Evaluation and control estimation strategy for three acting play diseases with six control variables

Muhammad Tahir\textsuperscript{1*}, Gul Zaman\textsuperscript{2} and Syed Inayat Ali Shah\textsuperscript{3}

\textbf{Abstract:} In this article, we prolate, the coinfection mathematical model for the implication of optimal control. Here the model (Tahir, 0004) AIDS/HIV/TB is extended for an optimal control purpose, and for sensitivity analysis of the dominant parameters involved in infection. For this purpose, initially, we apprized the threshold number of the concern model. Then the sensitivity analysis is discussed for dominant parameters which mostly spread infection in population. Moreover, simulation is shown in simple graph and area graph which shows the effected area of any population in any community by using Matlab programming. Here our mission is to minimize the coinfection problem from any community. Also we defined six control variables with different schemes to control and minimized infection. In the last section, numerical simulation is presented in a new way by Runge-Kutta method of order four, and Matlab programming which is with and without control or vaccination for the concern model.

\textbf{Subjects:} Advanced Mathematics; Applied Mathematics; Mathematical Biology

\textbf{Key words:} Mathematical model; threshold number; sensitivity analysis; biological region; optimal control; TB/HIV/AIDS; numerical simulation

\textbf{ABOUT THE AUTHORS}

Muhammad Tahir\textsuperscript{1*} is the corresponding author of this research article. His area of research, is Mathematical Biology, working in department of Mathematics, Northern University, Wattar, Nowshera Pakistan. E-mail addresses: tahir@northern.edu.pk; Tel: +92-345-9063508

Gul Zaman\textsuperscript{2} currently working as a Vice Chancellor at University of Malakand, lower Dir, 18800, Chakdara, Pakistan. His Ph.D from, Pusan National University, South Korea in 2008. E-mail addresses: talash74@yahoo.com

Syed Inayat Ali Shah\textsuperscript{3} currently working as a professor and dean in Mathematics at Islamia College University Peshawar, 25000 Pakistan. His Ph.D degree from Saga University Japan in 2002. E-mail addresses: inayat64@gmail.com.

\textbf{PUBLIC INTEREST STATEMENT}

In this study we presented the optimal control for a super infection model. As we know all the diseases of this study are so harmful and transmissible, even if an individual get infection it can transmit in to other individual or in family member, from where it circulate in the entire world. In this study we shown that vaccination is the key thing to fight against these coinfeected diseases if some one infected, or expel all the unhygienic environment, because it enter in the whole community. The study is valuable for a single common man to avoid from these virus should adopt good and healthy environment, isolation from infected individuals, vaccination at proper time, etc. The study also provide a wide range of safety if precaution are adopted in advance, and if infected any individual should treated at time is one of the necessary advise for all man kind. Otherwise we shown the infection spread in whole population and in last in the entire world.
1. Related literature

Work in mathematical biology is typically a collaboration between mathematicians and biologists. Mathematical models having great role in science field. Developing a mathematical model is termed “mathematical modeling” which is used in natural sciences, like physics, chemistry, biology, as well as, in engineering sciences like, computer sciences, electrical sciences. It is the art to transfer any problems from application area into tractable mathematical formulation. Mathematical models are the process that uses maths to represent, analyze, make predictions, or otherwise provide insight into the real-world phenomena. Similarly the control of an infectious disease is obligatory; therefore for some mathematical models and methodology are adopt to control the infection is known optimal control.

1.1. Acquired immune deficiency syndrome

The HIV virus leads AIDS which stands for Acquired Immune Deficiency Syndrome considered a global problem of all human health. HIV is a serious global health problem now a day. In 2017, there are 1.8 million people infected by HIV, while 940,000 have died with AIDS-related issues and causes. The arrival of HIV/AIDS in United States nearly 1970. If CD4 T cells are fewer in number make weaker the immunity system and turn in AIDS. In 1986 Robertson et al. discussed AIDS with its related virus (LAV/HTLV-III) (Robertson et al., 1986). To diagnosed AIDS the number of CD4 T cells less than 200 or you have an AIDS-defining complication. AIDS transmitted through sex, transfusions of blood, needles sharing, pregnancy, delivery, and breastfeeding. A recent study about AIDS was presented by Han et al. on 27 September 2018 which related to CD4 and CD8 cell normalization (Etefagh et al.; Han et al., 2018; Tahir et al., 2018). Tahir et al. presented optimal control for MERS-Corona Virus on 19 December 2018. In this situation a control law is required through which we judge the problem and minimize the infection. A recent study about AIDS was presented by Han et al. on 27 September 2018 which related to CD4 and CD8 cells normalization and Muhammad Tahir, Syed Inayat ali shah presented coinfection model (Zaman et al., 2009; Zheng, 2016). Optimal control theory is one of the powerful tools used in mathematical to control or reduced infection from community and population. In this situation a control law is required through which we judge the problem and minimize the infection.

1.2. Human immunodeficiency virus and tuberculosis

Human Immunodeficiency Virus is a global health problem that is lentivirus and creates HIV infection and one of the most studied infectious diseases in the world. Its believed that the HIV was originated in Congo(Kinshasa), in 1920 while, HIV first case occurs in a man determined by its sample, s blood whose was died in Congo, showed confirmed HIV infection (Pence, 2008; Zhu et al., 1998, Evian, 2006). HIV is categorized into two forms HIV 1 and HIV 2. The HIV 1 virus easily transmitted and more virulent, so why majority human infected by first type and found more globally (Reeves & Doms, 2002) and the virus chain is closely related to chimpanzees. While HIV 2 is slow in transmission as compared to HIV 1 and mostly confined in West Africa. Optimal control was presented by B.M.Adam et al. HIV dynamics Modeling, data analysis, and optimal treatment protocols (Adamsa et al.). Optimal controls of multidimensional and principle of time-optimal controls were discussed by (Zheng, 2016), (Zheng, 2015). Also for the optimal control purpose Joshi et al. discussed the optimal control of an HIV immunology model (Khan et al., 2013; Joshi, 2002; Thornley et al., 2008). Recently Ciaranello et al. presented Simulation modeling and metamodeling to inform national and international HIV policies for children and adolescents (Iaranello et al., 2018; Loe et al.; Tahir et al., 2018). Recent work on optimal control at 2018 has been done by M Tahir et al. presented the stability and optimal control of MERS CoV (Swierczynski, UNAID, 2007b).

