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Optimal Control Strategy to Reduce the Infection of the Pandemic HIV Associated with Tuberculosis in Bangladesh

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Abstract

Tuberculosis (TB) associates with HIV/AIDS at any stage of the total infection period. In recent years, HIV and TB have become the leading causes of death due to infectious and long lasting disease. On the basis of the characteristics of disease transmission of HIV and TB, we formulate a mathematical model. The model consists of ten compartments with nonlinear ordinary differential equations. The model is locally asymptotically stable in case of disease free equilibrium point when basic reproduction number is less than unity and locally asymptotically stable in case of endemic equilibrium point when the basic reproduction number is greater than unity. We apply optimal control theory to the co-infection model in the form of Pontryagin's Maximum Principle by introducing the treatment control and the vaccination control to decrease the transmission of the disease burden. Finally, we perform the numerical simulations of the optimal control model to observe the dynamics of the system in support of analytical findings.

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Introduction

Infectious diseases have been threatening throughout the world day by day and these diseases have a great influence on the human population. The history referrers that plague, nipah, swine flu, hepatitis B, HIV/AIDS, TB, COVID-19 etc are most dangerous infectious diseases that cause a huge loss of human life. From its very beginning, scientists have been trying to control these kinds of fatal diseases. After the manifestation of any infectious virus it starts to increase very fast sensibly or insensibly and people need the effective method to resist the outbreak of the disease or at least to control the number of infections (AIDS Report 2016).

Transmission diseases have ever been a great concern of human being from the very beginning of our history. Millions of people die annually from tuberculosis and HIV/AIDS and billions other are being infected. AIDS indeed is a terribly dangerous disease found almost everywhere in human society. But it has not affected all the societies equally throughout the world (Biswas 2012).

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People having AIDS are always under the threat of death and this disease is caused by the Human Immunodeficiency Virus usually known as HIV. HIV is a kind of virus which makes the human body almost incapable of fighting any kind of infections. HIV virus causes gradual destruction of immune system of human body by reflecting a decrease of CD4+T cell counts (Nunn *et al.* 2005). Significant immune destruction helps opportunistic processes develop and thereby infections start taking place in the body. Our human body heavily depends on the immune system to fight infections, the same way it depends on the digestive system to digest food. The immune system also prevents some types of infections from taking place in the body. If the immune system is totally destroyed then a person will have to die even from a simple infection like cold or flu (Sahani *et al.* 2017).

Tuberculosis more commonly known as TB is a bacterial infectious disease which can co-infect with HIV. TB can be latent (inactive) or active (Bowong and Tewa 2010). Close to one third of the world's population has dormant or latent TB. People living with TB gradually loss the immune system and as a result it causes a great health hazard. A complex interaction exists between TB and human immunodeficiency virus (Samad and Biswas 2018). The HIV and TB co-infection can spread out at an individual and community level. Human immunodeficiency virus and Tuberculosis jointly become the serious global mass health challenge. The incarnation of AIDS make the relation between HIV and TB. The co-infection of HIV and TB exist when individual are HIV positive and are either exposed or active to TB. Getting infected with TB bacteria is not automatic for HIV infected individuals. Similarly individuals infected with TB do not automatically get HIV stage unless in contact with HIV positive individuals (Brosch 2000). Till today the world's most serious epidemic as well as leading infectious killer disease is AIDS/HIV and TB, the ultimate destiny of which is the early death of the infected patient (Nura 2013).

