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First and Second Line of Treatment for Tuberculosis: A Mathematical Model with Drug Resistance.

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Abstract - This study proposed a mathematical model of tuberculosis with drug resistance to a firstand second lineoftreatment.Thebasicreproductionnumberforthemodelusingnextgenerationmethodisobtained.Theequilibrium point of the model was investigated and also found the global stability of the disease freeequilibrium and endemic equilibrium for the model. This study shows the effect of resistance rate of the first and second line of treatment to the infected and resistant population. If basic reproduction number is less than one, the disease free equilibrium is globally asymptotically stable and if basic reproduction number is greater than one, then the endemic equilibrium is a globally asymptotically stable.

Keywords - Tuberculosis, Mycobacterium tuberculosis bacteria [Mtb], developed multi-drug resistant [MDR], Basic reproduction number, Stability.

1. Introduction

Tuberculosis is an airborne disease caused by Mycobacterium tuberculosisbacteria (Mtb).Ullahet al. [8] discuss a general SIR epidemic model which represents the directtransmission of infectious disease. It is an ancient disease with evidence of its existence being found in relics from ancient Egypt, India and China [1]. Today, this disease ranks as the second leading cause of morbidity and mortality in the world from a single infectious agent, after the human immunodeficiency virus (HIV) according to Daniel. [10] Interestingly, about one third of the world's population is infected with Mycobacterium tuberculosis bacteriawith approximately nine million people developing active tuberculosis and million people worldwide die from the disease every year. Approximately 480,000 people developed multidrug resistant (MDR) tuberculosis globally with 210,000 of those who developed MDR tuberculosis succumbing to it. In addition to posing a, major health concern to low and middle income countries, tuberculosis affect economic growth negatively. [3] Psycho-social distress that communities go through is enormous. This involves thinking about the loss of their loved ones and the economic impact of taking care of sick ones especially among the low income individuals. This impacts not only the individuals, but also the economic progress of the country. Zaman [7] gives, another category of people largely at risk of contracting tuberculosis are those who work closely or live close to a person with active tuberculosis and they could include health care workers, people living in crowded living spaces or confined places such as schools or prisons. According to Semenza et al. [5] over the last twenty five years, the mortality rate of tuberculosis has greatly decreased by 45% since and this is largely due to effective diagnosis and treatment. However, the world is still far from defeating the disease. About 8 billion US dollars per year is needed for a full response to the global tuberculosis epidemic in low and middle income countries by the year 2015 with a funding gap of 2 billion US dollars per year. This

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amount excluded resources required for research and development, which was estimated to be about 2 billion US dollars yearly. Clearly, this reveals that the current investment in tuberculosis falls below the low and middle income country'sneeds.

Tuberculosis is responsible for more deaths worldwide than any other infectious agent. Waaler and Anderson [4] developed a first tuberculosis model for the transmission dynamics of tuberculosis. The enormous progress in prevention and treatment, tuberculosis disease remains a leading cause of death worldwide and one of the major sources of concern is the drug resistant strain, MDR-TB (multidrug resistant tuberculosis) and XDR-TB (extensively drug resistant tuberculosis). Young et al. [2] studies, tuberculosis is curable provided an early diagnosis is made and one follows the proper treatment regimen which would take six months upto two years for the active tuberculosis to clear. Sharma et al. [9] given that the infected population is similar on the sociological and psychological effect rate. Cohen and Murray[11] modelled epidemics of multi-drug resistant tuberculosis of heterogeneous fitness.

ModelAnalysis

This study will first extend the standard SEIRS mathematical model for the transmission of tuberculosis which will demonstrate the transmission of the Mycobacterium tuberculosis in human hosts taking into account the multidrug resistant (MDR) tuberculosis.

The ModelEquations

This study presents a simple model that can easily be analysed so as to properly understand the dynamics of this disease. Humans can contract MTB tuberculosis through contact with individuals who are infected with the disease after which they enter the exposed phase where a proportion of this class develop active tuberculosis thus moving into the infectious class. If treatment is administered promptly, those who recover from the disease will move to the recovered class and those who delay treatment and develop MDR tuberculosis will move to the resistant class. Those who recover from MDR tuberculosis will move to the recovered class. Given that there is no permanent immunity to tuberculosis, the recovered can lose their immunity and become susceptible again. Figure represent the flow of individuals into the different compartments and it has been constructed with these assumptions: recruitment isby
birth only, a variable population, a constant mortality rate, no permanent immunity to tuberculosis, no immediate infectively.