Tuberculosis considered one of the ancient diseases. According to hypothesize TB originated 150 million ago (Hayman, 1984, Samanta 2010a, Samanta 2010b). TB was considered 3 million years ago, in community of East Africa, but it only infected hominid that time (Gutierrez et al., 2005). Treatment and prevention of TB is permanent challenge considered in the course of human life and history (Luca & Mihaescu, 2013; Salvioli, 2001). TB worldwide infects approximately
2 billion of people, and each year infects 10.4 million new peoples. Simply one third population are carriers TB and a chance to develop active disease in the world (Global Tuberculosis Report, 2016; Mac Donald & Izzo, 2015). Recently Murphyet et al. presented the gender differences of tuberculosis with treatment (Murphy et al., 2018). Tuberculosis chemotherapy discussed by Tweed et al. in the previous year 2018 (Tweed et al., 2018, Samanta 2011, Sharma & Samanta, 2014). Efforts are required for TB patient about health care, knowledge of TB, diagnosis, and finding strategies to improve in active TB (Lambert & Van der Stuyft, 2005; Sreeramareddy et al., 2009; Starla et al., 2008). The optimal control strategy of an fractional multistrain TB model was presented by N. H. Sweilam, and S. M. AL Mekhlafi (Sweilam & AL-Mekhlafi, 2016). Similarly numerical approach for Optimal control was presented by (Sweilam & AL-Mekhlafi, 2016) for the time delay of multistrain fractional model tuberculosis. The optimal control strategy of an fractional multistrain TB model was presented by N. H. Sweilam, and S. M. AL Mekhlafi (Khan et al., 2012). Similarly numerical approach for Optimal control was presented by (Markowitz et al., 2007) for the time delay of multistrain fractional model tuberculosis.

Here the model (Tahir et al.) lengthen for minimization of coinfection AIDS/HIV and TB from any population, also for the analysis of $R_0$ dominant parameters involve in infection. For this objective we proceed as, after the literature and reproductive number, we discussed the sensitivity index of $R_0$, to know the role of main parameters in infection spreading. Then six control variables are defined which are characterized as: $q_1$ represent and used treatment for TB, $q_2$ assigned to avoid closeness with the TB patient, $q_3$ assigned for multidrug and cotreatment and resistant HIV and TB, or start HIV and TB therapy, $q_4$ represented for health care center, $q_5$ are using for air precaution again TB, and $q_6$ using stigma of TB-HIV/AIDS respectively to (2002b) control infection there. We observed that by using the control variables it is obvious that the coinfection get abate from community. We presented numerical interpretation with and without control in the final section, also different images of the graph are also presented to know about the population involved. The numerically results shown with and without vaccination by RK4 and Matlab programming are also adopted.

2. Materials, methods and problems formulation
This part of the article possess, the mathematical coinfection model defined in (Tahir et al.) that is, AIDS/HIV and TB with eleven infection classes. Here our model contain coinfection characteristics of TB/HIV and chronic stage AIDS(HIV) transmission stage. So we divided the whole population in to 11 classes as follows:

- $a_1$. Susceptible individual are represented by $M_1(t)$.
- $a_2$. Latent TB individual are represented by $M_2(t)$ with no symptom of TB.
- $a_3$. Active TB individuals are represented by $M_3(t)$ with TB infection.
- $a_4$. Recovered TB individuals assigned by $M_4(t)$.
- $a_5$. HIV infected individuals represented by $M_5(t)$ with no symptom of AIDS.
- $a_6$. HIV infected individuals having AIDS symptom are represented by $M_6(t)$.
- $a_7$. HIV infected individuals represented by $M_7(t)$ which are under HIV treatment.
- $a_8$. Latent TB individuals represented by $M_8(t)$ with coinfected HIV(pre-AIDS).
- $a_9$. HIV infected individual (pre-AIDS) represented by $M_9(t)$ and having active TB symptom.
- $a_{10}$. HIV infected individual represent by $M_{10}(t)$ with no AIDS symptom.
- $a_{11}$. Active TB individuals and infected by HIV with AIDS. Now the assumptions from $a_1$ upto $a_{11}$ leads a compartmental mathematical coinfection model with differential equations at time “t” is given by:
\[ M_1^* = \mu - |M_1 - M_1 - d_\theta M_1|(t), \]
\[ M_2^* = |(S - k_1 + \tau_1 + d_\theta M_2)t + \gamma_2(M_3)|](t), \]
\[ M_3^* = [(k_1 M_2 - (\tau_2 + d_\theta + d_\theta) M_3)](t), \]
\[ M_4^* = [(\tau_2 M_2 - \tau_3 M_3 - (\gamma_3 + + d_\theta) M_4)](t), \]
\[ M_5^* = [(M_1 + \alpha_1 M_6 + M_4 + \omega_1 M_5)t - (\rho_1 + \phi + \psi + d_\theta) M_5)](t), \]
\[ M_6^* = [(\rho_1 M_5 + \omega_2 M_{10} - \alpha_3 M_6 - (d_\theta + d_\theta) M_6)](t), \]
\[ M_7^* = [(\phi M_6 + u_2 M_9 + r_1 M_9 - (\omega_2 + d_\theta) M_7)](t), \]
\[ M_8^* = [(\gamma_2 M_{10} - (k_2 + k_3 + d_\theta) M_8)](t), \]
\[ M_9^* = [(\delta M_3 + \psi M_5 + \alpha_2 M_6 + \tau_2 M_8 - (\rho_2 + d_\theta + d_\theta) M_9)](t), \]
\[ M_{10}^* = [(u_1 M_9 + (1 - r) M_3 M_{10} - (\gamma_2 + \omega_2 + d_\theta) M_{10})](t), \]
\[ M_{11}^* = [((1 - (u_1 + u_2)) \phi M_9 - (\alpha_2 + d_\theta + d_\theta) M_{11})](t). \]  

(1)

We fix the following initial conditions for model (Hayman, 1984) as:
\[ [(M_1, M_2, M_3, M_4, M_5, M_6, M_7, M_8, M_9, M_{10}, M_{11})](t) \geq 0. \]

Here certain assumptions are drawn in model [1] like:

- \( \eta_{\alpha}, \delta, \psi, \gamma_1, \gamma_2, \eta_C \) are the modification parameters.
- \( \mu \) represent recruitment rates.
- \( \beta_1 \) represents TB transmission rate.
- \( \beta_2 \) shown HIV transmission rate.
- \( k_1, \) show the rate through individuals leave compartment \( a_2 \) and become infected.
- \( k_2 \) assign for the individuals to leave compartment \( a_8 \) and enter in TB infection compartment.
- \( k_3 \) assign for the individual to leave from compartment \( a_8. \)
- \( \rho_1 \) represents individuals rate leave compartment \( a_5 \) and join compartment \( a_6. \)
- \( \rho_2 \) individuals leave compartment \( a_9. \)
- \( \alpha_1 \) represent the individual leave compartment \( a_9. \)
- \( \omega_2 \) represents the individuals leave compartment \( a_{10}. \)
- \( \phi \) assign HIV infected individuals treatment rate for compartment \( a_5 \) infected individuals.
- \( \tau_1 \) assign for TB individuals treatment rate of compartment \( a_2 \) infected individuals.
- \( \gamma_2 \) represent the treatment rate of compartment \( a_3 \) infected individuals.
- \( \alpha_1 \) AIDS individuals treatment rate.
- \( \alpha_2 \) HIV individuals treatment rate of all 11 classes individuals.
- \( r \) represents fraction for compartment \( a_8 \) individuals who used TB/HIV combine treatment.
- \( d_\theta \) assign rate for TB individuals induced death.
- \( d_\theta A \) is the rate assign for AIDS and TB-induced death.
- \( d_\theta \) assign for natural death.
- \( d_\theta \) assign rate for AIDS individuals induced death.

The population of model (Hayman, 1984), are represented by \( N(t) \) as under,
\[ N(t) = [(M_1 + M_2 + M_3 + M_4 + M_5 + M_6 + M_7 + M_8 + M_9 + M_{10} + M_{11})](t). \]

Here we assume the following:

The “Active TB” infected individuals will infect susceptible “latent TB” individuals by the rate of transmission \( T. \)
\[ T(t) = \frac{\beta_1}{N(t)}(M_3 + M_9 + M_{11})(t). \]

Also individuals with HIV, infect susceptible HIV individuals transmission rate \( C, \)

\[ C(t) = \frac{\beta_2}{N(t)} [M_4 \Psi_4 + M_9 + M_8 + M_{10} + \xi M_7 + \xi_4(M_6 + M_{11})](t). \]

Also we need the following more assumptions as:

\( \beta_1 \) considered the effectiveness TB individuals infected rate.

and \( \beta_2 \) represents the effectiveness rate to HIV infected individuals.

\( \xi_1 \geq 1 \) represent for parameter of modification with relative infectiousness of AIDS symptom individuals.

\( \xi_c < 1 \) represent the parameter of modification with body immunity of HIV suffered individual produced with antiretroviral treatment.

Now the population of model (Hayman, 1984), is represented by \( N(t) \), so differentiate the above model (Hayman, 1984) we get,

\[ \frac{dN(t)}{dt} \leq -\mu - d_N N(t). \]

Thus model (Hayman, 1984) will study in the following biological closed region,

\[ \Psi = \{ \{M_1, M_2, M_3, M_4, M_5, M_6, M_7, M_8, M_9, M_{10}, M_{11}\} | t \in M_{11} \}, 0 < V \leq \mu - d_N N(t) \}. \]

While we have value “V” as,

\[ V = \{(M_1 + M_2 + M_3 + M_4 + M_5 + M_6 + M_7 + M_8 + M_9 + M_{10} + M_{11})\}(t). \]

3. Calculation of reproductive number “\( R_0 \)"

The mathematical models are studied with basic reproduction number \( R_0 \) which is considered a fundamental parameter. Now \( R_0 \) is the basic value and key factor in mathematical epidemiological model (Tahir et al., 2020). The value of \( R_0 \) has been derived by different techniques, but an easy method is the next generation matrix approach which is very useful for biologically meaning of the basic reproduction number or threshold number for continuous time differential equations (Thornley et al., 2008). We proceed in mode (Hayman, 1984) defined in (Tahir et al.) as, the rate of secondary infectious \( F \) represented the infectious class also the rate of a disease progression is represented by \( F \) of non-infected class. Now from above statement, the basic reproduction value of proposed model (Hayman, 1984) is given.

\[ R_0 = \text{Max} \left( \frac{\psi(t)}{\xi_2 + \xi_7 + \xi_9}, \frac{\psi(t)}{\mu_1 + \phi + d_0} \right). \]

The above \( R_0 \) is the required value of our model.

4. Sensitivity analysis of reproductive number “\( R_0 \)"

In this subsection, we discuss the sensitivity indices of our model. To check the disease transmission in any population at any time we need to discuss the parameters that are highly effects and involve in the reproductive number. Sensitivity analysis determine and predict about the parameters values involve in a model.
Definition: The normalized sensitivity reproductive number, $S$ index which depends on differentiability on parameter $\phi$, can be defined by,

$$S_{\phi} = \frac{\phi \partial R_0}{R_0 \partial \phi}$$

We analyze the most highly important effective parameters of reproductive number which can be necessity further use in the control of infection.

The Table 1 shows that there are two influences parameters involve on the rate of reproductive number, e.g. positive and negative. In addition, $\mu, \alpha_2, \gamma_1$ and $\gamma_2$ have positive influences while $r_2, \alpha_2$, and $k_1$ have negative effect on the rate of reproductive number. From this we describe that, increasing or decreasing 10 percent will increase or decrease the rate of reproductive number 10 percent, 8.087 percent, 1.245 percent and 8.315 percent are given in Figures 1-3 and 6.

On the other side we see that the parameters index by, $r_2, \alpha_2$ and $k_1$ describe that increase its values 10 percent should decrease it 10 percent reproductive number upto 7.687, 7.761 and 9.011 given in Figures 4, 5, 7 and 8.

