Research Article

Exploring the Stochastic Host-Pathogen Tuberculosis Model with Adaptive Immune Response

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In this literature, we probe a stochastic host-pathogen tuberculosis model with the adaptive immune response of four states of epidemiological classification: *Mycobacterium tuberculosis*, uninfected macrophages, infected macrophages, and immune response CD4+ T cells. This model is pertinent to the latent stage of tuberculosis infection and active tuberculosis-infected individuals. The stochastic host-pathogen tuberculosis model in pathology is constituted based on the environmental influence on the *Mycobacterium tuberculosis* and macrophage population, elucidated by stochastic perturbations, and it is proportional to each state. We evince the existence and a unique global positive solution of a stochastic tuberculosis model. We attain sufficient conditions for the extinction of the tubercle bacillus. Moreover, we acquire the existence of the stationary distribution of the positive solutions by the Lyapunov function method. Eventually, numerical simulations validate analytical findings and the dynamics of the stochastic TB model.

1. Introduction

In the annals of history, there have been many threats such as natural calamity, diseases, and wild animals for the existence of humans; among these, diseases seem to be the main cause of death. In the previous centuries, tuberculosis posed a great threat to the survival of human beings. It is believed that it was the cause of death of more than a third population [1]. And block death in Europe is the standing testimony for these facts. Fortunately, due to the development of medical science, tuberculosis is completely curable but still persists.

Tuberculosis is traced back to 3400-2400 BC. It is as ancient as that of ancient countries such as Egypt, Greece, Rome, and India. The German Nobel laureate Robert Koch (1843-1910) discovered the tubercle bacillus (March 24, 1882) at the backdrop of one in seven who died in Europe due to mysterious disease.

Infection of the lungs bacteria (*Mycobacterium tuberculosis* (MTB)) leads to tuberculosis (TB). The bacterial

infection may also spread into the brain, kidneys, spine, etc., but it is fortunate that tuberculosis is curable and preventable [1]. Tuberculosis is contagious and spreads through the air. Even the inhalation of a few of these germs is potential enough to infect a person. The physical contact, the nearness, and the air around the infected person can also infect. Sharing the same space with the infected person, weak immunity, malnutrition, unemployment, poor lifestyle, poor food habits, lack of shelter, unhygienic environment, drug abuse, imperfect sexual attitude, ill-literacy, and smoking are vulnerable factors for the spread of tuberculosis [2].

Infection is mainly occurred by the aerosol route like inhalation, wherein bacilli contained droplet nuclei sets in the alveoli. Here, alveolar macrophages [3] engulf the bacteria and ultimately bring out the infection to dendritic cells and all other cells as epithelial cells. These alveolar macrophages possess multiple microbicidal mechanisms which include phagolysosome fusion and respiratory burst to prevent postinfective mechanisms. For successful

sustainability of infection, the tuberculosis bacilli must understand its encounter with the collection of activated macrophages (granuloma) [4, 5] and eventually gain access to the lymphocytes, neutrophils, fibroblasts, eosinophils, or the bloodstream [6, 7]. Macrophages with the potential to sterile and kill the bacteria are segmented apart in the tissue. In the case of adaptive immunity with the accumulation of effector CD4⁺ and CD8⁺ T cells setting in lungs, the multiplication of the bacterial population is contained and enumerable patients become asymptomatic and unable to shed bacteria, and they are then considered as vulnerable to latent TB infection (LTBI). Varied mechanisms cause the limited ability with adaptive immune responses to encounter and eradicate MTB, some of which are then categorized and characterized such as weakened histocompatibility complex (MHC) class II-mediated antigen presentation; adaptation of the anti-inflammatory mediator lipoxin A₄; containing by regulatory T cells; monitoring bacterial antigen gene expression and hence incapable of reducing antigen-specific CD4⁺ T cells; and immune to the macrophages activating effector cytokines such as interferon- γ (INF- γ) and tumour necrosis factor- α (TNF- α) [4, 8].

The latent stage of the tuberculosis infection is non-challenged; though the germs are present in the body, they are inactive and harmless. Antibiotics such as isoniazid (INH), rifampin (Rifadin, Rimactane), and rifapentine can also be used to contain the aggravation of the germs at this stage. It is very easy to wipe out the germs from the body at this stage. Indications of active tuberculosis infection are coughing, sudden weight loss, loss of appetite, sweating during nights, fever, and chest pain.

The potential roles for adjunctive immunotherapy in multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) [9–11] consist in enhancing cure rates and reducing time spent to cultural shifts, reducing the tissue damage concerned with nonproductive postimmune reactions, and elevating overall health status by subdoing systematic impacts of prolonged chronic inflammation. In addition, enumerable powerfully useful cytokines and other immunomodulatory agents already exist in medical use for other conditions.

A significant role in the immunity against pathogen agent is played by T-cell differentiation and memory and effector T cells [12–14]. Hence, an effective T-cell response decides if the infection decreases or develops into a medically evident disease. Studies prove that CD4⁺ T cells [13–15] do their part in the protection against MTB as strengthened by the evidence that CD4⁺ T cells such as T helper 1 (Th1), Th2, Th17, and regulatory T cells (Tregs) and all these subsets support one another to restrict infection. MTB-specific CD4⁺ Th1 cell response is recognized as possessing a protective role for the power to generate cytokines such as INF- γ and TNF- α that involve the processes of recruitment and activation of innate immune cells as monocytes and granulocytes. In this way, when other antigen-specific T cells such as CD8⁺ cells [14], natural killer (NK) cells, $\gamma\delta$ T cells, nonclassical (MHC) class I molecule CD1, controlled T cells

are able to raise INF- γ during MTB infection and they are unable to equalize the lack of CD4⁺ T cells.

Of late, studies have revealed that multifunctional/polyfunctional T cells (i.e., T cells possessed with multiple effector functions) [13, 14] can produce INF- γ coupled with IL-2, and subsequently, a subset of cells is able to concurrently produce INF- γ , TNF- α , IL-2, and IL-17 and was diagnosed in patients with active TB disease compared to LTBI, which rapidly decreased on anti-TB treatment. And also, the polyfunctional T cells were recognized for their potentiality to proliferate and to secrete very many cytokines, and these cells were discovered to act a protective role in antiviral immunity in chronic infections (when the antigen load is low).

Memory T cells are a subset of infection-fighting T cells (T lymphocytes) that are highly proliferative and possess a strong immune response. Based on the role of L-selectin and CC-chemokine receptor 7, memory T cells can be segmented into CD62L^{hi} CCR7⁺ and CD62L^{lo} CCR7[−] [12–14]. In the case of in vitro stimulation, human CD62L^{hi} CCR7⁺ memory CD4⁺T cells caused the production of IL-2 but hardly produce interferon- γ , IL-4, or IL-5. But CD62L^{lo} CCR7[−] cells rapidly produced these effector cytokines but produced little IL-2. CCR7⁺ cells named as central memory (T_{CM}) cells [13, 14] are potential enough to produce numerous IL-2 but low lying of effector cytokines and home to secondary lymphoid tissues. But CCR7[−] cells termed as effector memory (T_{EM}) cells [14] are capable of producing high order of cytokines and home to peripheral tissues. Subsequently, there are various other subpopulations of memory T cells such as memory T stem cells (T_{SCM} , multiple stem-like properties), T naive phenotype (T_N), and transitional memory T cells (T_{TM}) [13, 14], very many of which were secreted in the peripheral blood of healthy individuals.

Regulatory T cells (T_{reg}) [16] are inevitable for monitoring peripheral tolerance, preventing self-generating immunity, and reducing chronic inflammatory disease. In fact, T_{reg} have varied mechanisms within their powers, and one such mechanism is the suppression by inhibitory cytokines which include IL-10, transforming (TGF- β), and latest identified IL-35 which are prime mediators of T_{reg} cell function. CD4⁺CD25⁺FOXP3⁺ circulating T_{reg} play a primary role in restricting immune responses by downregulating CD4⁺ or CD8⁺ cell functions. Hectic suppression by T_{reg} is important in regulating immune responses against MTB.

In spite of the fact that the role of CD8 T cells [13] in TB is less clear than that of CD4 T cells, they are considered in general to impart optimal immunity and protection. CD8 T cells contain enumerable antimicrobial effector mechanisms that are less vital or cease to exist in CD4 Th1 and Th17 T cells. CD8 T cells emit cytokines or cytotoxic molecules, which cause apoptosis of target cells. Th1 CD4 T cells propel effector functions in macrophages that contain intracellular MTB, and their role has been monitored with protection. Besides, many studies have depicted that Th17 cells, which can produce IL-17, are implicated in immune protection against MTB, mainly due to the effect of this

cytokine in incurring and vibrating neutrophils. Th 17 cells have been implicated in the protection against TB at initial levels, for their power to employ monocytes and Th1 lymphocytes to the space of granuloma formation [5]. Contrarily, very many studies have manifested that unrestricted Th17 stimulation confirms an exaggerated inflammation catalyzed by neutrophils and inflammatory monocytes that rush to the place of disease during the damage of tissue.

MTB-specific CD4+ T-cell protective response is simply due to Th1 cells and is negotiated by IFN- γ and TNF- α that employ monocytes and granulocytes and enhance their antimicrobial attitudes. Subsequently, higher part of antigen-specific effector memory cells and diminished frequency of central memory CD4+ T cells have been discovered in patients with active TB in comparison with distribution witness in LTBI individuals. All the information converges on the increase of this complicated disease with the aim of improving diagnosis, prognosis, drug therapy, and vaccination.

Zhang [17] acclaimed the following host tuberculosis model:

$$\begin{aligned}\frac{dB}{dt} &= \delta B \left(1 - \frac{B}{K}\right) + M_i \left(\eta_1 b + \eta_2 \gamma \frac{T}{c+T}\right) - M_u B (\zeta + \eta_3 \beta), \\ \frac{dM_u}{dt} &= s_M - \mu_M M_u - \beta M_u B, \\ \frac{dM_i}{dt} &= \beta M_u B - b M_i - \gamma M_i \frac{T}{c+T}, \\ \frac{dT}{dt} &= s_T + c_M M_i \frac{T}{1+e_m T} + c_B B \frac{T}{1+e_B T} - \mu_T T.\end{aligned}\quad (1)$$

The biological meaning of all positive parameters and symbols in the deterministic TB model (1) are listed in Table 1. According to the theory in [17], the deterministic TB model (1) has the following properties:

The positive invariant set Γ is given by

$$\Gamma = \left\{ (B, M_u, M_i, T) \in \mathbb{R}_+^4 : B(t) < \mathcal{B}, (M_u + M_i)(t) \leq \frac{s_M}{\min\{\mu_M, b\}}, T(t) < \frac{1}{\mu_T} \left(s_T + \frac{c_M}{e_M} \mathcal{M} + \frac{c_B}{e_B} \mathcal{B} \right), \text{ where } \mathcal{M} := \frac{s_M}{\min\{\mu_M, b\}} \right\}. \quad (2)$$

The disease-free equilibrium is given by $E_0 = (M_{u_0}, T_0, B_0, M_{i_0}) = ((s_M/\mu_M), (s_T/\mu_T), 0, 0)$.

If $\mathcal{R}_0 \leq 1$, then the disease-free equilibrium is globally asymptotically stable, where $\mathcal{R}_0 = \delta \mu_M / 2(\eta_3 \beta + \zeta) s_M + (1/2) \sqrt{(4\beta(c\mu_T + s_T)(\eta_1 b + (\eta_2 \gamma s_T / \mu_T c + s_T)) / (\eta_3 \beta + \zeta)(bc\mu_T + bs_T + \gamma s_T)) + (\delta^2 \mu_M^2 / (\eta_3 \beta + \zeta)^2 s_M^2)}$.