Thehumanpopulationiscategorizedintosuch that at time $t\geq 0$ there are S, susceptible humans, E, exposed humans to tuberculosis, I, infected humans with active tuberculosis,R_1,resistanthumanstothefirstlineoftreatment,R_2,resistanthumanstothe second line of treatment, R, recovered humans. Thus the size of the human population is given as$N=S+E+I+R_{ES}+R$.Inourmodel,therecruitmentintothesusceptiblehuman populationisbybirthh.Thesizeofthehumanpopulationisfurtherincreasedbythepartial immune humans in R after they lose their immunity at the rate q. The size of human populationisdecreasedbynaturaldeaths(μ)andexposuretoMtb.Theexposedsusceptible to Mtb move to the exposed classes E with the force of infection being þ resulting in an increaseintheexposedclass.Theexposedclassisfurtherdecreasedbynaturaldeath(μ)and the proportion who move to the infected class I after developing active tuberculosis. The infectedclassIisalsoreducedbynaturaldeaths(μ),diseaseinduceddeath(α_1),thosewho recover (ð) and also by those resistance rate to the first and second line of treatment$r_1$and $r_2$respectively.Thustheinfectedclass(I),andtheresistantcl

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asses(R_1andR_2)gainpartial immunity at the rates (ð) and (f) respectively thus moving to the recovered class R thus reducingtheirrespectiveclassesandalsoincreasingtherecoveredclass.Theresistantclasses R_1 ,R_2also reduced by natural deaths (μ) and disease induced deaths while the recoveredclass is reduced by natural deaths ( ) and those who lose their partial immunity at the rateq.
Following Table (1) and (2) gives the description of variables and parameters

Table 1

Description of variables
S(t) = Susceptible humans
E(t) = exposed humans
I(t) = infected humans
R_1(t) = resistant to the first line of treatment
R_2(t) = resistant to the second line of treatment
R(t) = Recovered humans

Table 2

Description of Parameters
þ = Rate at which the susceptible become exposed to Mtb
y = Infection rate
α_1= Disease induced death rate
μ = Rate of natural death
r_1= Resistance rate of first line treatment
r_2= Resistance rate of second line treatment
ð = Recovery after first line of treatment
f = Recovery after second line of treatment
q = Rate at which recovered loss their immunity
α_2, α_3 = Disease induced death rate after first and second resistance respectively

DifferentialEquations
From the above discussion, we get the following system of ordinary differential equations

$$\frac{ds}{dt} = \lambda N - \mu S - \beta SI + \rho R$$

$$\frac{dE}{dt} = \beta SI - (\mu + \gamma)E$$

$$\frac{dl}{dt} = \gamma E - (\mu + \alpha_1 + r_1 + r_2)l,$$

$$\frac{dR_1}{dt} = r_1 i - (\mu + \alpha_2 + \delta)R_1$$

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$$\frac{dR_2}{dt} = r_2 i - (\mu + \alpha_3 + \varphi)R_{2,}$$
$$\frac{dR}{dt} = \delta R_1 + \pi R_2 - (\mu + \rho)\mathrm{R}$$

The above system of equations is (1),

To obtain the equilibrium points for the system of differential equation (1) by equating each of the equations to 0 as shown inbelow

$$\frac{ds}{dt} = \lambda\mathrm{N} - \mu\mathrm{S} - \beta SI + \rho\mathrm{R} = 0$$
$$\frac{dE}{dt} = \beta SI - (\mu + \gamma)E = 0,$$
$$\frac{dl}{dt} = \gamma E - (\mu + \alpha_1 + r_1 + r_2)l = 0,$$
$$\frac{dR_1}{dt} = r_1 i - (\mu + \alpha_2 + \delta)R_1 = 0,$$
$$\frac{dR_2}{dt} = r_2 i - (\mu + \alpha_3 + \varphi)R_{2,} = 0,$$
$$\frac{dR}{dt} = \delta R_1 + \pi R_2 - (\mu + \rho)\mathrm{R} = 0,$$

The above system of equations is (2).

Solving System (2),to get two equilibrium points,one being the disease free equilibrium while the other being the endemic equilibrium .

Disease free equilibrium points (S,E,I,R_1,R_2,R) is expressed as follows:

X0=((S,E,I,R1,R2,R)=((S,E,I,R1,R2,)=($\frac{\lambda\mathrm{N}}{\mu}$, 0,0,0,0,0) and endemic equilibrium point (S*,E*,I*,R1*,R2*,R*p)is expresse3 as follows:

$$\left.\begin{aligned} \mathrm{S} * &= \frac{(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)}{\beta\gamma}, \\ \mathrm{E} * &= \frac{\beta x\,((\mu+\rho)(\lambda\mathrm{N}-\mu x)}{(\mu+\gamma)(\beta x\,(\mu+\rho)-\mathrm{p})} \\ \mathrm{I} * &= \frac{((\mu+\rho)(\lambda\mathrm{N}-\mu x)}{(\beta x\,(\mu+\rho)-\mathrm{p})}, \\ R1 * &= \frac{r_1((\mu+\rho)(\lambda\mathrm{N}-\mu x)}{(\mu+\alpha_2+\delta)(\beta x\,(\mu+\rho)-\mathrm{p})}, \\ , \ R2 * &= \frac{r_2((\mu+\rho)(\lambda\mathrm{N}-\mu x)}{((\mu+\alpha_3+\varphi))(\beta x\,(\mu+\rho)-\mathrm{p})} \end{aligned}\right\} (3)$$

