using random data in MATLAB tool to simulate the result of the model through the diagrammatic representation. The flowchart of the model is depicted in figure 1.

MODEL OF THE DIAGRAM

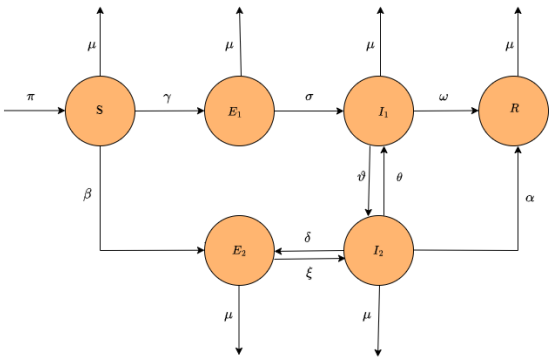

Fig-1. Flow chart of TB Model

MODEL OF THE EQUATION

Using the transmission illustration and our presumptions, the model can be expressed through the following six ordinary differential equations:

$$\frac{ds}{dt} = \pi - \gamma s - \beta s - \mu s$$

$$\frac{dE_1}{dt} = \gamma s - \sigma E_1 - \mu E_1$$

$$\frac{dE_2}{dt} = \beta s + \delta I_2 - \xi E_2 - \mu E_2 (1)$$

$$\frac{dI_1}{dt} = \sigma E_1 + \theta I_2 - \omega I_1 - \vartheta I_1 - \mu I_1$$

$$\frac{dI_2}{dt} = \vartheta I_1 + \xi E_2 - \delta I_2 - \theta I_2 - \alpha I_2 - \mu I_2$$

$$\frac{dR}{dt} = \omega I_1 + \alpha I_2 - \mu R$$

SUBJECT TO THE NONNEGATIVE INITIAL CONDITIONS

$$S \geq 0, E_1 \geq 0, E_2 \geq 0, I_1 \geq 0, I_2 \geq 0, R \geq 0$$

STATE OF EQUILIBRIUM

Equilibrium is the state of a solution that doesn't change over time. This implies that since the systems start in balance, the state will continue to exist in equilibrium until the end of time. A dynamic structure is always changing. Here, we have a discrete dynamical system at the discrete unit estimating point of a period. From the perspective of mathematics, a discrete dynamical system is defined as a set of numbers that are interconnected by the function f(yn), where f is a real-valued function. $yn + 1 - yn = g(yn)$is the iteration form for a function. By replacing yn and $yn + 1$ with the same quantity, one can find the equilibria in different configurations. For example, one can substitute $yn + 1 = yn = a. a = f(a)$ or $0 = g(a)$to find the value "a" that ensures $yn = a$is the equilibrium of the dynamic structure. A continuous dynamical system is characterized by the

solution to the differential equation (Eq.) $\frac{dy}{dt} = f(y)$ .By setting $\frac{dy}{dt} = 0$, one can determine equilibrium. We then need to solve the equation. $0 = g(a)$ to find values "a" such that the dynamical system's equilibrium is $y(t) = a$.

DISEASE FREE EQUILIBRIUM POINT (DFEP)

The model (1) has a DFE given by

$$\frac{ds}{dt} = \pi - \gamma s - \beta s - \mu s$$

$$S = \pi$$

DFEPDisease free equilibrium point is$(\pi, 0,0,0,0,0)$(2)

ENDEMIC EQUILIBRIUM POINT

Let $(E^*=E^*= (S^*, {E_1}^*, {E_2}^*, {I_1}^*, {I_1}^*, R^*) \in \psi$ be the equilibrium points of the organization that the equations arrange. First of all, Implementing the condition yields the states of equilibrium.

$S^* = 0$(3)

${E_1}^* = 0$(4)

${E_2}^* = \frac{\beta\left(\frac{\pi}{\gamma+\beta+\mu}\right)+\delta I_2}{\xi+\mu}$(5)

${I_1}^* = \frac{\sigma\left(\frac{\gamma s}{\sigma+\mu}\right)+\theta I_2}{\omega+\vartheta+\mu}$ (6)

${I_2}^* = \frac{\vartheta\left(\frac{\sigma E_1+\theta I_2}{\omega+\vartheta+\mu}\right)-\xi\left(\frac{\beta s+\delta I_2}{\xi+\mu}\right)}{\delta+\theta+\alpha+\mu}$ (7)

$R^* = \frac{\omega\left(\frac{\sigma E_1+\theta I_2}{\omega+\vartheta+\mu}\right)+\alpha\left(\frac{\vartheta I_1+\xi E_2}{\delta+\theta+\alpha+\mu}\right)}{\mu}$ (8)

REPRODUCTION NUMBER

The next-generation matrix method will be used to determine R_0 after we have distinguished the classes in our model. One of the infectious virus classes is tuberculosis. The TB reproduction number R_0will therefore be established.

We determine the Reproduction number R_0 and identify the infected cases of I_2 such as,

$F =$ Incoming of infected region

$V =$outgoing of infected region

$$F = \begin{pmatrix} \vartheta I_1 + \xi E_2 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} V = \begin{pmatrix} \delta I_2 + \theta I_2 + \alpha I_2 + \mu I_2 \\ \gamma s + \beta s + \mu s \\ \sigma E_1 + \mu E_1 \\ \xi E_2 + \mu I_2 \\ \omega I_1 + \vartheta I_1 + \mu I_1 \\ \mu R \end{pmatrix} \quad (9)$$

$$F = \vartheta I_1 + \xi E_2$$

$$V = (\delta + \theta + \alpha + \mu) I_2$$

$$FV^{-1} = \frac{\vartheta I_1 + \xi E_2}{(\delta + \theta + \alpha + \mu) I_2}$$

$$R_0 = \frac{\vartheta I_1 + \xi E_2}{(\delta + \theta + \alpha + \mu) I_2} \qquad (10)$$

The fundamental reproduction number R_0 is obtained from equation (9). Therefore, in the disease-free case, the equilibrium points of the $SE_1E_2I_1I_2R$ model is asymptotically stable.

