International Journal of Mathematics And its Applications
Volume 5, Issue 4–E (2017), 793–799.
ISSN: 2347-1557
Available Online: http://ijmaa.in/

International Journal of Mathematics And its Applications

A Mathematical Model of Typhoid with Drug Resistance Effect

Research Article

Priya Baghel[1]*, V.H.Badshah[1], T.K.Jhala[2] and Shivram Sharma[3]

1 School of Studies in Mathematics, Vikram University, Ujjain, Madhya Pradesh, India.

2 Department of Mathematics, Government P.G. College Mandsaur, Ujjain, Madhya Pradesh, India.

3 Medicaps University, Indore, Madhya Pradesh, India.

Abstract: In this paper, we consider a mathematical model of the type SIR (susceptible, infected and recovered) to understand the dynamic of the disease. We calculate the basic reproduction number R_0, using the next generation method, the disease free equilibrium and endemic equilibrium are established and their stability analysis done. We show that the disease free equilibrium point is globally asymptotically stable if $R_o < 1$ and if $R_o > 1$, there exist the endemic equilibrium state, which is also globally asymptotically stable.

Keywords: Typhoid, S. typhi, Multidrug Drug Resistance, basic reproduction number, Stability.

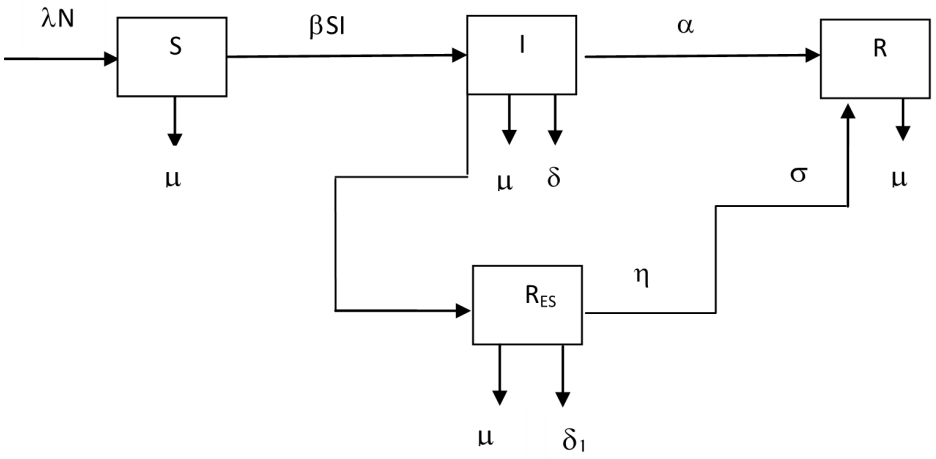
1. Introduction

Typhoid fever is an acute illness associated with fever caused by the Salmonella typhi bacteria, a Gram-negative bacterium. It can also be caused by Salmonella serotype paratyphi A, a related bacterium that usually causes a less severe illness. Salmonella nomenclature is complex, and scientists use different systems to refer to and communicate about this genus. The criteria for designating bacteria as individual species is not clear, making the nomenclature of these bacteria a bit confusing. There are two main views on the nomenclature of the genus Salmonella.

Two species are to be recognized: Salmonella bongori and Salmonella enterica. S.enterica include six subspecies, of which subspecies I (one) contain all the pathogens of warm-blooded animals. S.typhi was a serotype within subspecies I: Salmonella enterica subspecies I serotype typhi. The correct nomenclature for the causal agent of typhoid fever is Salmonella typhi as noted in the International Journal of Systematic and Evolutionary Microbiology. During an acute infection, S.typhi multiplies in mononuclear phagocytic cells before being released into the bloodstream. After ingestion in food or water, typhoid organisms pass through the pylorus and reach the small intestine [16].

It is endemic in Southeast Asia [5, 13], Central America [1, 12, 4] and Indian subcontinent [7, 10] some parts of Africa. We formulate the mathematical model and define all the parameters there in. The basic reproduction is obtained to study the local stability and global stability of the disease free and endemic equilibrium.