Where x=S*,$p = \rho(\frac{\delta r_1}{((\mu+\alpha_2+\delta)} + \frac{\varphi r_2}{(\mu+\alpha_3+\varphi)},)$

2.4 Condition of Existence /positivity of Equlibrium:

The System will remain positive provided this condition holds:

$$\frac{(\lambda\mathrm{N}-\mu x)}{(\beta x(\mu+\rho)-\mathrm{p})} > 0 \leftrightarrow (\lambda\mathrm{N}-\mu x) > 0 \leftrightarrow \lambda\mathrm{N} > \mu x$$

Substituting for x,

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$$\lambda N > \mu \frac{(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)}{\beta\gamma} \leftrightarrow \lambda N\beta\gamma > (\mu+\gamma)(\mu+\alpha_1+r_1+r_2) > 1.$$

The expression is the condition of existence.

Let us look at the following system of following equations:

$$\frac{dE}{dt} = \beta SI - (\mu+\gamma)E \,, \frac{dl}{dt} = \gamma E - (\mu+\alpha_1+r_1+r_2)l = 0, \frac{dR_1}{dt} = r_1 i - (\mu+\alpha_2+\delta)R_1$$

$$\frac{dR_2}{dt} = r_2 i - (\mu+\alpha_3+\varphi)R_2,$$

,

Let $X=(E,I,R1,R2)^T$ Then above system can be expressed in matrix form as shown below:

$$\frac{dX}{dt} = F(X) - V(X)$$

Where

$$\begin{pmatrix} \beta SI \\ 0 \\ 0 \\ 0 \end{pmatrix}, V(X) = \begin{pmatrix} -\gamma E + \mu + \alpha 1 + r1)I \\ (\mu+\gamma)E \\ -r1 + (\mu+\alpha 2+\delta)R1 \\ r2 - (\mu+\alpha 3+\pi)R2 \end{pmatrix}$$

O9

$$F(X) = \begin{pmatrix} \beta SI \\ 0 \\ 0 \\ 0 \end{pmatrix}, \qquad V(X) = \begin{pmatrix} \gamma E + (\mu+\alpha_1+r_1+r_2)I \\ (\mu+\gamma)E \\ -r_1 + (\mu+\alpha_2+\delta)R_1 \\ r_2 - (\mu+\alpha_3+\pi)R_2 \end{pmatrix}$$

The Jacobian matrix of F(X) and V(X) at the disease free equilibrium X_0 are,

$DF(X_0) = \begin{bmatrix} F_1 & 0 \\ 0 & 0 \end{bmatrix}$, $\mathrm{DV}(X_0) = \begin{bmatrix} V_1 & 0 \\ 0 & 0 \end{bmatrix}$ respectively

Where

$$F_1 = \begin{pmatrix} 0 & \frac{\beta\lambda N}{\mu} & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$ and

$$V1 = \begin{pmatrix} (\mu+\gamma) & 0 & 0 & 0 \\ 0 & (\mu+\alpha_1+r_1+r_2) & 0 & 0 \\ 0 & 0 & \mu+\alpha_2+\delta & 0 \\ 0 & 0 & 0 & -(\mu+\alpha_3+\varphi) \end{pmatrix}$$

Now

$$V^{-1} = \begin{pmatrix} \frac{1}{(\mu+\gamma)} & \frac{0}{r1} & 0 & 0 \\ \frac{\gamma}{(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)} & \frac{}{(\mu+\alpha_1+r_1+r_2)} & 0 & 0 \\ \frac{\gamma r_1}{(\mu+\alpha_1+r_1+r_2)(\mu+\gamma)(\mu+\alpha_2+\delta)} & \frac{r_1}{(\mu+\alpha_1+r_1+r_2)(\mu+\alpha_2+\delta)} & \frac{1}{(\mu+\alpha_2+\delta)} & 0 \\ \frac{\gamma r_2}{(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)(\mu+\alpha_3+\pi)} & \frac{r_2}{(\mu+\alpha_1+r_1+r_2)(\mu+\alpha_3+\pi)} & 0 & \frac{-1}{(\mu+\alpha_3+\pi)} \end{pmatrix}$$

