

Mathematical Modelling Approach for Uncertainty and Sensitivity Analyses of Cholera Infection in an Aquatic Environment

Umoh, Ezekiel S.

General Studies Department

Akwa Ibom State Polytechnic, Ikot Osurua, Ikot Ekpene, Nigeria

E-mail: elzekumoh@gmail.com

Nwagor, Peters O.

Department of Mathematics and Statistics,

Ignatius Ajuru University of Education, Port Harcourt, Rivers State

E-mail: peter.nwagor@iaue.edu.ng, pnwagor@yahoo.com

ABSTRACT

A mathematical modelling approach for uncertainty and sensitivity analyses of cholera infection in aquatic environment is formulated for the degree of a dynamical system which aid cholera transmission, spread and control. A numerical approach was adopted using the ODE45 numerical scheme to tackle uncertainty and sensitivity problems. Results of analyses have significant epidemiological importance in cholera control. The study further shows that long term precise predictions of the concentration of infected cells during cholera infection could be difficult until the key parameters are correctly determined. It is evident from this analysis that the most important parameter to cholera transmission is the contact between susceptible and infected persons, while the most crucial parameter to cholera control is the rate of cholera awareness and a continuous system of 1st Order Non-linear Differential Equation was adopted together with a MATLAB ODE45 numerical scheme.

Keywords: *Mathematical modelling approach, uncertainty, sensitivity analyses, cholera infection*

INTRODUCTION

Sensitivity analysis characterizes the response of model outputs to parameter variations (Tarantola 2008), helping to allocate resources to follow up experimentation and field study to isolate vital sources of parameter uncertainty, to identify parameters that can be shed to yield a simpler model to elucidate the plausible range of system outcome for

forecasting purposes, when data are not available, and to determine the robustness of a modelling study's qualitative conclusions (Gatelli, 2008). The model outputs (the ODE solutions over a simulation interval) provides a dynamic representation of the transmission process. Recent advances in Computational Sciences, Numerical Analysis and Information Technology have made widespread application of mathematical modelling possible, Fraser (2008) said model outputs often have complex, non-linear relationship with model parameter, values and inappropriate choices of parameter values can lead to bias in model outputs as opined by Ecohard (2010). Mathematical modelling refers to the process of describing a system by means of mathematical concepts and language (Numfor, 2010). In other words, mathematical modelling is a process of encoding and decoding reality in which a natural phenomenon is reduced to a formal numerical expression by a causal process.

Sensitivity and stability can affect the reliability of the results at every stage of computations; they may grow or shrink as the solution of the model evolves (Umoh, 2022). And there inherent uncertainties can be made small by a more complex model or additional computation and we must know how uncertainty in the model parameters leads to uncertainties in the model predictions.

The issues of model misspecification (in which the item modelled differs from the item of interest) and parameter uncertainty (in which the true values of the parameter are impossible to estimate correctly, as they pertain to this cholera model) include:

β , the rate at which each of the N persons get contaminated water.

ξ , the rate at which infected persons contribute to the concentration of vibrio in the water reservoir.

δ , rate of removal of the infectious vibrios from water supply.

ϕ rate at which the infected persons recovered from vibrio cholera.

K , the concentration of cholera that affects 50% of exposed people.

The model assumes the ratio of asymptomatic to symptomatic infection is constant throughout the epidemic and that dose determines the likelihood of infection but not likelihood of being symptomatic (Hornick 1971), and violation of the assumption generates two consequences. First, severity affects the intensity of shedding and so the average contribution of an infectious person to transmission may change within a short time as distribution of infectious dose change. Second, only symptomatic infectious persons are reported and that affect the distribution of infections, and therefore the infectious terms suffers misspecification and creates uncertainty since there is no physically plausible processes that relates the modelled state variables (concentration of vibrios and "rate of contact with contaminated water") to a rate (or probability per unit of time) at which susceptible persons become infected.