Reproduction number R_0 is derived from equation (9). Thus, the equilibrium point of this model is disease-free case and its asymptotically stable.

LOCAL STABILITY OF DISEASE-FREE EQUILIBRIUM POINT

Theorem1.

If $R_0 < 1$ the disease-free equilibrium is locally asymptotically stable, otherwise unstable if $R_0 > 1$ the Jacobian matrix of the model is given.

Proof

The local stability of the TB disease-free equilibrium is determined by using the Jacobian matrix of Equation (1) at the disease-free equilibrium point. Using Equation (1) of the system as follows,

The model's Jacobian matrix is provided by

$$J = \begin{vmatrix} -(\gamma + \beta + \mu) & 0 & 0 & 0 & 0 & 0 \\ \gamma & -\sigma - \mu & 0 & 0 & 0 & 0 \\ \beta & 0 & -\xi - \mu & 0 & \delta & 0 \\ 0 & \sigma & 0 & -\omega - \vartheta - \mu & \theta & 0 \\ 0 & 0 & \zeta & \vartheta & -\delta - \theta - \alpha - \mu & 0 \\ 0 & 0 & 0 & \omega & \alpha & -\mu \end{vmatrix} \qquad (11)$$

Finding the determinant of the DFEP using Jacobian matrix are follows,

$$|J - \lambda I| = 0$$

$$\begin{vmatrix} -(\gamma + \beta + \mu) - \lambda & 0 & 0 & 0 & 0 & 0 \\ \gamma & -\sigma - \mu - \lambda & 0 & 0 & 0 & 0 \\ \beta & 0 & -\xi - \mu - \lambda & 0 & \delta & 0 \\ 0 & \sigma & 0 & -\omega - \vartheta - \mu - \lambda & \theta & 0 \\ 0 & 0 & \zeta & \vartheta & -\delta - \theta - \alpha - \mu - \lambda & 0 \\ 0 & 0 & 0 & \omega & \alpha & -\mu - \lambda \end{vmatrix} =$$

0(12)

Here we got six negative Eigen values, the DFE (Disease free equilibrium point) is locally asymptotically stable.

Consequently, the evidence which $R_0 < 1$ implies the disease-free equilibrium point is LAS.

Theorem2.

The system of solutions (1) is positive boundaries for all individuals(S, E_1, E_2, I_1, I_2, R) $\in \mathbb{R}_+^6$ and also construct with a positive magnitude of time 't' as well.

Proof

$$\frac{ds}{dt}(\text{ at}S = 0) \Rightarrow \pi \geq 0 \quad (13)$$

$$\frac{dE_1}{dt}(\text{ at}E_1 = 0) \Rightarrow \gamma s \geq 0 \quad (14)$$

$$\frac{dE_2}{dt}(\text{ at}E_2 = 0) \Rightarrow \beta s + \delta I_2 \geq 0 \quad (15)$$

$$\frac{dI_1}{dt}(\text{at}I_1 = 0) \Rightarrow \sigma E_1 + \theta I_2 \geq 0 \quad (16)$$

$$\frac{dI_2}{dt}(\text{ at}I_2 = 0) \Rightarrow \vartheta I_1 + \xi E_2 \geq 0 \quad (17)$$

$$\frac{dR}{dt}(\text{ at}R = 0) \Rightarrow \omega I_1 + \alpha I_2 \geq 0 \quad (18)$$

The solution to the problem above will therefore remainand this following region therefore becomes possible.

$$\Xi = (S(0), E_1(0), E_2(0), I_1(0), I_2(0), R(0)) \in \mathbb{R}_+^6 \quad (19)$$

$$(S(0), E_1(0), E_2(0), I_1(0), I_2(0), R(0)) \geq 0.$$

DIMENSIONLESSTRANSFORMATION

We apply dimensionless modifications to the model to enhance its analysis. With the help of the state variables S, E_1, E_2, I_1, I_2 and$R$, the standard arrangement of models transforms into

$$\dot{S}(t) = \pi - (\gamma + \beta + \mu)s \quad (20)$$

$$\dot{E_1}(t) = \gamma s - (\sigma + \mu)E_1 \quad (21)$$

$$\dot{E_2}(t) = \beta s + \delta I_2 - (\xi + \mu)E_2 \quad (22)$$

$$\dot{I_1}(t) = \sigma E_1 + \theta I_2 - (\omega + \vartheta + \mu)I_1 \quad (23)$$

$$\dot{I_2}(t) = \vartheta I_1 + \xi E_2 - (\delta + \theta + \alpha + \mu)I_2 \quad (24)$$

$$\dot{R}(t) = \omega I_1 + \alpha I_2 - \mu R \quad (25)$$

Adding … yields

$$\dot{S}(t) + \dot{E_1}(t) + \dot{E_2}(t) + \dot{I_1}(t) + \dot{I_2}(t) + \dot{R}(t) = \pi - N\mu \quad (26)$$

Where $S + E_1 + E_2 + I_1 + I_2 + R = 1$ (27)

REGION OF FEASIBLE

In the TB simulations, every state variable is continuously positive because the population that's subject to consideration represents the human population. Thus, in the region ψ, the model equations of system (1) are restricted to a non-negative condition,

$$\psi = (S(t), V(t), E(t), I(t), Q(t), R(t)): S > 0, V > 0, E > 0, I > 0, Q > 0, R > 0 \in \mathbb{R}_{+}^{6}$$

where the feasible region is positively invariant, our model Eqs. (1)is biologically meaningful; otherwise, it is not.