TB continues to be a major source of illness and death in Bangladesh, which ranks sixth in the globe in terms of TB patient burden (Mahmood 2010). In Bangladesh, it is estimated that 70,000 people die from tuberculosis each year, with 300,000 new cases appearing each year. Prior to 2014, the case notification rates for new smear-positive cases and all forms of TB cases were 68 and 122 per 100,000 population, respectively, but by the end of 2014, the number of all types of TB cases had increased, with a significant increase in the number of extra-pulmonary cases due to better case detection. However, overall progress in case detection was slow and steady in 2016, with a case notification rate of 138 per 100,000 people (Kuddus *et al.* 2021). In 1989, the first case of HIV was discovered in Bangladesh. Every year since then, 10, 20, 100, or 200 additional instances have been discovered (Risingbd.com 2022). According to a government source, a total of 1500 cases of HIV/AIDS were confirmed and recorded in 2009, up from 1207 cases in 2007 and 1495 cases in 2008. The number of instances that go undetected is substantially larger. According to a recent poll, 50% of males tested positive for HIV at a city hospital are students, and 80% of those infected caught the infection through interacting with prostitutes (Mahmood 2010). According to the most recent figures, a total of 6,104 HIV-positive persons have been treated. The remaining 1,125 AIDS patients are still unable to receive therapy. The Bangladesh National AIDS/STD Control Program, on the other hand, claims that the number of AIDS patients receiving treatment is growing every year. In 2019, 52 percent of people were aware of the problem, which increased to 63 percent in 2021. Two

years ago, 65 percent of AIDS-infected persons were receiving treatment, which has since risen to 77 percent (Risingbd.com 2022).

(Bhunu *et al.* 2009) proposed a mathematical model of HIV/AIDS and tuberculosis co-infection and showed that the dynamics of different stages of the model. They also applied anti-retroviral therapy for the AIDS case and treatment for active and latent form of TB. (Biswas *et al.* 2019) proposed a nonlinear model of HIV immunology to describe the interaction between virus and human along with optimal therapy strategy using Pontryagin maximum principle. (Fatmawati and Tasman 2016) studied a mathematical model of Tuberculosis-HIV co-infection with the anti-TB and antiretroviral treatment. Mahmud (2010) discussed HIV/AIDS and TB scenario in Bangladesh, their transmission process, link of TB with HIV/AIDS, organism of HIV and TB, economic impact of TB and HIV in Bangladesh and HIV-TB policy issues in Bangladesh. David (2015) formulated a mathematical model of HIV and TB co-infection to demonstrate the dynamics of them separately and then showed the transmission and changes of different compartments with the presence of one another.

Being motivated with the severity of HIV/AIDS and TB worldwide as well as in Bangladesh, we are intended to do the work about it. We extended the model (Bhunu *et al.* 2009) in context of Bangladesh. Bhunu *et al.* (2009) applied anti-retroviral therapy for the AIDS case and treatment for active and latent form of TB, but we applied vaccination for latent form of TB and treatment for co-infection taking the weight in Bangladesh perspective. The parameter specification has been carried out by estimation from secondary data. However, describing the epidemiology of these infectious diseases and adopting any control strategy is not an easy task. By using mathematical modeling, we analyze the epidemiological insights of the model. We use two control variables for the prevention and minimization of the disease transmission. We perform the numerical calculation of this model by using ODE45 solver in MATHLAB programming language.

Objectives of the Study

The objectives of this study are:

1. to study the biological features and insights of the transmission of HIV and TB diseases and their co-infection on human body.
2. to propose a model in case of HIV/AIDS and TB with control only in human body using compartmental model with ordinary differential equations.
3. to analyze the HIV/AIDS and TB model in presence with one another.
4. to detect the factor that accelerates the different stages of HIV-TB co-infection.
5. to find a control strategy of the pandemic HIV and TB to minimize the transmission.
6. to solve the nonlinear system of ordinary differential equations with optimal control strategy for both analytically and numerically.
7. to create awareness among the general people about HIV/AIDS and TB so that they become careful of getting infection easily.

Materials and methods

The entire population model is divided into ten compartments that are Susceptible individuals (S) Latent TB with no HIV (L_T), Exposed to TB only (L_{T0}), Symptom of TB (S_R), Infected with HIV only (I_H), Those who have recover with temporal immunity (R_T), HIV infected individuals (pre-AIDS) exposed to TB (E_{TH}), HIV infected displaying HIDS symptoms (H_S), AIDS individuals exposed to TB (E_{TH}) and AIDS individuals dually infected with TB (H_{DT}),

