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A Mathematical Model of the Transmission Dynamics of Tuberculosis with Exogenous Reinfection in the Infection-Free State

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Abstract **-In the present work, a perturbation of the model presented by Feng, Castillo-Chávez and Capurro (2000) will be carried out, where the dynamics of tuberculosis transmission will be described, where recovery from the disease will be incorporated. The model will include four epidemiological populations: Susceptible (S), Exposed (E), Infected (I) and Infected with treatment (T). This will allow to know how the interaction that exists with the infected can cause the permanence of the individuals with the disease. For which, its qualitative behavior will be analyzed as its evolution in time of the epidemiological populations for the model by the ordinary differential equations (ODE) and its perturbation to the dalay differential equations (DDE). In this way, it will allow us to know how the parameters influence the spread of the disease at the point free of infection and with a computational extension to evaluate an endemic situation.**

Keywords**—Epidemiology Mathematical. Tuberculosis. Ordinary Differential Equations. Delay Differential Equations. Computational Simulation.**

Introduction

A perturbation will be made to the Model presented by Feng et al. [1], as was also done by Palafox[2]. From these starting points, an introduction can begin with new guidelines on how the health system has introduced different forms of prevention and control so that the disease advances within society. Tuberculosis bacteria are known to spread from person to person through the air [3].

People who are nearby can inhale these bacteria and become infected. This is the central point of the dynamics that will represent the mathematical model in the section II and III of our research[4].

Therefore, we are going to consider the exogenous reinfection of tuberculosis where it can occur in a previously infected subject, who, when infected again by another individual, can in turn become ill again, developing tuberculosis of the "adult"' type, as express Directorate for Prevention and Control of Tuberculosis [5], and also Zuluaga [6]. The prevalence of the different forms of "adult" tuberculosis depends largely on the prevalence of sources of infection [7].

In addition, in communities with a high prevalence of infection, the most frequent types are post-primary tuberculosis and exogenous reinfection [3]. On the contrary, in communities with low prevalence, tuberculosis is more frequent due to endogenous reactivation, as stated by the institutions Centers for Disease Control and Prevention (CNE), the Ministry of Health of Peru (MINSA), and additionally the work of Tincopa and Sánchez [8].

The different forms of "adult"' tuberculosis is clinically and radiologically in distinguishable. Given this fact, a mathematical model should be proposed that can be considered the best way to represent the dynamics and how it can be addressed in an adequate epidemiological

intervention to reduce the prevalence and spread of tuberculosis[9].

Mathematical Model Without Delay

We consider the functions $S, E, I, T \in C^1([0;+\infty))$.These functions are non-negative and represent the following epidemiological populations: Susceptible (S), Exposed (E), Infected (I) and Infected with Treatment (T). We also consider the total epidemiological population N), that is, $N = S + E + I + T$. In addition, in our model, we consider parameters that represent epidemiological rates, so their values are always positive. With these considerations we propose the model (1). In Section 4, we will present computational simulations of the Feng et al. model [1].
These simulations will make it possible to generate interpretations with an epidemiological meaning, and draw conclusions about how the disease affects both people and society[10].

As stated in section I, the contagion of tuberculosis occurs through contact between the infected person and a susceptible person and that at the same time there may be a reinfection of the disease (exogenous) that through contact of an Infected in treatment (T) with another infected (I) can generate the transition to the exposed population (E) so that it goes through the disease process again, which we call a latent period to be able to infect to other people.

In addition, it can currently be considered that there is a recovery from the disease through the dosage schedules for the treatment of tuberculosis disease have an initial phase of two months, followed by the continuation phase in which several treatment options are chosen, with a duration of 4 or 7 months (for a total of six to nine months of treatment).

According to the hypotheses that have been mentioned, as expressed by the national institutions[3]-[4] and international institutions [6], and at the same time, as evidenced by the works of Alarcón et al. [10], Ibarguen-Mondragón and Esteva[11], Raimundo and Yang [12], and finally Ziegler[7], we can perform a diagramming of our behavioural model of the dynamics of tuberculosis transmission.

$$\begin{cases} \frac{dS}{dt} = \Lambda - c\beta_1 \frac{SI}{N} + r_1 E + r_2 I + r_3 T - \mu S & , \quad S(0) = S_o \\ \frac{dE}{dt} = c\beta_1 \frac{SI}{N} - \rho\beta_2 \frac{EI}{N} - (\theta + r_1)E - \mu E + \sigma\beta_3 \frac{IT}{N} & , \quad E(0) = E_o \\ \frac{dI}{dt} = \rho\beta_2 \frac{EI}{N} + \theta E - (k + r_2 + d_1)I - \mu I & , \quad I(0) = I_o \\ \frac{dT}{dt} = kI - (r_3 + d_2)T - \mu T - \sigma\beta_3 \frac{IT}{N} & , \quad T(0) = T_o \\ 0 < c, \beta_1, \beta_2, \beta_3, \theta, \rho, k, \sigma, \mu, r_1, r_2, r_3, d_1, d_2 < 1 \\ \Lambda > 0 \end{cases} \quad (1)$$

First, we will show the existence of solutions of the system of ordinary differential equations [1]. Then, since the system (1) models the dynamics of epidemiological species, we also show the positivity of the solutions [13]. With these justifications, the hypotheses of the epidemiological phenomenon among the four populations that interact in society for the proper definition of the Ziegler model will be guaranteed [7].