THE MODEL OF THE DYNAMICS

$N(t)$ is differentiated with respect to time along the model's layouts in equation (1) to represent a complete population.

$$N(t) = S(t) + E_1(t) + E_2(t) + I_1(t) + I_2(t) + R(t)$$

we obtain

$$\frac{dN(t)}{dt} = \frac{dS(t)}{dt} + \frac{dE_1(t)}{dt} + \frac{dE_2(t)}{dt} + \frac{dI_1(t)}{dt} + \frac{dI_2(t)}{dt} + \frac{dR(t)}{dt} \quad (28)$$

Adding the equation of the system (1) we get

$$\frac{dN(t)}{dt} = \pi - N\mu \quad (29)$$

As a result, an equation (28) can be used to find the variation in population or the variation of population over dynamics.

Lemma1.

$\Omega \{ (t); E_1(t); E_2(t); I_1(t); I_2(t); R(t) \in \mathbb{R}^6: N(t) \leq \frac{\pi}{\mu} \}$ determines the feasible region Ω.

$S(0) \geq 0, E_1(0) \geq 0, E_2(0) \geq 0, I_1(0) \geq 0, I_2(0) \geq 0, R(0) \geq 0$, as the initial conditions, is positively invariant in the system of equation (1).

Proof

Adding the equation (1) we obtain

$$\frac{dN(t)}{dt} = \pi - N\mu$$

resolving the differential equations

$$N(t) \leq \frac{\pi}{\mu} + N(0)e^{-\mu t} \quad (30)$$

$$\lim t \to \infty \sup N(t) \leq \frac{\pi}{\mu}$$

It suggests that the area

$$\Omega: \{ (t); E_1(t); E_2(t); I_1(t); I_2(t); R(t) \in \mathbb{R}^6: N(t) \leq \frac{\pi}{\mu} \} \quad (31)$$

Is positively correlated with systems (1)

Theorem3.

The system of equation describes a deterministic model that all solutions are uniformly bounded on$\Omega \subset \mathbb{R}^6$.

Proof

$$N = S + E_1 + E_2 + I_1 + I_2 + R$$

$$\frac{dN}{dt} = \frac{ds}{dt} + \frac{dE_1}{dt} + \frac{dE_2}{dt} + \frac{dI_1}{dt} + \frac{dI_2}{dt} + \frac{dR}{dt} \quad (32)$$

$$\frac{dN}{dt} = \pi - N\mu$$

$$\frac{dN}{\pi - N\mu} \leq dt \quad (33)$$

By integrating

$$\int \frac{dN}{\pi - N\mu} \leq \int dt \Rightarrow -\frac{1}{\pi - \mu} In(\pi - N\mu) \leq t + c$$

$$\Rightarrow In(\pi - N\mu) \geq (\pi - \mu)t - (\pi - \mu)c$$

$$e^{In(\pi - N\mu)} = e^{-(\pi - \mu)t - (\pi - \mu)c}$$

By simplification

$$\pi - N\mu = ce^{-(\pi - \mu)t} \quad (34)$$

Where c is constant, Ast $\longrightarrow \infty$

$ce^{-(\pi - \mu)t} \longrightarrow 0$

(35) then $\pi - N\mu < 0$

We have the population size

$$N \leq \frac{\pi}{\mu} \Rightarrow 0 \leq N \leq \frac{\pi}{\mu}$$

$$(S, E_1, E_2, I_1, I_2, R) \in \mathbb{R}_+^6 \; N \leq \frac{\pi}{\mu} \quad (36)$$

Theorem 4.

The proposed model (1) solution set $\{S(t), E_1(t), E_2(t), I_1(t), I_2(t), R(t)\}$ combined with (2), is positive for all $t > 0$.

Proof

We evaluate equation (1) while taking into consideration the non-linear system of equations.

$$\frac{ds}{dt} = \pi - \gamma s - \beta s - \mu s$$

Which means that

$$\frac{ds}{dt} \geq -(\gamma + \beta + \mu)S \quad (37)$$

By integrating, we get

$$S(t) \geq S(0)e^{-(\gamma+\beta+\mu)t} \quad (38)$$

This goes $S(t) \geq 0$

THE PREDOMINANT EQUILIBRIUM POINT'S GLOBAL STABILITY

The Lyapunov functional is utilized to evaluate the global stability of the indigenous equilibrium point Σ_c. To this end, we define the definition that follows $L(S, E_1, E_2, I_1, I_2, R) = \frac{1}{2}((S - S^*)+(E_1 - E_1{}^*) + (E_2 - E_2{}^*) + (I_1 - I_1{}^*) + (I_2 - I_2{}^*) + (R - R^*))$