* *E-mail: priyabaghel66@gmail.com*



2. Mathematical Model

Ronoh, M.,et al. [8] analysed SIR model of tuberculosis with drug resistance effects,the proposed model is

$$\left.\begin{aligned} \tfrac{dS}{dt} &= \lambda N - \beta SI - \mu S \\ \tfrac{dI}{dt} &= \beta SI - (\mu + \delta + \alpha + \eta)\, I \\ \tfrac{dR_{ES}}{dt} &= \eta I - (\mu + \delta_1 + \sigma)\, R_{ES} \\ \tfrac{dR}{dt} &= \alpha I - \mu R + \sigma R_{ES} \end{aligned}\right\} \tag{1}$$

Parameter Description

β : Rate at which the susceptible become infectious to S.typhi

δ : disease induced death rate

α : recovery rate due to prompt treatment

δ_1 : disease induced death rate after resistance

η : Resistance rate to treatment

σ : recovery rate after second line of resistance treatment

μ : natural death rate

2.1. Reproduction Number

To find the reproduction number using the next generation method for the model and define the basic reproduction number, $R_o = \rho\left(FV^{-1}\right)$ where $F = \left[\frac{\partial F_i(x_0)}{\partial x_j}\right]$ and $V = \left[\frac{\partial V_i(x_0)}{\partial x_j}\right]$

$$F = \begin{bmatrix} \frac{\beta\lambda N}{\mu} & 0 \\ 0 & 0 \end{bmatrix},\ V = \begin{bmatrix} (\mu + \delta + \alpha + \eta) & 0 \\ 0 & (\mu + \delta_1 + \sigma) \end{bmatrix},$$

$$V^{-1} = \frac{1}{(\mu + \delta + \alpha + \eta)\,(\mu + \delta_1 + \sigma)} \begin{bmatrix} (\mu + \delta_1 + \sigma) & 0 \\ 0 & (\mu + \delta + \alpha + \eta) \end{bmatrix}$$

By calculating largest eigen value of FV^{-1}, the basic reproduction number R_o is expressed as

$$R_o = \frac{\beta\lambda N}{\mu\,(\mu + \delta + \alpha + \eta)}$$

2.2. Equilibrium Points

The equilibrium points of the system (1) are the solution of the following system

$$\left.\begin{aligned} &\lambda N - \beta SI - \mu S = 0 \\ &\beta SI - (\mu + \delta + \alpha + \eta)\, I = 0 \\ &\eta I - (\mu + \delta_1 + \sigma)\, R_{ES} = 0 \\ &\alpha I - \mu R + \sigma R_{ES} = 0 \end{aligned}\right\} \tag{2}$$

Solving above system, we always get an equilibrium points $E_0 = \left(\frac{\lambda N}{\mu}, 0, 0, 0\right)$ which is called the disease free equilibrium of the system (1) and the endemic equilibrium $E^* = (S^*, I^*, R^*_{ES}, R^*)$, exist only if $R_o > 1$, where

$$\left.\begin{aligned} &S^* = \tfrac{(\mu+\delta+\alpha+\eta)}{\beta}, \quad I^* = \tfrac{\left(\lambda N - \mu S^*\right)}{\beta S^*} \\ &R^*_{ES} = \tfrac{\eta I^*}{\mu+\delta_1+\sigma}, \quad R^* = \left(\tfrac{\alpha(\mu+\delta_1+\sigma)+\eta\sigma}{\mu(\mu+\delta_1+\sigma)}\right) I^* \end{aligned}\right\} \tag{3}$$

3. Stability of Equilibriums

The local stability of the equilibrium point is determined from the jacobian matrix of the system of ordinary differential equation (1) evaluated at each equilibrium point and we will find the global stability of both equilibrium points by Lyapunov Lasalle function.

3.1. Disease Free Equilibrium

The jacobian matrix at E_o is shown as:

$$J\left(E_0\right) = \begin{bmatrix} -\mu & -\frac{\beta\lambda N}{\mu} & 0 & 0 \\ 0 & -(\mu+\delta+\alpha+\eta) & 0 & 0 \\ 0 & \eta & -(\mu+\delta_1+\sigma) & 0 \\ 0 & \alpha & \sigma & -\mu \end{bmatrix}$$

The characteristic equation of the jacobian matrix is $|J_0 - tI| = 0$, that is

$$\begin{bmatrix} -\mu - t & -\frac{\beta\lambda N}{\mu} & 0 & 0 \\ 0 & \frac{\beta\lambda N}{\mu} - (\mu+\delta+\alpha+\eta) - t & 0 & 0 \\ 0 & \eta & -(\mu+\delta_1+\sigma) - t & 0 \\ 0 & \alpha & \sigma & -\mu - t \end{bmatrix} = 0$$

