Journal of the Nigerian Society for Mathematical Biology
Volume 1 (2018), 47 - 58

Sensitivity analysis of a transmission dynamics model for Typhoid fever and its control

W. Atokolo[*] and D. Omale[†]

Abstract

In this article, we investigated the sensitivity analysis of the transmission dynamics of typhoid fever model with control formulated by Atokolo and Mbah [1]. The existence of the steady state of the model was determined, after which the effective reproduction number of the model was computed using the next generation matrix approach. Sensitivity analysis was then carried out to determine which parameters that should be targeted by control intervention strategies of which the result shows that an increase in the enlightenment campaign, treatment rate and rate of vaccination leads to a reduction in the prevalence of the disease.

Keywords: modeling; typhoid; enlightenment; treatment; vaccination

1 Introduction

Typhoid is an endemic infectious disease caused by bacteria called Salmonella Typhi (S.Typhi) [11]. It is spread through contaminated food, water or drink. The constipated food or water that contains these bacteria causes illness by drinking or eating and enters the body. They travel in the human intestines, and then enter the blood [10].

Abdominal pain, headache and general ill feeling, constipation in Adults and diarrhea in Children are the symptoms of this disease. A complicated case results into an intestinal perforation (Holes occurring in the wall of the intestine), this causes the leakage of intestinal contents into the abdominal cavity. Intestinal perforation is frequently fatal as it is accompanied by a sudden rise in pulse rate, hypertension [2]. The incubation period is about 10-14 days. It is endemic in Central America, Indian subcontinent, south East Asia and some parts of Africa, including Nigeria. In 2000, it was estimated that the disease caused 21.6 million illness and 216, 500 deaths globally [10].

[*]Department of Mathematical Sciences, Kogi State University, Ayingba, Kogi State; williamsatokolo@gmail.com
[†] Department of Mathematical Sciences, Kogi State University, Ayingba, Kogi State; davidubahi@gmail.com

The infection is transmitted by ingestion of food or water contaminated with Bacteria. The infected person continues to shed bacteria in their stool or urine for years thereby sustaining transmission, this prolonged shedding likely increases transmission, particularly in regions with poor sanitation [5]. It was discovered that, in a country where open sewage is accessible to insects, these insects land on the sewage, pick up the bacteria and then contaminates food or water to be taken by humans [1]. After taken in contaminated food/water, the S-typhi bacteria head down to the digestive tract where they are taken in by the phagocytes cells. The Phagocytes are cells of the immune system whose job is to engulf and kill the invading bacteria. In the case of S- typhi, the bacteria are able to survive the ingestion by the phagocytes and multiply within these cells [1].

The period of time within which the bacteria are multiplying in the phagocytes is between 8 to 14 days which represents the incubation period of typhoid fever. When huge numbers of bacteria fill an individual's phagocyte, they move into the blood stream where their presence brings out the disease symptoms. The presence of these bacteria in the blood stream is responsible for an increasing high fever [6].

Ciprofloxacins are widely regarded as optimal for the treatment of typhoid fever in adults [3]. They are relatively inexpensive, well tolerated and more rapidly and reliably effective than the former first line drugs; Chloramphenicol, Ampicillin, Amoxicillin. Surgery is usually indicated in cases of intestinal perforation. Death occurs on 10% to 30% of untreated cases [7].

The major routes of transmission of typhoid fever are through drinking water or eating food contaminated with Salmonella typhi. Prevention is based on ensuring access to safe water and by promoting safe food handling practices [1].

Sensitivity Analysis is used to determine how "sensitive" a model is, to changes in the value of the parameters of the model and to changes in the structure of the model [12]. Sensitivity analysis helps to build confidence in a model by studying the uncertainties that are often associated with parameters in such models. Sensitivity indexes allow us to measure the relative change in a state variable when a parameter changes, it is also commonly used to determine the robustness of model predictions to parameter values [12].The analysis shows us how to reduce human mortality due to typhoid fever; it helps us to find out those parameters that should be targeted by intervention strategies which also enable us to know how crucial each parameter is to the transmission of the disease.