The next generation matrix of the system is given by

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$$E_1 v_1^{-1} = \begin{pmatrix} \left(\frac{\beta\gamma\lambda}{\mu(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)}\mathrm{N}\right) & \frac{\beta N\lambda}{(\mu+\alpha_1+r_1+r_2)} & 0 & 0 \\ 0 & (\mu+\alpha_1+r_1+r_2) & 0 & 0 \\ 0 & 0 & \underline{0} & 0 \\ 0 & 0 & & \end{pmatrix}$$

Now,toobtainthespectralradiusof F_1V_1-^{1}, whichisdefinedasthelargesteigenvalueofandthespectralradiusfortheabovesystemisthebasicreproductionnumberandits expression is given by

$$R_0 = \frac{\beta\lambda\mathrm{N}\gamma}{(\mu+\alpha_1+r_1+r_2)(\mu+\gamma)\mu}$$

StabilityAnalysis

In this section this study will determine the stability of the diseases free equilibrium point. This study can easily establish the local stability of the equilibriums by Routh Hurwitz criteria, so left it. This study will discuss only on the global stability of the disease free and endemic equilibrium.

Global Stability of the Disease Free Equilibrium

The local dynamics of a general SEIRS model is determined by the reproduction number R_0.

If R_0<=I. then each infected individual in its entire period of infectiousness will producelessthanoneinfectedindividualonaverage.Thismeansthatthediseasewillbewipedoutofthepopulation.

If R_0>I,theneach infected individual in its entire infectious period having contact with susceptible individuals will produce more than one infected individual implying that the disease persist in the population.

If R_0=1thisisdefinedasthediseasethreshold, then one individual infects one more individual. For R_0<=I the disease free equilibrium is locally asymptotically stable while for R_0>I the disease free equilibrium becomesunstable.Thediseasefreeequilibriumpoint is points

$(\mathrm{S},\mathrm{E},\mathrm{I},\mathrm{R}_1,R_2,\mathrm{R}) = (\frac{\lambda\mathrm{N}}{\mu},0,0,0,0,0)$.

Theorem: I If R_0<= thenthediseasefreeequilibriumisofthesystem

$(\mathrm{S},\mathrm{E},\mathrm{I},\mathrm{R}_1,R_2,\mathrm{R}) = (\frac{\lambda\mathrm{N}}{\mu},0,0,0,0,0)$.is globally asymptotically stable on Ω.

Proof.ConstructthefollowingLasalle-Lyapunovfunction

$\mathrm{V}(\mathrm{S},\mathrm{E},\mathrm{I},\mathrm{R}_1,R_2,\mathrm{R}) = (\frac{\lambda\mathrm{N}}{\mu},0,0,0,0,0)$.on the thepositively invariant compact setΩ.

Define $\mathrm{V}(\mathrm{S},\mathrm{E},\mathrm{I},\mathrm{R}_1,R_2,\mathrm{R}) = \gamma E + (\mu+\gamma)I$……(4)

Differentiate above equation and using the second and third equations of the system (1), we get

$$\frac{dV}{dt} = \gamma\frac{dE}{dt} + (\mu+\gamma)\frac{dI}{dt}$$

$$\frac{dV}{dt} = [\,\beta\gamma\mathrm{S}\text{-}(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)]I$$

$$\frac{dV}{dt} = [(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)(R_0-1)]I$$

Which is strictly decreasing for R_0<I.

Definetheset$(\mathrm{E},\mathrm{I},\mathrm{R}_1,R_2,\mathrm{R}) \in \Omega$.

Thelargestinvariantset is contained in the set E for which E= 0 or I = 0 or R_1= 0, R_2= 0 Thus

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by Lasalle invariantprincipalthediseasefreeequilibriumisgloballyasymptoticallystableonΩ.

Global Stability of The Endemic Equilibrium Theorem 2. The endemicequilibrium

$$\emptyset = (\mathrm{E}, \mathrm{I}^*, {R_1}^*, {R_2}^*,)$$

Given by equ(3) is globally asymptotically stable on Ω.

Proof: To establish the global stability of the endemic equilibrium $\emptyset$, so constructLypunao function V_1= $\Omega \rightarrow$R where Ω={E(t),I(t),R_1(t),R_2(t)/E(t)>0,I(t)>0, R_1>0,R_2>0}as described by UllahZaman and Islam and it is given as

$$V_1(\mathrm{E}, \mathrm{I}, \mathrm{R}_1, R_2, \mathrm{R}) = L_1[\mathrm{E} - E^* \ln\left(\frac{E}{E^*}\right) + L_2\left[I - I^* ln\left(\frac{l}{I^*}\right)\right] + L_3\left[R_1 - {R^*}_1 \ln\left(\frac{R_1}{{R^*}_1}\right)\right] +$$

$$L_4\left[R_2 - {R^*}_2 \ln(\frac{R_2}{{R^*}_2})\right] \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(5)$$

Where L_1,L_2,L_3,L_4 are positive constants to be later considered.