For the treatment strategies of HIV and TB we considered two control variables like u_1 and u_2. We have u_1 representing the vaccinations that will treat tuberculosis so that the disease transmission can be minimized and u_2 that take HIV and TB treatment simultaneously. So here u_1 is the vaccination control and u_2 is the treatment control. Now we aim to reduce the number of infected individuals of HIV and TB patients along with the cost of the respective control measures. The optimal control model with nonlinear ODEs are:

$$S'(t) = A - \lambda_2 S - \lambda_1 S - \mu S \tag{1}$$

$$L_T{}'(t) = \lambda_2 S - \lambda_1 L_T (c_2 E_{TH} + c_3 I_H) - (\mu + \nu_1) L_T - u_1 L_T \tag{2}$$

$$I_H{}'(t) = \lambda_1 S + \lambda_1 R_T - (\rho_1 + \mu) I_H - \lambda_2 I_H + c_3 \lambda_1 L_T I_H \tag{3}$$

$$H_S{}'(t) = \rho_1 I_H - \eta_1 \lambda_2 H_S - \mu H_S - d_2 H_S \tag{4}$$

$$E_{TH}{}'(t) = \lambda_1 E_{T0} + \lambda_2 I_H - c_2 \lambda_1 L_T E_{TH} - (\kappa_4 + \mu) E_{TH} - u_2 E_{TH} \tag{5}$$

$$E_{HT}{}'(t) = \kappa_4 E_{HT} + \eta_1 \lambda_2 H_S - (\kappa_5 + \mu + d_2 + \psi_2 \lambda_2) E_{HT} \tag{6}$$

$$H_{DT}{}'(t) = (\kappa_5 + \psi_2 \lambda_2) E_{HT} - (\mu + d_1 + \varepsilon d_2) H_{DT} \tag{7}$$

$$E_{T0}{}'(t) = \nu_1 L_T + \lambda_2 R_T - (\lambda_1 + \psi_3 \lambda_2) E_{T0} - (\mu + \kappa_1) E_{T0} \tag{8}$$

$$S_T{}'(t) = r_2 R_T + (\kappa_1 + \psi_3 \lambda_2) E_{T0} - (\mu + r_1 + d_1) S_T \tag{9}$$

$$R_T{}'(t) = r_1 S_T - (\mu + r_2 + \lambda_1 + \lambda_2) R_T + u_1 L_T + u_2 E_{TH} \tag{10}$$

with the initial conditions

$$S(0)=S_0>0, L_T(0)=L_{T0}\geq 0, I_H(0)=I_{H0}\geq 0, H_S(0)=H_{S0}\geq 0, E_{TH}(0)=E_{TH0}\geq 0, E_{HT}(0)=$$
$$E_{HT0}\geq 0, H_{DT}(0)=H_{DT0}\geq 0, E_{T0}(0)=E_{T00}\geq 0, S_T(0)=S_{T0}\geq 0, R_T(0)=R_{T0}\geq 0$$

Here, the model is now the optimal control model and the set of control variables $(u_1(t),u_2(t))\in U$ is Lebesgue measurable, where

$$U=\{(u_1(t),u_2(t)): 0\leq a_i\leq u_i(t)\leq b_i\leq 1, i=1,2\}, \forall t\in[0,T]$$

Taking these two control variables under consideration, the performance index is given by

$$\text{Minimize } J(u_1,u_2)=\int_0^T\left(L_T(t)+I_{TH}(t)+\frac{Au_1^2}{2}+\frac{Bu_2^2}{2}\right)dt \qquad (11)$$

where A and B are weight parameters and the constant A represents the costs associated with vaccine of Latent TB with no HIV and B represents the costs associated with HIV infected individuals (pre-AIDS) co-infected with active TB. So our model can be stated as an optimal control problem with the performance index (11) as follows:

$$\begin{cases}\text{Minimize } J(\mathrm{x},u)=\int_0^T L(x(t),\mathrm{u}(t))\,dt\\ \textit{subject to}\\ \dot{x}(t)=f(x(t))+g(x(t))u(t), \forall t\in[0,T]\\ u(t)\in U, \forall t\in[0,T]\\ x(0)=x_0\end{cases} \qquad (12)$$

For analytical validation, the following Theorem 1 and Theorem 2 are very important.