The tuberculosis model (1) has a unique positive infected equilibrium E_1 if and only if $\mathcal{R}_0 > 1$ and it is globally asymptotically stable when it exists. The positive infected equilibrium $E_1 = (M_{u_1}, T_1, B_1, M_{i_1})$, where $M_{u_1} = (s_M / \beta B_1 + \mu_M)$, $M_{i_1} = (\beta s_M B_1 (T_1 + c) / (\beta B_1 + \mu_M)(bc + bT_1 + \gamma T_1))$, and

$$T_1 = \frac{-c(((\beta B_1 + \mu_M)\delta + ((\eta_1 - \eta_3)\beta - \zeta)s_M)K - \delta B_1(\beta B_1 + \mu_M))b}{((\gamma + b)(\beta B_1 + \mu_M)\delta + (((\eta_1 - \eta_3)b + \gamma(\eta_2 - \eta_3))\beta - \zeta(\gamma + b)s_M)K - \delta B_1(\gamma + b)(\beta B_1 + \mu_M))}, \quad (3)$$

and B_1 is determined by

$$f(B_1) = \frac{dT}{dt}|_{M_{u_1}, T_1, M_{i_1}} = (c_B T_1 (e_M T_1 + 1))B_1 + (-e_M \mu_T T_1^2 + (c_M M_{i_1} + e_M s_T - \mu_T)T_1 + s_T)(e_B T_1 + 1) = 0. \quad (4)$$

In reality, the environmental noise perverts through and medal with the population dynamics, ecology, environmental sciences, and mathematical biology. Stochasticity has its impact upon various biological [18–25] and other models [26–30]. Many researchers probed stochastic tuberculosis models in which the total host population can be divided into three, four, and five epidemiological classes,

respectively, such as susceptible (S), exposed (E), and infected (I) [31]; susceptible (S), latent (L), infectious (I), and treated (T) [32]; susceptible (S), exposed (E), infected (I), and recovered (R) [33]; and susceptible (S), vaccinated (V), infected with TB in latent stage (L), infected with TB in active stage (I), and treated individuals infected with TB (T) [34, 35]. On the other hand, Khalid Hattaf et al. [36, 37]

TABLE 1: Biological meaning of variables and parameters of the deterministic model (1).

Symbol	Interpretation
<i>Variables</i>	
$B(t)$	<i>Mycobacterium tuberculosis</i> (MTB) population at time t
$M_u(t)$	Population of uninfected macrophages at time t
$M_i(t)$	Population of infected macrophages at time t
$T(t)$	Population of immune response CD4+ T cells at time t
<i>Parameters</i>	
δ	Bacterium growth rate
K	Carrying capacity
η_1	Death rate of infected macrophages
η_2	Extracellular bacteria (B) rate by burst
η_3	Engulfment rate of uninfected macrophages
c	Half saturation rate in uninfected macrophages
ζ	Killing rate of extracellular bacteria
s_M	Influx rate of uninfected macrophages
μ_M	Death rates of uninfected macrophages
β	Infection rates of uninfected macrophages
b	Killing rate of infected macrophages
γ	Cell-mediated adaptive immune response rate
s_T	Natural recruitment rate of activated CD4+ T cells
c_B	Maximum killing rates of extracellular bacteria macrophages
c_M	Maximum killing rates of infected macrophages
e_B	Saturating factor of extracellular bacteria macrophages
e_M	Saturating factor of infected macrophages
μ_T	Death rate of activated CD4+ T cells

investigated specific functional response and temporary immunity and delayed viral infection models with adaptive immune response like cytotoxic T lymphocyte (CTL) cells which is in MHC class I molecules. In all the above models such as SEI, SLIT, SEIR, SVLIT, the researchers probed on host population, temporary immunity, and CTL cells. However, the authors have not examined the functions of macrophages and immune response CD4+ T cells which are in MHC class II molecules so far.

The macrophages inundate the MTB and quarantine them in a cellular compartment where the bacteria are killed or cannot thrive. If the number of MTB is higher than that of macrophages, it will result in the death of the macrophages in the granuloma. Then the granuloma's core liquidizes and is transmitted through airways to other people. During infection, the MTB cells set sporadically in the alveoli of an individual. The immunologic effects of both infected and uninfected macrophages vary randomly due to environmental sources of MTB. The adaptive immune responses in

an individual start with very few number of cells and later vary greatly among individual immune systems. This variation is random, and on the other hand, individuals with smoking habit, weak immunity, malnutrition, etc., possess low immune response and have to be treated with more dosages of antigens to increase the immunity contingently.

This study is challenging and useful in the sense that TB in its various dimensions and nature can be disclosed. Based on the above factors, we put forth the stochastic host-pathogen TB model with adaptive immune response. The stochastic host-pathogen TB model on the basis of the influence of the environment on the *Mycobacterium tuberculosis* and macrophage population was manifested by stochastic perturbations and it is proportional to each state [38, 39].

We establish the following stochastic host-pathogen TB model:

$$\begin{aligned}
 dB(t) &= \left[\delta B \left(1 - \frac{B}{K} \right) + M_i \left(\eta_1 b + \eta_2 \gamma \frac{T}{c+T} \right) - M_u B (\zeta + \eta_3 \beta) \right] dt + \sigma_1 B dW_1(t), \\
 dM_u(t) &= [s_M - \mu_M M_u - \beta M_u B] dt + \sigma_2 M_u dW_2(t), \\
 dM_i(t) &= \left[\beta M_u B - b M_i - \gamma M_i \frac{T}{c+T} \right] dt + \sigma_3 M_i dW_3(t), \\
 dT(t) &= \left[s_T + c_M M_i \frac{T}{1+e_M T} + c_B B \frac{T}{1+e_B T} - \mu_T T \right] dt + \sigma_4 T dW_4(t).
 \end{aligned} \tag{5}$$

Let $W(t) = (W_1(t), W_2(t), W_3(t), W_4(t))$ be a 4-dimensional Wiener process defined on the given probability space. The components of $W(t)$ are supposed to be mutually independent. In the stochastic model (5), the nonnegative constants $\sigma_1, \sigma_2, \sigma_3$, and σ_4 denote the intensities of the environmental white noise.

The intention of this literature is structured as follows. In Section 2, the existence of the global and positive solutions to the stochastic host-pathogen TB model (5) is examined. In Section 3, sufficient conditions for the extinction of the tubercle bacillus are probed. In Section 4, we probe that there is a unique ergodic stationary distribution of the positive solutions of the stochastic TB model (5) under some conditions. In Section 5, we demonstrate some numerical simulations that validate our analytical findings. Eventually, Section 6 provides conclusions and future directions.

2. Global Positive Solutions of the Stochastic TB Model

Since B, M_u, M_i , and T in the stochastic TB system (5) denotes the population of MTB, uninfected macrophages, infected macrophages, and immune response CD4+ T cells, respectively, they should be nonnegative. For a stochastic differential equation to have a unique global (i.e., no explosion in a finite time) solution for any given initial value,

the coefficients of the equation are eventually required to satisfy the linear growth condition and local Lipschitz condition. Yet, the coefficients of equation (5) do not satisfy the linear growth condition; nevertheless, they are locally Lipschitz continuous, and thus, the solution of equation (5) may explode at a finite time. Hence, for further studies, we should set some preconditions under which stochastic system (5) has unique global positive solutions.

Theorem 1. *For any given initial value $(B(0), M_u(0), M_i(0), T(0)) \in \mathbb{R}_+^4$, there exists unique positive solutions $(B(t), M_u(t), M_i(t), T(t))$ of the stochastic TB model (5) on $t \geq 0$ and the solution will remain in $\mathbb{R}_+^4$ with probability one.*

Proof. It is clear that the stochastic TB system (5) satisfies the local Lipschitz condition for any given initial value $(B(0), M_u(0), M_i(0), T(0)) \in \mathbb{R}_+^4$. Then, there exist unique maximum local solutions $(B(t), M_u(t), M_i(t), T(t))$ on $t \in [0, \tau_*)$, where τ_* is the explosion time [43]. To exhibit that the solution is universal, i.e., inevitable to affirm that $\tau_* = \infty$ a.s. Basically, we exhibit that $B(t), M_u(t), M_i(t)$, and $T(t)$ do not explode to infinity in a finite time. Let $\kappa_0 > 0$ be adequately large $(B(0), M_u(0), M_i(0), T(0)) \in [(1/\kappa_0), \kappa_0]$. For each integer $\kappa \geq \kappa_0$, define the stopping time [40]:

$$\tau_\kappa = \inf \left\{ t \in [0, \tau_*) : \min\{B(t), M_u(t), M_i(t), T(t)\} \leq \frac{1}{\kappa} \text{ or } \max\{B(t), M_u(t), M_i(t), T(t)\} \geq \kappa \right\}, \quad (6)$$

with the typical format $\inf \phi = \infty$, where ϕ reflects the empty set. Evidently, τ_κ is increasing as $\kappa \rightarrow \infty$. We have $\tau_\infty = \lim_{\kappa \rightarrow \infty} \tau_\kappa$; therefore, $\tau_\infty \leq \tau_*$ a.s. If we evince that $\tau_\infty = \infty$ a.s., then $\tau_* = \infty$ and $(B(t), M_u(t), M_i(t), T(t)) \in \mathbb{R}_+^4$ a.s. for all $t \geq 0$. Presume that $\tau_\infty < \infty$, then there is a pair of constants $\tilde{T} > 0$ and $\varepsilon \in (0, 1)$ such that

$$\mathbb{P}\{\tau_\infty \leq \tilde{T}\} > \varepsilon. \quad (7)$$

Thus, there exists an integer $\kappa_1 \geq \kappa_0$ such that

$$\mathbb{P}\{\tau_\kappa \leq \tilde{T}\} \geq \varepsilon, \quad \text{for all } \kappa \geq \kappa_1. \quad (8)$$

Define a $\mathcal{C}^2$ -function $V: \mathbb{R}_+^4 \rightarrow \mathbb{R}_+$ by

$$V(B, M_u, M_i, T) = \varphi_2 \left(B - \varphi_1 - \varphi_1 \ln \frac{B}{\varphi_1} \right) + (M_u - 1 - \ln M_u) + (M_i - 1 - \ln M_i) + \varphi_2 (T - 1 - \ln T), \quad (9)$$

where $\varphi_1 > 0$ and $\varphi_2 > 0$ will be determined later. The nonnegativity of $V(B, M_u, M_i, T)$ function occurs from $u - 1 - \ln u \geq 0, \forall u > 0$.

By Itô's formula to V , we obtain

$$\begin{aligned} dV = & \mathcal{L}V dt + \varphi_2 \sigma_1 (B - \varphi_1) dW_1 + \sigma_2 (M_u - 1) dW_2 \\ & + \sigma_3 (M_i - 1) dW_3 + \varphi_2 \sigma_4 (T - 1) dW_4, \end{aligned} \quad (10)$$

where $\mathcal{L}V: \mathbb{R}_+^4 \rightarrow \mathbb{R}_+$ is defined as

$$\begin{aligned}
\mathcal{L}V &= \varphi_2 \left(1 - \frac{\varphi_1}{B}\right) \left[\delta B \left(1 - \frac{B}{K}\right) + M_i \left(\eta_1 b + \eta_2 \gamma \frac{T}{c+T}\right) - M_u B (\zeta + \eta_3 \beta) \right] + \frac{\varphi_1 \varphi_2 \sigma_1^2}{2} \\
&+ \left(1 - \frac{1}{M_u}\right) \left[s_M - \mu_M M_u - \beta M_u B \right] + \frac{\sigma_2^2}{2} + \left(1 - \frac{1}{M_i}\right) \left[\beta M_u B - b M_i - \gamma M_i \frac{T}{c+T} \right] \\
&+ \frac{\sigma_3^2}{2} + \varphi_2 \left(1 - \frac{1}{T}\right) \left[s_T + c_M M_i \frac{T}{1+e_m T} + c_B B \frac{T}{1+e_B T} - \mu_T T \right] + \frac{\varphi_2 \sigma_4^2}{2}, \\
\mathcal{L}V &= -\frac{\varphi_2 \delta}{K} B^2 + \frac{\varphi_2 \delta (\varphi_1 + K)}{K} B - \varphi_1 \varphi_2 \delta + \varphi_2 M_i \left(\eta_1 b + \eta_2 \gamma \frac{T}{c+T}\right) - \varphi_2 M_u B (\zeta + \eta_3 \beta) \\
&- \frac{\varphi_1 \varphi_2 M_i}{B} \left(\eta_1 b + \eta_2 \gamma \frac{T}{c+T}\right) + \varphi_1 \varphi_2 M_u (\zeta + \eta_3 \beta) + s_M - \mu_M M_u - \frac{s_M}{M_u} + \mu_M + \beta B \\
&- b M_i - \gamma M_i \frac{T}{c+T} - \frac{1}{M_i} (\beta M_u B) + b + \gamma \frac{T}{c+T} + \varphi_2 s_T + \frac{\varphi_2 c_M M_i T}{1+e_m T} + \frac{\varphi_2 c_B B T}{1+e_B T} \\
&- \varphi_2 \mu_T T - \frac{\varphi_2 s_T}{T} - \frac{\varphi_2 c_M M_i}{1+e_m T} - \frac{\varphi_2 c_B B}{1+e_B T} + \varphi_2 \mu_T + \frac{\varphi_1 \varphi_2 \sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \frac{\sigma_3^2}{2} + \frac{\varphi_2 \sigma_4^2}{2}, \\
\mathcal{L}V &\leq \max_{B \in \mathbb{R}_+} \left\{ -\frac{\varphi_2 \delta}{K} B^2 + \frac{\varphi_2 \delta (\varphi_1 + K) + K\beta + K\varphi_2 c_B}{K} B \right\} + (\varphi_1 \varphi_2 (\zeta + \eta_3 \beta) - \mu_M) M_u \\
&+ (\varphi_2 (\eta_1 b + \eta_2 \gamma + c_M) - b) M_i + s_M + \mu_M + b + \gamma + \varphi_2 s_T + \varphi_2 \mu_T + \frac{\varphi_1 \varphi_2 \sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \frac{\sigma_3^2}{2} + \frac{\varphi_2 \sigma_4^2}{2}.
\end{aligned} \tag{11}$$