Sensitivity Analysis is extremely important for mathematical models. It studies the variation of a model caused by variations in the inputs [9].In essence, Sensitivity Analysis determines which parameters and initial conditions (inputs) affect the quantities (outputs) of the model the most. The first reason why Sensitivity Analysis is required is that, it tells the Researcher which parameters deserve the most numerical attention [9].A very sensitive parameter should be carefully estimated as a small variation in that parameter will lead to large quantitative changes to the quantity of interest and may even produce qualitatively different results. Qualitative changes to a quantity of interest fall under the scope of bifurcation theory and will not be considered in this paper.

An insensitive parameters, on the other hand does not require as much effort to estimate, as small variation in that parameter will not produce large changes to a quantity of interest.

The second reason why Sensitivity Analysis becomes so vital is that, it highlights which parameters should be targeted in management strategies. One of the objectives of Mathematical Modeling is to determine what the current outcome of a system may be and if necessary, discover how to change any negative outcomes [9]. Changing the values of the most sensitive parameters will be the most effective strategy in changing the model results. The Researcher will then implement any applicable real-world scenarios that will alter the value of the most sensitive parameter to get the best control over the outcome.

2 Model Formulation

The model flow diagram and the developed model as given by [1] are shown in Figure 1 and equations (1) to (7) respectively.

$$\frac{dS}{dt} = \pi - \psi(1-x)BS + \alpha R - \theta(1+z)S - \mu S \qquad (1)$$