Theorem 1: We consider a system of n variables

$$\overline{x}(t)=\begin{pmatrix}x_1(t)\\ \vdots\\ x_n(t)\end{pmatrix}$$

Let $u(t)$ be a control variable with set of admissible controls U that satisfies the following differential equation

$x_i'(t) = g\left(t, x_i(t), u(t)\right)$ for $i = 1, ..., n$

With associated objective functional $J(u) = \int f\left(t, \overline{x}(t), u(t)\right) dt$

There exists an optimal control which minimizes $\overline{J}(u)$ if the following conditions are satisfied

i) F is non empty

ii) The control set U must be closed and convex

iii) The right hand side of the state system is continuous, bounded above by a linear combination of the control and state and can be written as a linear function of u with coefficients defined by the time and state.

iv) The integrand of the objective functional is convex on U and is bounded below by

$-C_2 + C_1(u)^{\eta}$, with $C_1 > 0$ and $\eta > 0$.

Theorem 2: There exists optimal control $\left(u_1^*, u_2^*\right)$ that minimizes the objective functional J over U given by $u_1^* = \max\left\{0, \min\left(1, \frac{\left(P_{L_T} - P_{R_T}\right)L^*_T}{A}\right)\right\}$ and $u_2^* = \max\left\{0, \min\left(1, \frac{\left(P_{E_{TH}} - P_{R_T}\right)E^*_{TH}}{B}\right)\right\}$.

Proof: We search for the characterization of u_1^* where there arise three cases for

$u_1^* = \max\left\{0, \min\left(1, \frac{\left(P_{L_T} - P_{R_T}\right)L^*_T}{A}\right)\right\}$ and $u_2^* = \max\left\{0, \min\left(1, \frac{\left(P_{E_{TH}} - P_{R_T}\right)E^*_{TH}}{B}\right)\right\}$.

In terms of Hamiltonian, we get the optimality conditions,

$$\frac{\partial H}{\partial u_1} = Au_1 - P_{L_T}L_T + P_{R_T}L_T$$

Case I: When $\frac{\partial H}{\partial u_1} > 0$, then

$$Au_1 - P_{L_T}L_T + P_{R_T}L_T > 0$$

$$\Rightarrow u_1 > \frac{\left(P_{L_T} - P_{R_T}\right)L_T}{A}$$

Let $\frac{\left(P_{L_T} - P_{R_T}\right)L_T}{A} = \overline{u}_1$

So $u_1 > \overline{u}_1$

$\therefore 0 \geq \overline{u}_1$

Case II: When $\frac{\partial H}{\partial u_1} = 0$, then

$$Au_1 - P_{L_T} L_T + P_{R_T} L_T = 0$$

$$\Rightarrow u_1 = \frac{\left(P_{L_T} - P_{R_T}\right) L_T}{A}$$

$$\Rightarrow 0 < \frac{\left(P_{L_T} - P_{R_T}\right) L_T}{A} < 1$$

$$\therefore 0 < \overline{u}_1 < 1$$

Case III: When $\frac{\partial H}{\partial u_1} < 0$, then

$$Au_1 - P_{L_T} L_T + P_{R_T} L_T < 0$$

$$\Rightarrow u_1 < \frac{\left(P_{L_T} - P_{R_T}\right) L_T}{A}$$

$$\therefore 1 \le \overline{u}_1$$

Therefore $u_1^* = \begin{cases} 0 & \text{if } \overline{u}_1 \le 0 \\ \overline{u}_1 & \text{if } 0 < \overline{u}_1 < 1 \\ 1 & \text{if } \overline{u}_1 \ge 1 \end{cases}$

In compact form

$$u_1^* = \max\left\{0, \min\left(1, \frac{\left(P_{L_T} - P_{R_T}\right) L^*{}_T}{A}\right)\right\} \tag{13}$$