Sensitivity Analysis Methods

Scatter Plots

Scatter plots are occasionally used to visually examine the correlation between a model output variable and parameters. An output variable that is sensitive to the selected parameter will yield an obvious correlation pattern in the scatter plot. Generally, a Monte Carlo algorithm is used to sample the parameter space, and multiple scatter plots are drawn illustrating the relationship between each parameter and each output variable of interest (Rodrigues, Monteiro & Torres, 2013). Visual recognition of the correlation between parameter and model output values can be contingent on the choice of axis scales.

The Morris Method

The Morris method, also called the elementary effects method, is based on the ratio of the change in an output variable to the change in an input parameter. Given the general relationship between a model's output Y and input parameters, X , $Y = f(X)$, the elementary effect of x_i can be expressed as, Morris (1991)

$$EE_i(X) = \frac{y_i(x_1, x_2, \dots, x_i + \Delta, x_{i+1}, \dots, x_k) - y_i(X)}{\Delta}, \quad (1)$$

Where $X \in [0,1]^k$ is a scaled vector of k input parameters, y_i is the state variable of interest, Δ is a value in the set $\left\{\frac{1}{(p-1)}, \dots, 1 - \frac{1}{(p-1)}\right\}$ and p is the number of levels into which each dimension of the parameter space is divided. The distribution of $EE_i(X)$, denoted F_i , is obtained by repeated random sampling of X from its k -dimensional, p -level parameter space, as opined by Saltelli (2007).

The mean of F_i (denoted μ), the mean of $|F_i|$ (denoted μ^*), and the standard deviation of F_i (denoted σ) are the resulting sensitivity measures of an output variable to a parameter. A large μ suggests that the parameter has strong influence on the output, while a large σ suggests either that the relationship between the parameter and output is nonlinear or the parameter interacts with other parameters. Importantly, when the F_i distribution contains both positive and negative values, elementary effects may cancel each other to produce a small μ , but the parameter may still be influential; thus, the use of the absolute elementary effect, μ^* , as a remedy, has been recommended. As the elementary effect of x_i as estimated by the Morris method bears more resemblance to $\Delta y_j / \Delta x_i|_x$ rather $\partial y_j / \partial x_i|_x$, the accuracy of the Morris index depends on the smoothness of y over the parameter domain.

Latin Hypercube Sampling - Partial Rank Correlation Coefficient

A measure of the nonlinear, but monotonic, relationship between two variables, the PRCC is an efficient and reliable sampling-based SA method that provides a measure of monotonicity between parameters and model output after removing the linear effects of all parameters except the parameter of interest. A standard correlation coefficient, ρ , for two variables, x and y , is calculated as follows (Gomero, 2012):

$$\rho = \frac{\sum_i(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_i(x_i - \bar{x})^2} \sqrt{\sum_i(y_i - \bar{y})^2}} \quad (2)$$

where $\{x_i, y_i | x_i \in x, y_i \in y\}$ are the set of paired, sampled data, \bar{x} is the sample mean of x , and \bar{y} is the sample mean of y (Ray, 2008). The PRCC determines the sensitivity of an output state variable to an input parameter as the linear correlation, ρ , between the residuals, $(X_j - \hat{X}_j)$ and $(Y - \hat{Y})$, where X_j is the rank transformed, sampled j th input parameter, and Y is the rank transformed output state variable, while keeping all other parameter values fixed; \hat{X}_j and \hat{Y} are determined for k samples by the linear regression models

$$\hat{X}_j = c_0 + \sum_{\substack{p=1 \\ p \neq j}}^k c_p X_p \quad (3)$$

and

$$\hat{Y} = b_0 + \sum_{\substack{p=1 \\ p \neq j}}^k b_p X_p \quad (4)$$

The Sobol' Method

The Sobol' method is a variance-based GSA technique capable of estimating the influence of individual parameters, or a group of parameters on the output variables of a nonlinear model. Given a model of the relationship between output variables and parameters, $Y = f(X) = f(x_1, x_2, \dots, x_k)$ that is square integrable over its unit hypercube parameter space, the model function a single state variable, $y = f(X)$, can be decomposed into summands of increasing dimensionality, known as the high-dimensionality model representation (Sobol, 1990):

$$y = f(X) = f_0 + \sum_{i=1}^k f_i(x_i) + \sum_{i>1}^k f_{ij}(x_i, x_j) + \dots + f_{1,2,\dots,k}(x_1, x_2, \dots, x_k) \quad (5)$$