On the other hand, we note that the proposed mathematical model expressed in (1) is non-homogeneous[14].

*Theorem 1.*Let function $G: \mathbb{R}^4_+ \to \mathbb{R}^4_+$, where $G(X) = (G_1(X), G_2(X), G_3(X), G_4(X))$ with $X = (x_1, x_2, x_3, x_4)$, associated to the system (1), are continuous functions and there are $\frac{\partial G_j}{\partial x_j}$ continuous in $\mathbb{R}^4_+, \forall j = \overline{1,4}$. Then, the function G is locally lipschitz continuous on $\mathbb{R}^4_+$.

Theorem 2. Let function$G: \mathbb{R}^4_+ \to \mathbb{R}^4_+$ locally lipschitz continues in $\forall j = \overline{1,4}$and satisfice $G_j(X) \geq 0$ for any $x \in \mathbb{R}^4_+$, $x_j = 0$. Then, for each $x_o \in \mathbb{R}^4_+$, there is a unique solution $X' = G(X)$ with $X(0) = X_o \in \mathbb{R}^4_+$ where is defined on some interval $[0, b]$ with $b \in (0;+\infty)$

Theorem 3. All solutions of the system (1) are bounded in the long time.

The result obtained with theorems 1, 2 and 3 indicate that the solution of the system (1) is bounded in the long time. This means that the feasible region of the system is obtained.

$$\mathfrak{C} = \{(S, E, I, T): S + E + I + T \leq \frac{\Lambda}{\mu} \; ; \; S \geq 0, E \geq 0, I \geq 0, T \geq 0\}$$

I. Qualitative Analysis

After having presented the existence and uniqueness, and also positivity of solutions in Theorem 1 and 2, and in a complementary way that the solutions of the system (1) are bounded according to the theorem 3. We will proceed to carry out the qualitative analysis of the mathematical model (1) that allows us to know how its behavior is in a long term of time [15]. Therefore, the critical points in the steady state of the model will be determined to evaluate its stability in the long term[1].

The equilibrium points (2) associated with system (1) in its steady state are as follows

$$\begin{aligned} w_1 &= (\frac{\Lambda}{\mu} \; ; \; 0 \; ; \; 0 \; ; 0) \\ w_2 &= (\, S^* \; ; \; E^* \; ; \; I^* \; ; \; T^* \,) \end{aligned} \quad (2)$$

Two critical points of the equation have been obtained that give the possibility of local stability associated with the system (1). First, it must be justified that the critical points must be non-negative since the functions represent populations of the epidemiological populations [16]. In this sense, the existence of the critical points (2) will be determined according to the restrictions provided in each coordinate of the point must be positive[15].

After obtaining the equilibrium points (2), we will proceed to determine the Jacobian matrix $J(S, E, I, T)$ associated with the mathematical model (1). The Jacobian matrix represents a linear system, associated to the non-

linear model, in the neighborhood of an equilibrium point [2].We will focus on the infection-free point(w_1).

$$J\left(\frac{\Lambda}{\mu};0;0;0\right)=\begin{bmatrix}-\mu & r_1 & -\frac{c\beta_1\Lambda}{\mu N}+r_2 & r_3\\ 0 & -(\theta+\mu+r_1) & \frac{c\beta_1\Lambda}{\mu N} & 0\\ 0 & \theta & -k-\mu-r_2-d_1 & 0\\ 0 & 0 & k & -\mu-r_3-d_2\end{bmatrix}$$

Having the Jacobian matrix associated with the system (1) at the infection-free point. The characteristic polynomial will be determined to analyze the sign of the eigen values of the matrix, and thus determine the local stability of the infection-free point [1]; there are other methods to determine local stability as given in Pino[15]-[17].

$$p(\lambda)=(\lambda+\mu)(\lambda+\mu+d_2+r_3)(\lambda+\mu+\theta+r_1)(\lambda+\mu+k+r_2+d_1)$$

As all parameters of the system (1) are positive quantities. It is easy to see that the signs of the eigen values are negative.

$$\lambda_1=-\mu \qquad \lambda_2=-(\mu++d_2+r_3)$$
$$\lambda_3=-(\mu++\theta+r_1) \quad \lambda_4=-(\mu+k+r_2+d_1)$$

Therefore,the infection-free poin t$w_1=(\frac{\Lambda}{\mu}\ ;\ 0\ ;\ 0\ ;0\ )$ associated with the system (1) is locally stable [15]-[16].