Now if we want to control HIV infection we need to focus on parameter $\mu$ which have highest sensitivity index 1.0000, which means decreasing its value 10 percent will decrease the rate of reproductive number by 10 percent. The parameters $\mu, \alpha_1, \gamma_1$ and $\gamma_2$ have collective got 2.7648 sensitivity index, then by decreasing above parameters 10 percent, will decrease the rate of reproductive number by 27.648 percent. In the way, the parameters $r_2, \alpha_2$ and $k_1$ collectively got 2.4459 sensitivity index. If we want to increasing HIV infection up to 24.459 by 10 percent, causes to decreased reproductive number 24.459. From these parameters we see that it easy to develop control strategy for model defined in (Tahir et al., 2019).

| Parameter                      | Sensitivity Index | Value   |
|--------------------------------|-------------------|---------|
| Recruitment rate               | $S_\mu$           | +1.0001 |
| AIDS treatment rate            | $S_{\alpha_1}$    | +0.8087 |
| Rate through class change      | $S_{\alpha_2}$    | -0.7687 |
| HIV Rate treatment             | $S_{\gamma_1}$    | -0.7761 |
| Modified parameter             | $S_{\gamma_2}$    | +0.1245 |
| Rate through individual left class | $S_{\beta}$    | -0.9011 |
| Modified parameter             | $S_{\beta_1}$     | +0.8315 |

Figure 1. The plot shows TB/ HIV/AIDS individuals.
Figure 2. The plot shows TB/HIV/AIDS individuals.

Figure 3. The plot shows TB/HIV/AIDS individuals.

Figure 4. The plot show sensitivity analysis for reproductive number $R_0$ verses $\sigma$, and $\mu$. 
Figure 5. The plot show sensitivity analysis for reproductive number $R_0$ verses $\omega_1$ and $\alpha_1$.

Figure 6. The plot show sensitivity analysis for reproductive number $R_0$ verses $\omega_2$ and $\gamma_2$.

Figure 7. The plot show sensitivity analysis for reproductive number $R_0$ verses $\sigma$ and $\mu$. 
5. Optimal control problem of the proposed model

Optimal control in mathematical models for any problem is considered one of the best tools for the complex dynamical system (Robertson et al., 1986). The said technique applied to the dynamics structure of the epidemic disease study, and for more study refer to (Kumar et al., 2007; Lawn & Zumla, 2011; Tuberculosis, 2002; UNAIDS, WHO, 2007a). Now we apply optimal control to minimized infected individuals and increase susceptible as well as, recovered individuals. Now we are going to define six control variables for $q_{11}$ states variables, which are $(M_1, M_2, M_3, M_4, M_5, M_6, M_7, M_8, M_9, M_{10})$ and $M_{11}(t)$ . In Equation [2] we define the control variables in time “t” which are define as below,

$$
M^*_1 = \mu - M_1 - M_2 - d_
u M_1 + q_1 L_{TH} + q_2 I_T + q_3 M + M_4 M_H + q_5 I_{TH} + q_6 A,
$$

$$
M^*_2 = S + r_1 M_3 - (k_1 + r_1 + d_N) M_2 + q_1 L_{TH} + q_2 I_T + q_3 X,
$$

$$
M^*_3 = k_1 M_2 - (r_2 + d_T + d_N + d) M_3 + q_1 L_{TH} + q_2 I_T + q_3 X,
$$

$$
M^*_4 = r_3 M_4 + r_2 M_3 - (r_1 + r_1 + d_N) M_4 + q_2 I_T,
$$

$$
M^*_5 = M_1 - (\phi + \gamma + d_0) M_5 + 1 M_6 + M_7 + \omega_1 M_8 + M_9 + L_{TH} + \omega_3 X + q_4 X_H + q_5 I_{TH},
$$

$$
M^*_6 = \phi_1 M_5 + \omega_2 M_10 - \alpha_3 M_6 - (d_N + d_0) M_6 + q_1 L_{TH} + q_2 I_T + q_3 M + q_4 X_H + q_5 A.
$$

(2)

$$
M^*_7 = \phi M_2 + u_1 r_2 M_3 + r_3 M_8 - (\omega_1 + d_N) M_7 + q_1 L_{TH} + q_2 I_T + q_3 R + q_4 M_H + q_5 I_{TH},
$$

$$
M^*_8 = r_2 M_{10} - (k_2 + d_0) M_7 + q_2 I_T + q_3 M + q_4 M_H + q_5 I_{TH},
$$

$$
M^*_9 = \delta M_3 + \gamma M_5 + \alpha_2 M_6 + \alpha_2 M_8 + \alpha_2 + d_M + d_T) M_6 + q_1 L_{TH} + q_2 I_T + q_3 M + q_4 M_H + q_5 I_{TH},
$$

$$
M^*_10 = u_2 r_1 M_3 + (1 - \tau_1) k_1 M_3 - (r_2 + r_1 + d_N + d_T) M_10 + q_4 M_H(t) + q_5 I_{TH},
$$

$$
M^*_11 = (1 - (u_1 + u_2)) r_2 M_3 - (a_2 + d_N + d_2) M_{11} + q_1 X.
$$

Here following conditions are subjected for Equation [2], for control variables, $q_1, q_2, q_3, q_4, q_5$ and $q_6$ are assigned for,

- $q_1$: used treatment for TB,
- $q_2$: take isolation from TB patient.
- $q_3$: assigned for multidrug and cotreatment and resistant HIV and TB, or start HIV and TB therapy.
- $q_4$: represented for health-care center, to control infection there.
- $q_5$: air precaution again TB.
- $q_6$: using stigma of TB-HIV/AIDS respectively.

Now we define an objective functional which control our problem that minimized infection individuals of all classes, and maximized susceptible also recovered individuals. For the required objective we defining six control variables given above. Now to control the problem our required objective functional is given by,
\[
J(q_1, q_2, q_3, q_4, q_5, q_6) = \min_{t_0}^{t_{\text{end}}} \{(Z_1 M_1 + Z_2 M_2 + Z_3 M_3 + Z_4 M_4 + Z_5 M_5 + Z_6 M_6) \\
+ 7 M_7 + Z_8 M_8 + Z_9 M_9 + Z_{10} M_{10} + Z_{11} M_{11}(t) \\
+ \frac{1}{2} \left\{(W_1 q_1^2 + W_2 q_2^2 + W_3 q_3^2 + W_4 q_4^2 + W_5 q_5^2 + W_6 q_6^2)\right\}(t) dt
\]

(3)