Sobol (2001) demonstrated that if each term in this expansion has a zero mean, then the total variance of an output variable can be decomposed into the HDMR ANOVA represented as (Saltelli, 2007):

$$V(y) = \int f(X)^2 dX - f_0 = \sum_{i=1}^k V_i + \sum_i \sum_{i>1}^k V_{ij} + \sum_i \sum_{j>i}^k \sum_{h>j}^k V_{ijh} + \dots + V_{1,2,\dots,k} \quad (6)$$

where $V(y)$ is the variance of the model output y , k is the number of parameters and $V_{i_1, i_2, \dots, i_5} = \int f^2_{i_1, i_2, \dots, i_5} dx_{i_1}, dx_{i_2}, \dots, dx_{i_5}$ for a given set of indices, i_1, \dots, i_5 . The Sobol' sensitivity indices are the ratios of the partial variance given an individual parameter or the interactions of a parameter subset to the total variance. Two Sobol' indices are often calculated; the main effects also called the 'first-order index' and the total effects of a parameter are expressed, respectively, as (Sobol, 2001):

$$S_i = \frac{V[E(y|x_i)]}{V(y)} \quad (7)$$

and

$$S_{r_i} = 1 - \frac{V[E(y|x_{-i})]}{V(y)} \quad (8)$$

In disease model formulation, we make simplifications and assumptions on the model itself and on the parameters that represent the different transition and interaction in the model in question. The disease model provides a mathematical representation of the dynamic transmission cycle, involving interactions between infected and susceptible hosts that are generally expressed as a set of coupled ordinary differential equations, ODEs (Keeling, 2007). Owing to sensitivity on parameter values, it is important to correctly understand the possible effects of such parameter values to the expected model output (Stockholm, 2006). Sensitivity in the set of parameter values creates variability in the models predictive capabilities. The less the number of uncertain parameters in the model, the less the significance of variability introduced into a model, and vice-versa (Gomero, 2012).

Edward & Nyerere (2015) made a Mathematical Model that entailed some vital dynamics of cholera transmission with public health educational campaigns, vaccination, sanitation and treatment as control strategies in limiting the disease. Sensitivity analysis was carried out by them in the basic reproduction number with all control strategies and was discovered that the most sensitive parameters are educational campaigns, therapeutic treatment, and effective contact between the susceptible and infected persons, bacteria carrying capacity and recruitment rate. And they concluded that any strategy aimed at eliminating cholera should target these parameters. Mondal & Kar (2013) showed a waterborne disease epidemic model amenable to cholera dynamics including multiple transmissions namely, water-to-person and person-to-person transmission. Their study of the sensitivity analysis of the system in reference to some crucial parameters and discovered that the number of infected persons and pathogen concentrations are directly proportional to the two type disease transmission rate. It was also disarmed that if person-to-person contact was not applied, then the disease may be transmitted through the contaminated reservoir and within a very small time it might speed into the entire population. Kadaleka (2011) indicated that the

cholera epidemic can be controlled when intervention, nutrition and treatment are introduced.

The cholera epidemic is a fatal water-borne disease causing diarrhea, dehydration, and vomiting in an individual (WHO, 2019). It is caused by a bacterium called *Vibrio cholerae*. Cholera transmitted through ingesting contaminated feces and touching vomit and corpse killed by the bacterium without using protective devices (Panja, 2019). The disease has incubation period of less than 24 hours to 5 days and the infection is often asymptomatic that is not showing signs and symptoms readily. Less than 25% of the infected persons are asymptomatic and of these 10 – 20% of the infected persons show severe symptoms. A constant loss of body fluids leads to dehydration, and rejecting treatment as the incident occurs, hastens the death of the infected person within a few hours (Mosler & Kessely, 2015).