II. Basic Reproduction Number($\mathfrak{R}_o$)

The Basic Reproduction Number($\mathfrak{R}_o$)represents the average number of new cases that a given case generates, throughout an infectious period [18]. To determine the Basic Reproduction Number, we will use the Next Generation Matrix method[19]-[20].To determine the Basic Reproduction Number ($\mathfrak{R}_o$)we will define some matrices for the construction of the Next Generation Matrix. We will apply the method associated with the infection-free point to determine the evolution of the tuberculosis epidemic.

$$F\left(\frac{\Lambda}{\mu};0;0;0\right)=\begin{bmatrix}0 & c\beta_1 & 0\\ 0 & 0 & 0\\ 0 & 0 & 0\end{bmatrix}$$

$$V\left(\frac{\Lambda}{\mu};0;0;0\right)=\begin{bmatrix}\mu+\theta+r_1 & 0 & 0\\ -\theta & \mu+k+r_2+d_1 & 0\\ 0 & -k & \mu+r_3+d_2\end{bmatrix}$$

With the matrices obtained, the Basic Reproduction Number($\mathfrak{R}_o$)can be determined, where the parameter obtained is similar to that obtained by Feng et al. [1]-[19]. This helps us to confirm the results obtained by these authors as expressed in Palafox [2]; but at the same time, it is different due to some additional considerations that were introduced to the model (1), so that it can consider the reality currently faced by tuberculosis disease [3]-[5].

$$\mathfrak{R}_o=\left(\frac{c\beta_1}{\mu+k+d_1+r_2}\right)\left(\frac{\theta}{\theta+\mu+r_1}\right)$$

The Basic Reproduction Number ($\mathfrak{R}_o$)is made up of the product of two epidemiological terms [1].

The first term $\left(\frac{c\beta_1}{\mu+k+d_1+r_2}\right)$ represents the product of the average number of Susceptible infected by an Infected during his effective infectious period [4]-[5], and the second term $\left(\frac{\theta}{\theta+\mu+r_1}\right)$ represents the fraction of the population that survives the latent period [3]. Therefore, this indicator($\mathfrak{R}_o$) gives us the number of secondary infectious cases produced by an infected individual during its effective infectious period in a susceptible population as expressed by the works mentioned in section 1 both the mathematical references and the epidemiological references related to tuberculosis disease [19]-[20].

Mathematical Model With Delay

An important consideration contained in the model expressed in section 2, through the equation (1), is the hypothesis of exogenous reinfection that occurs in the interaction between those infected with treatment (T) with the infected (I) as expressed in the research of Feng et al. [1]. This transition is made immediately, that is, as soon as they come into contact with the probability of contagion and infection, they are considered in the population of the Exposed (E) [3]. But this consideration would be better modeled by a delay coefficient because there is a latent period for this transition to happen where the collection of individuals requires time to analyze their impact [4].

Therefore, the term will be introduced with the discrete delay in the rate of change of the population of the Exposed due to the fact that a latent period must pass[10]; It must be taken into account that the SEIT mathematical model considers a latent period from the population of the Susceptible (S) to the population of the Exposed (E) so that they can be placed in the population of the Infected (I) so they can spread the disease [15]-[21].

On the other hand, a mathematical model has been considered omitting the population of the Exposed (E) by means of differential equations with delay, for greater detail Hal Smith's book can be reviewed, where the period will be included latent; but this consideration is not good because it is important to consider the population of individuals who have the disease but are not yet actively contagious [12].

Therefore, this consideration would generate a factor that allows better analysis of how exogenous reinfection affects the transmission dynamics of tuberculosis and can be better addressed for the good of society [6]-[10].

$$\begin{cases} \frac{dS}{dt} = \Lambda - c\beta_1 \frac{SI}{N} + r_1 E + r_2 I + r_3 T - \mu S \\ \frac{dE}{dt} = c\beta_1 \frac{SI}{N} - \rho\beta_2 \frac{EI}{N} - (\theta + r_1)E - \mu E + \sigma\beta_3 \frac{I(t-\tau)T(t-\tau)}{N} \\ \frac{dI}{dt} = \rho\beta_2 \frac{EI}{N} + \theta E - (k + r_2 + d_1)I - \mu I \\ \frac{dT}{dt} = kI - (r_3 + d_2)T - \mu T - \sigma\beta_3 \frac{IT}{N} \\ S(0) = S_o \quad E(0) = E_o(t): [-\tau, 0] \to [0; +\infty) \\ I(0) = I_o \qquad T(0) = T_o \\ 0 < c, \beta_1, \beta_2, \beta_3, \theta, \rho, k, \sigma, \mu, r_1, r_2, r_3, d_1, d_2 < 1 \\ \Lambda, \tau > 0 \end{cases} \quad (3)$$

In order to analyze in greater detail, the theorems of existence and uniqueness of solutions of the system (3), it is presented in detail in chapter 3 (page 25) and specifically in section 3.1, 3.2 and 3.3 of Hall Smith's book [21]. There you can follow in a structured and detailed way how the formalities of our model are guaranteed[15]-[17].