This implies

$$(\mu + t)^2 \left(\frac{\beta\lambda N}{\mu} - (\mu+\delta+\alpha+\eta) - t\right)(\mu+\delta_1+\sigma+t) = 0$$

Three eigen values of the jacobian matrix has negative real part and forth eigen value namely $\frac{\beta\lambda N}{\mu} - (\mu+\delta+\alpha+\eta)$ is negative when $R_o < 1$. So by Routh Hurwitz criteria the disease free equilibrium is locally asymptotically stable. From the above discussion we have the following theorem.

Theorem 3.1. *The disease free equilibrium E_o is locally asymptotically stable if $R_o < 1$.*

Now we will discuss the global stability of disease free equilibrium, using Lyapunov-Lasalle function. We consider the lyapunov-Lasalle function

$$\begin{aligned}\frac{dV}{dt} &= \frac{dI}{dt}\\ &= \beta SI - (\mu+\delta+\alpha+\eta)\,I\\ &= (\mu+\delta+\alpha+\eta)\,I\left[\frac{\beta\lambda N}{\mu\,(\mu+\delta+\alpha+\eta)} - 1\right]\\ &= (\mu+\delta+\alpha+\eta)\,I\,[R_0 - 1]\\ &\leq 0\end{aligned}$$

when $R_o < 1$. Further more $\frac{dV}{dt} = 0$ when $I = 0$. Hence the largest invariant set contained in the set $E = \{(S,I) \in O|\dot{V}\,(S,I) = 0\}$ is reduced to DFE. Thus by Lasalle's invariance principle the DFE is globally asymptotically stable on Ω. So we have the following theorem.

Theorem 3.2. *If $R_o < 1$, then the disease free equilibrium E_o is globally asymptotically stable.*

3.2. Endemic Equilibrium

First we shall discuss on the local stability of endemic equilibrium. Jacobian matrix of the system at endemic equilibrium is given by

$$J\,(E^*) = \begin{bmatrix} -\beta I^* - \mu & -\beta S^* & 0 & 0\\ \beta I^* & \beta S^* - (\mu+\delta+\alpha+\eta) & 0 & 0\\ 0 & \eta & -(\mu+\delta_1+\sigma) & 0\\ 0 & \alpha & \sigma & -\mu \end{bmatrix}$$

The characteristic equation of the jacobian matrix is $|J(E^*) - tI| = 0$, that is

$$\begin{bmatrix} -\beta I^* - \mu - t & -\beta S^* & 0 & 0\\ \beta I^* & \beta S^* - (\mu+\delta+\alpha+\eta) - t & 0 & 0\\ 0 & \eta & -(\mu+\delta_1+\sigma) - t & 0\\ 0 & \alpha & \sigma & -\mu - t \end{bmatrix} = 0$$

This implies

$$(t+\mu)\,(t+\mu+\delta_1+\sigma)\left(t^2 + a_1 t + a_2\right) = 0$$

where $a_1 = \beta I^* + 2\mu + \delta + \alpha + \eta - \beta S^* = \beta I^* + \mu > 0$, $a_2 = (\beta I^* + \mu) + (\mu+\delta+\alpha+\eta) > 0$. It is clear that first two eigen values namely $-\mu$, $-(\mu+\delta_1+\sigma)$ are negative and since $a_1 > 0$, $a_2 > 0$ so the roots of equation $t^2 + a_1 t + a_2 = 0$ have negative real parts. Thus all the eigen values of the jacobian matrix at endemic equilibrium has negative real part. So by Routh Hurwitz criteria the endemic equilibrium is locally asymptotically stable. From the above discussion we have the following theorem.