The uncertainty and sensitivity analyses indicate each parameter to disease transmission and are used for accessing sensitive model variations in the value of the parameters in the structure of the model (Numfor, 2010 & Rodrigues et al., 2013). Sensitivity analysis determines variability of input causing variability in the outputs. The model is carried out by dividing the population denoted by $N(t)$ according to the infection status into $S(t)$ – susceptible, $I(t)$ – infected, $R(t)$ – recovered and $B(t)$ is the amount of concentration of *vibrio cholerae* in aquatic habitat at time t . And the model parameters are π , human recruitment rate, ξ , the rate of human contribution to the population of *Vibrio cholera*, β_1 , rate of human exposure to contaminated water, δ , natural death rate of *vibrio cholera*, μ , death rate unrelated to cholera, μ_c , death rate due to cholera, β_2 , rate of contact between susceptible and infected persons, θ , rate of cholera awareness, ω , rate of sanitation, ν , rate of vaccination, ρ , rate of cholera treatment and N , pathogen concentration that yields 50% catching cholera. Therefore, the work presents the sensitivity indices of each parameter in relating to R_0 of the model. Numerical simulations are carried out to validate the theoretical results.

MATERIALS AND METHODS

Model Formation

The interaction between the population of susceptible persons, the infected, the recovered persons and the *vibrio cholerae* concentration in the aquatic habitat which are time dependent is being studied in formulating the system of non-linear ordinary differential equations. This mathematical formulation describes an aspect of *vibrio cholerae* infection which defines a set of deterministic values with application in health informatics modelling.

Mathematical Formation

The model used in this research work is a set of deterministic system of time non-linear first order differential equation proposed by Wang and Mondak (2011) which describes the transmission of the vibrio cholerae infection.

$$\frac{ds}{dt} = \pi - \mu s - (1 - \theta) \frac{\beta_1 BS}{B+N} - (1 - \theta) \beta_2 IS + \sigma R - \nu S \quad S(o), S \geq 0$$

$$\frac{dI}{dt} = (1 - \theta) \beta_1 BS + (1 - \theta) \beta_2 IS - (\mu + \mu_c + \rho) I \quad I(o), I \geq 0$$

$$\frac{dR}{dt} = \sigma s - \mu R - \sigma R + \rho I \quad R(o), R \geq 0$$

$$\frac{dB}{dt} = (1 - \theta) \xi I - (\sigma + \omega) B \quad B(o), B \geq 0$$

initial conditions.

Table 1: The definitions for the model parameters, their values, units and sources

Parameter	Symbol	Values	Units	Sources
Human recruitment rate	π	10	day ⁻¹	Kadeleka, 2011
Rate of Human contribution to the population of Vibrio Cholerae	ξ	10	cells/ μ l/day	Iserere et al, 2014
Rate of human exposure to contaminated water	β_1	0.075	day ⁻¹	Wang, 2011
Pathogen concentration that yields 50% chance of catching cholera	N	10 ⁵	cells/ μ l	Edward & Nyerere, 2015
Natural death rate for Vibrio Cholerae	ν	0.4	day ⁻¹	Iserere et al, 2014
Death rate unrelated to Cholera	μ	0.02	day ⁻¹	Kadeleka, 2011
Human death rate due to cholera	μ_c	0.015	day ⁻¹	Kadeleka, 2011
Rate of contact between susceptible and infected persons	β_2	0.00011	day ⁻¹	Wang & Modnak, 2011
Rate of Cholera awareness	θ	0.6	Dimensionless	Assumed
Rate of Vaccination	σ	0.2	Dimensionless	Assumed
Rate of Sanitation	ω	0.5	Dimensionless	Ochoche, 2013
Rate of Cholera treatment	ρ	0.98	day ⁻¹	Kadeleka, 2011

Source: Wang X. and Wang J. (2014) & Umoh (2022)