$$\frac{dE}{dt} = \psi(1-x)BS + \delta(1-\omega)BV - (\lambda+\mu)E \qquad (2)$$

$$\frac{dI}{dt} = \lambda E - \gamma(1+y)I - (d_1+\mu)I \qquad (3)$$

$$\frac{dI_T}{dt} = \gamma(1+y)I - (\phi + d_2 + \mu)I_T \qquad (4)$$

$$\frac{dV}{dt} = \theta(1+z)S - \delta(1-\omega)BV - \mu V \qquad (5)$$

$$\frac{dR}{dt} = \phi I_T - (\alpha+\mu)R \qquad (6)$$

$$\frac{dB}{dt} = KI - \mu_1 B \qquad (7)$$

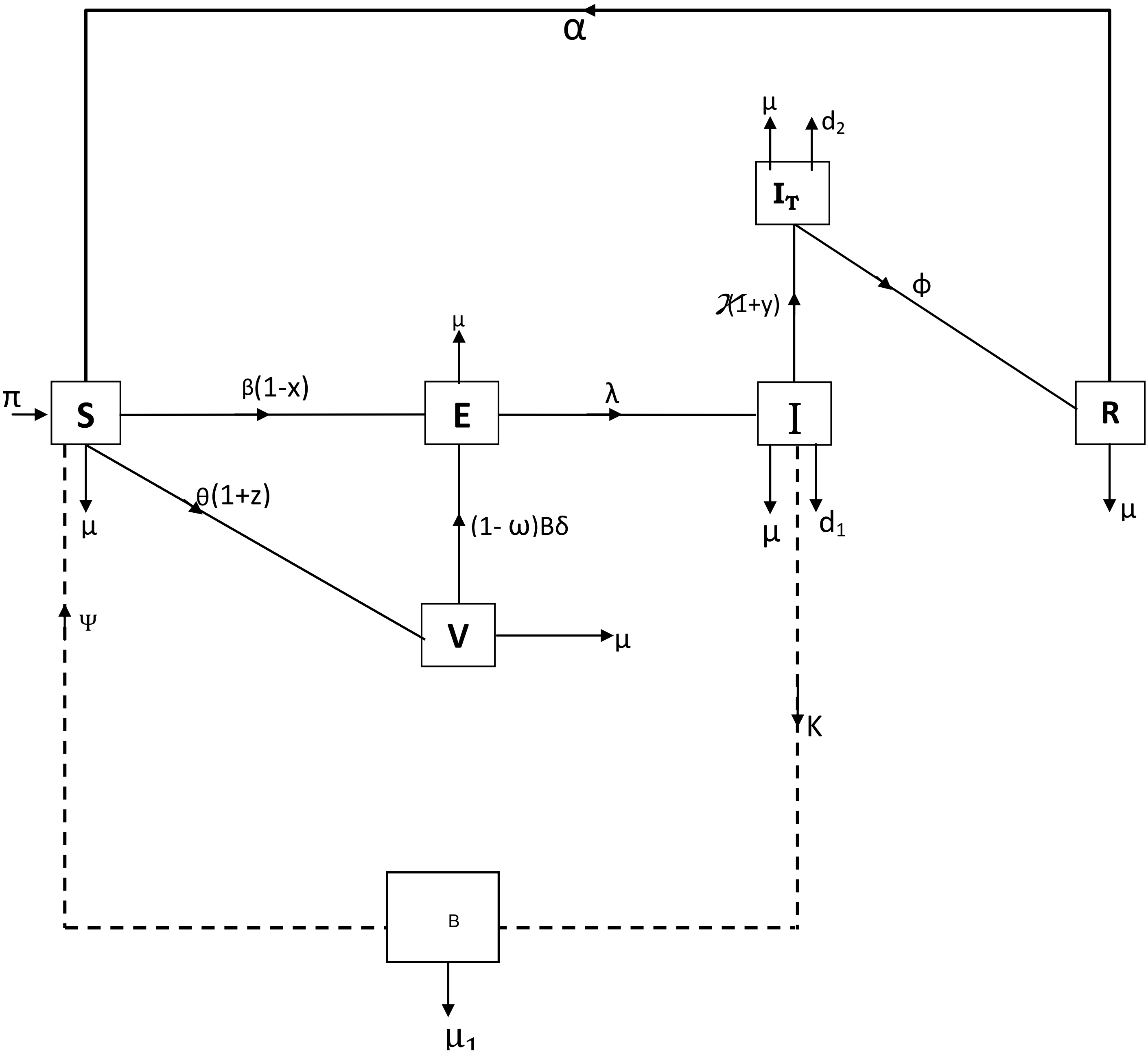

Fig 1: Model flow diagram for Transmission Dynamics of Typhoid fever and its control [12]

Variables and parameters	**Description**
S	Susceptible class
E	Exposed class
I	Infected class
I_T	Infected but on treatment
V	Vaccinated class
R	Recovered class
B	Bacteria class
Π	Recruitment
W	Waning rate of the vaccine
Ψ	Interaction rate
α	Rate at which the Recovered are susceptible again
$\boldsymbol{\gamma}$	Treatment rate
μ	Natural death rate of human
μ_1	Death rate of bacteria
d_1	Death rate for the infected
d_2	Death rate for the infected but on treatment
Θ	Rate of vaccination
Φ	Recovery rate
δ	Exposure rate of the vaccinated class
K	Shedding rate of bacteria
B	Contact rate
$\boldsymbol{\lambda}$	Rate of infection
X	Enlightenment rate for the exposed
Y	Enlightenment rate to go for treatment
Z	Enlightenment rate to go for vaccination

Table 1: Model parameters and variables

3 Equilibria of Model

The DFE of the model is given by

$$\left[\frac{\Pi}{\theta(1+Z)+\mu},\quad 0,\quad 0,\quad 0,\quad \frac{\theta(1+Z)\,\pi}{\mu\,[\theta(1+Z)\,+\mu]},\quad 0,\quad 0\right], \tag{8}$$

while the endemic equilibrium is given by

$$B^* = \frac{KI^*}{\mu_1} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \tag{9}$$

$$E^* = \frac{[\gamma\,(1+y) + (d_1+\mu)]I^*}{\lambda} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \tag{10}$$

$$I_T^* = \frac{\gamma(1+y)]I^*}{(\Phi+d_2+\mu)} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \tag{11}$$

$$R^* = \frac{\Phi\gamma(1+y)I^*}{(\alpha+\mu)(\Phi+d_2+\mu)} \ldots\ldots\ldots\ldots\ldots\ldots \tag{12}$$

$$S^* = \frac{\{[\pi(\alpha+\mu)\left(\Phi+d_2+\mu\right]+\alpha\gamma\Phi(1+y)I^*\}\mu_{1.}}{\left[(\alpha+\mu)\left(\Phi+d_2+\mu\right)\right]\{\psi(1-x)KI^*+\theta(1+Z)+\mu\}\mu_{1.}} \ldots\ldots\ldots\ldots \tag{13}$$

$$V^* = \frac{\{\theta(1+Z)[\pi(\alpha+\mu)\left(\Phi+d_2+\mu\right]+\alpha\gamma\Phi(1+y)I^*\}\mu_{1.}\mu_1}{\left[(\alpha+\mu)\left(\Phi+d_2+\mu\right)\right]\{\psi(1-x)KI^*+\theta(1+Z)+\mu\}\mu_{1.}\delta(1-w)KI^*} \ldots\ldots\ldots \tag{14}$$

$$I^* = \frac{\lambda E^*}{[\gamma\,(1+y) + (d_1+\mu)]} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \tag{15}$$