I. Qualitative Analysis

Similarly, to what was done for the model (1) in section 2, the qualitative analysis (steady state of the system) will be done for our model [1]. Where the equilibrium points associated with our model without delay (1) will be determined to describe the behavior of the long-term solutions. The critics points of the model with delay (3), will be determined in a similar way to the model (1) as indicated by Smith [21]. Therefore, the equilibrium points determined will be the critical points for our model and to analyze the stability in its steady state.

After having obtained the critical points (2) associated with the system (3), we will proceed to determine the Jacobian matrix without delay ($J(S,E,I,T)$), as the Jacobian matrix with delay ($J_\tau(S,E,I,T)$) associated to the mathematical model (3). These matrices represent a linear system associated with the nonlinear model at an equilibrium point where the steady state associated with the system is found.

The Jacobian matrix without delay associated with the system (3) would be the following:

$$J\left(\frac{\Lambda}{\mu}; 0; 0; 0\right) = \begin{bmatrix} -\mu & r_1 & -\frac{c\beta_1\Lambda}{\mu N} + r_2 & r_3 \\ 0 & -(\theta + \mu + r_1) & \frac{c\beta_1\Lambda}{\mu N} & 0 \\ 0 & \theta & -k - \mu - r_2 - d_1 & 0 \\ 0 & 0 & k & -\mu - r_3 - d_2 \end{bmatrix}$$

$$J_\tau\left(\frac{\Lambda}{\mu}; 0; 0; 0\right) = \begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

The Jacobian matrices associated with the system (3) at the infection-free point (w_1), will proceed to determine the characteristic polynomial to analyze the sign of the eigenvalues it possesses to determine if it is locally stable.

$$p(\lambda) = det\left(\lambda \cdot Id - J - J_\tau \cdot e^{-\lambda\tau}\right) = 0$$

The characteristic polynomial obtained for the associated system without delay will be equivalent to the characteristic polynomial obtained for the associated system with delay at the infection-free point for the steady state of the model [21].

$$p(\lambda) = (\lambda + \mu)(\lambda + \mu + d_2 + r_3)(\lambda + \mu + \theta + r_1)(\lambda + \mu + k + r_2 + d_1)$$

As all parameters of the system (3) are positive quantities. It is easy to see that the signs of the eigen values are negative.

$$\lambda_1 = -\mu \qquad \lambda_2 = -(\mu + +d_2 + r_3)$$
$$\lambda_3 = -(\mu + +\theta + r_1) \quad \lambda_4 = -(\mu + k + r_2 + d_1)$$

Therefore, the infection-free point$w_1 = (\frac{\Lambda}{\mu}\ ;\ 0\ ;\ 0\ ;\ 0\ )$ associated with the system (3) is locally stable (Pino, 2017). An important observation that has been obtained when analyzing the model without delay(1), and the model with delay (3) is that at the infection-free point (w_1) are locally stable [15]. Therefore, in the long run they converge to the same steady state [1]. This leads to considering a numerical analysis to visualize how the disease evolves in the short and medium term to have an epidemiological perspective according to the spread that may be generated[2]-[10].

Numerical Simulation

Within the mathematical modeling oriented to Epidemiology, the Qualitative Analysis is carried out (section 2 (ODE) and section 3 (DDE)) which is complemented by the Numerical Analysis to see its evolution over time [1]; Smith, 2011). This helps us to visualize the behavior of the approximate solutions, through the computational simulations are complemented with the hypotheses to guarantee the local stability of the model (1) and (3). From here, epidemiological interpretations can be considered in the short, medium and long term[5]-[10]. In addition, the evolution of the curves helps us to make adequate decisions in Public Health such as the implementation of strategies to control the disease [3].

It would be possible to carry out the computational simulation of the model (1) with the values of the table 1, and deduce epidemiological interpretations of the dynamics that presents the spread of tuberculosis disease [3]-[5].

A simulation time of 500 days will be determined, to know the behavior of the populations, their respective evolution when they interact with each other and the impact on society. The values obtained are based on the parameters of the work of Feng et al.[1],Palafox[2] and the reports of the national health institutions.