Method of Solution

Determination of the Steady State Solution

$$\frac{ds}{dt} = \pi - \mu s - (1 - \theta) \frac{\beta_1 BS}{B+N} - (1 - \theta) \beta_2 IS + \sigma R - \nu S \quad (9)$$

$$\frac{dI}{dt} = (1 - \theta)\beta_1BS + (1 - \theta)\beta_2IS - (\mu + \mu c + \rho)I \quad (10)$$

$$\frac{dR}{dt} = \sigma S - \mu R - \sigma R + \rho I \quad (11)$$

$$\frac{dB}{dt} = (1 - \theta)\xi I - (\sigma + \omega)B \quad (12)$$

At steady state,

$$\frac{ds}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = \frac{dB}{dt} = 0 \quad (13)$$

From (9), $\frac{ds}{dt} = 0$. Using (13) in (9) – (12) yields (14), (15), (16) and (17) respectively

$$\begin{aligned} &\Rightarrow \pi - \mu S - (1 - \theta) \frac{\beta_1BS}{B + N} - (1 - \theta)\beta_2IS + \sigma R - \nu S = 0 \\ &\Rightarrow \pi(B + N) - \mu S(B + N) - (1 - \theta)\beta_1BS - (1 - \theta)(B + N)\beta_2IS + \sigma R(B + N) \\ &\quad - \nu S(B + N) = 0 \\ &\Rightarrow \pi B + \pi N - \mu BS - \mu NS - (1 - \theta)\beta_1BS - (1 - \theta)\beta_2IBS - (1 - \theta)N\beta_2IS + \sigma BR \\ &\quad + \sigma NR - \nu BS - \nu S = 0 \\ &\Rightarrow \pi B - \mu BS - \mu NS - (1 - \theta)\beta_1BS - (1 - \theta)\beta_2IBS - (1 - \theta)N\beta_2IS + \sigma BR + \\ &\quad \sigma NR - \nu BS - \nu S = -\pi N \end{aligned} \quad (14)$$

From (10);

$$\begin{aligned} &\frac{dI}{dt} = 0, \\ &\Rightarrow (1 - \theta)\beta_1BS + (1 - \theta)\beta_2IS - (\mu + \mu c + \rho)I = 0 \end{aligned} \quad (15)$$

From (11)

$$\begin{aligned} &\frac{dR}{dt} = 0, \\ &\Rightarrow \sigma S - \mu R - \sigma R + \rho I = 0 \end{aligned} \quad (16)$$

And from (12)

$$\begin{aligned} &\frac{dB}{dt} = 0, \\ &\Rightarrow (1 - \theta)\xi I - (\sigma + \omega)B = 0 \\ &\Rightarrow I = \frac{(\sigma + \omega)B}{(1 - \theta)\xi} = 0 \end{aligned} \quad (17)$$

Putting (18) in (17); we have

$$\begin{aligned} \sigma S - (\mu + \sigma)R + \rho \frac{(\sigma + \omega)B}{(1 - \theta)\xi} &= 0 \\ \Rightarrow \sigma\xi(1 - \theta)S - (1 - \theta)(\mu + \sigma)\xi R + \rho(\sigma + \omega)B &= 0 \end{aligned} \quad (18)$$

Putting (18) in (15), then

$$\begin{aligned} (1 - \theta)\beta_1 BS + \frac{(\sigma + \omega)\beta_2 BS}{\xi} - \frac{(\sigma + \omega)(\mu + \mu c + \rho)B}{(1 - \theta)\xi} &= 0 \\ \Rightarrow (1 - \theta)^2 \xi \beta_1 BS + (1 - \theta)(\sigma + \omega)\beta_2 BS - (\sigma + \omega)(\mu + \mu c + \rho)B &= 0 \\ \Rightarrow B[(1 - \theta)^2 \xi \beta_1 S + (1 - \theta)(\sigma + \omega)\beta_2 S - (\sigma + \omega)(\mu + \mu c + \rho)] &= 0 \\ \Rightarrow B = 0 \text{ or} \\ (1 - \theta)^2 \xi \beta_1 BS + (1 - \theta)((\sigma + \omega)\beta_2 BS - (\sigma + \omega)(\mu + \mu c + \rho)B) &= 0 \\ \Rightarrow [(1 - \theta)^2 \xi \beta_1 + (1 - \theta)(\sigma + \omega)\beta_2]S = (\sigma + \omega)(\mu + \mu c + \rho). \end{aligned}$$