3.1 Effective Reproduction Number [R_e]

It is the expected number of secondary infections produced when one infected individual is introduced completely into a susceptible population [4]. Computations of $\boldsymbol{R_e}$ typically involve product of infection rates and duration of infection. The effective reproductive number, $R_e = \rho\,(Fv^{-1})$, was calculated using the next generation matrix approach as:

$$R_e = \frac{\boldsymbol{\Pi\lambda k(1-x)\psi}}{(\boldsymbol{\theta}(\mathbf{1}+\boldsymbol{Z})+\mu)\,\{\mu_1\,(\boldsymbol{\lambda}+\mu)[\boldsymbol{\gamma}(\mathbf{1}+\mathbf{y})+(\boldsymbol{d_1}+\mu)]-\boldsymbol{\lambda k}[\boldsymbol{\psi}(\mathbf{1}-\mathbf{x})\mathbf{s}+\boldsymbol{\delta}(\mathbf{1}-\mathbf{w})\mathbf{v}]\}} \ldots\ldots\ldots\ldots \tag{16}$$

4 Sensitivity analysis of the Typhoid fever model

The following values as given by [1] for the parameters involved in Model (1) - (7) are presented in Table 2.

Parameters	Description	Estimated values	Source
Π	Recruitment	500	[1]
W	Waning rate of the vaccine	$0<w<1$	[11]
Ψ	Interaction rate	0.0011	[11]
α	Rate at which the Recovered are susceptible again	0.9	[1]
γ	Treatment rate	0.9	[11]
μ	Natural death rate of human	0.016	[11]
μ_1	Death rate of bacteria	0.0345 daily	[8]
d_1	Death rate for the infected	0.005	[11]
d_2	Death rate for the infected but on treatment	0.001	[1]
Θ	Rate of vaccination	0.5	[1]
Φ	Recovery rate	0.0357daily	[11]
δ	Exposure rate of the vaccinated class	$0< \delta<1$	[1]
K	Shedding rate of bacteria	0.014daily	[8]
B	Contact rate	0.0002	[11]
λ	Rate of infection	0.2	[10]
X	Enlightenment rate for the exposed	$0<x<1$	[1]
Y	Enlightenment rate to go for treatment	$0<y<1$	[1]
Z	Enlightenment rate to go for vaccination	$0<z<1$	[1]

Table 2: Parameters and variables estimated values

We calculate the sensitivity indexes of the Reproduction number for the Control model R_0^C to the parameters involved in the model (1) –(7), To check which of this parameter in the model (1) - (7) has high impact on R_0^C , and also to find out key parameter that contributes in the reduction of typhoid fever transmission in the population. The normalized forward sensitivity index of the variable to a parameter is the ratio of the relative change in the parameter.

The sensitivity index of π with respect to R_0^C is given as:

$$X_{\pi}^{R_0^C} = \frac{\partial R_0^C}{\partial \pi} \times \frac{\pi}{R_0^C} =$$

$$\frac{[\mu_1\gamma(1+y)(\lambda+\mu)+\mu_1(\lambda+\mu)(d_1+\mu)+\mu_1(\lambda+\mu)-\lambda k\psi(1-x)s-\lambda k\delta v(1-w)]}{[\mu_1\gamma(1+y)(\lambda+\mu)+\mu_1(\lambda+\mu)(d_1+\mu)+\mu_1(\lambda+\mu)-\lambda k\psi(1-x)s-\lambda k\delta v(1-w)]} = 1$$