Choose $\varphi_2 = (b/\eta_1 b + \eta_2 \gamma + c_M)$ such that $\varphi_2 (\eta_1 b + \eta_2 \gamma + c_M) - b = 0$ and let $\varphi_1 = (\mu_M/\varphi_2 (\zeta + \eta_3 \beta))$ such that $\varphi_1 \varphi_2 (\zeta + \eta_3 \beta) - \mu_M = 0$, and then we have

$$\mathcal{L}V \leq \max_{B \in \mathbb{R}_+} \left\{ -\frac{\varphi_2 \delta}{K} B^2 + \frac{\varphi_2 \delta (\varphi_1 + K) + K\beta + K\varphi_2 c_B}{K} B \right\} + s_M + \mu_M + b + \gamma + \varphi_2 s_T + \varphi_2 \mu_T + \frac{\varphi_1 \varphi_2 \sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \frac{\sigma_3^2}{2} + \frac{\varphi_2 \sigma_4^2}{2} := \Lambda, \tag{12}$$

where Λ is a positive constant. Thus,

$$\begin{aligned}
dV &\leq \Lambda dt + \varphi_2 \sigma_1 (B - \varphi_1) dW_1 + \sigma_2 (M_u - 1) dW_2 \\
&+ \sigma_3 (M_i - 1) dW_3 + \varphi_2 \sigma_4 (T - 1) dW_4.
\end{aligned} \tag{13}$$

Integrate both sides of equation (13) from 0 to $\tau_\kappa \wedge \tilde{T} = \min\{\tau_\kappa, \tilde{T}\}$,

$$\begin{aligned}
\int_0^{\tau_\kappa \wedge \tilde{T}} dV(B(\tau), M_u(\tau), M_i(\tau), T(\tau)) &\leq \int_0^{\tau_\kappa \wedge \tilde{T}} \Lambda dt + \int_0^{\tau_\kappa \wedge \tilde{T}} (\varphi_2 \sigma_1 (B - \varphi_1) dW_1 + \sigma_2 (M_u - 1) dW_2 \\
&+ \sigma_3 (M_i - 1) dW_3 + \varphi_2 \sigma_4 (T - 1) dW_4).
\end{aligned} \tag{14}$$

Taking expectations on both sides of (14) yields

$$\begin{aligned} \mathbb{E}V(B(\tau_\kappa \wedge \tilde{T}), M_u(\tau_\kappa \wedge \tilde{T}), M_i(\tau_\kappa \wedge \tilde{T}), T(\tau_\kappa \wedge \tilde{T})) &\leq V(B(0), M_u(0), M_i(0), T(0)) + \mathbb{E} \int_0^{\tau_\kappa \wedge \tilde{T}} \Lambda d\tau, \\ \mathbb{E}V(B(\tau_\kappa \wedge \tilde{T}), M_u(\tau_\kappa \wedge \tilde{T}), M_i(\tau_\kappa \wedge \tilde{T}), T(\tau_\kappa \wedge \tilde{T})) &\leq V(B(0), M_u(0), M_i(0), T(0)) + \Lambda \tilde{T}. \end{aligned} \quad (15)$$

Let $\Omega_\kappa = \{\tau_\kappa \leq \tilde{T}\}$ for all $\kappa \geq \kappa_1$, and by (8), then $\mathbb{P}(\Omega_\kappa) \geq \varepsilon$. Notice that for every $\omega \in \Omega_\kappa$, there exists at least

$B(\tau_\kappa, \omega)$ or $M_u(\tau_\kappa, \omega)$ or $M_i(\tau_\kappa, \omega)$ or $T(\tau_\kappa, \omega)$ which is equal to either κ or $(1/\kappa)$.

If $B(\tau_\kappa, \omega) = \kappa$ or $(1/\kappa)$, then

$$\begin{aligned} (B(\tau_\kappa, \omega), M_u(\tau_\kappa, \omega), M_i(\tau_\kappa, \omega), T(\tau_\kappa, \omega)) &\geq \varphi_2 \left[\left(\kappa - \varphi_1 - \varphi_1 \ln \frac{\kappa}{\varphi_1} \right) \wedge \left(\frac{1}{\kappa} - \varphi_1 - \varphi_1 \ln \frac{1}{\varphi_1 \kappa} \right) \right] \\ &= \varphi_1 \varphi_2 \left[\left(\frac{\kappa}{\varphi_1} - 1 - \ln \frac{\kappa}{\varphi_1} \right) \wedge \left(\frac{1}{\kappa \varphi_1} - 1 + \ln \varphi_1 \kappa \right) \right]. \end{aligned} \quad (16)$$

Similarly, if $M_u(\tau_\kappa, \omega) = \kappa$ or $(1/\kappa)$, then

$$\begin{aligned} (B(\tau_\kappa, \omega), M_u(\tau_\kappa, \omega), M_i(\tau_\kappa, \omega), T(\tau_\kappa, \omega)) \\ \geq (\kappa - 1 - \ln \kappa) \wedge \left(\frac{1}{\kappa} - 1 + \ln \kappa \right). \end{aligned} \quad (17)$$

If $M_i(\tau_\kappa, \omega) = \kappa$ or $(1/\kappa)$, then

$$\begin{aligned} (B(\tau_\kappa, \omega), M_u(\tau_\kappa, \omega), M_i(\tau_\kappa, \omega), T(\tau_\kappa, \omega)) \\ \geq (\kappa - 1 - \ln \kappa) \wedge \left(\frac{1}{\kappa} - 1 + \ln \kappa \right). \end{aligned} \quad (18)$$

If $T(\tau_\kappa, \omega) = \kappa$ or $(1/\kappa)$, then

$$\begin{aligned} (B(\tau_\kappa, \omega), M_u(\tau_\kappa, \omega), M_i(\tau_\kappa, \omega), T(\tau_\kappa, \omega)) \\ \geq \varphi_2 \left[(\kappa - 1 - \ln \kappa) \wedge \left(\frac{1}{\kappa} - 1 + \ln \kappa \right) \right]. \end{aligned} \quad (19)$$

Therefore,

$$\begin{aligned} (B(\tau_\kappa, \omega), M_u(\tau_\kappa, \omega), M_i(\tau_\kappa, \omega), T(\tau_\kappa, \omega)) &\geq \varphi_1 \varphi_2 \left[\left(\frac{\kappa}{\varphi_1} - 1 - \ln \frac{\kappa}{\varphi_1} \right) \wedge \left(\frac{1}{\kappa \varphi_1} - 1 + \ln \varphi_1 \kappa \right) \right] \\ &\quad \wedge (\kappa - 1 - \ln \kappa) \wedge \left(\frac{1}{\kappa} - 1 + \ln \kappa \right) \wedge \varphi_2 (\kappa - 1 - \ln \kappa) \wedge \left(\frac{1}{\kappa} - 1 + \ln \kappa \right). \end{aligned} \quad (20)$$

Then, we attain

$$\begin{aligned} V(B(0), M_u(0), M_i(0), T(0)) + \Lambda \tilde{T} &\geq \mathbb{E}(1_{\Omega_\kappa}(\omega) V(B(\tau_\kappa \wedge \tilde{T}), M_u(\tau_\kappa \wedge \tilde{T}), M_i(\tau_\kappa \wedge \tilde{T}), T(\tau_\kappa \wedge \tilde{T}))), \\ &= \mathbb{E}(1_{\Omega_\kappa}(\omega) V(B(\tau_\kappa, \omega), M_u(\tau_\kappa, \omega), M_i(\tau_\kappa, \omega), T(\tau_\kappa, \omega))), \\ &\geq \mathbb{E} \left[1_{\Omega_\kappa}(\omega) \varphi_1 \varphi_2 \left(\left(\frac{\kappa}{\varphi_1} - 1 - \ln \frac{\kappa}{\varphi_1} \right) \wedge \left(\frac{1}{\kappa \varphi_1} - 1 + \ln \varphi_1 \kappa \right) \right) \wedge (\kappa - 1 - \ln \kappa) \wedge \left(\frac{1}{\kappa} - 1 + \ln \kappa \right) \wedge \varphi_2 ((\kappa - 1 - \ln \kappa) \wedge \left(\frac{1}{\kappa} - 1 + \ln \kappa \right)) \right], \\ V(B(0), M_u(0), M_i(0), T(0)) + \Lambda \tilde{T} &\geq \varepsilon \left\{ \varphi_1 \varphi_2 \left(\left(\frac{\kappa}{\varphi_1} - 1 - \ln \frac{\kappa}{\varphi_1} \right) \wedge \left(\frac{1}{\kappa \varphi_1} - 1 + \ln \varphi_1 \kappa \right) \right) \wedge (\kappa - 1 - \ln \kappa) \wedge \left(\frac{1}{\kappa} - 1 + \ln \kappa \right) \wedge \varphi_2 ((\kappa - 1 - \ln \kappa) \wedge \left(\frac{1}{\kappa} - 1 + \ln \kappa \right)) \right\}, \end{aligned} \quad (21)$$

where 1_{Ω_κ} is the indicator function of $\Omega_\kappa(\omega)$. Letting $\kappa \rightarrow \infty$, we get $\infty > V(B(0), M_u(0), M_i(0), T(0)) + \Lambda\tilde{T} = \infty$. It is a contradiction, and hence, we obtain $\tau_\infty = \infty$ a.s., which completes the proof of Theorem 1. $\square$

Remark 1. Considering the region $\mathbb{R}_+^4$ is positively invariant, the unique solution of the stochastic TB model (5) exists for any given initial value in $\mathbb{R}_+^4$. Hence, it is sufficient to probe its dynamics of the host-pathogen stochastic TB model in the region $\mathbb{R}_+^4$.

Remark 2. As stated in the introduction, immunotherapy with LTBI and active TB individuals and adaptive immune responses are known to be quite effective against MTB. However, the prevailing opinion among public health and medical practitioners in the entire world, prior to 1944 [44], was a less effective treatment for TB patients. During the years between 2016 and 2035, the efforts at the global, regional, and national levels to ease and eradicate the burden of TB disease have the colossus objective “ceasing TB epidemic,” within the purview of the UN’s Agenda for Sustainable Development and based on the WHO’s End TB Strategy [1]. Hence, it is fruitful to study the eradication of the MTB among LTBI and active TB individuals. This is done as follows.

3. Extinction of the MTB

In this section, the extinction of the MTB is discussed. The death rate of uninfected macrophages and the intensities of the white noise in the stochastic system (5) are the consequences of the random fluctuations. The population dynamics show direct results on the qualitative outcome of the MTB dynamics in the system with regard to the factors that decide MTB eradication during the long course of time. Firstly, we shall present a lemma which will be used in our analysis.

Lemma 1. Let $(B(t), M_u(t), M_i(t), T(t))$ be the solution of the stochastic TB system (5) with any positive initial value $(B(0), M_u(0), M_i(0), T(0)) \in \mathbb{R}_+^4$. Then

$$\begin{aligned} \lim_{t \rightarrow \infty} \frac{B(t)}{t} &= 0, \\ \lim_{t \rightarrow \infty} \frac{M_u(t)}{t} &= 0, \\ \lim_{t \rightarrow \infty} \frac{M_i(t)}{t} &= 0, \\ \lim_{t \rightarrow \infty} \frac{T(t)}{t} &= 0 \text{ a.s.} \end{aligned} \quad (22)$$

Moreover, if $\mu_M > ((\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)/2)$, then

$$\begin{aligned} \lim_{t \rightarrow \infty} \frac{\int_0^t B(\tau) dW_1(\tau)}{t} &= 0, \\ \lim_{t \rightarrow \infty} \frac{\int_0^t M_u(\tau) dW_2(\tau)}{t} &= 0, \\ \lim_{t \rightarrow \infty} \frac{\int_0^t M_i(\tau) dW_3(\tau)}{t} &= 0, \\ \lim_{t \rightarrow \infty} \frac{\int_0^t T(\tau) dW_4(\tau)}{t} &= 0. \end{aligned} \quad (23)$$

Define a parameter as follows:

$$\widetilde{\mathcal{R}}_0 = \frac{4[\beta s_M + \mu_M(\delta + bN_1 + \gamma N_2)]}{\mu_M(\sigma_1^2 \wedge \sigma_3^2)}. \quad (24)$$

Theorem 2. For any given initial value $(B(0), M_u(0), M_i(0), T(0)) \in \mathbb{R}_+^4$, then the MTB of the stochastic TB system (5) will cease out if $\mu_M > ((\sigma_1^2 \vee \sigma_3^2)/2)$ and $\widetilde{\mathcal{R}}_0 < 1$, i.e., $\lim_{t \rightarrow \infty} B(t) = 0, \lim_{t \rightarrow \infty} M_i(t) = 0$ a.s.