We mention the above terms as: Z_1 Susceptible individuals, Z_2 TB unexposed individuals, Z_3 infected TB individuals, Z_4 recovered TB and HIV individuals without AIDS, Z_5 HIV/AIDS individuals, Z_6 HIV treatment individuals, Z_7 both TB and HIV infected individuals, Z_8 TB/HIV with no AIDS individuals, Z_9 HIV and TB recovered individuals without AIDS and HIV and AIDS individuals, Z_{10} TB/HIV no AIDS and Z_{11} TB/HIV/AIDS respectively. Here our goal is to increase recovered individuals and minimize infected individuals. For this mission we need to define the following control set, Also the terms used in equation [3] are characterized by the following:

- \(\frac{1}{2} W_1 q_1^2\) used treatment for “TB”.
- \(\frac{1}{2} W_2 q_2^2\) take isolation from TB patient.
- \(\frac{1}{2} W_3 q_3^2\) assigned for multidrug and co-treatment and resistant HIV and TB, or start HIV and TB therapy.
- \(\frac{1}{2} W_4 q_4^2\) represented for health care center, to control infection there.
- \(\frac{1}{2} W_5 q_5^2\) is using airborne precaution against “TB”.
- \(\frac{1}{2} W_6 q_6^2\) using stigma or injection of “TB” and “HIV/AIDS”.

Now to find control function for the Equation [3] processed as below:

\[
J(q_1, q_2, q_3, q_4, q_5, q_6) = \min_{\varphi(t)} \{J(q_1, q_2, q_3, q_4, q_5, q_6)\} \text{ such that } (q_1, q_2, q_3, q_4, q_5, q_6) = \varphi(t)
\]

Control system set for Equation [3] is defined as,

\[
Q=\{q_1, q_2, q_3, q_4, q_5, q_6(t)\} \text{ is lebesgue measurable on } [1,0], 0 \leq q_i(t) < 1
\]

with \((i = 1, 2, 3, 4, 5, 6)\)

6. Optimal control existence of model

By considering the control set system (Mac Donald & Izzo, 2015) in time \(t = 0\) now existence for optimal control, we define both of Equations [4] and [5] that is, “a Lagrangian” as well as, “Hamiltonian”. Now Lagrangian equation for optimal control problem, considered,

\[
L(M_1, M_2, M_3, M_4, M_5, M_6, M_7, M_8, M_9, M_{10}, M_{11}) = \{Z_1 M_1 + Z_2 M_2 + Z_3 M_3 + Z_4 M_4 + Z_5 M_5 + Z_6 M_6 + Z_7 M_7 + Z_8 M_8 + Z_9 M_9 + Z_{10} M_{10} + Z_{11} M_{11}\}(t) \\
+ \frac{1}{2} \left\{(W_1 q_1^2 + W_2 q_2^2 + W_3 q_3^2 + W_4 q_4^2 + W_5 q_5^2 + W_6 q_6^2)\right\}. 
\]

Now “Hamiltonian” “H" for the said purpose is given by,

\[
H = L(M_1, M_2, M_3, M_4, M_5, M_6, M_7, M_8, M_9, M_{10}, M_{11}) \\
\left( \frac{d}{dt} \left[ \xi_1 M_1 + \xi_2 M_2 + \xi_3 M_3 + \xi_4 M_4 + \xi_5 M_5 + \xi_6 M_6 + \xi_7 M_7 + \xi_8 M_8 + \xi_9 M_9 + \xi_{10} M_{10} + \xi_{11} M_{11} \right] \right) (t)
\]

Now existence of optimal control, is given below,
\[ H = L + \{ \xi_1 (\mu - M_1 - M_3 - d_6 M_1 + \xi_2 [S + r_1 M_3 - (k_1 + r_1 + d_6) M_1]) \\
+ \xi_3 [k_2 M_2 - (r_2 + d_7 + d_9 + \delta) M_5] + \xi_4 [r_2 M_2 + r_7 M_3 - (\gamma_1 + t) + d_9) M_4] \\
+ \xi_5 [M_1 - (p_1 + \phi + \psi + d_5) M_5] + \alpha_3 M_6 + M_6 + \alpha_1 M_7] \\
+ \xi_6 [r_2 M_2 + \rho_2 M_{10} - \alpha_1 M_6 - (d_6 + d_9) M_6] + \xi_7 [\phi M_6 + u_1 \rho_2 M_9 + r k_3 M_8 \\
- (\omega_1 + d_6) M_7] + \xi_8 [\gamma_2 M_{10} - (k_2 + k_3 + d_9) M_8] \\
+ \xi_9 [\omega M_3 + \psi (t) M_5 + \alpha_2 M_6 + k_3 M_6 - (\rho_2 + d_6 + d_7) M_9] \\
+ \xi_10 [u_2 (t) \rho_2 M_9 + (1 - \gamma) \gamma_3 M_6 - (\gamma_2 + u_2 + d_9) M_{10}] \\
+ \xi_{11} [(1 - (u_1 + u_2)) \rho_2 M_9 - \alpha_2 + d_6 + d_7) M_{11}]) (t) \] (4)

Now “Lagrangian” value, that is “L” is given,

\[ L = [Z_1 M_1 + Z_2 M_2 + Z_3 M_3 + Z_4 M_4 + Z_5 M_5 + Z_6 M_6 + Z_7 M_7 + Z_8 M_8 + Z_9 M_9 + Z_{10} M_{10} + Z_{11} M_{11}] (t) \\
+ \frac{1}{2} (W_1 q_1^2 + W_2 q_2^2 + W_3 q_3^2 + W_4 q_4^2 + W_5 q_5^2 + W_6 q_6^2). \] (5)

Now we have the following result for the existence of proposed model,

**Theorem 9.1** For existence of optimal control we take, \( u^* = (q_1, q_2, q_3, q_4, q_5, q_6) \) \( e Q, \) Such that,

\[ L(q_1, q_2, q_3, q_4, q_5, q_6) = \min L(q_1, q_2, q_3, q_4, q_5, q_6). \]

Subjected to initial conditions of the control system (2).