Theorem 3.3. *If $R_o > 1$, then endemic equilibrium $E^* = (S^*, I^*, R^*_{ES}, R^*)$ is locally asymptotically stable.*

Now for global stability of the endemic equilibrium, An equilibrium for system (1) is given by (S^*, I^*), where

$$S^* = \frac{\lambda}{\mu}\left(\frac{1}{R_o}\right)N,\ I^* = \frac{\mu R_o}{\beta}\left[1 - \frac{1}{R_o}\right]$$

It follows from first equation of the system (2),

$$\lambda S^* I^* = \lambda N - \mu S^* \tag{4}$$

Define a Lyapunov function as:

$$\begin{aligned} V(S,I) &= S^*\left(\frac{S}{S^*} - \log\frac{S}{S^*}\right) + I^*\left(\frac{I}{I^*} - \log\frac{I}{I^*}\right) \\ \frac{dV(S,I)}{dt} &= \lambda N - \mu S - \lambda N\frac{S^*}{S} + S^*\beta I + \mu S^* - \gamma I - \beta S I^* + \gamma I^* \\ &= \lambda N\left(1 - \frac{S^*}{S} - \frac{S}{S^*} + 1\right) \\ &= \lambda N\left(2 - \frac{S^*}{S} - \frac{S}{S^*}\right) \\ &= -\lambda N\frac{S^*}{S}\left(1 - \frac{S}{S^*}\right)^2 \\ &\leq 0 \end{aligned}$$

For all $S, I \geq 0$, then we conclude $\frac{dV}{dt}$ is semi-definite positive. Then the endemic equilibrium is globally asymptotically stable. Thus we can write the above result in the following theorem form.

Theorem 3.4. *If $R_o > 1$, then endemic equilibrium is globally asymptotically stable.*

4. Numerical Simulation

In this section we explain our result through graphically, using MATLAB. If we select parameter as: $\beta = 0.36$, $\lambda = 0.001$, $N = 1000$, $\mu = 0.3$, $\delta = 0.02$, $\delta_1 = 0.067$, $\eta = 0.570104$, $\alpha = 0.6$, $\sigma = 0.21$ and $(S, I, R_{ES}, R) = (2, 1, 1, 1)$. Then we have $R_o = 0.8753 < 1$ and from the Figure 1, we can easily see that $(S, I, R_{ES}, R) = (2, 1, 1, 1)$ goes to the disease free equilibrium $E_o = (3.33, 0, 0, 0)$. So disease free equilibrium is globally asymptotically stable.

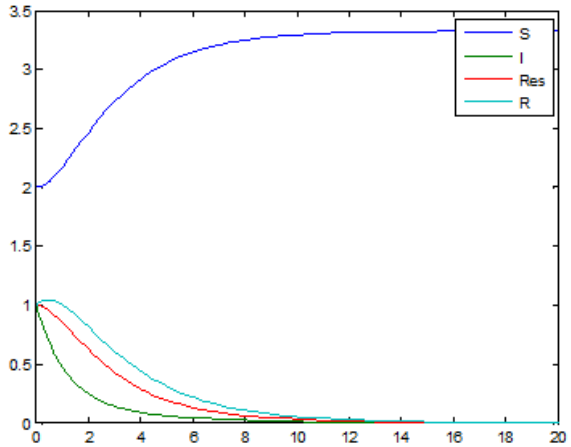


Figure 1. **when $\Re_o < 1$**

Again, if $\beta = 3$, $\lambda = 0.025$, $N = 1000$, $\mu = 0.3$, $\delta = 1.6$, $\delta_1 = 0.067$, $\eta = 0.570104$, $\alpha = 0.6$, $\sigma = 0.21$ and $(S, I, R_{ES}, R) = (2, 1, 1, 1)$. Then we have $R_o = 81.4304 > 1$ and from the Figure 2, we can easily see that $(S, I, R_{ES}, R) = (2, 1, 1, 1)$ goes to the endemic equilibrium $E^* = (1.023, 8.04, 7.95, 21.65)$. So endemic equilibrium is globally asymptotically stable.

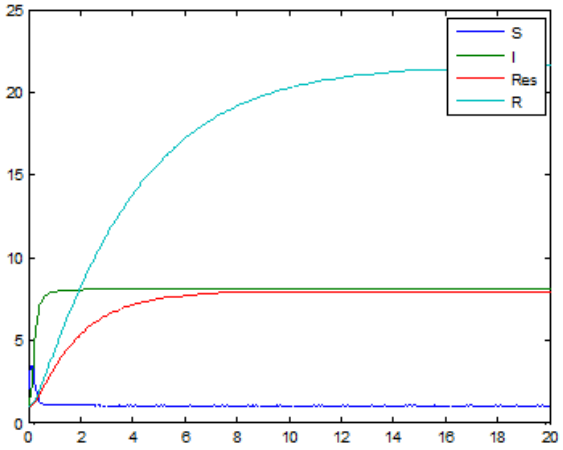


Figure 2. when $\Re_o > 1$

5. Conclusion

In this paper, we analyzed the existence and global stability of the equilibrium points. We found that when the basic reproduction number $R_o < 1$, then disease dies out and when the basic reproduction number $R_o > 1$, then disease persists.