TABLE I
TABLE OF NUMERICAL VALUES FOR THE MATHEMATICAL MODEL

Variable	Description	Value
S	Population of Susceptible	2000
E	Exposed Population	50
I	Infected Population	20
T	Population of Infected with treatment	0
Parameter	**Description**	**Value**
Λ	Steady Recruit Rate	420
c	Contact rate per capita Susceptible-Infected	0.600
β_1	Contagion rate of a Susceptible by an Infected	0.750
ρ	Per-capita contact rate Exposed-Infected	0.400
β_2	Contagion rate of an Exposed by an Infected	0.680
θ	Rate of latent period of the Exposed	0.080

σ	Contact rate per capita Treated-Infected	0.500
β_3	Contagion rate of a Treated by an Infected	0.920
k	Treatment rate of an Infected person per capita	0.350
r_1	Per-capita recovery rate of an Exposed	0.0045
r_2	Per-capita recovery rate of an Infected	0.0028
r_3	Recovery rate per capita of a Treaty	0.0060
μ	Per-capita natural mortality rate	0.0180
d_1	Mortality rate per capita of an Infected	0.0250
d_2	Per-capita mortality rate of a Treaty	0.0100
τ	Discrete Delay Coefficient	15

I. Computational Simulation

The computer simulation will be carried out where we can visualize the behavior of the populations (Susceptible, Exposed, Infected and Treated) over time. For the present simulation, the fourth order Runge-Kutta numerical method was used with an absolute margin of error (10^{-6}) to have a good approximation of the solution of the model (1) so that the generated curve can represent the evolution of the epidemiological population [1]. For the simulation of the model (3), the Multistep numerical method was used, which also gives us a good approximation and has an absolute margin of error[15]-[16].

Through figure 1, it will be possible to analyze a state where the disease does not spread with a high impact but in the medium term it decreases considerably until it disappears. This computational simulation presents the infection-free state $w_1 = (\frac{\Lambda}{\mu}\ ;\ 0\ ;\ 0\ ;\ 0\ )$ where it has a Basic Reproduction Number less than one ($\Re_o = 0.8874$).

This indicator makes it possible to carry out adequate epidemiological programs and methodologies to maintain a favorable situation for citizens, as the health institutions state within their epidemiological plans [3]-[4]-[5].

An increase in epidemiological rates can be considered to be able to evaluate other scenarios where a different evolution of the disease can be analyzed to evaluate ways of proposing adequate strategies to not allow an uncontrolled expansion and cause a greater impact on the health system and society. In the figure 1, on the left side, the mathematical model (ODE) expressed in (1) is presented, and on the right side, the mathematical model (DDE) expressed in (3). In this way, both models can be compared at simulation time to infer epidemiological interpretations.

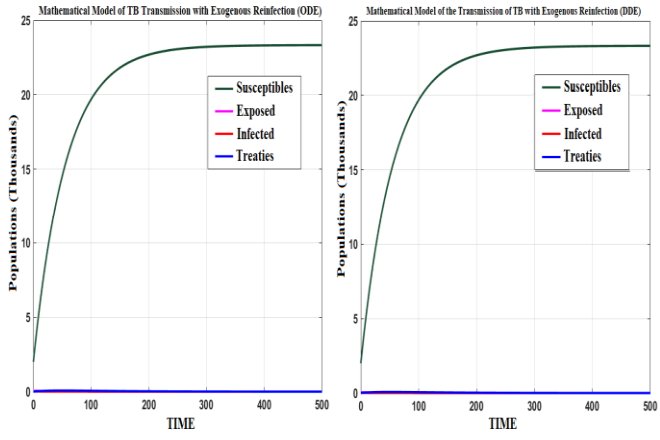

FIGURE I Computational Simulation of the Models at the Free Point of Infection (Table 1)

This is the scenario that is always sought when carrying out a study of the impact of the disease by the institutions in charge of MINSA [1]-[4] and CDC [5]. But it is also important to review situations where infection rates are increasing due to contact between the infected and the susceptible or a low level of detection of the infected [3]-[5].

In this sense, a brief reduction in the exposure rate initially considered in Table 1, ($\theta = 0.25$), has been considered; and with this disturbance, a Basic Reproduction Number greater than one ($\Re_o = 1.1874$) is obtained, where it is reflected in figure 2, generating an expectation of implementing adequate health strategies[3]-[5].

This will make it possible to analyze the evolution in light of the sensitivity of these parameters, since they mark an endemic evolution in the system [4], since the latent period is reduced, with which the infected person who cannot infect passes in a shorter time to an active infected capable of spreading the disease.