**Proof:** Now to prove the optimal control existence using in (Murphy et al., 2018) we define positive control variables as well as state variables. To minimizing the case define above the convexity required for the objective functional in Equations (4), \((q_1, q_2, q_3, q_4, q_5, q_6) (t),\) and \( q_6(t) = W \) so by the definition it closed and also convex. Here optimal control system is bounded which show the compactness and fulfill the existence of the proposed model and optimal control for further to integrand on objective functional (Global Tuberculosis Report, 2016),

\[ L = [Z_1 M_1 + Z_2 M_2 + Z_3 M_3 + Z_4 M_4 + Z_5 M_5 + Z_6 M_6 + Z_7 M_7 + Z_8 M_8 + Z_9 M_9 + Z_{10} M_{10} + Z_{11} M_{11}] (t) + \\
\frac{1}{2} (W_1 q_1^2 + W_2 q_2^2 + W_3 q_3^2 + W_4 q_4^2 + W_5 q_5^2 + W_6 q_6^2). \]

Taking the convex in optimal control, that is, set \( W \) which implies the ensure of optimal control, \((q_1, q_2, q_3, q_4, q_5, q_6)\) to minimize (Mac Donald & Izzo, 2015). For optimal control problem we need to find optimal control solution for our purposed model for this we use Maximum principle of Pontryagin, (Mac Donald & Izzo, 2015) to the Hamiltonian as below.

\[ H(y, p(y), u(y), \lambda (y)) = f(y, p(y), u(y)) + \lambda (g(p(y), u(y))). \] (6)

If \((q_1, q_2, q_3, q_4, q_5, q_6)\) we will considered the optimal control solution for the required proposed optimal control problem then obviously there a nontrivial vector exist,

\[ \lambda (y) = (\lambda_1 (y), \lambda_2 (y), \lambda_3 (y) \ldots \ldots \ldots \lambda_n (y)). \]

Such that \( y \) taking for time, that is, \( y = t \)

\[ \frac{dx}{dy} = \partial H(y, x(y), u(y), \lambda (y)) = \frac{\partial H(y, p(t), u(y), u(y), \lambda (y))}{\partial u} \frac{\partial H(y, p(t), u(y), u(y), \lambda (y))}{\partial x}. \] (7)

On Hamiltonian equation we apply the necessary condition and we processed as below.
Theorem 9.2 Suppose that \( \{M_1, M_2, M_3, M_4, M_5, M_6, M_7, M_8, M_9, M_{10}, M_{11}\}(t) \) are the optimal state solution regarding to optimal control variables \( q_1, q_1^*, q_2, q_2^*, q_3, q_3^* \) for the optimal problem (Global Tuberculosis Report, 2016) also (Mac Donald & Izzo, 2015). Then the adjoint variables will exist there \( \lambda_1(y), \lambda_2(y), \lambda_3(y), \lambda_4(y), \lambda_5(y), \lambda_6(y), \lambda_7(y), \lambda_8(y), \lambda_9(y), \lambda_{10}(y) \) and \( \lambda_{11}(y) \) are satisfied.

\[
\begin{align*}
\lambda_1'(y) &= \xi_1(\lambda_1(t) + \lambda_H(t) + dN) - (\xi_2 a_1 + 7N), \\
\lambda_2'(y) &= \xi_1(k_1 + r_1 + dN) - (\xi_3 k_1 + \xi_4 r_1 + Z_2), \\
\lambda_3'(y) &= \xi_1(r_1 + dN + dN) - (\xi_5 k_1 + 9N), \\
\lambda_4'(y) &= \xi_6(y_1 a_7(t) + \lambda_H(t) + dN) - (\xi_7 k_1 + \xi_8 t(t) + Z_4), \\
\lambda_5'(y) &= \xi_8(\lambda_1(t) + \lambda_H(t) + dN) - (\xi_9 k_1 + \xi_{10} t(t) + Z_5), \\
\lambda_6'(y) &= \xi_2(\lambda_1(t) + \lambda_H(t) + dN) - (\xi_3 a_1 + Z_6), \\
\lambda_7'(y) &= \xi_7(a_1 + dN) - (\xi_8 a_1 + Z_7), \\
\lambda_8'(y) &= \xi_9(k_2 + k_3 + dN) - (\xi_{10} k_2 + \xi_{11} k_2 + 1 - r) + Z_8), \\
\lambda_9'(y) &= \xi_{10}(r_2 + dN + dN) - (\xi_{11} r_2 + \xi_{12} r_2 + 1 - r_2) + Z_9), \\
\lambda_{10}'(y) &= \xi_{12}(\lambda_1(t) + \lambda_H(t) + dN) - (\xi_{13} a_1 + \xi_{14} a_1 + 1 - r) + Z_{10}), \\
\lambda_{11}'(y) &= \xi_{13}(\lambda_1(t) + \lambda_H(t) + dN) - (\xi_{14} a_1 - Z_{11}).}
\end{align*}
\]

Where \( \lambda_T = 0 \) and \( \lambda_H = C \)

with the transversality conditions (Boundary conditions).

\( \lambda_i(y) = 0, \) for \( i = 1, 2, 3, 4, 5, 6. \)

Further more the optimal control variables \( w_1^*, w_2^*, w_3^*, w_4^*, w_4^*, w_5^* \) and \( q_1, q_2, q_3, q_4, q_5, q_6 \) are as.

\[
\begin{align*}
q_1^* &= \max \left\{ \min \left\{ \frac{-7T_{11}(t)}{W_1}, 1 \right\}, 0 \right\}, \\
q_2^* &= \max \left\{ \min \left\{ \frac{-f_T(t)}{W_2}, 1 \right\}, 0 \right\}, \\
q_3^* &= \max \left\{ \min \left\{ \frac{-8R(t)}{W_3}, 1 \right\}, 0 \right\}, \\
q_4^* &= \max \left\{ \min \left\{ \frac{-7R_{10}(t)}{W_4}, 1 \right\}, 0 \right\}, \\
q_5^* &= \max \left\{ \min \left\{ \frac{-6T_{10}(t)}{W_5}, 1 \right\}, 0 \right\}, \\
q_6^* &= \max \left\{ \min \left\{ \frac{-3A(t)}{W_6}, 1 \right\}, 0 \right\}.
\end{align*}
\]

**Proof:** Now to find the adjoint Equation [3] for transversality conditions (Luca & Mihaescu, 2013), let considered the Hamiltonian (Global Tuberculosis Report, 2016) by representing \( \{M_1 = M_2 = M_3, M_4, M_5 = M_6 = M_7 = M_8, M_9, M_{10} = M_{11}\}(t) \) then differentiate Hamiltonian equation with respect to time \( (M_1, M_2, M_3, M_4, M_5, M_6, M_7, M_8, M_9, M_{10}, M_{11})(t) \) and we obtain the desired adjoint equation [10]. We find \( q_1^*, q_2^*, q_3^*, q_4^*, q_5^* \) and \( w_6 \). Now differentiate the Hamiltonian with respect to \( q_1, q_2, q_3, q_4, q_5 \) and \( w_6 \) we solve \( \frac{dt}{dt} = 0, \frac{dt}{dt} = 0, \frac{dt}{dt} = 0, \frac{dt}{dt} = 0, \frac{dt}{dt} = 0 \) on the interior on the control set we use optimality conditions. Finally we use a property of the control space \( W \) and to get Equations [10] and [11] which complete the required proof.