References

[1] A.Fica, S.Miranda, A.Ricci, K.D'ottone and F.Cabello, *Epidemic typhoid in Chile: analysis by molecular and conventional methods of Salmonella typhi strain diversity in epidemic (1977 and 1981) and non epidemic. 1990. Years*, J. C. Micbio., 34(1996), 1701-1707.

[2] A.Korobeinikov and G.C.Wake, *Lyapunov functions and global stability for SIR,SIRS,and SIS epidemiological models*, Appl. Math. Lett., 15(8)(2002), 955-960.

[3] F.Mills-Robertson, M.E.Addy, P.Mensah and S.S.Crupper, *Molecular characterization of antibiotic resistance in clinical salmonella typhi isolated in Ghana*, FEMS Micbio. Let., 215(2002), 249-253.

[4] J.Olarte and E.Galindo, *Salmonella typhi resistant to chloramphenicol, ampicillin and other antimicrobial agents: Strains isolated during an extensive typhoid fever epidemic in Mexico*, Anti A. Chem., 4(1973), 597-601.

[5] J.M.Ling, N.W.S.Lo and A.F.Cheng, *Molecular methods for the epidemiological typing of Salmonella enteric serotype Typhi from Hong Kong and Vietnam*, J.C. Mibol., 38(2000), 292-300.

[6] M.Parvej, S.Islam, I.Khan, S.Shafie and G.Taza, *Mathematical Analysis of Typhoid Model with Saturated Incidence Rate*, Advanced studies in Biology., 7(2)(2015), 65-78.

[7] M.Rahman, A.Ahmad and S.Shoma, *Decline in epidemic of multidrug resistant Salmonella typhi is not associated with increased incidence of antibiotic-susceptible strain in Bangladesh*, Epid. Inf., 129(29)(2002), 29-34.

[8] M.Ronoh, R.Jaroudi, P.Fotso, V.Kamdoum, N.Matendechere, J.Wairimu, R.Auma and J.Lugoye, *A Mathematical Model of Tuberculosis with Drug Resistant Effects*, Applied Mathematics., 7(2016), 1303-1316.

[9] P.Adda and D.Bichara, *Global Stability for SIR and SIRS models with differential Mortality*, International Journal of Pure and Applied Mathematics, 80(3)(2012), 425-433.

[10] P.M.Shanahan, M.V.Jesudason, C.J.Thomson and S.G.Amyes, *Molecular analysis of and identification of antibiotic resistance genes in clinical isolates of Salmonella typhi from India*, J.C Micbio., 36(1998), 1595-1600.

[11] S.Kariuki, C.Gilks, G.Revathi and C.A.Hart, *Genotypic analysis of multidrug resistant Salmonella enteric serovar Typhi, Kenya*, Emerh. Infect. Dis., 6(2000), 649-651.

[12] S.Kariuki, G.Revatni, J.Muyodi, J.Mwituria, A.Munyalo, S.Mirza and C.A.Hart, *Characterization of Multidrug-Resistant Typhoid Outbreaks in Kenya*, J. C. Micbol., 42(4)(2004), 1477-1482.

[13] S.H.Mirza, N.J.Beechmg and C.A.Hart, *Multidrug resistant typhoid: a globalproblem*, J. Med. Micbio., 44(1996), 317-319.

[14] S.Naowarat, P.Thongjaem and I.Ming Tang, *Effect of Mosquito Repellent on the Transmission Model of Chikunguniya Fever*, American Journal of Applied Sciences, 9(4)(2012), 563-569.

[15] S.Zaki and S.Karande, *Multidrug-resistant typhoid fever: a review*, J Infect Dev Ctries., 5(5)(2011), 324-337.

[16] www.who.int/int vaccines and Biologicals. Background document the diagnosis, treatment and prevention of typhoid fever communicable disease surveillance and response vaccines and Biologicals World Health Organization-2003.Department of vaccines and Biologicals CH-1211 Geveva 27, Switzerland.