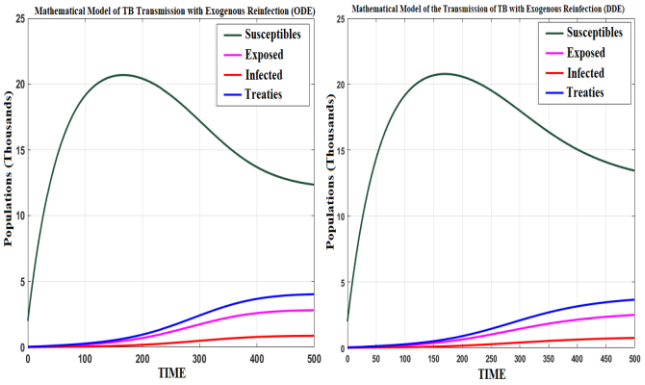

Figure II Computational Simulation of the Models (Scenario 1)

As shown in figure 2, a slight growth of the infected is generated in its three states (exposed, active and under treatment) where the susceptible population has a strong growth and then reaches a threshold, due to the interaction of the infected where the spread can still be controlled in a strategic and dynamic way in society [1], in such a way that it does not reach an epidemic explosion[3], as represented by the basic reproduction number($\Re_o = 1.1874$) and this indicates the spread of the disease over time [4], in such a way that an impact study is considered to reduce the spread of tuberculosis. Given this presentation of figures 2 and 3, the population curves are obtained over time before a differentiation of the exposure rate θ.As a third scenario, there will be an increase in epidemiological rates where they will generate an explosion of the disease in a short time [3].

The model using the delay differential equations (3) makes a significant difference in exogenous reinfection compared to the ordinary differential equations (1) studied in Feng et al. [1], and a good result is obtained when considering a latent period by the coefficient of delay introduced in the exogenous reinfection between the active Infected and those infected in treatment[3]-[5]. This consideration allows the impact and data collection to be adequately evaluated and to generate a better

epidemiological strategy, in addition to allowing a dynamic evaluation of patients who may acquire a reinfection.

The following parameters will be considered for the computational simulation, it will be a more critical case for both model (1) and (3) in order to analyze this situation (Feng et al., 2000).

Infectious contact rates between populations:$c = 0.90; \beta_1 = 0.95;\ \beta_2 = 0.85;\ \rho = 0.75$ and also exogenous reinfection: $\beta_3 = 0.92;\ \sigma = 0.60$. We continue with the treatment rates: $k = 0.25$ and the latent period rate: $\theta = 0.38$[3]. The recovery rates considered allow evaluating how the health system within its annual strategic plan allows it to continue evaluating the implementation of resources, for which these rates are as follows: $r_1 = 0.002;\ r_2 = 0.0010;\ r_3 = 0.0030,$ and finally the natural and disease mortality rates: $\mu = 0.015;\ d_1 = 0.008;\ d_2 = 0.010$ [10]. Where a basic reproduction number greater than one ($\Re_o = 2.9759$) is obtained, indicating that the disease will spread with considerable speed that intervention must be made to stop the epidemic [3]-[5].

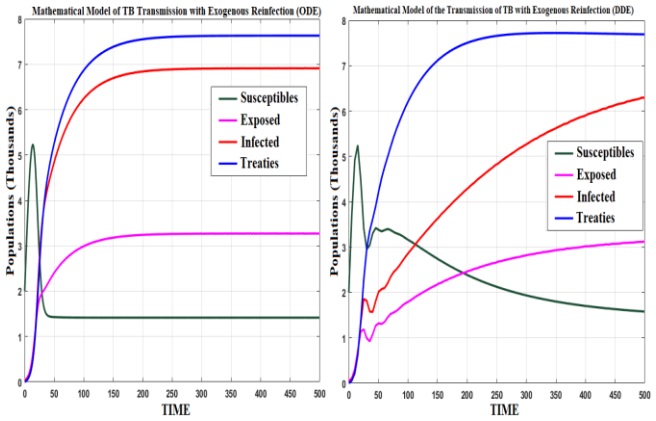

Figure III Computational Simulation of the Models (Scenario 2)

As commented in section 3, the delay helps to consider the data as a historical report to be able to more closely evaluate the exogenous reinfection suffered by those infected in treatment (T) and pass to the Exposed population (E) to incubate. the disease again in order to be actively infected capable of transmitting the disease [1]-[5]. An important consideration according to historical reports shows a slow growth and sometimes oscillating behavior [4], which allows evaluating a more strategic way to face the evolution of reinfection growth that has a critical impact for society [10].