The function L has a value greater than zero, and at the predominant equilibrium point Σ_c it equals zero. When we differentiation the function in relation to time, we get

$$\frac{dL}{dt} = ((S - S^*)+(E_1 - E_1{}^*) + (E_2 - E_2{}^*) + (I_1 - I_1{}^*) + (I_2 - I_2{}^*) + (R - R^*))$$

$$\frac{dS}{dt} + \frac{dE_1}{dt} + \frac{dE_2}{dt} + \frac{dI_1}{dt} + \frac{dI_2}{dt} + \frac{dR}{dt}$$

$$= \left(N - \frac{\pi}{\mu}\right)(\pi - \mu N)$$

$$\leq \left(N - \frac{\pi}{\mu}\right)(\pi - \mu N) \leq -\left(\frac{\pi - \mu N}{N}\right)^2 \leq 0 \quad (39)$$

In cases where, the function is strictly Lyapunov and from a global asymptotic perspective, the permanent equilibrium point Σ_c is stable. This is valid for $R_0^c > 1$, as this proves that Σ_c exists. Both epidemiologically and clinically, these results point to a very long survival period for tuberculosis in humans.

Theorem 5.

The mathematical subsystems (1) have unique solution if it is determined that $\frac{\partial T_i}{\partial Tb}, Tb = (1)$ are continuous and bounded on Ω.Let Ω be the region$\alpha T_i \in \mathbb{R}_+^6$

Proof

Let equation (1) represented by $T_i = T_1, T_2, T_3, T_4, T_5, T_6$ respectively from equation (1) of $Tb = S, E_1, E_2, I_1, I_2, R$ the following partal derivatives are obtained.

From equation (1), S following partial derivatives are obtained

$$\left|\frac{\partial T_1}{\partial S}\right| = |\gamma - \beta - \mu| < \infty \; ; \left|\frac{\partial T_1}{\partial E_1}\right| = 0 < \infty \; ; \left|\frac{\partial T_1}{\partial E_2}\right| = 0 < \infty \; ; \left|\frac{\partial T_1}{\partial I_1}\right| = 0 < \infty \; ; \left|\frac{\partial T_1}{\partial I_2}\right| = 0 < \infty; \left|\frac{\partial T_1}{\partial R}\right| = 0 < \infty; (40)$$

The above partial derivatives exist, are continuous and are bounded.

From equation (1),E_1 following partial derivatives are obtained.

$\left|\frac{\partial T_2}{\partial E_1}\right| = |-\sigma - \mu| < \infty$; $\left|\frac{\partial T_2}{\partial E_2}\right| = 0 < \infty$;$\left|\frac{\partial T_2}{\partial I_1}\right| = 0 < \infty$; $\left|\frac{\partial T_2}{\partial I_2}\right| = 0 < \infty$;$\left|\frac{\partial T_2}{\partial S}\right| = |\gamma|0 < \infty$; $\left|\frac{\partial T_2}{\partial R}\right| = 0 < \infty$;(41)

Existing, continuous, and constrained are the partial derivatives mentioned above.

From equation (1),E_2 following partial derivatives are obtained.

$\left|\frac{\partial T_3}{\partial E_2}\right| = |\zeta - \mu| < \infty$; $\left|\frac{\partial T_3}{\partial E_1}\right| = 0 < \infty$;$\left|\frac{\partial T_3}{\partial I_1}\right| = 0 < \infty$; $\left|\frac{\partial T_3}{\partial I_2}\right| = |-\delta|0 < \infty$;$\left|\frac{\partial T_3}{\partial S}\right| = |\beta| < \infty$; $\left|\frac{\partial T_3}{\partial R}\right| = 0 < \infty$;(42)

Existing, continuous, and constrained are the partial derivatives mentioned above.

From equation (1),I_1 following partial derivatives are obtained.

$\left|\frac{\partial T_4}{\partial I_1}\right| = |-\omega - \vartheta - \mu| < \infty$; $\left|\frac{\partial T_4}{\partial E_1}\right| = |\sigma| < \infty$;$\left|\frac{\partial T_4}{\partial E_2}\right| = 0 < \infty$; $\left|\frac{\partial T_4}{\partial I_2}\right| = |-\theta| < \infty$;$\left|\frac{\partial T_4}{\partial S}\right| = 0 < \infty$;$\left|\frac{\partial T_4}{\partial R}\right| = 0 < \infty$; (43)

Existing, continuous, and constrained are the partial derivatives mentioned above.

From equation (1), I_2following partial derivatives are obtained.

$\left|\frac{\partial T_5}{\partial I_2}\right| = |-\delta - \theta - \alpha - \mu| < \infty$; $\left|\frac{\partial T_5}{\partial E_1}\right| = 0 < \infty$;$\left|\frac{\partial T_5}{\partial E_2}\right| = |-\xi| < \infty$; $\left|\frac{\partial T_5}{\partial I_1}\right| = |\vartheta|0 < \infty$;$\left|\frac{\partial T_5}{\partial S}\right| = 0 < \infty$; $\left|\frac{\partial T_5}{\partial R}\right| = 0 < \infty$; (44)

Existing, continuous, and constrained are the partial derivatives mentioned above.

From equation (1),Rfollowing partial derivatives are obtained.

$\left|\frac{\partial T_6}{\partial R}\right| = |\mu| < \infty$; $\left|\frac{\partial T_6}{\partial E_1}\right| = 0 < \infty$;$\left|\frac{\partial T_6}{\partial E_2}\right| = 0 < \infty$; $\left|\frac{\partial T_6}{\partial I_1}\right| = |\omega| < \infty$;$\left|\frac{\partial T_6}{\partial I_2}\right| = |-\alpha| < \infty$;$\left|\frac{\partial T_6}{\partial S}\right| = 0 < \infty$;(45)

The above partial derivatives exist, are continuous and are bounded.