Proof. Consider the second and third equations of the stochastic TB system (5). Integrating these equations from 0 to t and dividing both sides by t , we get

$$\begin{aligned} \frac{M_u(t) - M_u(0)}{t} + \frac{M_i(t) - M_i(0)}{t} &= s_M - \mu_M \langle M_u \rangle \\ &\quad - b \langle M_i \rangle - \gamma \langle M_i \frac{T}{c+T} \rangle + \frac{\sigma_2}{t} \int_0^t M_u(\tau) dW_2(\tau) \\ &\quad + \frac{\sigma_3}{t} \int_0^t M_i(\tau) dW_3(\tau). \end{aligned} \quad (25)$$

It follows that

$$\langle M_u \rangle \leq \frac{1}{\mu_M} \left[s_M - \frac{M_u(t) - M_u(0)}{t} - \frac{M_i(t) - M_i(0)}{t} + \frac{\sigma_2}{t} \int_0^t M_u(\tau) dW_2(\tau) + \frac{\sigma_3}{t} \int_0^t M_i(\tau) dW_3(\tau) \right] \quad (26)$$

Consequently,

$$\lim_{t \rightarrow \infty} \langle M_u \rangle \leq \frac{1}{\mu_M} \lim_{t \rightarrow \infty} \left[s_M - \frac{M_u(t) - M_u(0)}{t} - \frac{M_i(t) - M_i(0)}{t} + \frac{\sigma_2}{t} \int_0^t M_u(\tau) dW_2(\tau) + \frac{\sigma_3}{t} \int_0^t M_i(\tau) dW_3(\tau) \right]. \quad (27)$$

By Lemma 1, we have

$$\lim_{t \rightarrow \infty} \langle M_u \rangle \leq \frac{s_M}{\mu_M} \text{ a.s.} \quad (28)$$

On the other hand, let $P(t) = B(t) + M_i(t)$. Applying Itô's formula, we obtain

$$\begin{aligned} d \ln P(t) &= \frac{1}{B + M_i} \left[\delta B \left(1 - \frac{B}{K} \right) + M_i \left(\eta_1 b + \eta_2 \gamma \frac{T}{c + T} \right) - M_u B (\zeta + \eta_3 \beta) + \beta M_u B - b M_i \right. \\ &\quad \left. - \gamma M_i \frac{T}{c + T} - \frac{1}{2(B + M_i)^2} (\sigma_1^2 B^2 + \sigma_3^2 M_i^2) \right] dt \\ &\quad + \frac{\sigma_1 B}{B + M_i} dW_1(t) + \frac{\sigma_3 M_i}{B + M_i} dW_3(t), \\ d \ln P(t) &\leq \frac{1}{B + M_i} \left[\delta B + M_i b (\eta_1 - 1) + M_i \gamma \frac{T}{c + T} (\eta_2 - 1) + \beta M_u B - \frac{1}{2(B + M_i)^2} (\sigma_1^2 B^2 + \sigma_3^2 M_i^2) \right] dt \\ &\quad + \frac{\sigma_1 B}{B + M_i} dW_1(t) + \frac{\sigma_3 M_i}{B + M_i} dW_3(t), \\ &\leq \left[\delta + b N_1 + \gamma N_2 + \beta M_u - \frac{1}{4} (\sigma_1^2 \wedge \sigma_3^2) \right] dt + \frac{\sigma_1 B}{B + M_i} dW_1(t) + \frac{\sigma_3 M_i}{B + M_i} dW_3(t), \end{aligned} \quad (29)$$

where $N_1 = (\eta_1 - 1) > 0$ and $N_2 = (\eta_2 - 1) > 0$.

Integrating both sides of (28) from 0 to t , we attain

$$\begin{aligned} \ln(B(t) + M_i(t)) &\leq \ln(B(0) + M_i(0)) + \beta \int_0^t M_u(\tau) d\tau + (\delta + b N_1 + \gamma N_2) t - \frac{t}{4} (\sigma_1^2 \wedge \sigma_3^2) \\ &\quad + \int_0^t \frac{\sigma_1 B}{B + M_i} dW_1(\tau) + \int_0^t \frac{\sigma_3 M_i}{B + M_i} dW_3(\tau). \end{aligned} \quad (30)$$

Dividing both sides of by t and then taking the limit superior yield

$$\begin{aligned} \limsup_{t \rightarrow \infty} \frac{\ln(B(t) + M_i(t))}{t} &\leq \beta \frac{s_M}{\mu_M} + (\delta + b N_1 + \gamma N_2) - \frac{1}{4} (\sigma_1^2 \wedge \sigma_3^2), \\ &= \frac{1}{4} (\sigma_1^2 \wedge \sigma_3^2) \left(\frac{4[\beta s_M + \mu_M (\delta + b N_1 + \gamma N_2)]}{\mu_M (\sigma_1^2 \wedge \sigma_3^2)} - 1 \right), \\ &= \frac{1}{4} (\sigma_1^2 \wedge \sigma_3^2) (\widetilde{\mathcal{R}}_0 - 1) < 0. \end{aligned} \quad (31)$$

The conclusion is confirmed. $\square$

Remark 3. The immunomodulatory agents are compatible to immune responses such as IL-2 and IL-4 to effectively active T helper cells. Immunosuppressive agents such as TNF- α moderate dangerous inflammation and cytokine therapy INF- γ tends to accelerate the mycobacterial activity of effector immune cells [42]. All these facts exist in reality, which wipe out the MTB.

Remark 4. Patients have lack of information, lack of money for treatment, side effects, lack of commitment to a long course, social barriers, irregular treatment and do not take proper drugs and so they have a low level of immunity. These are the factors for the TB persistent and prevalence among population.

4. Ergodic Stationary Distribution

When considering epidemic dynamical systems, we are interested in when the disease will persist and prevail in a population. In this section, we present some theories about the stationary distribution (see Has'minskii [43]), and we show that there exists an ergodic stationary distribution, which reveals that the disease will persist. Let $X(t)$ be a homogeneous Markov process in $\mathbb{R}_+^4$, which is described by the following stochastic differential equation:

$$dX(t) = f(X(t))dt + \sum_{r=1}^k g_r(X)dw_r(t). \quad (32)$$

The diffusion matrix is defined as follows:

$$A(x) = (a_{ij}(x)), \quad a_{ij}(x) = \sum_{r=1}^k g_r^i(x)g_r^j(x). \quad (33)$$

Lemma 2 (see [39]). *The Markov process $X(t)$ has a unique ergodic stationary distribution $\pi(\cdot)$ if there exists a bounded domain $D \subset \mathbb{R}_+^4$ with regular boundary Γ , having the following properties:*

A_1 : *there is a positive number M such that $\sum_{i,j=1}^4 a_{ij}(x)\xi_i\xi_j \geq M|\xi|^2$, for $x \in D$, $\xi = (\xi_1, \xi_2, \xi_3, \xi_4) \in \mathbb{R}_+^4$.*

A_2 : *there exist a nonnegative $\mathcal{C}^2$ -function $V(x)$ and a positive constant $\bar{C}$ such that $\mathcal{L}V \leq -\bar{C}$ for any $x \in \mathbb{R}_+^4 \setminus D$. Then*

$$\mathbb{P} \left\{ \lim_{T \rightarrow \infty} \frac{1}{T} \int_0^T f(X(t))dt = \int_{\mathbb{R}_+^4} f(x)\pi(dx) \right\} = 1, \quad (34)$$

for all $x \in \mathbb{R}_+^4$, where $f(\cdot)$ is a function integrable with respect to the measure π .

Define a parameter

$$\mathcal{R}_0^s = \frac{s_M \beta}{(\vartheta + (\sigma_1^2/2))(\mu_M + (\sigma_2^2/2))(b + \gamma + (\sigma_3^2/2))} \left(\eta_1 b + \frac{\eta_2 \gamma s_T}{s_T + c\mu_T + (c\sigma_4^2/2)} \right), \quad (35)$$

where $\vartheta = \left(\frac{\zeta + \eta_3 \beta}{\mu_M} \right) s_M + (\zeta + \eta_3 \beta) M_{u_1} + \left(\frac{\zeta + \eta_3 \beta}{\mu_M} \right) \frac{M_{u_1} \sigma_2^2}{2}$.

Theorem 3. *Assume that $\mathcal{R}_0^s > 1$, then for any initial value $(B(0), M_u(0), M_i(0), T(0)) \in \mathbb{R}_+^4$, the stochastic TB system (5) admits a unique stationary distribution $\pi(\cdot)$ and it has the ergodic property.*

Proof. The diffusion matrix of the stochastic TB system (5) is given by

$$\begin{pmatrix} \sigma_1^2 B^2 & 0 & 0 & 0 \\ 0 & \sigma_2^2 M_u^2 & 0 & 0 \\ 0 & 0 & \sigma_3^2 M_i^2 & 0 \\ 0 & 0 & 0 & \sigma_4^2 T^2 \end{pmatrix}. \quad (36)$$

Select $\tilde{M} = \min_{(B, M_u, M_i, T) \in \tilde{D}_K \subset \mathbb{R}_+^4} \{\sigma_1^2 B^2, \sigma_2^2 M_u^2, \sigma_3^2 M_i^2, \sigma_4^2 T^2\}$, and we have

$$\begin{aligned} \sum_{i,j=1}^4 a_{ij}(B, M_u, M_i, T) \xi_i \xi_j &= (\sigma_1 B \xi_1 \quad \sigma_2 M_u \xi_2 \quad \sigma_3 M_i \xi_3 \quad \sigma_4 T \xi_4) \begin{pmatrix} \sigma_1 B \xi_1 \\ \sigma_2 M_u \xi_2 \\ \sigma_3 M_i \xi_3 \\ \sigma_4 T \xi_4 \end{pmatrix} \\ &= (\sigma_1 B)^2 \xi_1^2 + (\sigma_2 M_u)^2 \xi_2^2 + (\sigma_3 M_i)^2 \xi_3^2 + (\sigma_4 T)^2 \xi_4^2 \\ &\geq \tilde{M} \|\xi\|^2 \quad \text{for any } (B, M_u, M_i, T) \in \tilde{D}_K, \xi = (\xi_1, \xi_2, \xi_3, \xi_4) \in \mathbb{R}_+^4, \end{aligned} \quad (37)$$

where $\tilde{D}_k = [(1/k), k] \times [(1/k), k] \times [(1/k), k] \times [(1/k), k]$ and $k > 1$ is an adequately larger integer, and then condition A_1 in Lemma 2 holds.

Next, we tend to prove the condition A_2 . Define

$$V_1(B, M_u, M_i) = -\ln B - k_1 \ln M_u - k_2 \ln M_i, \quad (38)$$

where k_1 and k_2 are positive constants to be resolved later. By applying Itô's formula to V_1 , we get

$$\begin{aligned} \mathcal{L}V_1 &= \frac{-1}{B} \left(\delta B \left(1 - \frac{B}{K} \right) + M_i \left(\eta_1 b + \eta_2 \gamma \frac{T}{c+T} \right) - M_u B (\zeta + \eta_3 \beta) \right) + \frac{\sigma_1^2}{2} \\ &\quad - \frac{k_1}{M_u} (s_M - \mu_M M_u - \beta M_u B) + k_1 \frac{\sigma_2^2}{2} - \frac{k_2}{M_i} \left(\beta M_u B - b M_i - \gamma M_i \frac{T}{c+T} \right) + k_2 \frac{\sigma_3^2}{2}, \\ &= \frac{\delta B}{K} - \frac{M_i \eta_1 b}{B} - \frac{M_i \eta_2 \gamma}{B} \frac{T}{c+T} + M_u (\zeta + \eta_3 \beta) - \delta + \frac{\sigma_1^2}{2} - k_1 \frac{s_M}{M_u} + k_1 \mu_M + k_1 B \beta + k_1 \frac{\sigma_2^2}{2} \\ &\quad - k_2 \frac{\beta M_u B}{M_i} + k_2 b + k_2 \gamma \frac{T}{c+T} + k_2 \frac{\sigma_3^2}{2}, \\ &= -\frac{M_i \eta_1 b}{B} - k_1 \frac{s_M}{M_u} - k_2 \frac{\beta M_u B}{M_i} + \frac{\delta B}{K} - \frac{M_i \eta_2 \gamma}{B} \frac{T}{c+T} + M_u (\zeta + \eta_3 \beta) - \delta + \frac{\sigma_1^2}{2} + k_1 B \beta \\ &\quad + k_1 \left(\mu_M + \frac{\sigma_2^2}{2} \right) + k_2 b + k_2 \gamma \frac{T}{c+T} + k_2 \frac{\sigma_3^2}{2}, \\ \mathcal{L}V_1 &\leq -3\sqrt[3]{\eta_1 b s_M \beta k_1 k_2} + \frac{\delta B}{K} - \frac{M_i \eta_2 \gamma}{B} \frac{T}{c+T} + M_u (\zeta + \eta_3 \beta) + \frac{\sigma_1^2}{2} + k_1 B \beta + k_1 \left(\mu_M + \frac{\sigma_2^2}{2} \right) \\ &\quad + k_2 \left(b + \gamma + \frac{\sigma_3^2}{2} \right) - \delta. \end{aligned} \quad (39)$$