Now again by recall Equations [10] and [11] from the optimal control \( w^* \) the characterization of the optimal control. We obtained the State variables and also optimal control variables by the solving optimality system which contain state variables (Global Tuberculosis Report, 2016) and adjoint system (Mac Donald & Izzo, 2015) by boundary condition (Lambert & Van der Stuyft, 2005) and (Sreeramreddy et al., 2009).

Putting the values of \( q_1, q_2, q_3, q_4, q_5, q_6 \) on the control system (Mac Donald & Izzo, 2015) we obtain the following.
\[ M_1^*(t) = \mu - |M_1 - M_1 - dW_3(t)|t + \max \left\{ \min \left\{ \frac{-7L_{TH}}{W_1}, 1 \right\}, 0 \right\} L_{TH}(t) + \max \left\{ \min \left\{ \frac{-6I_T}{W_2}, 1 \right\}, 0 \right\} I_T(t) + \max \left\{ \min \left\{ \frac{-8R}{W_3}, 1 \right\}, 0 \right\} M(t) + \max \left\{ \min \left\{ \frac{-7M_H}{W_4}, 1 \right\}, 0 \right\} M_H(t) + \max \left\{ \min \left\{ \frac{-6I_{TH}}{W_5}, 1 \right\}, 0 \right\} I_{TH}(t) + \max \left\{ \min \left\{ \frac{-3M}{W_6}, 1 \right\}, 0 \right\} M(t), \]

\[ M_2^*(t) = |S(t) + y_3M_3 - (k_1 + r_1 + dW_3(t)|t + \max \left\{ \min \left\{ \frac{-7L_{TH}}{W_1}, 1 \right\}, 0 \right\} L_{TH}(t) + \max \left\{ \min \left\{ \frac{-6I_T}{W_2}, 1 \right\}, 0 \right\} I_T(t) + \max \left\{ \min \left\{ \frac{-8R}{W_3}, 1 \right\}, 0 \right\} M(t), \]

\[ M_3^*(t) = |k_2M_2 - (\tau_2 + d\tau + dN + \delta M_3)|t + \max \left\{ \min \left\{ \frac{-7L_{TH}}{W_1}, 1 \right\}, 0 \right\} L_{TH}(t) + \max \left\{ \min \left\{ \frac{-6I_T}{W_2}, 1 \right\}, 0 \right\} I_T(t) + \max \left\{ \min \left\{ \frac{-8R}{W_3}, 1 \right\}, 0 \right\} M(t), \]

\[ M_4^*(t) = |x_1M_2 + x_2M_3 - (\tau_1 + t + dW_4)|t + \max \left\{ \min \left\{ \frac{-6I_T}{W_2}, 1 \right\}, 0 \right\} I_T(t), \]

\[ M_5^*(t) = |M_1 - (\tau_1 + \phi + \omega + dW_5)|t + \max \left\{ \min \left\{ \frac{-7M_H}{W_4}, 1 \right\}, 0 \right\} M(t) + \max \left\{ \min \left\{ \frac{-6I_{TH}}{W_5}, 1 \right\}, 0 \right\} I_{TH}(t), \]

\[ M_6^*(t) = |y_3M_3 - (\nu_3 + d\nu)|t + \max \left\{ \min \left\{ \frac{-7M_H}{W_4}, 1 \right\}, 0 \right\} M_H(t), \]

\[ M_7^*(t) = |y_3M_3 + (\nu_3 + d\nu)|t + \max \left\{ \min \left\{ \frac{-3A(t)}{W_6}, 1 \right\}, 0 \right\} A(t), \]

\[ M_8^*(t) = |x_1M_1 - (k_2 + k_3 + dW_4)|t + \max \left\{ \min \left\{ \frac{-6I_T}{W_2}, 1 \right\}, 0 \right\} I_T(t), \]

\[ M_9^*(t) = |k_2M_2 - (\tau_2 + d\tau + dN + \delta M_3)|t + \max \left\{ \min \left\{ \frac{-7M_H}{W_4}, 1 \right\}, 0 \right\} M_H(t), \]

\[ M_{10}^*(t) = \max \left\{ \min \left\{ \frac{-6I_T}{W_2}, 1 \right\}, 0 \right\} I_T(t), \]

\[ M_{11}^*(t) = |(1 - (u_1 + u_2))|x_2M_3 - (\omega_1 + d\omega)|t + \max \left\{ \min \left\{ \frac{-3A(t)}{W_6}, 1 \right\}, 0 \right\} A(t). \]

\[ (10) \]

Where the value of \( H \) is given by,

\[ H = |Z_1M_1 + Z_2M_2 + Z_3M_3 + Z_4M_4 + Z_5M_5 + Z_6M_6 + Z_7M_7 + Z_8M_8 + Z_9M_9 + Z_{10}M_{10} + Z_{11}M_{11}(t)| + \frac{1}{2} \left( W_1 q_1^2 + W_2 q_2^2 + W_3 q_3^2 + W_4 q_4^2 + W_5 q_5^2 + W_6 q_6^2 \right) + \xi_1 |M_1 - C M_1(t) - dW_3(t)| + \xi_2 |S + y_3M_3 - (k_1 + r_1 + dW_3(t)|t + \xi_3 |k_2M_2 - (\tau_2 + d\tau + dN + \delta M_3)|t + \xi_4 |x_2M_3 - x_2M_3 + x_2M_3 - (\tau_2 + C + dW_4)|t |t|}$
7. Discussion on numerical simulation

In this subsection of the article, numerical presentation of the model (1) defined in (Tahir et al.) which presented for verification and for analytical purpose. All numerical results obtained by the use of Runge-Kutta order four method. Parameters and its value of simulation given in Table 2, which are biologically feasible and shown then validating and existence of the model. Moreover, the time interval is taken from 0 to 10 units with out vaccination and from 0 to 2500 with vaccination for simulation, and different initial population sizes are taken for compartmental population given in Figures 9-18 with and without vaccination also we presented his different image with a vaccine. Using parameters value, non-negative initial population sizes and time intervals from 0 to 10 shown in Table 2. Here we see that vaccination is necessary for population to control the diseases. From the Figs 09 to 19 it is clear that recovery is fast in case of vaccination, the alternative graph(area covered graph) shows more rapid recovery, while it is noted that the concern proposed model shown that AIDS, HIV and TB individuals showing some minus character, which implies recovery in the early stage with vaccine is not possible, but after 2 months the individuals felling well but only a few individuals were recovered totally with vaccine, and most individuals remain suffer in the concern compartment. The other compartment individuals recovery in very fast from the alternative graph. It implies that consecutive vaccine is so necessary for such viral diseases.