Since all the partial derivatives exist and are bounded and defined, the system of equations (1) exists and has solutions.$\mathbb{R}_+^6$.

GLOBAL STABILITY OF ENDEMI EQUILIBRIUM

Theorem 6

The endemic point $\mathbb{E}^*$ unique equilibrium is globally asymptotically stable if $R_0 > 1$.

Proof

Let us assume that the accompanying Lyapunov function

$T_B\ (S^*\square,\ E_1{}^*\ ,E_2{}^*\ ,\ I_1{}^*\square I_2{}^*\ ,\ R^*\square)$

$(S - S^*\square - S_h In\frac{S^*\square}{S^*\square}) + (E_1 - E_1{}^* - E_1 In\frac{E_1{}^*}{E_1{}^*\square}) + (E_2 - E_2{}^* - E_2 In\frac{E_2{}^*}{E_2{}^*\square}) + (I_1 - I_1{}^* - I_1 In\frac{I_1{}^*}{I_1{}^*}) + (I_2 - I_2{}^* - I_2 In\frac{I_2{}^*}{I_2{}^*\square}) + (R - R^* - RIn\frac{R^*}{R^*\square})$ (46)

Computing the derivative of T_B, we get

$$\frac{LT_B}{dt} = \left(\left(\frac{S-S^*}{S^*}\right)\frac{dS}{dt} + \left(\frac{E_1-E_1{}^*}{E_1{}^*}\right)\frac{dE_1}{dt} + \left(\frac{E_2-E_2{}^*}{E_2{}^*}\right)\frac{dE_2}{dt} + \left(\frac{I_1-I_1{}^*}{I_1{}^*}\right)\frac{dI_1}{dt} + \left(\frac{I_2-I_2{}^*}{I_2{}^*}\right)\frac{dI_2}{dt} + \left(\frac{R-R^*}{R^*}\right)\frac{dR}{dt}\right)$$

Substituting our model equations in $\frac{LT_B}{dt}$ above we get

$$\frac{LT_B}{dt} = \left(\left(\frac{S-S^*}{S^*}\right)(\pi - \gamma s - \beta s - \mu s) + \left(\frac{E_1-E_1{}^*}{E_1{}^*}\right)(\gamma s - \sigma E_1 - \mu E_1) + \left(\frac{E_2-E_2{}^*}{E_2{}^*}\right)(\beta s + \delta I_2 - \xi E_2 - \mu E_2) + \left(\frac{I_1-I_1{}^*}{I_1{}^*}\right)(\sigma E_1 + \theta I_2 - \omega I_1 - \vartheta I_1 - \mu I_1) + \left(\frac{I_2-I_2{}^*}{I_2{}^*}\right)(\vartheta I_1 + \xi E_2 - \delta I_2 - \theta I_2 - \alpha I_2 - \mu I_1) + \left(\frac{R-R^*}{R^*}\right)(\omega I_1 + \alpha I_2 - \mu R)\right) \quad (47)$$

Here considered A and B values are positive and negative. Then $\frac{LT_B}{dt} = A - B$.

$$A = ((\gamma s + \beta s + \mu s)S^* + (\sigma E_1 + \mu E_1)E_1{}^* + (\xi E_2 + \mu E_2)E_2{}^* + (\omega I_1 + \vartheta I_1 + \mu I_1)I_1{}^* + (\delta I_2 + \theta I_2 + \alpha I_2 + \mu I_2)I_2{}^* + (\mu R)R^*)$$

$$B = (\pi)\frac{S^*}{S} + (\gamma s)\frac{E^*}{E_1} + (\beta s + \delta I_2)\frac{E_2{}^*}{E_2} + (\beta E + \theta I_2)\frac{I_1{}^*}{I_1} + (\vartheta I_1 + \xi E_2)\frac{I_2{}^*}{I_2} + (\omega I_1 + \alpha I_2)\frac{R^*}{R}$$

If $A < B$ then $\frac{LT_B}{dt} \leq 0$, $\frac{LT_b}{dt} = 0$

(48)

If and only If

$$S = S^* = E_1 = E_1{}^* = E_2 = E_2{}^* = I_1 = I_1{}^* = I_2 = I_2{}^* = R = R^*$$

$$(S, E_1, E_2, I_1, I_2, R) \in \frac{LT_B}{dt} = 0 \quad (49)$$

We demonstrate that the endemic equilibrium result is asymptotically stable [38].

NUMERICAL REPRODUCTION

We carried out numerical simulations show that the resultsofqualitative analysis. The process of simulation modeling is carried out with the use of variables and parameters. To demonstrate our parameters and area characteristics, we made a few assumptions about the parameter values. Numerical estimation has been established by using MATLAB,it has demonstrated the primary results of the theoretical TB models. Our investigation's final goal is to find out how prescription drugs affect TB patients are get recovered from the TB disease.In fig.2. explained, how some people get tuberculosis promptly and how most susceptible humans have an excessive infection rate.