[B* is an assumption]

$$S = \frac{(\sigma + \omega)(\mu + \mu c + \rho)B}{(1 - \theta)^2 \xi \beta_1 + (1 - \theta)(\sigma + \omega)\beta_2} \quad S^* \quad (19)$$

But by putting B=0 in (18), it becomes

$$\begin{aligned} \sigma\xi(1 - \theta)S - (1 - \theta)(\mu + \sigma)\xi R &= 0 \Rightarrow \sigma S - (\mu + \sigma)R = 0 \\ \Rightarrow R &= \frac{\sigma S}{\mu + \sigma} \end{aligned} \quad (20)$$

Putting B = 0 and I = 0 in (14) we have

$$\begin{aligned} -\mu NS + \sigma NR - N\nu S &= -\pi N \Rightarrow \mu S - \sigma R + \nu S = \pi \\ \Rightarrow (\mu + \nu)S - \sigma R &= \pi \end{aligned} \quad (21)$$

Putting (20) in (21), then

$$\begin{aligned} (\mu + \nu)S - \frac{\sigma^2 R}{\mu + \sigma} &= \pi \\ \Rightarrow (\mu + \sigma)(\mu + \nu)S - \sigma^2 S &= \pi(\mu + \sigma) \\ \Rightarrow [(\mu + \sigma)\mu + \nu - \sigma^2]S &= \pi(\mu + \sigma). \\ S = \frac{\pi(\mu + \sigma)}{(\mu + \sigma)(\mu + \nu) - \sigma^2} &= S^\wedge \quad (S^\wedge \text{ is an assumption}) \end{aligned} \quad (22)$$

Putting (22) in (20); then

$$R = \frac{\pi\sigma(\mu + \sigma)}{(\mu + \sigma)^2(\mu + \nu) - \sigma^2(\mu + \sigma)}$$

$$R = \frac{\pi\sigma}{(\mu+\sigma)(\mu+\nu)-\sigma^2} = R^{\wedge} \quad (R^{\wedge} \text{ is an assumption}) \quad (23)$$

RESULTS

To examine the sensitivity analysis (test) of cholera in aquatic habitat using the mathematical model: $\frac{ds}{dt} = \pi - \mu S + \sigma R - \nu S$

Table 2: Sensitivity Analysis $R = 40.6, S = 5.0, \gamma = 0.02, \pi - \text{varies}$

π	μ	$\frac{ds}{dt} = \pi - \mu S + \sigma R - \nu S$
1	0.020	6.90
2	0.018	7.91
3	0.016	8.92
4	0.014	9.93
5	0.012	10.94
6	0.010	11.95
7	0.008	12.96
8	0.006	13.97
9	0.004	14.98
10	0.002	15.99

On the basis of the calculations, it is observed that from Table 2, the sensitivity of the dependent variable S , for a fixed $\pi = 10$ (human recruitment rate) and a varying value of μ (death rate of cholera) range from 0.002 – 0.02 is 15.90. The sensitivity of the dependent variable S , for a varying π (Human recruitment rate) of 1 – 10, and a varying μ ranging from 0.002 – 0.020, increases from 6.90 – 15.99 which predict a decrease in the sensitivity of susceptible persons. On the sensitivity of susceptible persons scenario, the increase in human recruitment rate, predict a decrease in the sensitivity of susceptible persons, which is consistent with the work of Nwagor and Ekaka-a (2017). The numerical method which is being utilized in this work can be extended in tackling the effect of vaccination in the stability of the dynamical system.