The sensitivity index of Θ with respect to R_0^C is given as:

$$X_{\theta}^{R_0^C} = \frac{\partial R_0^C}{\partial \theta} \times \frac{\theta}{R_0^C}$$

$$-\frac{[\mu_1\gamma(1+y)(\lambda+\mu)(1+z+\mu)+\mu_1(\lambda+\mu)(d_1+\mu)(1+z+\mu)+\mu_1(\lambda+\mu)(1+z+\mu)-\lambda k\psi(1-x)s(1+z+\mu)-\lambda k\delta v(1-w)(1+z+\mu)]}{[\mu_1\gamma(1+y)(\lambda+\mu)+\mu_1(\lambda+\mu)(d_1+\mu)+\mu_1(\lambda+\mu)-\lambda k\psi(1-x)s-\lambda k\delta v(1-w)](\theta+z+\mu)}$$

$$= -1.907$$

The sensitivity index of ψ with respect to R_0^C is given as:

$$X_{\psi}^{R_0^C} = \frac{\partial R_0^C}{\partial \psi} \times \frac{\psi}{R_0^C} =$$

$$\frac{[\mu_1\gamma(1+y)(\lambda+\mu)+\mu_1(\lambda+\mu)(d_1+\mu)+\mu_1(\lambda+\mu)-\lambda k\psi(1-x)s-\lambda k\delta v(1-w)+\lambda k\delta(1-x)}{[\mu_1\gamma(1+y)(\lambda+\mu)+\mu_1(\lambda+\mu)(d_1+\mu)+\mu_1(\lambda+\mu)-\lambda k\psi(1-x)s-\lambda k\delta v(1-w)]} = 9.956$$

The sensitivity index of δ with respect to R_0^C is given as:

$$X_{\sigma}^{R_0^C} = \frac{\partial R_0^C}{\partial \sigma} \times \frac{\sigma}{R_0^C} =$$

$$\frac{[\lambda k v(1-w)]}{[\mu_1\gamma(1+y)(\lambda+\mu)+\mu_1(\lambda+\mu)(d_1+\mu)+\mu_1(\lambda+\mu)-\lambda k\psi(1-x)s-\lambda k\delta v(1-w)]} = 1.215$$

The sensitivity index of γ with respect to R_0^C is given as:

$$X_{\gamma}^{R_0^C} = \frac{\partial R_0^C}{\partial \gamma} \times \frac{\gamma}{R_0^C} =$$

$$-\frac{[\mu_1\gamma(1+y)(\lambda+\mu)]}{[\mu_1\gamma(1+y)(\lambda+\mu)+\mu_1(\lambda+\mu)(d_1+\mu)+\mu_1(\lambda+\mu)-\lambda k\varphi(1-x)s-\lambda k\sigma v(1-w)]} = -3.6182$$

The sensitivity index of μ_1 with respect to R_0^C is given as:

$$X_{\mu_1}^{R_0^C} = \frac{\partial R_0^C}{\partial \mu_1} \times \frac{\mu_1}{R_0^C} =$$

$$\frac{-\mu_1(\lambda+\mu)(\theta+z\theta+\mu)[\gamma(1+y)+(d_1+\mu)]}{[\mu_1\gamma(1+y)(\lambda+\mu)+\mu_1(\lambda+\mu)(d_1+\mu)+\mu_1(\lambda+\mu)-\lambda k\psi(1-x)s-\lambda k\delta v(1-w)]} = -4.2884$$

The sensitivity index of μ with respect to R_0^C is given as:

$$X_{\mu}^{R_0^C} = \frac{\partial R_0^C}{\partial \mu} \times \frac{\mu}{R_0^C} =$$

$$\frac{-\mu_1[(\lambda+2\mu)(\mu_1\gamma(1+y))+2\mu_1\mu+2\mu_1\mu+3\mu_1\mu^2+\mu_1\lambda+2\mu_1\mu-\lambda k\psi(1-x)s-\lambda k\delta v(1-w)]}{[\mu_1\gamma(1+y)(\lambda+\mu)+\mu_1(\lambda+\mu)(d_1+\mu)+\mu_1(\lambda+\mu)-\lambda k\psi(1-x)s-\lambda k\delta v(1-w)](\theta+z+\mu)}$$
$$= -0.02538$$

The sensitivity index of w with respect to R_0^C is given as:

$$X_{w}^{R_0^C} = \frac{\partial R_0^C}{\partial w} \times \frac{w}{R_0^C} =$$

$$\frac{[-w\lambda k\delta v]}{[\mu_1\gamma(1+y)(\lambda+\mu)+\mu_1(\lambda+\mu)(d_1+\mu)+\mu_1(\lambda+\mu)-\lambda k\psi(1-x)s-\lambda k\delta v(1-w)]} = 0.251$$