Taking the derivative of the Lyapunov function V_1as given in equation (5) yields

$$\frac{dV_1}{dt} = L_1[\mathrm{E} - E^* \quad \left(\frac{\beta \mathrm{SI}}{E} - (\mu + \gamma)\right)] + L_2\left[I - I^*\left(\frac{\gamma \mathrm{E}}{l} - (\mu + \alpha_1 + r_1 + r_2)\right)\right] + L_3\left[R_1 -\right.$$

$$R{*}1\, r1IR1 - (\mu + \alpha 2 + \delta) + L4R2 - R{*}2\, (r2lR2 - (\mu + \alpha 3 + \varphi) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots(6)$$

CHOOSING L_1=L_2=L_3=L_4 =1 equ(6) becomes

$$= (E - E^*)(\mu + \gamma)(VV_1R_0 - 1) + (I - I^*)(\mu + \alpha_1 + r_1 + r_2)(VV_1R_0 - 1) + r_1(R_1 -$$

$${R^*}_1)\frac{({R^*}_1 I - I^* R_1)}{{R^*}_1 R} + r_2(R_2 - {R^*}_2)(\frac{I{R^*}_2 - I^* R}{{R^*}_2 R_2})$$

Thus $\frac{dV_1}{dt} \leq 0\ iff R_0 < 1\ and\ {R^*}_1$ I<$I^* R_1\ and\ {R^*}_2\, I < R_2 I^*$.

To have Thus $\frac{dV_1}{dt} = 0\ iff\ E = E^*, I = I^*$.

$R_1 < {R^*}_1, R_1 = {R^*}_1, R_2 = {R^*}_2$ OR $R_0 = 1\ AND\ {R^*}_2$ I= $I^* R_2$

Define the set

$$\emptyset = \{(\mathrm{E}, \mathrm{I}^*, {R_1}^*, {R_2}^*,) \in \frac{\Omega}{\frac{dV_1}{dt} = 0}\}$$

Therefore the largest compact invariant set is singletone set Φ which is the endemic equilibrium. By Lasalle invariant principle Φ is globally asymptotically stable on Ω.

NumericalSimulation

Explain this result through graphically. Consider the parameters as:

□ □0.001, N □ 1, 000, □ □0.398,□□1, r_1 □0.4, r_2 □0.5, □ □0.7, □$_1$ □0.8,□$_2$ □ 0.4,□$_3$ □0.3,□ □ □1,□□1.2, □ □0.4 Then this study gives R_0 =0.1395 <1 and if the initial valuesof susceptible, exposed, infected, resistant of first and second line treatment population are 1, 2, 1, 1, 1 and 1 respectively. The susceptible population goes to its steady state value while exposed, infected, resistant of first and second line treatment population approach to zero as time increase as shown in Figure 1. So that the disease free equilibrium is globally asymptotically stable.