Choose

$$\begin{aligned} k_1 &= \frac{\eta_1 b s_M \beta}{\left(\mu_M + (\sigma_2^2/2) \right)^2 \left(b + \gamma + (\sigma_3^2/2) \right)}, \\ k_2 &= \frac{\eta_1 b s_M \beta}{\left(\mu_M + (\sigma_2^2/2) \right) \left(b + \gamma + (\sigma_3^2/2) \right)^2}. \end{aligned} \quad (40)$$

Then

$$\mathcal{L}V_1 \leq -\frac{\eta_1 b s_M \beta}{\left(\mu_M + (\sigma_2^2/2) \right) \left(b + \gamma + (\sigma_3^2/2) \right)} + \frac{\delta B}{K} - \frac{M_i \eta_2 \gamma}{B} \frac{T}{c+T} + M_u (\zeta + \eta_3 \beta) + \frac{\sigma_1^2}{2} + k_1 B \beta - \delta. \quad (41)$$

Define

$$V_2(B, M_u, M_i, T) = V_1(B, M_u, M_i) - k_3 c \ln T - k_4 \ln M_u - k_5 \ln M_i, \quad (42)$$

where k_3, k_4 , and k_5 are positive constants to be determined later. By calculating,

$$\begin{aligned}
 \mathcal{L}V_2 \leq & -\frac{M_i \eta_2 \gamma}{B} \frac{T}{c+T} - \frac{\eta_1 b s_M \beta}{(\mu_M + (\sigma_2^2/2))(b + \gamma + (\sigma_3^2/2))} + \frac{\delta B}{K} + M_u (\zeta + \eta_3 \beta) + \frac{\sigma_1^2}{2} + k_1 B \beta - \delta \\
 & - k_3 \frac{c}{T} \left(s_T + c_M M_i \frac{T}{1 + e_M T} + c_B B \frac{T}{1 + e_B T} - \mu_T T \right) + k_3 \frac{c \sigma_4^2}{2} - \frac{k_4}{M_u} (s_M - \mu_M M_u - \beta M_u B) + k_4 \frac{\sigma_2^2}{2} \\
 & - \frac{k_5}{M_i} \left(\beta M_u B - b M_i - \gamma M_i \frac{T}{c+T} \right) + k_5 \frac{\sigma_3^2}{2}, \\
 \leq & -\frac{M_i \eta_2 \gamma}{B} \frac{T}{c+T} - k_3 \frac{c+T}{T} s_T - k_4 \frac{s_M}{M_u} - k_5 \frac{\beta M_u B}{M_i} - \frac{\eta_1 b s_M \beta}{(\mu_M + (\sigma_2^2/2))(b + \gamma + (\sigma_3^2/2))} + \frac{\delta B}{K} \\
 & + M_u (\zeta + \eta_3 \beta) + \frac{\sigma_1^2}{2} + k_1 B \beta - \delta + k_3 s_T - k_3 c c_M M_i \frac{1}{1 + e_M T} - k_3 c c_B B \frac{1}{1 + e_B T} + k_3 c \mu_T \\
 & + k_3 \frac{c \sigma_4^2}{2} + k_4 \mu_M + k_4 B \beta + k_4 \frac{\sigma_2^2}{2} + k_5 b + k_5 \gamma \frac{T}{c+T} + k_5 \frac{\sigma_3^2}{2}, \\
 \mathcal{L}V_2 \leq & -4 \sqrt{\eta_2 \gamma s_T s_M \beta k_3 k_4 k_5} - \frac{\eta_1 b s_M \beta}{(\mu_M + (\sigma_2^2/2))(b + \gamma + (\sigma_3^2/2))} + \frac{\delta B}{K} + M_u (\zeta + \eta_3 \beta) + \frac{\sigma_1^2}{2} + k_1 B \beta \\
 & + k_4 B \beta + k_3 \left(s_T + c \mu_T + \frac{c \sigma_4^2}{2} \right) + k_4 \left(\mu_M + \frac{\sigma_2^2}{2} \right) + k_5 \left(b + \gamma + \frac{\sigma_3^2}{2} \right) - \delta.
 \end{aligned} \tag{43}$$

Choose

Hence,

$$\begin{aligned}
 k_3 &= \frac{\eta_2 \gamma s_T s_M \beta}{(s_T + c \mu_T + (c \sigma_4^2/2))^2 (\mu_M + (\sigma_2^2/2))(b + \gamma + (\sigma_3^2/2))}, \\
 k_4 &= \frac{\eta_2 \gamma s_T s_M \beta}{(s_T + c \mu_T + (c \sigma_4^2/2))(\mu_M + (\sigma_2^2/2))^2 (b + \gamma + (\sigma_3^2/2))}, \\
 k_5 &= \frac{\eta_2 \gamma s_T s_M \beta}{(s_T + c \mu_T + (c \sigma_4^2/2))(\mu_M + (\sigma_2^2/2))(b + \gamma + (\sigma_3^2/2))^2}.
 \end{aligned} \tag{44}$$

$$\begin{aligned}
 \mathcal{L}V_2 \leq & -\frac{\eta_2 \gamma s_T s_M \beta}{(s_T + c \mu_T + (c \sigma_4^2/2))(\mu_M + (\sigma_2^2/2))(b + \gamma + (\sigma_3^2/2))} - \frac{\eta_1 b s_M \beta}{(\mu_M + (\sigma_2^2/2))(b + \gamma + (\sigma_3^2/2))} \\
 & + M_u (\zeta + \eta_3 \beta) + \frac{\sigma_1^2}{2} + \left(\frac{\delta}{K} + k_1 \beta + k_4 \beta \right) B - \delta, \\
 \mathcal{L}V_2 \leq & -\frac{s_M \beta}{(\mu_M + (\sigma_2^2/2))(b + \gamma + (\sigma_3^2/2))} \left(\eta_1 b + \frac{\eta_2 \gamma s_T}{s_T + c \mu_T + (c \sigma_4^2/2)} \right) + M_u (\zeta + \eta_3 \beta) + \frac{\sigma_1^2}{2} \\
 & + \left(\frac{\delta}{K} + k_1 \beta + k_4 \beta \right) B - \delta.
 \end{aligned} \tag{45}$$

Define

$$\begin{aligned}
 U_1(B, M_u, M_i, T) &= V_2(B, M_u, M_i, T) + \left(\frac{\zeta + \eta_3 \beta}{\mu_M} \right) \left(M_u - M_{u_1} - M_{u_1} \ln \frac{M_u}{M_{u_1}} \right), \\
 \mathcal{L}U_1 &\leq - \frac{s_M \beta}{(\mu_M + (\sigma_2^2/2))(b + \gamma + (\sigma_3^2/2))} \left(\eta_1 b + \frac{\eta_2 \gamma s_T}{s_T + c\mu_T + (c\sigma_4^2/2)} \right) + M_u (\zeta + \eta_3 \beta) + \frac{\sigma_1^2}{2} \\
 &\quad + \left(\frac{\delta}{K} + k_1 \beta + k_4 \beta \right) B - \delta + \left(\frac{\zeta + \eta_3 \beta}{\mu_M} \right) \left(1 - \frac{M_{u_1}}{M_u} \right) (s_M - \mu_M M_u - \beta M_u B) + \left(\frac{\zeta + \eta_3 \beta}{\mu_M} \right) \frac{M_{u_1} \sigma_2^2}{2}, \\
 &\leq - \frac{s_M \beta}{(\mu_M + (\sigma_2^2/2))(b + \gamma + (\sigma_3^2/2))} \left(\eta_1 b + \frac{\eta_2 \gamma s_T}{s_T + c\mu_T + (c\sigma_4^2/2)} \right) + \left(\frac{\zeta + \eta_3 \beta}{\mu_M} \right) s_M + \frac{\sigma_1^2}{2} + (\zeta + \eta_3 \beta) M_{u_1} \\
 &\quad + \left(\frac{\zeta + \eta_3 \beta}{\mu_M} \right) \frac{M_{u_1} \sigma_2^2}{2} + \left(\frac{\delta}{K} + k_1 \beta + k_4 \beta + \left(\frac{\zeta + \eta_3 \beta}{\mu_M} \right) \beta M_{u_1} \right) B, \\
 \mathcal{L}U_1 &\leq - \frac{s_M \beta}{(\mu_M + (\sigma_2^2/2))(b + \gamma + (\sigma_3^2/2))} \left(\eta_1 b + \frac{\eta_2 \gamma s_T}{s_T + c\mu_T + (c\sigma_4^2/2)} \right) + \vartheta + \frac{\sigma_1^2}{2} + \phi B \\
 &= - \left(\vartheta + \frac{\sigma_1^2}{2} \right) (\mathcal{R}_0^s - 1) + \phi B = -\lambda + \phi B,
 \end{aligned} \tag{46}$$

where

$$\begin{aligned}
 \lambda &:= - \left(\vartheta + \frac{\sigma_1^2}{2} \right) (\mathcal{R}_0^s - 1), \\
 \mathcal{R}_0^s &:= \frac{s_M \beta}{(\vartheta + (\sigma_1^2/2))(\mu_M + (\sigma_2^2/2))(b + \gamma + (\sigma_3^2/2))} \left(\eta_1 b + \frac{\eta_2 \gamma s_T}{s_T + c\mu_T + (c\sigma_4^2/2)} \right), \\
 \vartheta &:= \left(\frac{\zeta + \eta_3 \beta}{\mu_M} \right) s_M + (\zeta + \eta_3 \beta) M_{u_1} + \left(\frac{\zeta + \eta_3 \beta}{\mu_M} \right) \frac{M_{u_1} \sigma_2^2}{2}, \\
 \phi &:= \left(\frac{\delta}{K} + k_1 \beta + k_4 \beta + \left(\frac{\zeta + \eta_3 \beta}{\mu_M} \right) \beta M_{u_1} \right).
 \end{aligned} \tag{47}$$

Define a $\mathcal{C}^2$ -function $U: \mathbb{R}^4 \rightarrow \mathbb{R}$, as follows:

$$U(B, M_u, M_i, T) = MU_1 + U_2 + U_3 + U_4 + U_5 + U_6, \tag{48}$$

where $U_2 = -\ln B$, $U_3 = -\ln M_u$, $U_4 = -\ln M_i$, $U_5 = -\ln T$, $U_6 = (1/\theta + 1)((B/\eta_1 b + \eta_2 \gamma) + M_u + M_i + (T/4))^{\theta+1}$, in

which θ is a sufficiently small constant satisfying $0 < \theta < \min \{(\mu_M/\sigma_2^2), (b/1 + (c_M/4) + \sigma_3^2), (T/\sigma_4^2)\}$; $b > (1 + (c_M/4))$, and select a suitable constant $M > 0$ which satisfies the following condition:

$$-M\lambda + E \leq -2, \tag{49}$$

where

$$E = \sup_{(B, M_u, M_i, T) \in \mathbb{R}_+^4} \left\{ \frac{\delta B}{K} + M_u (\zeta + \eta_3 \beta) + \beta B - \frac{\delta B^{\theta+2}}{2(\eta_1 b + \eta_2 \gamma)K} - \frac{\mu_M}{2} (M_u)^{\theta+1} \right. \\ \left. - \frac{(b - (1 + c_M/4))}{2} (M_i)^{\theta+1} - \frac{\mu_T}{8} (T)^{\theta+1} + F - \delta + \mu_M + b + \gamma + \mu_T + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \frac{\sigma_3^2}{2} + \frac{\sigma_4^2}{2} \right\}. \quad (50)$$

Easily we can check that

$$\liminf_{n \rightarrow \infty (B, M_u, M_i, T) \in \mathbb{R}_+^4 \setminus \mathbb{D}_n} U(B, M_u, M_i, T) = +\infty, \quad (51)$$

where $\mathbb{D}_n = ((1/n), n) \times ((1/n), n) \times ((1/n), n) \times ((1/n), n)$. Furthermore, $U(B, M_u, M_i, T)$ is not only continuous.