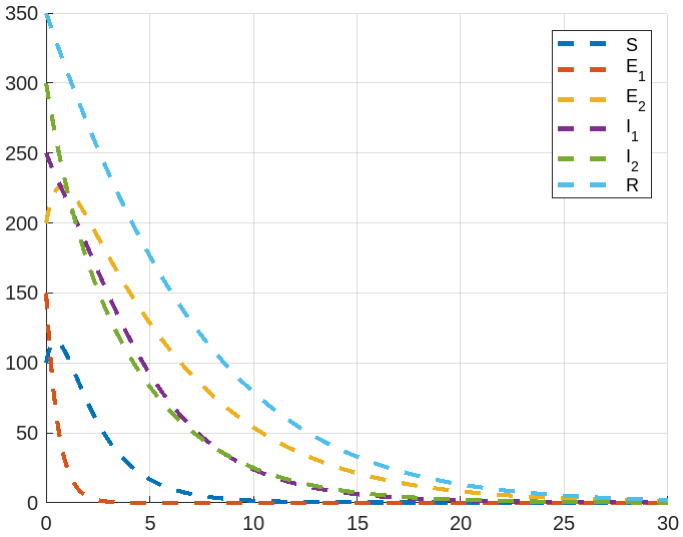

Fig.2. Stability analysis of TB population.

Many individuals did not receive enough information about the treatment, even though some individuals who were infected with tuberculosis went on to develop the disease after receiving the necessary care the individual get reinfected again.TShe values of the parameters, In fig.2. We used random values such as $\delta = 0.10016; \vartheta = 0.45; \sigma = 0.3;\ \gamma = 0.078;\ \omega = 0.9;\ \pi = 0.03; \beta = 0.7; \mu = 0.12;\ \theta = 0.10;\ \alpha = 0.05;\ \xi = 0.030$. All the stages of the people are controlled and stable by using random values.

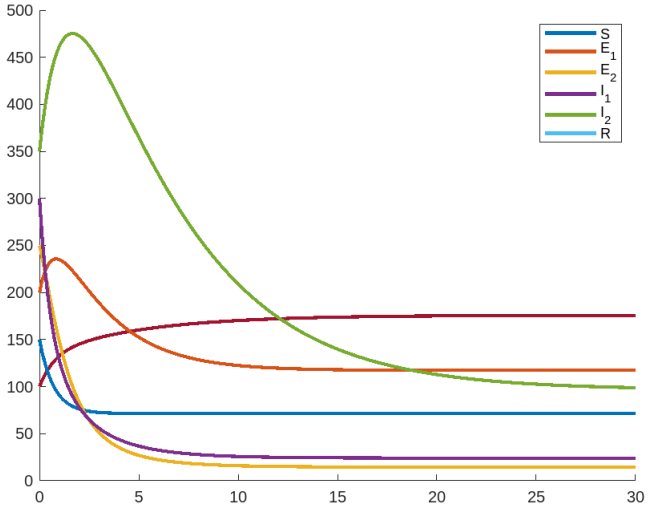

Fig.3. Stability analysis of TB population $\pi = 100$.

Infig.3 some people contract TB rapidly and that the majority of the disease is reduced, the stability analysis of TB population is controlled and stable. The random values such as $\delta = 0.3571; \vartheta = 0.5; \sigma = 0.003;\ \gamma = 0.50; \omega = 0.05; \pi = 100; \beta = 0.7;\ \mu = 0.20;\ \theta = 0.7;\ \alpha = 0.5; \xi = 0.30$. All the stages of the people are controlled and stable by using random values.

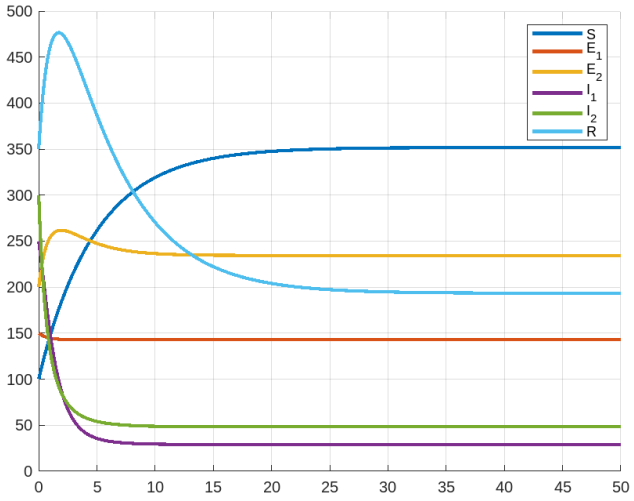

Fig.4.Stability analysis of TB population $\pi = 200$.

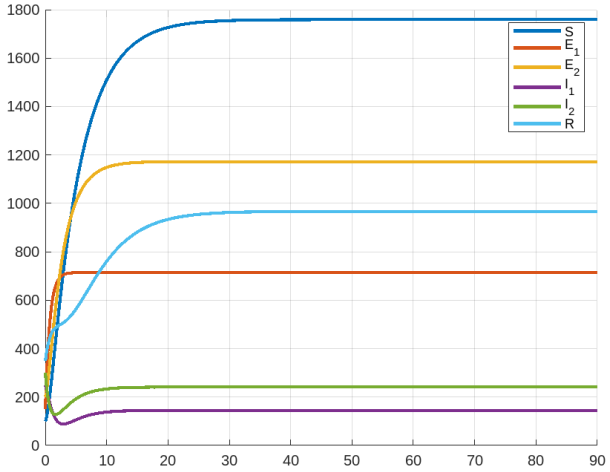

Fig.5. Stabilityanalysisof TB Population $\pi = 1000$.