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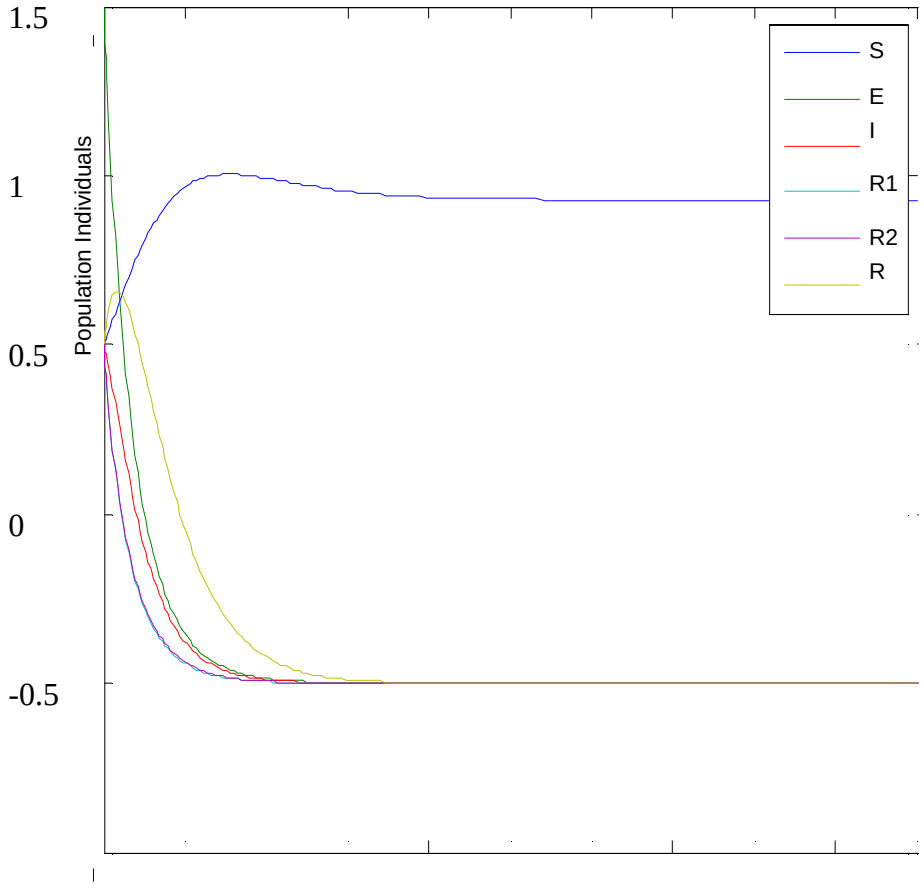
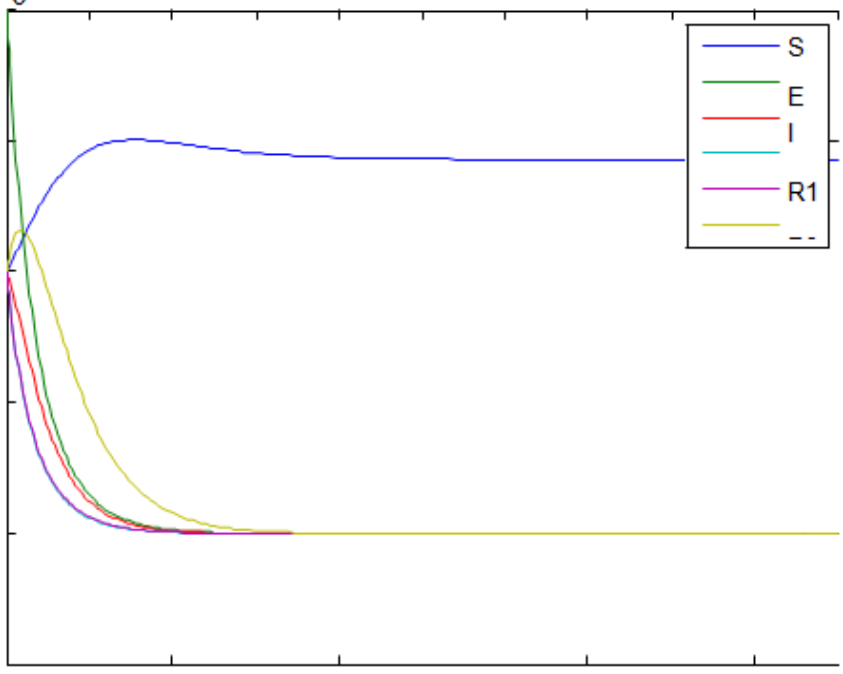


re 1. When R_0 □ 0.1395 □ 1.



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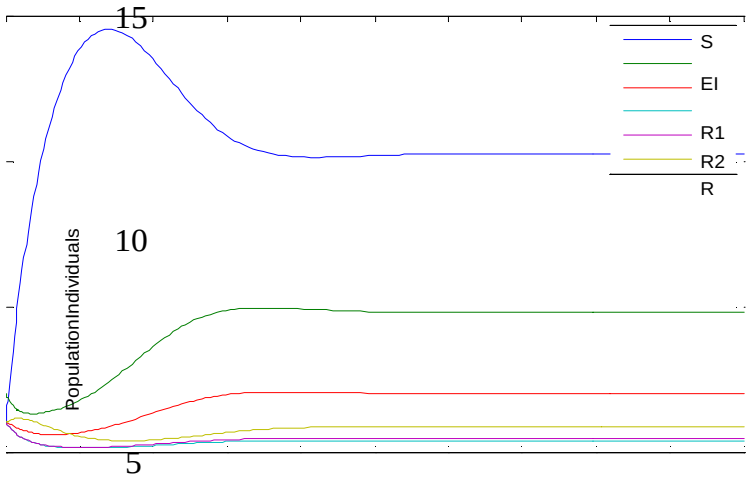
Again if, we take the parameters of the system as: = 0.015, γ N=1,000,β= 0.398,λ= 1, r1 = 0.4, r2= 0.5, μ =0.7, α1= 0.8,α2= 0.4, α 3=0.3, δ =1,π = 1.2,ρ= 0.4.
Then(E* S*, E* ,I*, R1, *,R2* ,R*)= (10.25,4.8,2,38,45,84)and R0 = > 2.091 1.
If the initial values of susceptible, exposed, infected, resistant of first and second line treatment population are 1, 2, 1, 1, 1 and 1 respectively. Therefore by theorem (2), the endemic equilibrium is a global asymptotically stable as shown in Figure 2