Hence, $U(B, M_u, M_i, T)$ has a minimum point $(\tilde{B}_0, \tilde{M}_{u_0}, \tilde{M}_{i_0}, \tilde{T}_0)$ in the interior of $\mathbb{R}_+^4$. Then, we define a $\mathcal{C}^2$ -function

$$\tilde{U}(B, M_u, M_i, T) = U(B, M_u, M_i, T) - \tilde{U}(\tilde{B}_0, \tilde{M}_{u_0}, \tilde{M}_{i_0}, \tilde{T}_0).$$

By applying Itô's formula, we obtain

$$\mathcal{L}U_2 = -\delta \left(1 - \frac{B}{K}\right) - \frac{M_i}{B} \left(\eta_1 b + \eta_2 \gamma \frac{T}{c+T}\right) + M_u (\zeta + \eta_3 \beta) + \frac{\sigma_1^2}{2} \\ \leq -\delta + \frac{\delta B}{K} + M_u (\zeta + \eta_3 \beta) + \frac{\sigma_1^2}{2},$$

$$\mathcal{L}U_3 = -\frac{s_M}{M_u} + \mu_M + \beta B + \frac{\sigma_2^2}{2},$$

$$\mathcal{L}U_4 = -\frac{\beta M_u B}{M_i} + b + \gamma \frac{T}{c+T} + \frac{\sigma_3^2}{2} \leq -\frac{\beta M_u B}{M_i} + b + \gamma + \frac{\sigma_3^2}{2},$$

$$\mathcal{L}U_5 = -\frac{s_T}{T} - c_M M_i \frac{1}{1 + e_M T} - c_B B \frac{1}{1 + e_B T} + \mu_T + \frac{\sigma_4^2}{2} \\ \leq -\frac{s_T}{T} + \mu_T + \frac{\sigma_4^2}{2},$$

$$\mathcal{L}U_6 = \left(\frac{B}{\eta_1 b + \eta_2 \gamma} + M_u + M_i + \frac{T}{4} \right)^\theta \left(\frac{1}{\eta_1 b + \eta_2 \gamma} \left(\delta B \left(1 - \frac{B}{K}\right) + M_i \left(\eta_1 b + \eta_2 \gamma \frac{T}{c+T} \right) - M_u B (\zeta + \eta_3 \beta) \right) + s_M \right. \\ \left. - \mu_M M_u - b M_i - \gamma M_i \frac{T}{c+T} + \frac{s_T}{4} + c_M M_i \frac{T}{4(1 + e_M T)} + c_B B \frac{T}{4(1 + e_B T)} - \frac{\mu_T T}{4} \right) \\ + \frac{\theta}{2} \left(\frac{B}{\eta_1 b + \eta_2 \gamma} M_u + M_i + \frac{T}{4} \right)^{\theta-1} \times \left(\left(\sigma_1 \frac{B}{\eta_1 b + \eta_2 \gamma} \right)^2 + \sigma_2^2 M_u^2 + \sigma_3^2 M_i^2 + \sigma_4^2 \left(\frac{T}{4} \right)^2 \right), \\ \leq \left(\frac{B}{\eta_1 b + \eta_2 \gamma} + M_u + M_i + \frac{T}{4} \right)^\theta \left(s_M + \frac{s_T}{4} + \left(\frac{\delta}{\eta_1 b + \eta_2 \gamma} + \frac{c_B B}{4} \right) B - \frac{\delta B^2}{(\eta_1 b + \eta_2 \gamma)K} - \mu_M M_u - \left(b - \left(1 + \frac{c_M}{4}\right) \right) M_i - \frac{\mu_T T}{4} \right) \\ + \frac{\theta}{2} \left(\frac{B}{\eta_1 b + \eta_2 \gamma} M_u + M_i + \frac{T}{4} \right)^{\theta-1} \times \left(\sigma_1^2 \left(\frac{B}{\eta_1 b + \eta_2 \gamma} \right)^2 + \sigma_2^2 M_u^2 + \sigma_3^2 M_i^2 + \sigma_4^2 \left(\frac{T}{4} \right)^2 \right),$$

$$\begin{aligned}
&\leq \left(s_M + \frac{s_T}{4}\right) \left(\frac{B}{\eta_1 b + \eta_2 \gamma} + M_u + M_i + \frac{T}{4}\right)^\theta + \left(\frac{\delta}{\eta_1 b + \eta_2 \gamma} + \frac{c_B B}{4}\right) \\
&\quad \times \left(\frac{B}{\eta_1 b + \eta_2 \gamma} + M_u + M_i + \frac{T}{4}\right)^\theta B - \frac{\delta B^{\theta+2}}{(\eta_1 b + \eta_2 \gamma)K} - \mu_M (M_u)^{\theta+1} \\
&\quad - \left(b - \left(1 + \frac{c_M}{4}\right)\right) (M_i)^{\theta+1} - \frac{\mu_T T}{4} (T)^{\theta+1} + \frac{\theta}{2} \left(\sigma_1^2 \left(\frac{B}{\eta_1 b + \eta_2 \gamma}\right)^{\theta+1} + \sigma_2^2 M_u^{\theta+1} + \sigma_3^2 M_i^{\theta+1} + \sigma_4^2 \left(\frac{T}{4}\right)^{\theta+1}\right), \\
\mathcal{L}U_6 &\leq -\frac{\delta B^{\theta+2}}{2(\eta_1 b + \eta_2 \gamma)K} - \frac{\mu_M}{2} (M_u)^{\theta+1} - \frac{(b - (1 + (c_M/4)))}{2} (M_i)^{\theta+1} - \frac{\mu_T}{8} (T)^{\theta+1} + F,
\end{aligned} \tag{52}$$

where

$$\begin{aligned}
F = \sup_{(B, M_u, M_i, T) \in \mathbb{R}_+^4} &\left\{ -\frac{\delta B^{\theta+2}}{2(\eta_1 b + \eta_2 \gamma)K} - \frac{\mu_M}{2} (M_u)^{\theta+1} - \frac{(b - (1 + (c_M/4)))}{2} (M_i)^{\theta+1} - \frac{\mu_T}{8} (T)^{\theta+1} \right. \\
&+ \left(s_M + \frac{s_T}{4}\right) \left(\frac{B}{\eta_1 b + \eta_2 \gamma} + M_u + M_i + \frac{T}{4}\right)^\theta + \left(\frac{\delta}{\eta_1 b + \eta_2 \gamma} + \frac{c_B}{4}\right) \times \left(\frac{B}{\eta_1 b + \eta_2 \gamma} + M_u + M_i + \frac{T}{4}\right)^\theta B \\
&\left. + \frac{\theta}{2} \left(\sigma_1^2 \left(\frac{B}{\eta_1 b + \eta_2 \gamma}\right)^{\theta+1} + \sigma_2^2 M_u^{\theta+1} + \sigma_3^2 M_i^{\theta+1} + \sigma_4^2 \left(\frac{T}{4}\right)^{\theta+1}\right) \right\}.
\end{aligned} \tag{53}$$

It follows that

$$\begin{aligned}
\mathcal{L}\hat{U} &\leq -M\lambda + M\phi B + \frac{\delta B}{K} + M_u(\zeta + \eta_3 \beta) - \frac{s_M}{M_u} + \beta B - \frac{\beta M_u B}{M_i} - \frac{s_T}{T} - \frac{\delta B^{\theta+2}}{2(\eta_1 b + \eta_2 \gamma)K} \\
&\quad - \frac{\mu_M}{2} (M_u)^{\theta+1} - \frac{(b - (1 + (c_M/4)))}{2} (M_i)^{\theta+1} - \frac{\mu_T}{8} (T)^{\theta+1} + F - \delta + \mu_M + b + \gamma + \mu_T + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \frac{\sigma_3^2}{2} + \frac{\sigma_4^2}{2}.
\end{aligned} \tag{54}$$

Now we are in the portion to construct a compact subset $\mathbb{D}_\epsilon$ such that condition A_2 in Lemma 2 holds. Define the following bounded closed set

$$\mathbb{D}_\epsilon = \left\{ (B, M_u, M_i, T) \in \mathbb{R}_+^4 : \epsilon \leq B \leq \frac{1}{\epsilon}, \epsilon \leq M_u \leq \frac{1}{\epsilon}, \epsilon^3 \leq M_i \leq \frac{1}{\epsilon^3}, \epsilon \leq T \leq \frac{1}{\epsilon} \right\}, \tag{55}$$

where $0 < \epsilon < 1$ is a sufficiently small constant. In the set $\mathbb{R}_+^4 \setminus \mathbb{D}_\epsilon$, we can choose ϵ sufficiently small such that the following conditions hold:

$$-M\lambda + M\phi\epsilon + E \leq -1, \tag{56}$$

$$-\frac{s_M}{\epsilon} + G \leq -1, \tag{57}$$

$$-\frac{\beta}{\epsilon} + G \leq -1, \tag{58}$$

$$-\frac{s_T}{\epsilon} + G \leq -1, \tag{59}$$

$$-\frac{\delta}{4(\eta_1 b + \eta_2 \gamma)K} \frac{1}{\epsilon^{\theta+2}} + H \leq -1, \tag{60}$$

$$-\frac{\mu_M}{4} \frac{1}{\epsilon^{\theta+1}} + J \leq -1, \quad (61)$$

$$-\frac{(b - (1 + (c_M/4)))}{4} \frac{1}{\epsilon^{3\theta+3}} + N \leq -1, \quad (62)$$

$$-\frac{\mu_T}{16} \frac{1}{\epsilon^{\theta+1}} + O \leq -1, \quad (63)$$

where E, G, H, J, N , and O are positive constants which can be found from the equations (50), (66), (70), (72), (74), and (76). Conveniently, we can divide $\mathbb{R}_+^4 \setminus \mathbb{D}_\epsilon$ into the following eight domains:

$$\begin{aligned} \mathbb{D}_1 &= \{(B, M_u, M_i, T) \in \mathbb{R}_+^4: 0 < B < \epsilon\}, \quad \mathbb{D}_2 = \{(B, M_u, M_i, T) \in \mathbb{R}_+^4: 0 < M_u < \epsilon\}, \\ \mathbb{D}_3 &= \{(B, M_u, M_i, T) \in \mathbb{R}_+^4: 0 < M_i < \epsilon^3, B \geq \epsilon, M_u \geq \epsilon\}, \\ \mathbb{D}_4 &= \{(B, M_u, M_i, T) \in \mathbb{R}_+^4: 0 < T < \epsilon\}, \\ \mathbb{D}_5 &= \{(B, M_u, M_i, T) \in \mathbb{R}_+^4: B > (1/\epsilon)\}, \\ \mathbb{D}_6 &= \{(B, M_u, M_i, T) \in \mathbb{R}_+^4: M_u > (1/\epsilon)\}, \\ \mathbb{D}_7 &= \{(B, M_u, M_i, T) \in \mathbb{R}_+^4: M_i > (1/\epsilon^3)\}, \\ \mathbb{D}_8 &= \{(B, M_u, M_i, T) \in \mathbb{R}_+^4: T > (1/\epsilon)\}. \end{aligned}$$

Clearly, $\mathbb{D}_\epsilon^c = \mathbb{D}_1 \cup \mathbb{D}_2 \cup \mathbb{D}_3 \cup \mathbb{D}_4 \cup \mathbb{D}_5 \cup \mathbb{D}_6 \cup \mathbb{D}_7 \cup \mathbb{D}_8$. Next, we prove that $\mathcal{L}\hat{U} \leq -1$ on $\mathbb{D}_\epsilon^c$, which is equivalent to proving it on the above eight domains, respectively.

Case 1. If $(B, M_u, M_i, T) \in \mathbb{D}_1$, we have

$$\begin{aligned} \mathcal{L}\hat{U} &\leq -M\lambda + M\phi B + \frac{\delta B}{K} + M_u(\zeta + \eta_3\beta) + \beta B - \frac{\delta B^{\theta+2}}{2(\eta_1 b + \eta_2 \gamma)K} - \frac{\mu_M}{2}(M_u)^{\theta+1} \\ &\quad - \frac{(b - (1 + (c_M/4)))}{2}(M_i)^{\theta+1} - \frac{\mu_T}{8}(T)^{\theta+1} + F - \delta + \mu_M + b + \gamma + \mu_T + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \frac{\sigma_3^2}{2} + \frac{\sigma_4^2}{2}, \\ &\leq -M\lambda + M\phi B + E \leq -M\lambda + M\phi\epsilon + E. \end{aligned} \quad (64)$$

According to (56) and (64), we get that $\mathcal{L}\hat{U} \leq -1$ for any $(B, M_u, M_i, T) \in \mathbb{D}_1$.