Table 3: Quantifying the effect of no variation of rate of human exposure to contaminated water on the dynamical system($\beta_1 = 0.075$)

Time (t)	β_1	S(t)	I(t)	R(t)	B(t)
0.00	0.075	1000.000000	50.000000	20.000000	120.000000
0.05	0.075	9789.36323	467.604462	62.716212	2036.10642
0.10	0.075	9571.62411	1344.237742	162.230471	5104.93966
0.15	0.075	9331.33419	3560.336908	398.876767	13453.29046
0.20	0.075	9028.25972	9206.240301	986.390846	35227.15485
0.25	0.075	8578.24947	23207.982986	2456.293529	90661.84571
0.30	0.075	7853.04729	56145.174207	06054.628982	227039.50549
0.35	0.075	6826.74446	127166.329228	14424.706228	543977.97787
0.40	0.075	5926.34334	267298.048443	32521.766082	1226250.83258
0.45	0.075	5705.55651	546704.174662	69676.337172	2620436.49870
0.50	0.075	5809.69580	1138510.629000	146361.652049	5493368.46306
0.55	0.075	5822.39792	2391545.706767	307051.018499	11514253.03030
0.60	0.075	5827.20872	5022615.918847	644546.532746	24162104.87039
0.65	0.075	5831.04661	10548050.597243	1353324.713415	50725892.86920
0.70	0.075	5829.24985	22152411.650861	2841839.929496	106514620.20671
0.75	0.075	5828.43012	46523024.255695	5967910.308883	223679636.04418
0.80	0.075	5828.98202	97704602.838878	12533073.976454	469743286.67893
0.85	0.075	5829.99327	205193035.459849	26320812.430304	986511933.33221
0.90	0.075	5829.35116	430933786.606197	55276963.387465	2071798677.27492
0.95	0.075	5832.21481	905020628.448932	116088891.373109	4351052464.02423
1.00	0.075	5830.11501	1900669211.471159	243802383.016390	9137803080.07970

Table 3 shows the variation of data value of the rate of human exposure to contaminated water (β_1) ranging from 0.075 to 0.1485 yields a fluctuating pattern of the data set of the eigenvalues ($\lambda_1, \lambda_2, \lambda_3$ and λ_4). The results predict a predominantly unstable state solution of the dynamical system. With no variation of human exposure rate to contaminated water on the dynamical system, that is constant β_1 of 0.075. The value of susceptible persons increases even as infected persons, and the value of recovered persons likewise increase as well as the total population/concentration of cholera vibrio in that habitat.

Table 4: Quantifying the effect of 10% variation of rate of human exposure to contaminated water on the dynamical system($\beta_1 = 0.075$)

Time (t)	β_1	S(t)	I(t)	R(t)	B(t)
0.00	0.0075	1000.000000000000	50.000000000000	20.000000000000	120.000000000000
0.05	0.0075	979.591987364246	81.182300010017	45.500872272003	134.832357682902
0.10	0.0075	960.024498818397	114.409772291615	73.148413974624	160.612234385295
0.15	0.0075	941.314.692627377	152.267176422852	103.246551833984	197.727373661316
0.20	0.0075	923.479494323779	197.235773857825	136.320740289395	247.415720551232
0.25	0.0075	906.537839133412	251.789364962090	173.137068246353	311.816693264859
0.30	0.0075	890.517824728392	318.712935297366	214.690885173226	393.843572322504
0.35	0.0075	875458559092120	401.174003936125	262.248363971623	497.321181731835
0.40	0.0075	861.415805989765	502.971972257721	317.383049885002	627.055239804064
0.45	0.0075	848.464517006677	628.647498484801	382.039001757182	789.041391871032
0.50	0.0075	836.705076565613	783.779753605760	458.608920768520	990.681518202128
0.55	0.0075	826.266767344155	975.179478878350	550.032103943846	1241.108843301104
0.60	0.0075	817.315692852690	1211.339808401815	659.928660310351	1551.587823269608
0.65	0.0075	810.059331135194	1502.807480240954	792.757378258524	1936.040357762632
0.70	0.0075	804.756634565558	1862.954082082231	954.045536990950	2411.758504449836
0.75	0.0075	801.723504276388	2308.732254439054	1150.656879514565	3000.302721334482
0.80	0.0075	801.344639168330	2862.101997841409	1391.203215812687	3728.823310399562
0.85	0.0075	804.078747657475	3551.634584045606	1686.527131260514	4631.688463938120
0.90	0.0075	810.469156535430	4415.318514607173	2050.482021326027	5753.068372252369
0.95	0.0075	821.144526934345	5504.061264432333	2500.854823502280	7150.065517697770
1.00	0.0075	836.817790043535	6887.470724293232	3060.905766898180	8897.946665264065