Again for the characterization of u_2^*, we get

$$\frac{\partial H}{\partial u_2} = Bu_2 - P_{E_{TH}} E_{TH} + P_{R_T} E_{TH}$$

Case I: When $\frac{\partial H}{\partial u_1} > 0$, then

$$Bu_2 - P_{E_{TH}} E_{TH} + P_{R_T} E_{TH} > 0$$

$$\Rightarrow u_2 > \frac{\left(P_{E_{TH}} - P_{R_T}\right) E_{TH}}{B}$$

Let

$$\frac{\left(P_{E_{TH}} - P_{R_T}\right) E_{TH}}{B} = \overline{u}_2$$

$$\Rightarrow u_2 > \overline{u}_2$$

$$\therefore 0 > \overline{u}_2$$

$$\text{Therefore } u_2^* = \begin{cases} 0 & \text{if } \overline{u}_2 \le 0 \\ \overline{u}_2 & \text{if } 0 < \overline{u}_2 < 1 \\ 1 & \text{if } \overline{u}_2 \ge 1 \end{cases}$$

In compact form

$$u_2^* = \max\left\{0, \min\left(1, \frac{\left(P_{E_{TH}} - P_{R_T}\right)E_{TH}}{B}\right)\right\} \tag{14}$$

From (13) and (14) we get

$$u_i^* = \begin{cases} 0 & \text{if } \overline{u}_i \le 0 \\ \overline{u}_i & \text{if } 0 < \overline{u}_i < 1 \\ 1 & \text{if } \overline{u}_i \ge 1 \end{cases}$$

This completes the proof.

Results and discussion

In this section we discuss the numerical simulations with the responsible parameters. Our observation is that these two parameters which are the disease contact rate for HIV and TB respectively are mainly liable for dangerous threat. So we intend to control these parameters by applying controls measures, the vaccination control and the treatment control. To illustrate this we have considered 20 years of total time period because the transmission process of HIV and TB is quite long.

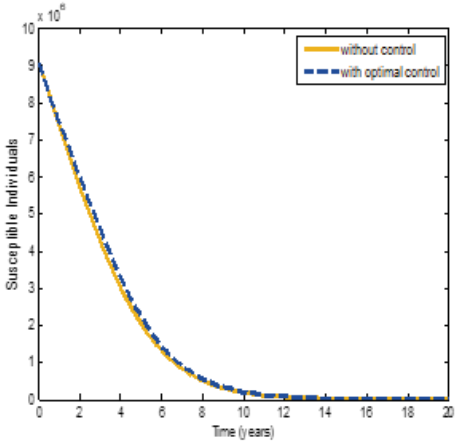

Fig. 1. Dynamic behavior of susceptible individuals considering vaccination as optimal control

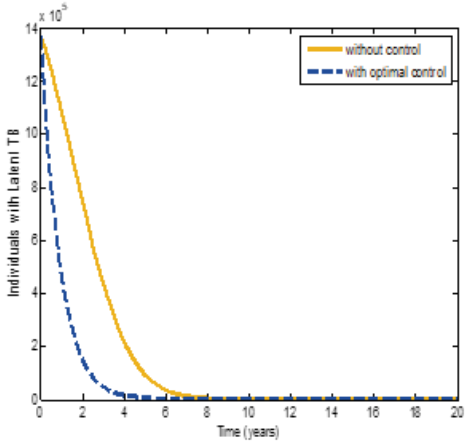

Fig. 2. Dynamic behavior of individuals with latent TB considering vaccination as optimal control

Fig. 1 describes the dynamics of susceptible individuals with the optimal vaccination control where a close look reveals that vaccination has slight impact on the susceptible population that decrease it. Fig. 2 states the dynamics of latent TB individuals applying the vaccination control which has a great impact to decrease the patients with latent TB. That means if we apply vaccination to the patients who have latent

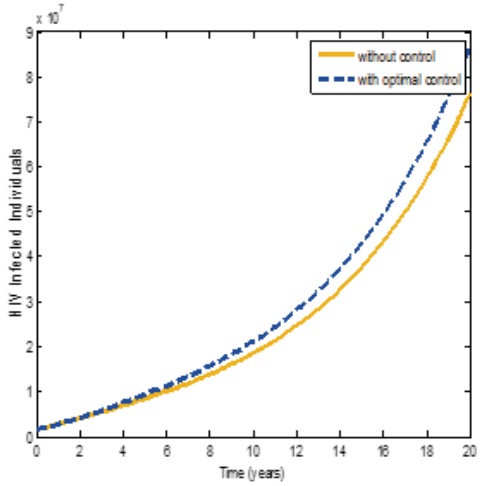

Fig. 3. Dynamic behavior of HIV infected individuals considering vaccination as optimal control