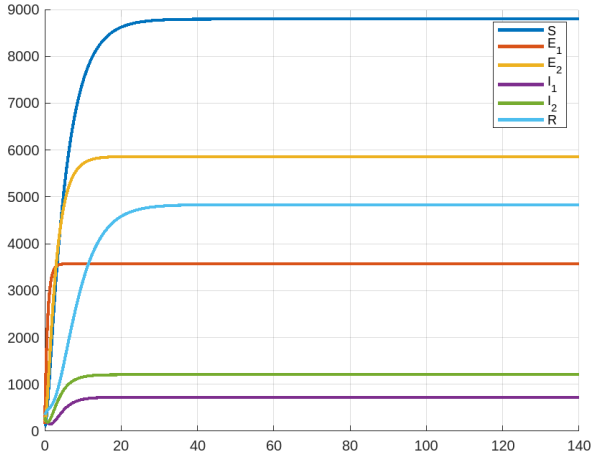

Fig.6. Stability analysis of TB population $\pi = 5000$.

In fig.4. We used random values such as $\delta = 0.3571$;ϑ =0.5;σ =0.03; γ =0.50;$\omega = 0.05$;$\pi = 200$;$\beta = 0.7$; $\mu = 0.20$; $\theta = 0.7$; $\alpha = 0.5$; $\xi = 0.30$. All the stages of the people are controlled and stable.

In fig.5. We used random values such as $\delta = 0.3571$;$\vartheta = 0.5$;$\sigma = 0.03$; $\gamma = 0.50$;$\omega = 0.05$;$\pi = 1000$; $\beta = 0.7$; $\mu = 0.20$; $\theta = 0.7$;$\alpha = 0.5$;$\xi = 0.30$. All the stages of the people are controlled and stable.

In fig.6. We used random values such as$\delta = 0.3571$;$\vartheta = 0.5$;$\sigma = 0.003$;$\gamma = 0.50$;$\omega = 0.5$; π =5000; $\beta = 0.7$; $\mu = 0.20$; $\theta = 0.7$;$\alpha = 0.5$; $\xi = 0.30$. All the stages of the people are controlled and stable.

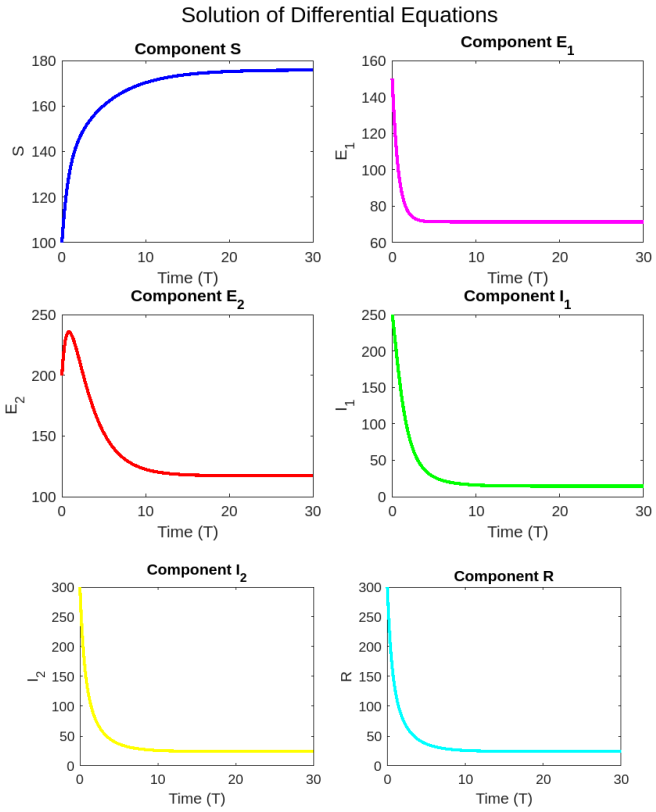

Fig.7.Visualizing the dynamics Solution of differentialequation.

In fig.7. We used random values such as $\delta = 0.3571$; $\vartheta = 0.5$; $\sigma = 0.03$;$\gamma = 0.50$; $\omega = 0.05$; $\pi = 100$; $\beta = 0.7$; $\mu = 0.20$; $\theta = 0.7$; $\alpha = 0.5$; $\xi = 0.30$. All the stages of the people are controlled and stable. We visualizing the all the compartments of the people through solution of differential equation.

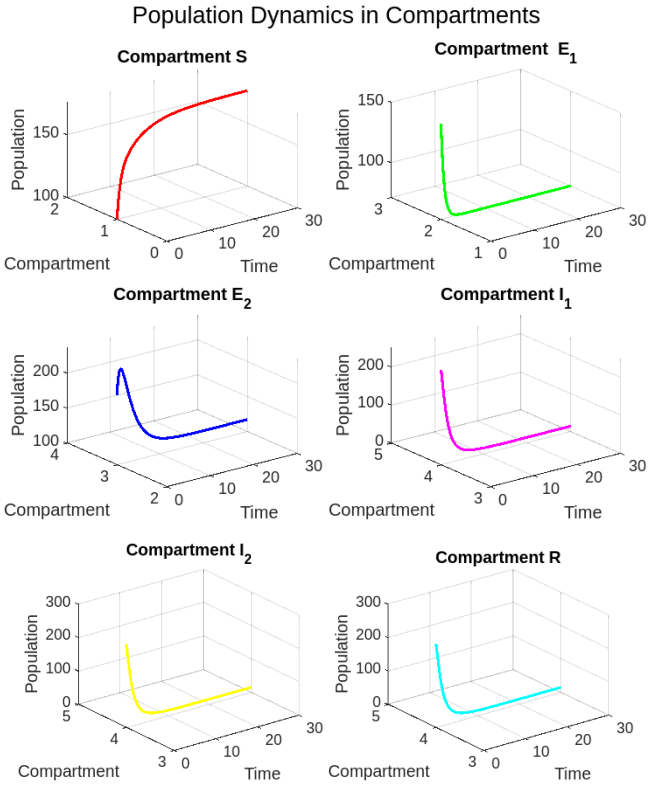

Fig.8.Stability analysis of TB population over dynamics.