8. Conclusion

In this subsection of the article, we fore a model of superinfection for optimal control purpose defined in (Tahir et al.) also the the sensitivity analysis of splendid parameters which affect the infection in population has been analyzed. In first the model formulated in related infectious classes, then we apprized basic reproductive number, R₀ by next-generation matrix. After we discussed the sensitivity analysis of the reproductive number R₀, shown in Table 1 from Figs 01 to 08. Here first we showed the graph of all infectious classes without control. Also we discussed the optimal control by introducing six control variables q₁, q₂, q₃, q₄, q₅ and q₆ to minimize the infection from population and show the behavior of the graphs in Figs 09 to 19 with and without control. The graph are shown without control, with control also we discussed the graph with area covered in population. We observed that with vaccination the recovery of individuals is very fast in early stages of most compartments observing from figures. Only figure 19 shown minus behavior indicated that with control only few individuals were able to fully recovered and most of them were remain infected in that compartment. All the parameters and their values are given in Table 2.

In this article, we presented a new way of optimal control graphing with area covered in population, which shows more rapid and fast recovery toward any infection accurately. This new optimal control graph and technique helps the scholar and scientist to provide new images in upcoming work to get recovery fast and more accurate. Also this type of graph provide description and an image that in any pandemic the population need to keep precaution to save maximum number of individual or population.
| Notation | Parameter description                              | Value |
|----------|---------------------------------------------------|-------|
| $q_1$    | Parameter of optimal control                      | 2.1200|
| $q_2$    | Parameter of optimal control                      | 1.3200|
| $q_3$    | Parameter of optimal control                      | 0.9400|
| $q_4$    | Parameter of optimal control                      | 2.4567|
| $q_5$    | Parameter of optimal control                      | 3.1000|
| $q_6$    | Parameter of optimal control                      | 1.3560|
| $\mu$   | Recruitment rate                                  | 0.0235|
| $d_\mu$ | Natural death rate                                | 0.0213|
| $\tau_1$| TB treatment rate for $L_I(t)$ individuals        | 0.2230|
| $y_1$   | Parameter of modification                         | 0.1123|
| $y_2$   | Parameter of modification                         | 0.11889|
| $k_1$   | Rate when individuals left $L_I(t)$ and get infection | 0.0125|
| $k_2$   | Rate when individuals left $L_{in}(t)$ and get TB  | 0.0825|
| $k_3$   | Rate when individuals left $L_{in}(t)$ class       | 0.2358|
| $\tau_2$| TB treatment rate $I_I(t)$ class                  | 0.2893|
| $d_I$   | TB-induced death rate                             | 0.1110|
| $\delta$| Modification of the parameter                     | 0.3100|
| $\rho_1$| Rate of individuals left $I_H(t)$ class to A       | 0.5000|
| $\rho_2$| Rate of individuals left $I_{in}(t)$ class         | 0.5800|
| $\Xi$   | HIV treatment rate for $I_{in}(t)$ class          | 0.1969|
| $\alpha_1$| Treatment rate of AIDS                            | 0.0035|
| $\alpha_2$| HIV treatment rate $A_I(t)$ class                  | 1.0000|
| $\omega_1$| Rate individuals leave $C_H(t)$ individual        | 0.1030|
| $\omega_2$| Rate individuals leave $R_H(t)$ individual        | 0.0921|
| $d_A$   | AIDS-induced death rate                           | 0.0035|
| $r$     | $L_{in}(t)$ treatment rate for TB and HIV individual | 0.6660|
| $\lambda$| Susceptible individual with active TB             | 0.2345|
| $\lambda_h$| HIV active individuals rate                       | 0.345|
| $\omega_1$| Parameter of control                              | 0.2212|
| $\omega_1$| Parameter of control                              | 0.0011|
| $d_{A_1}$| Induced death rate of AIDS-TB                      | 0.2100|
| $\eta_A$| Modification parameter                            | 0.6000|
| $\theta_1$| HIV transmission rate                             | 0.1000|
| $\eta_C$| Modification parameter                            | 0.0900|
| $\theta_1$| TB transmission rate                              | 1.7000|
Figure 9. The plot shows sensitivity analysis for reproductive number $R_0$ versus $\alpha_1$ and $\gamma_1$.

Figure 10. The plot shows sensitivity analysis for reproductive number $R_0$ versus $k_1$ and $\eta$.

Figure 11. The plot shows sensitivity analysis for reproductive number $R_0$ versus $k_2$ and $\gamma_2$. 
**Figure 12.** The plot shows sensitivity analysis of different parameters of the reproductive number $R_0$.

**Figure 13.** The plot shows sensitivity analysis of different parameters of the reproductive number $R_0$.

**Figure 14.** The plot shows sensitivity analysis of different parameters of the reproductive number $R_0$. 
Figure 15. The plot shows sensitivity analysis of different parameters of the reproductive number $R_0$.

Figure 16. The plot shows TB/HIV/AIDS individuals behavior with and without vaccination.

Figure 17. The plot shows TB/HIV/AIDS individuals behavior with and without vaccination.
Figure 18. The plot shows TB/HIV/AIDS individuals affected area in population.

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Author details
Muhammad Tahir1
E-mail: tahir@northern.edu.pk
ORCID ID: http://orcid.org/0000-0003-4300-3861
Gul Zaman2
Syed Inayat Ali Shah3
1 Department of Mathematics, Northern University, Nowshera, Pakistan.
2 Department of Mathematics, University of Malakand, Chakdara, Pakistan.
3 Department of Mathematics, Islamia College, University Peshawar, Peshawar, Pakistan.

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