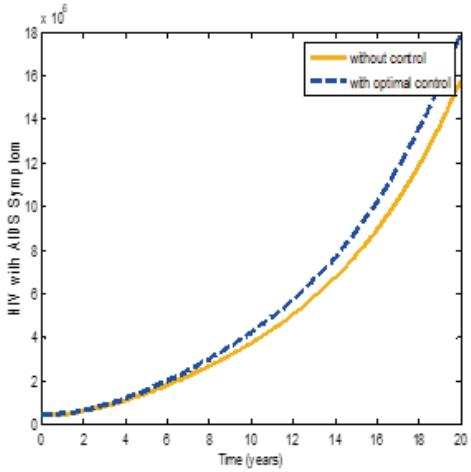

Fig. 4. Dynamic behavior of HIV with AIDS symptom considering vaccination as optimal control

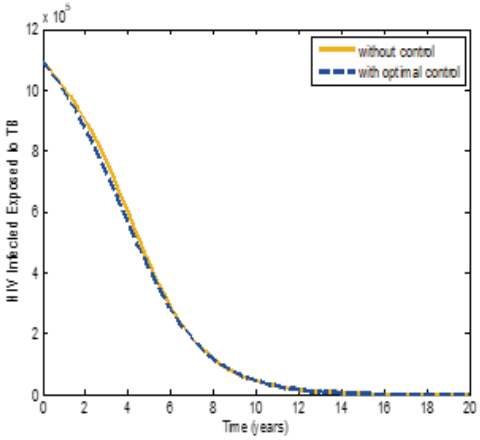

Fig. 5. Dynamic behavior of HIV infected exposed to TB considering vaccination as optimal control

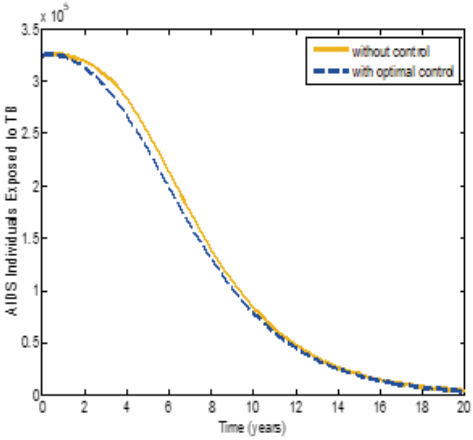

Fig. 6. Dynamic behavior of AIDS individuals exposed to TB considering vaccination as optimal control

TB, they might be get rid of it. Figs. 3 and 4 explain the dynamic behavior of HIV infected individuals and the HIV infected individuals with AIDS symptom without control and with control. From the both Figs. 3-4, we see that after applying the control strategy, the disease has no mode to decrease it means vaccination control has no impact on HIV infected population and HIV infected population with AIDS symptom in this model. Figs. 5 and 6 describe the dynamics of HIV infected individuals exposed to TB and AIDS infected individuals exposed to TB along with optimal control. Both Figs 5-6 show that HIV infected exposed to TB patients and AIDS infected exposed to TB have been decreased from the community when vaccination is induced. Figs. 7 and 8 show the dynamic behavior of AIDS individuals dually infected with TB and exposed to TB individuals with optimal control and without optimal con-

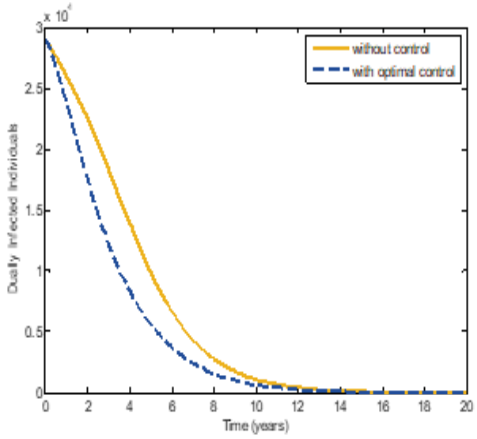

Fig. 7. Dynamic behavior of AIDS individuals dually infected with TB considering vaccination as optimal control