Let us take all the parameters are fixed except the resistance rate of the first and second lineof treatments, found that the infected population decreases as the resistance rate of the firstand second line of treatment increases which is shown in figure 3(a) and (b). Thereforeinfected population moves to resistant population of the first line of treatment and to theresistantpopulationofthesecondlineoftreatment,asresistantrateincreasesrespectively.

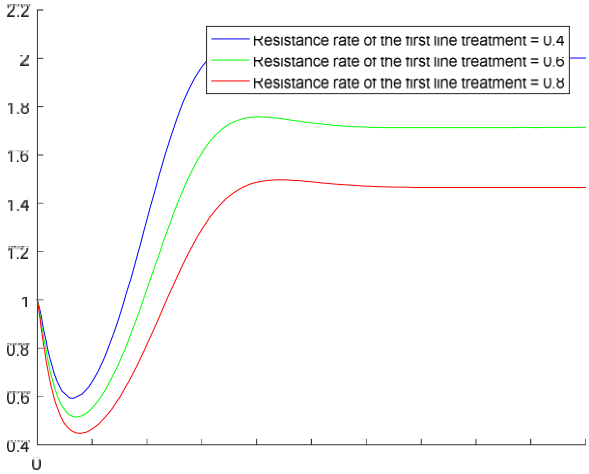


Figure.3(a) Changes in the infected population with respect to resistance rate of the first line treatment, keepingallotherparametersare fixed.

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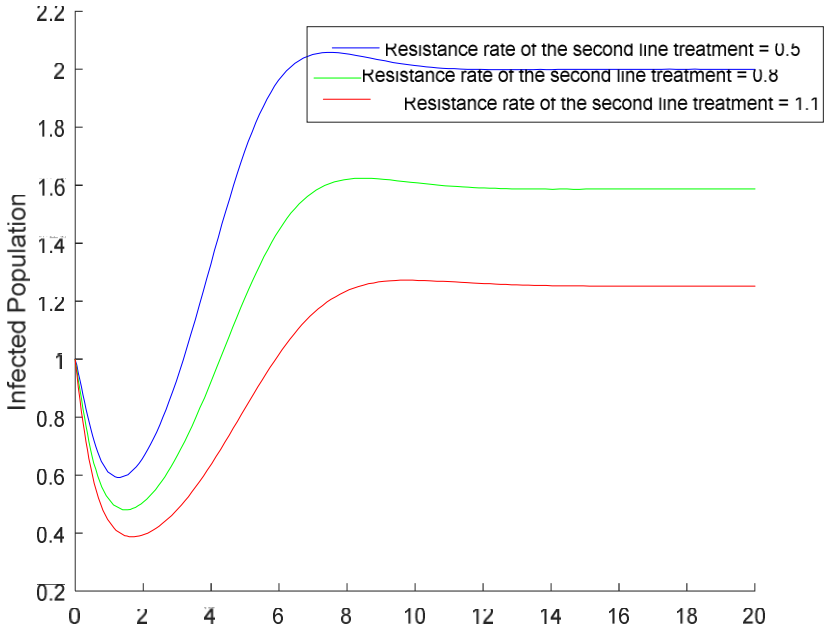

Figure.3(b)Changesintheinfectedpopulationwithrespecttoresistancerateofthesecondlinetreatment,keepingall otherparametersare fixed

Similarly again we take all parameters are fixed except the resistance rate of the first line andthe second line of treatment, found that the resistant population of the first line treatmentdecreaseswhenresistancerateofthefirstlinetreatmentincreasesi.e.resistantpopulation moves to recovered population while the resistant population of the second line treatmentincreases when the resistance rate of the second line of treatment increases i.e. after thesecond line treatment, the infected population comes into resistant population which showninfigure4(a)and 4(b)respectively.