In the mathematical sense, model (2) presents us with a slow growth with oscillations before stabilizing in the growth in the populations that generate the expansion of the disease (Infected and Exposed) where in time they converge at the same level [22]-[23]-[24], but in the short term its slow growth allows analysis and intervention so that over time it does not grow enormously and cause a collapse in the health system [9]. Differential equations with delay allow the presence of oscillatory solutions in time [20], this allows a better perspective on the behavior of infected populations, especially the consideration of exogenous reinfection that is not immediately its transition between populations [1].

Discussion And Conclusion

The mathematical model expressed in (1) adequately represents the spread of the tuberculosis disease by the Infected (I), in addition to the fact that this population generates an exogenous reinfection without it being possible to calculate it directly in order to analyze and evaluate the necessary means to prevent and control [3]-[10]. On the other hand, tuberculosis currently already has a cure to be able to consider a recovery, but not in a population distinction because there are variants of tuberculosis, the type of tuberculosis cannot be specifically recognized [5].

According to reports from national and international institutions, the evolution of tuberculosis has been controlled with intervention strategies and measures [3]. In this sense, epidemiological studies must be continued that allow knowing the rate of exogenous reinfection and the time that passes to present the symptoms of its latent period [4]. This dynamic is better modelled by the discrete delay coefficient (DDE), since it is not an immediate transition like ordinary differential equations [6]-[21]-[25]. The short-term evolution presented by both models (1) and (3) represent the consideration of a delay in the introduction of the Exposed population (E), despite the fact that in the long term both models converge to the same steady state of free of infection (w_1) so that the disease is eradicated in the long term [1]-[22].

Consequently, the evolution of the disease must be analyzed in its endemic state where the coexistence of epidemiological populations is provided [1]. And here, one of the pillars of public health must be ensured, which is the life of all the citizens that make up society [3]. Given this fact, the basic reproduction number ($\Re_o$)associated with model (1) allows us to see how the disease can develop in the short term, which allows us to guide control strategies and measures [3]-[4].

An important consideration that has not been incorporated in this work is the analysis of the endemic point where the coexistence of epidemiological populations is located, as developed in [2], but the incorporation of the retardation coefficient is introduced to model exogenous reinfection [15]-[21] to evaluate a better transition from the population infected with treatment to the population exposed by exogenous reinfection and how it affects the spread of the disease [26].

Therefore, the following can be concluded:

- The mathematical model (1) is an extension of the model developed by Feng, Chávez-Castillo and Capurro[1] where it has been perturbed by introducing a delay coefficient (2) that allowed a better approximation of the transition of the population infected with treatment (T) to the exposed population

(E) as a cause of exogenous reinfection of tuberculosis disease.

- An adequate construction of the model (1) allows an adequate evolution of the disease over time, the transition is immediate, where the consideration of recovery through intervention and monitoring strategies help reduce the spread [3]-[5], and is expressed in the basic reproduction number as an important epidemiological indicator to measure the spread of tuberculosis [4].
- The delay coefficient in model (3) helps to better approximate the growth of the population of Exposed (E) and Infected (I) because in reality there is not an explosive growth but a progressive one, even more oscillatory [3]- Smith, 2011). This perspective supports a better structure of strategies for intervention, control and prevention of the disease.
- The mathematical models (1) and (2) have unique solutions and are bounded in the long term according to the initial condition. In addition, the stability at the infection-free point$w_1 = (\frac{\Lambda}{\mu}\ ;\ 0\ ;\ 0\ ;0\ )$, is locally stable for both models in the long term [1]. In this steady state, it allows us to visualize the scenario where the spread of the disease has been overcome, where the basic reproduction number is less than one$(\Re_o < 1)$.

References

[1] Feng, Z., Castillo-Chávez, C., Capurro, A. 2000. A model for tuberculosis with exogenous reinfection. Theoretical population biology, 57(3):235-247. DOI: 10.1006/tpbi.2000.1451

[2] Palafox Lacarra, N. 2017. Modelos epidemiológicos para la Tuberculosis: Resistencia multiple, reinfección exógena y bifurcación hacia atrás. División de ciencias exactas y naturales, Universidad de Sonora, Mexico.

[3] Centro Nacional de Epidemiología, Prevención y Control de Enfermedades. 2021. Análisis de la situación epidemiológica de la tuberculosis en el Perú 2015, Lima, Perú. Ministerio de Salud, Perú.

[4] Dirección de Prevención y Control de la Tuberculosis. 2021. Informe operacional de Tuberculosis. Lima, Perú. Ministerio de Salud, Perú.

[5] Centers for Desease Control and Prevention (CDC). 2021. Tuberculosis (TB).Estados Unidos U.S. Department of Heatlh& Human Services.