In fig.8. We used random values such as $\delta = 0.3571;\ \vartheta = 0.5;\ \sigma = 0.03;\ \gamma = 0.50;\ \omega = 0.05;\ \pi = 100;\ \beta = 0.7;\ \mu = 0.20;\ \theta = 0.7;\ \alpha = 0.5;\ \xi = 0.30$. All the stages of the people are controlled and stable by using random values. The stability analysis of TB population over dynamics explored all the compartments of the disease rate, its decrease the infection and growth rate of thedisease is stable.

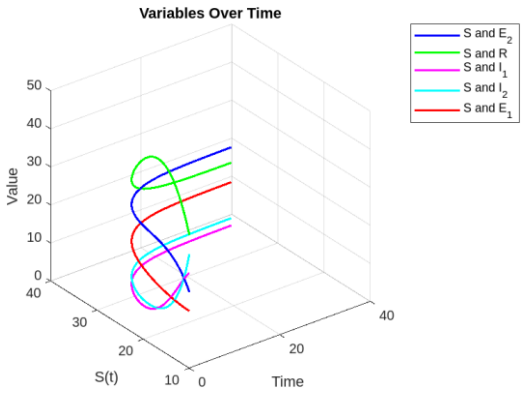

Fig.9.Comparision of TB population in all stages.

In fig.9. We used random values such as $\delta = 0.3571;\ \vartheta = 0.5;\ \sigma = 0.003;\ \gamma = 0.50;\ \omega = 0.5;\ \pi = 0.20;\ \beta = 0.7;\ \mu = 0.20;\ \theta = 0.7;\ \alpha = 0.5;\ \xi = 0.30$. All the stages of the people are controlled and stable.

3. CONCLUSION

In this paper we explored the mathematical simulations of the tuberculosis dynamics model. Whereby the impact of the density of populations on the spread of the tuberculosis disease is examined. It is obvious that the population density affects the frequency of interpersonal contact, which is turn affects the frequency of tuberculosis infections transmitted through the air. Overcrowding is thought to be an important contributor to the rising incidence rate of tuberculosis. The state of equilibrium points in the model has been determined and their equilibrium stabilities are analyzed for the purpose of qualitative analysis. The Basic Reproduction numberR_0 is derived and it is observed that if $R_0 < 1$ the DFE is locally asymptotically stable. The TB infectious at hospital $I_1$and TB infectious at publicI_2stage of the people controlled and stable from the infection of the TBdisease. The simulated version of the mathematical framework that is attached here, the analytical results and demonstrates how population density affects the prevalence of tuberculosis. A mathematical model clearly demonstrates the consequences of latent periods (E_1 and E_2) on the number of people and it can be seen that the number of residents decreases or the size of the occupied area increases, the emission rate of the epidemic from latent classes (short and long) to infectiousclass declines. We used Lyapunov function stability to find out the global stability of endemic equilibrium. In summary, the increase of population density will raise the possibility of an unstable disease-free equilibrium. These results show that thetuberculosis infection is decreased. This can be accomplished by either reducing the amount of overpopulation or growing the area in which the population lives. All the stages of the population are controlled and stable.The process of analysing and assessing each stage of the patient's case study is included in the interpretation of suggested controls. This helps to rectify the earlier stages of the disease's evaluation and supports the corrective actions of the disease-controlled system. The process of interpreting proposed controls encompasses keeping track of and evaluating each level of the patient's case study. This aids in the disease-controlled system's corrective actions and helps to correct the earlier stages of the disease's evaluation. Despite previous experience being under control, effective control is impossible. To enable follow-up when needed, control constantly looks to the future. To maintain control, revival approaches must be used, and changes must be made wherever feasible. It is a dynamic function because constant control must be the primary objective. In the current state of research, TB disease is theoretically managed through the use of mathematical models. We can practically control the tuberculosis disease after some medical case studies, depending on the stage of the patient. In future we plan to work on developing drugs resistant to chemotherapy,it helps to control the infection among population.

AUTHOR DECLARATIONS

CONFLICT OF INTEREST

The authors have no conflicts to disclose.

AUTHOR CONTRIBUTIONS

The authors have equal contributions. All authors drafted thepaper, perused it, and supported the last rendition of it.**Naresh Kumar Jothi**: Conceptualization (equal); Methodology(equal); Validation (equal); Visualization (equal); Writing – originaldraft (equal); Writing – review & editing (equal).

Lakshmi. A: Conceptualization (equal); Data curation (equal); Formal analysis(equal); Funding acquisition (equal); Methodology (equal);Writing – review & editing (equal). **Jayant Giri**:Conceptualization (equal); Data curation (equal); Formal analysis(equal); Investigation (equal); Methodology (equal); Writing –review & editing (equal). **T. Sathish**: Conceptualization (equal);Data curation (equal); Formal analysis (equal); Funding acquisition(equal); Investigation (equal); Methodology (equal).

DATA AVAILABILITY

The data that support the findings of this study are available within the article.

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