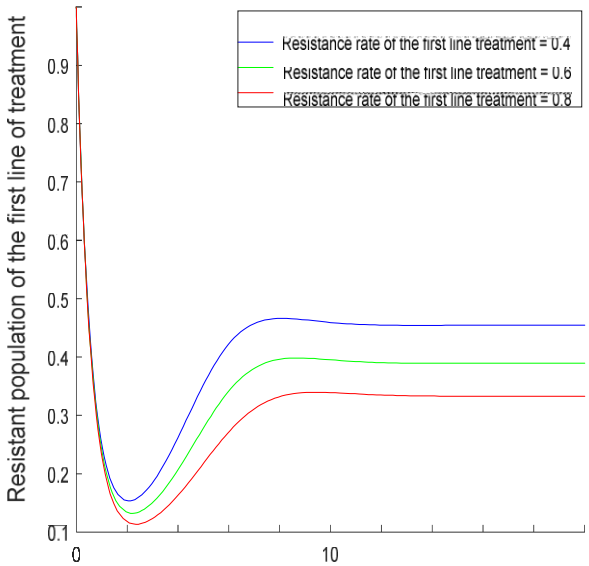

Figure.4(a)Changesintheresistantpopulationwithrespecttoresistancerateofthefirstlineoftreatment,keepingall the otherparametersarefixed.

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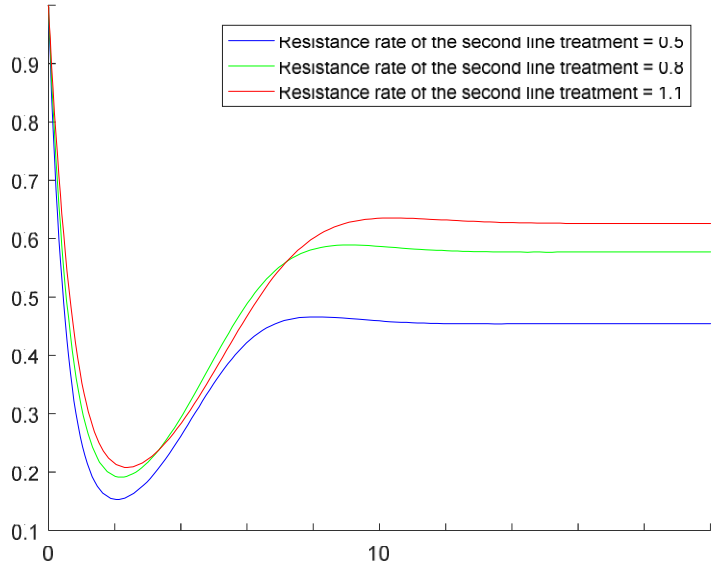

Figure.4(b)Changesintheresistantpopulationwithrespecttoresistancerateofthesecondlineoftreatment,keepingall theotherparametersarefixed.

Conclusion

This study analyzed the local and global stability of the equilibrium points, found that whenthe basic reproduction number R_O 1, then disease dies out and when the basic reproductionnumberR_O 1,then diseasepersists.

References

[1] D. Morse, Brothwell and PJ. Ucko, (1964), Tuberculosis in Ancient Egypt, Am RevRespir.Dis., 90: 524-541.

[2] D. Young, J. Stark and D. Kirschner, (2008), System Biology of Persistent Infection:TuberculosisasaCaseStudy,NatureReviewsMicrobiology, 6:520-528.

[3] E. Klein, R. Laxminarayan, D. Smith and C. Gilligan, (2007), Economic incentives andMathematical Models of Disease, Environment and Development Economics, 12: 707-732.

[4] H. Waaler, and S. Anderson, (1962), The Use of Mathematical Models in the Study of theEpidemiologyofTuberculosis, AmericanJournalofPublicHealth, 52:1002-1013.

[5] J. Semenza, J. Suk and S. Tsolova, (2010), Social Determinants of Infectious Diseases: APublicHealth Priority, Euro Surveil, 15 : 1-3.

[6] J. Trauer, J. Denholm and E. McBryde, (2014), Construction of a Mathematical Model forTuberculosis Transmission in Highly Endemic Regions of the Asia-Pacific. Journal ofTheoreticalBiology, 358: 74-84.

[7] Zaman, (2010), Tuberculosis: A Global Health Problem. Journal of Health PopulationandNutrition, 28: 111-113.

[8] R. Ullah, G. Zaman , and S. Islam, (2013), Stability Analysis of a General SIR

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 3, 2021, Pages. 1810 - 1821
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EpidemicModel,VFASTTransaction on Mathematics,1: 16-20.

[9] S. Sharma, V.H. Badshah, and V.K. Gupta,(2017), Analysis of a SIRI Epidemic ModelwithModifiedNonlinearincidenceRateandLatentPeriod,AsianjournalofMathematicsand statistics, 10: 1-12.

[10] T.M.Daniel,(2006),HistoryofTuberculosis,RespiratoryMedicine,100:1862-1870.

[11] T. Cohen, and M. Murray,(2004) Modelling Epidemics of Multidrug-Resistantm.TuberculosisofHeterogeneousFitness. NatureMedicine, 10:1117-1121.