[6] Zuluaga, M. 2015. ¿Reinfección o reactivación en la tuberculosis pulmonar? Un reto diagnóstico. Revista Fac. Nac. Salud Publica, 33(3):425-428. DOI: 10.17533/udea.rfnsp.v33n3a12

[7] Ziegler, J., Edwards, M., Smith, D. 1985. Exogenous reinfection in experimental airborne tuberculosis. Tubercle, 66(2):121-128. DOI: 10.1016/0041-3879(85)90077-7

[8] Tincopa Wong, O., Sánchez Saldaña, L. 2003. Tuberculosis cutánea.Dermatología Peruana, 13(3):195-214.

[9] Herrera Polanco, D. 2013. Ajuste de un modelo SEIR para la tuberculosis en El Salvador. Facultad de ciencias naturales y matemática, Universidad de El Salvador.

[10] Alarcón, V., Alarcón, E., Figueroa, C, Mendoza-Ticona, A. 2017. Tuberculosis en el Perú: situación epidemiológica, avances y desafíos para su control. Revista Peruana de Medicina Experimental y Salud Pública, 34(2):299-310. DOI: 10.17843/rpmesp.2017.342.2384

[11] Ibarguen-Mondragón, E., Esteva, L. 2012. Un modelo matemático sobre la dinámica del Mycobacterium tuberculosis en el granuloma. Revista colombiana de matemáticas, 46(1):39-65.

[12] Raimundo, S., Yang, H.M. 2005. Tuberculose: Questões sobre Reinfecção Exógena. Tend. Matematica Aplicada e Computacional, 6(1):121-130. DOI: 10.5540/tema.2005.06.01.0121

[13] Pino Romero, N., Salazar Fernández, C., López Cruz, R. 2019. Solución uniformemente acotada y estabilidad asintótica del punto libre de infección de un modelo matemático SI con dinámica vital (crecimiento logístico) mediante las ecuaciones diferenciales con retardo. Revista Selecciones Matemáticas, 6(1):66-76.

[14] Liu, L., Wang, Y. 2014. A mathematical study of a TB model with treatment interruptions and two latent periods. Computational and mathematical methods in medicine, 1-15. DOI: 10.1155/2014/932186

[15] Pino Romero, N. 2017. Análisis y simulación numérica de un modelo matemático SI con retardo discreto para las enfermedades de transmisión sexual. Facultad de ciencias matemáticas, Universidad Nacional Mayor de San Marcos, Perú.

[16] López Cruz, R. 2006. Structured SI epidemic models with applications to HIV epidemic. College of Science, Arizona State University.

[17] Pino Romero, N., López Cruz, R. 2017. Teoremas de estabilidad en un modelo matemático SI con dinámica vital estructurado por sexo para el estado libre de infección desarrollado mediante Ecuaciones Diferenciales Ordinarias y las Ecuaciones Diferenciales con Retardo aplicado a la Salud Pública. Revista Selecciones Matemáticas, 4(2):202-210. DOI: 10.17268/sel.mat.2017.02.07

[18] Ridenhour, B., Kowalik, J., Shay, D. 2014. Unraveling Ro: considerations for public health applications. American journal public health, 38(2):167-176. DOI: 10.2105/AJPH.2013.301704

[19] Van den Driessche, P. 2017. Reproduction numbers of infectious diseases models. Infectious disease modelling, 2(3):288-303.DOI: 10.1016/j.idm.2017.06.002

[20] Diekmann, O., Heesterbeek, A., Roberts, M. 2010. The construction of next-generation matrices for compartmental epidemic models. Journal Real Society Interface, 7(47):873-885.

[21] Smith, H. 2011. An introduction to Delay Differential Equations with applications to the Life Sciences. New York:Springer-Verlag. DOI: 10.1007/978-1-4419-7646-8

[22] Egonmwan, A., Okuonghae, D. 2019. Analysis of a mathematical model for tuberculosis with diagnosis. Journal of applied mathematics and computing (59):129-162. DOI: 10.1007/s12190-018-117

[23] De la Pava, E., Salguero, B., Alzate, A. 2002. Modelo matemático del riesgo anual de infección tuberculosa en Cali. Revista panamericana salud pública, 11(3):166-171.

[24] Yi, Y., Yi, S, Wei, Y. 2018. Dynamic model of tuberculosis considering multi-drug resistance and their applications. Infectious disease modelling, 3:362-372. DOI: 10.1016/j.idm.2018.11.001

[25] Tian, Y., Alawami, F., Al-Azem, A., Osgood, N., Hoeppner, V., Dutchyn, C. 2011. A system dynamics model of tuberculosis difusión with respect to contact tracing investigation. Proceedings of the 2011Winter Simulation conference (WSC), 1362-1373. DOI: 10.1109/WSC.2011.6147857

[26] Istianingsih et.al. et.al.(2022). The Role of Self-Control in the Impact of Artificial Intelligence Innovation on Lending Decisions in Online Fintech. International Journal of Applied Engineering & Technology, Vol.4(2022).

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