Case 2. If $(B, M_u, M_i, T) \in \mathbb{D}_2$, we attain

$$\begin{aligned} \mathcal{L}\hat{U} &\leq -\frac{s_M}{M_u} + M\phi B + \frac{\delta B}{K} + M_u(\zeta + \eta_3\beta) + \beta B - \frac{\delta B^{\theta+2}}{2(\eta_1 b + \eta_2 \gamma)K} - \frac{\mu_M}{2}(M_u)^{\theta+1} \\ &\quad - \frac{(b - (1 + (c_M/4)))}{2}(M_i)^{\theta+1} - \frac{\mu_T}{8}(T)^{\theta+1} + F - \delta + \mu_M + b + \gamma + \mu_T + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \frac{\sigma_3^2}{2} + \frac{\sigma_4^2}{2}, \\ &\leq -\frac{s_M}{M_u} + G \leq -\frac{s_M}{\epsilon} + G, \end{aligned} \quad (65)$$

where

$$\begin{aligned} G &= \sup_{(B, M_u, M_i, T) \in \mathbb{R}_+^4} \left\{ M\phi B + \frac{\delta B}{K} + M_u(\zeta + \eta_3\beta) + \beta B - \frac{\delta B^{\theta+2}}{2(\eta_1 b + \eta_2 \gamma)K} - \frac{\mu_M}{2}(M_u)^{\theta+1} \right. \\ &\quad \left. - \frac{(b - (1 + (c_M/4)))}{2}(M_i)^{\theta+1} - \frac{\mu_T}{8}(T)^{\theta+1} + F - \delta + \mu_M + b + \gamma + \mu_T + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \frac{\sigma_3^2}{2} + \frac{\sigma_4^2}{2} \right\}. \end{aligned} \quad (66)$$

In view of (57), we obtain that $\mathcal{L}\hat{U} \leq -1$ for any $(B, M_u, M_i, T) \in \mathbb{D}_2$.

Case 3. If $(B, M_u, M_i, T) \in \mathbb{D}_3$, we obtain

$$\begin{aligned} \mathcal{L}\hat{U} &\leq -\frac{\beta M_u B}{M_i} + M\phi B + \frac{\delta B}{K} + M_u(\zeta + \eta_3\beta) + \beta B - \frac{\delta B^{\theta+2}}{2(\eta_1 b + \eta_2 \gamma)K} - \frac{\mu_M}{2}(M_u)^{\theta+1} \\ &\quad - \frac{(b - (1 + (c_M/4)))}{2}(M_i)^{\theta+1} - \frac{\mu_T}{8}(T)^{\theta+1} + F - \delta + \mu_M + b + \gamma + \mu_T + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \frac{\sigma_3^2}{2} + \frac{\sigma_4^2}{2}, \\ &\leq -\frac{\beta M_u B}{M_i} + G \leq -\frac{\beta}{\epsilon} + G. \end{aligned} \quad (67)$$

By virtue of (58), we can conclude that $\mathcal{L}\hat{U} \leq -1$ for any $(B, M_u, M_i, T) \in \mathbb{D}_3$.

Case 4. If $(B, M_u, M_i, T) \in \mathbb{D}_4$, we get

$$\begin{aligned} \mathcal{L}\hat{U} &\leq -\frac{s_T}{T} + M\phi B + \frac{\delta B}{K} + M_u(\zeta + \eta_3\beta) + \beta B - \frac{\delta B^{\theta+2}}{2(\eta_1 b + \eta_2 \gamma)K} - \frac{\mu_M}{2}(M_u)^{\theta+1} \\ &\quad - \frac{(b - (1 + (c_M/4)))}{2}(M_i)^{\theta+1} - \frac{\mu_T}{8}(T)^{\theta+1} + F - \delta + \mu_M + b + \gamma + \mu_T + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \frac{\sigma_3^2}{2} + \frac{\sigma_4^2}{2}, \\ &\leq -\frac{s_T}{T} + G \leq -\frac{s_T}{\epsilon} + G. \end{aligned} \quad (68)$$

In view of (59), we can deduce that $\mathcal{L}\hat{U} \leq -1$ for any $(B, M_u, M_i, T) \in \mathbb{D}_4$.

Case 5. If $(B, M_u, M_i, T) \in \mathbb{D}_5$, then one can see that

$$\begin{aligned} \mathcal{L}\hat{U} &\leq -\frac{\delta B^{\theta+2}}{4(\eta_1 b + \eta_2 \gamma)K} + M\phi B + \frac{\delta B}{K} + M_u(\zeta + \eta_3\beta) + \beta B - \frac{\delta B^{\theta+2}}{4(\eta_1 b + \eta_2 \gamma)K} - \frac{\mu_M}{2}(M_u)^{\theta+1} \\ &\quad - \frac{(b - (1 + (c_M/4)))}{2}(M_i)^{\theta+1} - \frac{\mu_T}{8}(T)^{\theta+1} + F - \delta + \mu_M + b + \gamma + \mu_T + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \frac{\sigma_3^2}{2} + \frac{\sigma_4^2}{2}, \\ &\leq -\frac{\delta B^{\theta+2}}{4(\eta_1 b + \eta_2 \gamma)K} + H \leq -\frac{\delta}{4(\eta_1 b + \eta_2 \gamma)K} \frac{1}{\epsilon^{\theta+2}} + H, \end{aligned} \quad (69)$$

where

$$\begin{aligned} H = \sup_{(B, M_u, M_i, T) \in \mathbb{R}_+^4} &\left\{ M\phi B + \frac{\delta B}{K} + M_u(\zeta + \eta_3\beta) + \beta B - \frac{\delta B^{\theta+2}}{4(\eta_1 b + \eta_2 \gamma)K} - \frac{\mu_M}{2}(M_u)^{\theta+1} \right. \\ &\left. - \frac{(b - (1 + (c_M/4)))}{2}(M_i)^{\theta+1} - \frac{\mu_T}{8}(T)^{\theta+1} + F - \delta + \mu_M + b + \gamma + \mu_T + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \frac{\sigma_3^2}{2} + \frac{\sigma_4^2}{2} \right\}. \end{aligned} \quad (70)$$

By condition (60), we get that $\mathcal{L}\hat{U} \leq -1$ for any $(B, M_u, M_i, T) \in \mathbb{D}_5$. Case 6. If $(B, M_u, M_i, T) \in \mathbb{D}_6$, we get

$$\begin{aligned} \mathcal{L}\hat{U} &\leq -\frac{\mu_M}{4}(M_u)^{\theta+1} + M\phi B + \frac{\delta B}{K} + M_u(\zeta + \eta_3\beta) + \beta B - \frac{\delta B^{\theta+2}}{2(\eta_1 b + \eta_2 \gamma)K} - \frac{\mu_M}{4}(M_u)^{\theta+1} \\ &\quad - \frac{(b - (1 + (c_M/4)))}{2}(M_i)^{\theta+1} - \frac{\mu_T}{8}(T)^{\theta+1} + F - \delta + \mu_M + b + \gamma + \mu_T + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \frac{\sigma_3^2}{2} + \frac{\sigma_4^2}{2}, \\ \mathcal{L}\hat{U} &\leq -\frac{\mu_M}{4}(M_u)^{\theta+1} + J \leq -\frac{\mu_M}{4} \frac{1}{\epsilon^{\theta+1}} + J, \end{aligned} \quad (71)$$

where

$$\begin{aligned} J = \sup_{(B, M_u, M_i, T) \in \mathbb{R}_+^4} &\left\{ M\phi B + \frac{\delta B}{K} + M_u(\zeta + \eta_3\beta) + \beta B - \frac{\delta B^{\theta+2}}{2(\eta_1 b + \eta_2 \gamma)K} - \frac{\mu_M}{4}(M_u)^{\theta+1} \right. \\ &\left. - \frac{(b - (1 + (c_M/4)))}{2}(M_i)^{\theta+1} - \frac{\mu_T}{8}(T)^{\theta+1} + F - \delta + \mu_M + b + \gamma + \mu_T + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \frac{\sigma_3^2}{2} + \frac{\sigma_4^2}{2} \right\}. \end{aligned} \quad (72)$$

According to condition (62), we attain that $\mathcal{L}\hat{U} \leq -1$ for any $(B, M_u, M_i, T) \in \mathbb{D}_6$. Case 7. If $(B, M_u, M_i, T) \in \mathbb{D}_7$, we have

$$\begin{aligned} \mathcal{L}\hat{U} &\leq -\frac{(b - (1 + (c_M/4)))}{4}(M_i)^{\theta+1} + M\phi B + \frac{\delta B}{K} + M_u(\zeta + \eta_3\beta) + \beta B - \frac{\delta B^{\theta+2}}{2(\eta_1 b + \eta_2 \gamma)K} \\ &\quad - \frac{\mu_M}{2}(M_u)^{\theta+1} - \frac{(b - (1 + (c_M/4)))}{4}(M_i)^{\theta+1} - \frac{\mu_T}{8}(T)^{\theta+1} + F - \delta + \mu_M + b + \gamma + \mu_T + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \frac{\sigma_3^2}{2} + \frac{\sigma_4^2}{2}, \\ &\leq -\frac{(b - (1 + (c_M/4)))}{4}(M_i)^{\theta+1} + N \leq -\frac{(b - (1 + (c_M/4)))}{4} \frac{1}{\epsilon^{3\theta+3}} + N. \end{aligned} \quad (73)$$

where

$$\begin{aligned} N = \sup_{(B, M_u, M_i, T) \in \mathbb{R}_+^4} &\left\{ M\phi B + \frac{\delta B}{K} + M_u(\zeta + \eta_3\beta) + \beta B - \frac{\delta B^{\theta+2}}{2(\eta_1 b + \eta_2 \gamma)K} - \frac{\mu_M}{2}(M_u)^{\theta+1} \right. \\ &\left. - \frac{(b - (1 + (c_M/4)))}{4}(M_i)^{\theta+1} - \frac{\mu_T}{8}(T)^{\theta+1} + F - \delta + \mu_M + b + \gamma + \mu_T + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \frac{\sigma_3^2}{2} + \frac{\sigma_4^2}{2} \right\}. \end{aligned} \quad (74)$$

It leads to $\mathcal{L}\hat{U} \leq -1$ for any $(B, M_u, M_i, T) \in \mathbb{D}_7$ if condition (62) is satisfied. Case 8. If $(B, M_u, M_i, T) \in \mathbb{D}_8$, we attain

$$\begin{aligned} \mathcal{L}\hat{U} &\leq -\frac{\mu_T}{16}(T)^{\theta+1} + M\phi B + \frac{\delta B}{K} + M_u(\zeta + \eta_3\beta) + \beta B - \frac{\delta B^{\theta+2}}{2(\eta_1 b + \eta_2 \gamma)K} - \frac{\mu_M}{2}(M_u)^{\theta+1} \\ &\quad - \frac{(b - (1 + (c_M/4)))}{2}(M_i)^{\theta+1} - \frac{\mu_T}{16}(T)^{\theta+1} + F - \delta + \mu_M + b + \gamma + \mu_T + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \frac{\sigma_3^2}{2} + \frac{\sigma_4^2}{2}, \\ \mathcal{L}\hat{U} &\leq -\frac{\mu_T}{16}(T)^{\theta+1} + O \leq -\frac{\mu_T}{16} \frac{1}{\epsilon^{\theta+1}} + O, \end{aligned} \quad (75)$$

TABLE 2: List of parameters.

Parameters	Interpretation	Values	Reference
δ	Bacterium growth rate	5×10^{-4}	[17]
K	Carrying capacity	1×10^8	[17]
η_1	Death rate of an infected macrophages	50	[17]
η_2	Extracellular bacteria (B) rate by burst	20	[17]
η_3	Engulfment rate of uninfected macrophages	25	[17]
c	Half saturation rate in uninfected macrophages	150	[17]
ζ	Killing rate of extracellular bacteria	1.25×10^{-8}	[17]
s_M	Influx rate of uninfected macrophages	5000	[17]
μ_M	Death rates of uninfected macrophages	25	Assumed
β	Infection rates of uninfected macrophages	2×10^{-7}	[17]
b	Killing rate of infected macrophages	1.1×10^{-4}	Assumed
γ	Cell-mediated adaptive immune response rate	5×10^{-8}	[17]
s_T	Natural recruitment rate of activated CD4+ T cells	6.6	[17]
c_B	Maximum killing rates of extracellular bacteria macrophages	5×10^{-3}	[17]
c_M	Maximum killing rates of infected macrophages	1×10^{-3}	[17]
e_B	Saturating factor of extracellular bacteria macrophages	1×10^{-4}	[17]
e_M	Saturating factor of infected macrophages	1×10^{-4}	[17]
μ_T	Death rate of activated CD4+ T cells	0.33	[17]

FIGURE 1: The first segment of the figure represents the stochastic TB system (5) which fluctuates around the endemic equilibrium of deterministic TB system (1) if the environmental white noises are sufficiently small. The second segment of the figure reflects the probability distribution of the unique ergodic stationary distribution of the stochastic TB system (5).

where

$$\begin{aligned}
 O = & \sup_{(B, M_u, M_i, T) \in \mathbb{R}_+^4} \left\{ M\phi B + \frac{\delta B}{K} + M_u(\zeta + \eta_3\beta) + \beta B - \frac{\delta B^{\theta+2}}{2(\eta_1 b + \eta_2 \gamma)K} - \frac{\mu_M}{2}(M_u)^{\theta+1} \right. \\
 & \left. - \frac{(b - (1 + (c_M/4)))}{2}(M_i)^{\theta+1} - \frac{\mu_T}{16}(T)^{\theta+1} + F - \delta + \mu_M + b + \gamma + \mu_T + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \frac{\sigma_3^2}{2} + \frac{\sigma_4^2}{2} \right\}. \quad (76)
 \end{aligned}$$

FIGURE 2: Simulations of the stochastic TB model (5) with initial conditions $B(0), M_u(0), M_i(0), T(0) = (0.4, 0.2, 0.3, 0.1)$. Parameter values used are as given in Table 1.