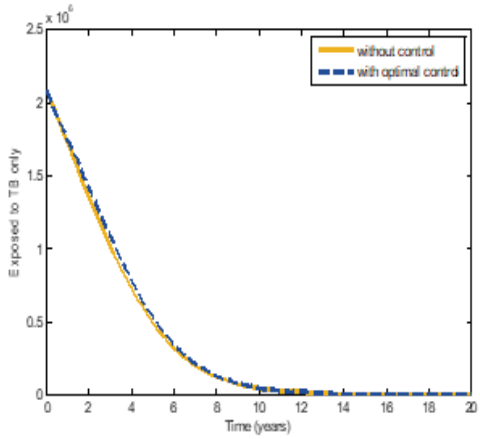

Fig. 8. Dynamic behavior of exposed to TB individuals considering vaccination as optimal control

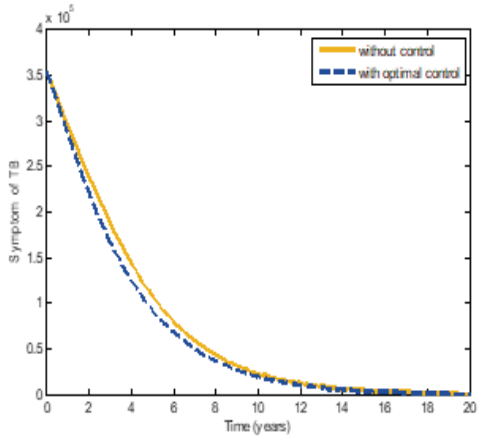

Fig. 9. Dynamic behavior of symptom of TB considering vaccination as optimal control.

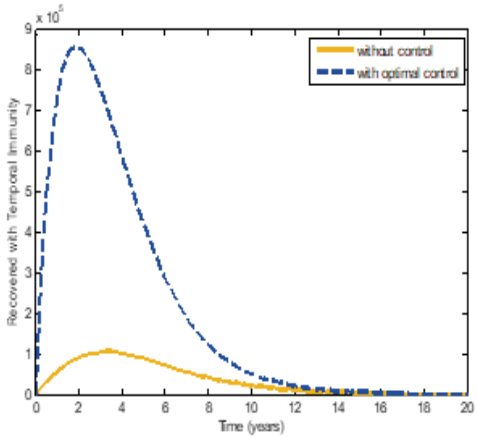

Fig. 10. Dynamic behavior of recovered with temporal considering vaccination as optimal control

trol. Vaccination is equally effective to these two compartments which elicit that AIDS dually infected with TB and exposed to TB patients have decreased after applying the strategy of vaccination control. Fig. 9 shows that the dynamic pattern of symptom of TB is decreasing and vaccination has direct impact on this compartment. If the patients who have symptom of TB get vaccination, the numbers of patients decrease gradually from the community. From the Fig. 10, we get the idea of dynamics of recovered population along with the impact of vaccination control. When the vaccination is applied the recovered population increased with a great extends. This means considerable recovery from the co-infection of HIV and TB is possible by applying vaccination among the general mass population.

Conclusion

In the modern day's public health scenarios, HIV and TB are top at the list of infectious diseases worldwide. So to eradicate or to minimize these kinds of contagious diseases is the gigantic challenge through the world. So proper program for HIV-TB, to create opportunity for reaches on HIV-TB and create awareness among the mass population can be helpful to control the infection rates. Counseling for HIV-TB coinfected persons to a great extent, availability of treatment and antidote, early detection of HIV-TB and plan to reduce the virus transmission should be emphasized. The government and the infectious diseases institutes should take all round steps against HIV and TB to eliminate this curse from the human planet.

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Declaration

The authors declare that this work is their own research findings and it has not been presented and published and will not be presented and published to any other university for similar or any other degree award.

Author's Contributions

This study is a collaborative efforts of all authors. MHA Biswas conceptualized the study, conducted methodological analysis, wrote parts of the computational studies, perform the programming code and formulated the initial draft of the manuscript. SA Samad studied the model analytically, produced some of the literature, checked the parameters, and computed real data to estimate the parameters. The final version of the work has been reviewed and approved by all authors.

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