The sensitivity index of z with respect to R_0^C is given as:

$$X_{z}^{R_0^C} = \frac{\partial R_0^C}{\partial z} \times \frac{z}{R_0^C} =$$

$$\frac{-z[\theta(\lambda+\mu)\mu_1\gamma(1+y)+(d_1+\mu)+\mu_1(\lambda+\mu)+\mu_1\theta(\lambda+\mu)-\theta\lambda k\psi(1-x)s-\theta\lambda k\delta v(1-w)]}{[\mu_1\gamma(1+y)(\lambda+\mu)+\mu_1(\lambda+\mu)(d_1+\mu)+\mu_1(\lambda+\mu)-\lambda k\psi(1-x)s-\lambda k\delta v(1-w)](\theta+z+\mu)}$$
$$=-0.000039$$

The sensitivity index of y with respect to R_0^C is given as:

$$X_y^{R_0^C}=\frac{\partial R_0^C}{\partial y}\times\frac{y}{R_0^C}=$$

$$\frac{-y(\lambda+\mu)\mu_1\gamma}{[\mu_1\gamma(1+y)(\lambda+\mu)+\mu_1(\lambda+\mu)(d_1+\mu)+\mu_1(\lambda+\mu)-\lambda k\psi(1-x)s-\lambda k\delta v(1-w)]}=-0.0006676$$

The sensitivity index of x with respect to R_0^C is given as:

$$X_x^{R_0^C}=\frac{\partial R_0^C}{\partial x}\times\frac{x}{R_0^C}=$$

$$\frac{-x\{[\mu_1\gamma(1+y)(\lambda+\mu)+\mu_1(\lambda+\mu)(d_1+\mu)+\mu_1(\lambda+\mu)-\lambda k\psi(1-x)s-\lambda k\delta v(1-w)]-(1-x)(\lambda k\psi s)\}}{[\mu_1\gamma(1+y)(\lambda+\mu)+\mu_1(\lambda+\mu)(d_1+\mu)+\mu_1(\lambda+\mu)-\lambda k\psi(1-x)s-\lambda k\delta v(1-w)](\theta+z+\mu)}$$
$$=-0.2015$$

The sensitivity index of k with respect to R_0^C is given as:

$$X_k^{R_0^C}=\frac{\partial R_0^C}{\partial k}\times\frac{k}{R_0^C}=$$

$$\frac{k\{[\mu_1\gamma(1+y)(\lambda+\mu)+\mu_1(\lambda+\mu)(d_1+\mu)+\mu_1(\lambda+\mu)-\lambda k\psi(1-x)-\lambda k\delta v(1-w)]+[\lambda\psi(1-x)s]-\lambda\delta v(1-w)]\}}{[\mu_1\gamma(1+y)(\lambda+\mu)+\mu_1(\lambda+\mu)(d_1+\mu)+\mu_1(\lambda+\mu)-\lambda k\varphi(1-x)s-\lambda k\sigma v(1-w)]}$$
$$=1.007$$

The sensitivity index of λ with respect to R_0^C is given as:

$$X_\lambda^{R_0^C}=\frac{\partial R_0^C}{\partial \lambda}\times\frac{\lambda}{R_0^C}=$$

$$\frac{\{[\mu_1(\lambda+\mu)[\gamma(1+y)+(d_1+\mu)]-\lambda k[\psi(1-x)s-\delta v(1-w)v]-\lambda[\mu_1\gamma+\mu_1 y+\mu_1((d_1+\mu)+\mu_1-k\varphi(1-x)s]-k\delta v(1-w)]\}}{[\mu_1\gamma(1+y)(\lambda+\mu)+\mu_1(\lambda+\mu)(d_1+\mu)+\mu_1(\lambda+\mu)-\lambda k\varphi(1-x)s-\lambda k\delta v(1-w)]}$$

$= 6.09$

Parameters	**Sensitivity Index**
Π	1
Θ	-1.907
Ψ	9.956
δ	1.215
γ	-3.6182
μ_1	-4.2884
μ	-0.02538
W	0.251
Z	-0.000039
Y	-0.0006676
X	-0.2015
K	1.007
λ	6.09

Table 3: Numerical value of the Sensitivity Index

The sensitivity indexes are given in Table 3. Positive index indicates that the value of R_0^C will increase with increase in the parameter and the one with negative index will decrease the value of R_0^C with increase in the parameter values.