It follows from (63) that $\mathcal{L}\hat{U} \leq -1$ for any $(B, M_u, M_i, T) \in \mathbb{D}_8$.

Obviously, from (64), (65), (67)–(69), (71), (73), and (75), we attain that for a sufficiently small ϵ , $\mathcal{L}V(B, M_u, M_i, T) \leq -1$, $\forall (B, M_u, M_i, T) \in \mathbb{R}_+^4 \setminus \mathbb{D}_\epsilon$. Hence, condition A_2 of Lemma 2 holds. It follows from Lemma 2 that the stochastic system (5) is ergodic and has a unique stationary distribution $\pi(\cdot)$. This completes the proof.

Remark 5. Notice that the expression of $\mathcal{R}_0^s$ converges with the basic reproduction number $\mathcal{R}_0$ for the deterministic model (1) if the environmental white noise is not taken into account. For example, we choose the real-life parameter values in Table 2, except $\delta = 7.2 \times 10^{-4}$, $b = 1.25$, $s_M = 1 \times 10^9$, $\mu_M = 7$, $\beta = 1.5 \times 10^{-9}$, $\gamma = 2 \times 10^{-2}$, $s_T = 2 \times 10^{-4}$, $c_M = 1 \times 10^{-4}$, $e_M = 1 \times 10^{-6}$, $c_B = 5 \times 10^{-6}$, $e_B = 1 \times 10^{-2}$, $\mu_T = 50$ with $\sigma_1 = 0 = \sigma_2 = \sigma_3 = \sigma_4$. We have $\mathcal{R}_0 = 1.3507$ and $\mathcal{R}_0^s = 1.3500$.

On the other hand, we select the above parameters except the environmental white noises $\sigma_1 = 0.3$, $\sigma_2 = 0.2$, $\sigma_3 = 0.4$, and $\sigma_4 = 0.3$. We have $\mathcal{R}_0^s = 1.2589$, and the

conditions of Theorem 2 are satisfied. Figure 1 represents the stochastic TB system (5) fluctuates around the endemic equilibrium $E_1 = (B_1, M_{u_1}, M_{i_1}, T_1)$ of deterministic TB system (1), where $B_1 = 4.5202 \times 10^{10}$, $M_{u_1} = 1.3368 \times 10^7$, $M_{i_1} = 7.1372 \times 10^8$, and $T_1 = 1.4269 \times 10^9$.

$$\widetilde{\mathcal{R}}_0 = \frac{4[\beta s_M + \mu_M(\delta + bN_1 + \gamma N_2)]}{\mu_M(\sigma_1^2 \wedge \sigma_3^2)} \approx \frac{0.5931}{2.2500} \approx 0.2636 < 1, \quad (78)$$

5. Numerical Simulations

In this section, we probe the extinction of the MTB, ergodic stationary distribution of the stochastic system (5), and the effect of varied environmental noise on model dynamic behavior based on the real-life parameters of theoretical outcomes by numerical simulations. Here, we utilize Milstein's higher-order method [44] and the host-pathogen stochastic TB model can be written as the subsequent discretization equations:

$$\begin{aligned} B_{k+1} &= B_k + \left[\delta B_k \left(1 - \frac{B_k}{K} \right) + M_{i_k} \left(\eta_1 b + \eta_2 \gamma \frac{T_k}{c + T_k} \right) - M_{u_k} B_k (\zeta + \eta_3 \beta) \right] \Delta t + \sigma_1 B_k \sqrt{\Delta t} \vartheta_k + \frac{\sigma_1^2}{2} B_k (\Delta t \vartheta_k^2 - \Delta t), \\ M_{u_{k+1}} &= M_{u_k} + \left[s_M - \mu_M M_{u_k} - \beta M_{u_k} B \right] \Delta t + \sigma_2 M_{u_k} \sqrt{\Delta t} \psi_k + \frac{\sigma_2^2}{2} M_{u_k} (\Delta t \psi_k^2 - \Delta t), \\ M_{i_{k+1}} &= M_{i_k} + \left[\beta M_{u_k} B_k - b M_{i_k} - \gamma M_{i_k} \frac{T_k}{c + T_k} \right] \Delta t + \sigma_3 M_{i_k} \sqrt{\Delta t} \rho_k + \frac{\sigma_3^2}{2} M_{i_k} (\Delta t \rho_k^2 - \Delta t), \\ T_{k+1} &= T_k + \left[s_T + c_M M_{i_k} \frac{T_k}{1 + e_m T_k} + c_B B_k \frac{T_k}{1 + e_B T_k} - \mu_T T_k \right] \Delta t + \sigma_4 T_k \sqrt{\Delta t} \nu_k + \frac{\sigma_4^2}{2} T_k (\Delta t \nu_k^2 - \Delta t), \end{aligned} \quad (77)$$

where $\vartheta_k, \psi_k, \rho_k$, and ν_k , $k = 1, 2, \dots, n$, are the k th perception of four mutually independent Gaussian random variables with $N(0, 1)$, σ_i , $i = 1, 2, 3, 4$ are the intensities of environmental noise, and $\Delta t > 0$ is the increase of time. Here we choose time step $\Delta t = 0.02$.

Throughout the literature, the initial values $B(0) = 0.4$, $M_u(0) = 0.2$, $M_i(0) = 0.3$, $T(0) = 0.1$ and suppose that the

unit of time is two hours in a day. We choose the parameter values of deterministic TB system (1) as given in Table 2.

Note that, $\mathcal{R}_0 = 0.2816 < 1$ and the deterministic TB model (1) has an infection-free equilibrium $E_0 = (M_{u_0}, T_0, B_0, M_{i_0}) = (200, 20, 0, 0)$, which is globally asymptotically stable on Γ . We fix the parameter values in Table 2 and intensities of environmental noise $\sigma_1 = 0.4$, $\sigma_2 = 0.4$,

FIGURE 3: The first and second segments of the figures exhibit the existence of the unique stationary distribution of the stochastic TB model (5) and the probability distribution of the stationary distribution, respectively.

FIGURE 4: The intensities of large environmental white noise $\sigma_1 = 1.25, \sigma_2 = 0.4, \sigma_3 = 1.25$ and $\sigma_4 = 0.2$ cause extinction of the MTB.

$\sigma_3 = 0.3, \sigma_4 = 0.3$. By calculating, and $25 = \mu_M > ((\sigma_1^2 \vee \sigma_2^2)/2) = \min(0.08, 0.045) = 0.045$, the conditions of Theorem 2 are satisfied. Figure 2 exhibits that the population of MTB and population of infected macrophages (LTBI or active TB) of the stochastic TB system (5) to eradicate the tuberculosis bacilli germs are almost surely from the infected TB individuals at this stage.

On the other hand, increasing the infected macrophage killing rate b from 1.1×10^{-4} to 1.25, increasing bacterium growth rate B , increasing the death rate of activated CD4+ T cells, and decreasing the natural recruitment rate of activated CD4+ T cells, etc., are vulnerable factors for tubercle bacillus which can grow from latency TB infection to oscillation and then reach as to active TB infection.

Keep all the parameter values same as in Table 2, except $\delta = 5 \times 10^{-3}, s_M = 3 \times 10^9, \beta = 3 \times 10^{-9}, b = 1.25, \gamma = 0.4$,

$s_T = 2 \times 10^{-4}, c_B = 5 \times 10^{-6}, c_M = 1 \times 10^{-4}, e_B = 1 \times 10^{-2}, e_M = 1 \times 10^{-4}, \mu_T = 50$, with the intensities of environmental white noise as follows: $\sigma_1 = 0.2, \sigma_2 = 0.5, \sigma_3 = 0.2$, and $\sigma_4 = 0.1$. By computing $\mathcal{R}_0^s = (s_M \beta / (\vartheta + (\sigma_1^2/2)))(\mu_M + (\sigma_2^2/2))(b + \gamma + (\sigma_3^2/2))((\eta_1 b + (\eta_2 \gamma s_T / s_T + c \mu_T + (c \sigma_4^2/2))) = 1.0171 > 1$, the conditions of Theorem 2 are fulfilled. Elseways, the deterministic TB model (1) has a unique positive infected equilibrium $E_1 = (B_1, M_{u_1}, M_{i_1}, T_1)$, where $B_1 = 2.4718 \times 10^{10}, M_{u_1} = 3.0256 \times 10^7, M_{i_1} = 1.3598 \times 10^9$, and $T_1 = 2.7432 \times 10^7$, which is globally asymptotically stable on Γ . For the already stipulated small intensities of white noise, the stochastic TB system (5) oscillates around the positive infected equilibrium E_1 . Figure 3 evinces the existence of the unique ergodic stationary distribution of the stochastic TB model (5) if $\mathcal{R}_0^s > 1$, which indicates that the disease will persist and prevail in an MTB population. The

second segment of Figure 3 evaluates the probability density distribution functions of the stationary distribution.

We keep all the parameter values as in Figure 3 with different intensities of environmental large white noise $\sigma_1 = 1.25$, $\sigma_2 = 0.4$, $\sigma_3 = 1.25$, and $\sigma_4 = 0.2$. Figure 4 reveals that the population of MTB and population of infected macrophages are swept away in the stochastic TB model (5) even while they are still persistent in the deterministic TB system (1). Hence, large intensity environmental white noise may be helpful for suppressing the disease outbreak and eradicating the MTB.

6. Conclusions and Future Directions

MTB is a leading communicable opportunistic disease in many countries and the main cause of chronic lung disease. In this literature, we studied the dynamical behavior of a stochastic host-pathogen tuberculosis model with adaptive immune response. Firstly, we exhibited that the stochastic TB model (5) has certain unique global positive solutions. We established sufficient conditions for the extinction of the tubercle bacillus. Also, we attained sufficient conditions for the existence of a unique ergodic stationary distribution of the positive solutions to the stochastic TB model (5) by applying a suitable Lyapunov function. Finally, the numerical simulations are provided to validate analytical outcomes and the dynamics of the stochastic host-pathogen TB model.

Certain interesting topics and practical realism earn further consideration. On the flip side, one may suggest some more realistic but complex models, such as considering the effects of impulsive perturbations on the stochastic TB system (5). The motivation for impulsive perturbations is that discontinuity is a common phenomenon and the real-life scenarios are generally discontinuous fashion like time and space. During the anti-TB treatment, pharmacokinetic variation and association of several drugs in a regimen are naturally nonlinear and occur only within some limited precise data spaces and often in a discontinuous manner [45]. Additionally, in the summer the incidence of TB is high, since it is speculated that the disease may have been obtained during the winter season. Due to air pollution, carbon monoxide stimulates bacillary reactivation and other factors such as poor water quality, soil pollution, and inadequate sanitation, which increase the risk of TB outbreaks. Owing to these sudden environmental changes, it is arousing curiosity to introduce the colored noise, for instance, continuous-time Markov chain into the stochastic TB system (5). Often, the switching among distinct environments is memoryless and the waiting time for the next switch is exponentially distributed [46, 47].

Finally, the memory CD8⁺ T cells can swiftly obtain effector functions to destroy infected cells and/or secrete inflammatory cytokines such as IL-2, IL-4, and IL-5 prevent replication of the host-pathogen [14]. The predominant bestow factor is that the exhibition of MHC-I molecules is nearly omnipresent, whereas MHC-II molecules are revealed on a more limited set of cells. In this connection, the memory CD8⁺ T cells have more opportunities to encounter antigen [14]. Hence, in the stochastic TB model (5), another compartment has to be added like

immune response CD8⁺ T cells which may be more effective and efficient to eradicate the tuberculosis bacilli. We leave these explorations for our future work.

Data Availability

No data were used to support this study.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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