4.1 Impact of the parameters on the reproduction number

The negatively indexed parameters like Treatment rate(γ), Vaccination rate(Θ), Enlightenment rate to avoid been exposed to Bacteria, (x), Enlightenment rate to go for treatment (y) and Enlightenment rate to go for Vaccination(z) will decrease the response function (the reproduction number) with the increase in the parameter values and as such, reduces the endemicity of the disease.

Similarly, an increase in the positively indexed parameters like Interaction rate(Ψ), waning rate of the vaccine (w), exposure rate of the vaccinated class (δ), shedding rate of the bacteria (k) and the rate of infection(λ) increase the value of the reproduction number(R_0^C) and as such increases the endemicity of the disease.

5 Conclusion

The most significant parameters affecting the reproduction number are the Treatment rate (γ), Vaccination rate (Θ), Enlightenment rate to avoid been exposed to Bacteria (x), Enlightenment rate to go for treatment (y) and Enlightenment rate to go for Vaccination (z) and as such these parameters should be targeted by control intervention strategies. Increasing these values will decrease the reproduction number for the control model (R_0^C), similarly if the values are decreased, the reproduction number will be increased and as such the spread of the disease increases. An increase in the positively indexed parameters like, Interaction rate(Ψ), waning rate of the vaccine (w), exposure rate of the vaccinated class (δ), shedding rate of the bacteria (k) and the rate of infection(λ) increase the value of the reproduction number and as such the disease invades the population.

References

[1] W. Atokolo and G.C.E. Mbah (2018). *Mathematical Model of the Transmission Dynamics of Typhoid Fever and its Control.* Journal of Nigeria Association of Mathematical Physics, 44, 61 - 68.

[2] Centers for Disease Control and Prevention (CDC) (2014) "*National Centre for Emerging and Zoonotic Infectious Disease, Atlanta USA.http://www.cdc.gov/nczved/divisions/ dfbmd/disease/typhoid fever/technical.html.accessed 31-01-14*

[3] N.T. Chinh, et al (2000). *A randomized Controlled Comparison of Azithronycin and Oflaxacin for multidrug – resistant and resistant enteric fever.* Antimicrobial Agents and Chemotherapy *2000:44:1855-9.*

[4] O. Diekmann. & Heesterbeck, J.A.P. (2000): *Mathematical epidemiology of infectious disease.* Wiley series in Mathematical and computational biology. John Wiley & Sons, West Sussex, England.

[5] T. Gale (2006) *"Typhoid fever Encyclopedia of Medicine*", Third edition.

[6] Hsu S-B (2005) A survey of Constructing Lyapunuv function for Mathematical Model in population biology. Taiwanese Journal of Mathematics, 9(2) :15 – 173

[7] Hsu S-B and Huang T-W. (1995). *Global stability for a class of Predator- Prey System.* SIAM J, Appl. Math, SS(3):763-783.

[8] Jones, M. M. et al (2015); *Modeling Malaria and Typhoid Fever Co-Infection Dynamics.* Mathematical Biosciences 264 (2015). 128 – 144.

[9] Micheal A. Mikueki (2012) *Sensitivity Analysis of the Basic Reproduction Number and other quantities for infectious Disease models.*.M.Sc. Dissertation, submitted to the Department of Mathematics, Colorado State University, Fort Collins, Colorado, Spring.

[10] Muhammad, A.K *et al* (2015); *Mathematical analysis of typhoid model with Saturated Incidence Rate*, Advanced Studies in Biology, Vol. 7(2): 65-78.

[11] Nthiiri T.K *et al* (2016); *Mathematical modeling of Typhoid fever Disease Incorporating Perfection against Infection. British Journal* of Mathematics & Computer Science 14(1): 1-10.

[12] Stephen Edward, Dmitry Kuznetsov, Silas miraw (2004) "*Modeling and Stability Analysis for a varicella Zoster Virus Model with vaccination.* Applied and Computational Mathematics . Vol 3(4): 150-162.