Table 4 shows the contribution of contact between susceptible and infected persons on the dynamic system. The smaller value of the contact rate between the susceptible and infected persons (β_2) (ranges from 0.000011 to 0.000099) yield or predict a relatively high value of λ . Whereas, an increased value of β_2 , predicted smaller values of λ resulting to unstable steady state solution of the dynamical system. By quantifying 10% variation of human exposure to contaminated water, the susceptible persons' value decreases, unlike the infected, recovered and total concentration of vibrio cholera which shows a remarkable increase in population.

Table 5: Quantifying the effect of 10% variation of rate of contact between susceptible and infected persons on the dynamical system($\beta_2 = 0.00011$)

Time (t)	β_2	S(t)	I(t)	R(t)	B(t)
0.00	0.000011	1000.00000000	50.00000000	20.00000000	120.00000000
0.05	0.000011	989.79913392	234.17803476	36.51683663	142.27640358
0.10	0.000011	979.87616098	466.76102782	62.69250908	203.48864085
0.15	0.000011	970.32353896	807.99472548	102.19301397	317.08217256
0.20	0.000011	961.27106001	1341.68471417	162.08443747	509.71696246
0.25	0.000011	952.91774468	2194.48072004	254.39285814	827.12967436
0.30	0.000011	945.58421523	3567.56844539	398.86288647	1344.55391231
0.35	0.000011	939.78498539	5781.69463603	627.47961125	2183.98442080
0.40	0.000011	936.35452330	9358.00828980	992.08193591	3543.17115363
0.45	0.000011	936.63316235	15145.57836600	1576.49405324	5741.99392631
0.50	0.000011	942.78047840	24561.06049793	2518.00202900	9304.66721372
0.55	0.000011	958.25752688	40012.72500020	4042.46530177	15094.31919962
0.60	0.000011	988.58543503	65777.18767535	6533.41101042	24579.67400431
0.65	0.000011	1042.61199115	109822.50240127	10653.38135437	40302.72767256
0.70	0.000011	1134.02578860	188075.66655015	17627.96768232	66988.16995387
0.75	0.000011	1284.42613285	335106.83123722	29801.43986815	113699.88013467
0.80	0.000011	1521.72676010	632324.81765584	52216.76602222	200075.31939831
0.85	0.000011	1874.27372767	1291267.56594397	96343.10347066	370936.67223750
0.90	0.000011	2308.33492848	2873840.20395146	191092.14513541	739875.50533415
0.95	0.000011	2619.79730492	6814400.93741627	411071.60893039	1600566.50481003
1.00	0.000011	2638.66745859	16124877.23187691	934934.99752241	3655523.97738281

Table 5 shows the behavior of the control variable of the cholera infection due to variation of the data set of human exposure to contaminated water, when β_1 is constant at 0.075. The value of the susceptible persons ranges from 50.0000 to 1900669211.471159. The recovered persons ranges from 20.0000 to 243802383.016390, whereas the zolet population of cholera (bacteria) in the aquatic habitat which ranges from 120.0000 to 91378703080.07970. By quantifying 10% variation of rate of contact between susceptible and infected persons, and at constant β_2 , the susceptible persons' value increases, likewise the infected, recovered and total concentration of vibrio cholera.

Table 6: Effect of human exposure to contaminated water on the stability of the dynamical system

β_1	λ_1	λ_2	λ_3	λ_4	TOS
0.075	-39812.71658669595	-17.41682184082	7.42003594031	-0.55361051806	Unstable
0.0075	-10.274244434883473	8.821119747921539	-0.554962766574937	-0.554962766574937	Unstable
0.015	-7.256844086446767	-7.256844086446767	8.091947754763949	-0.573257526961217	Unstable
0.0225	-23.095180665399170	-23.095180665399170	7.160009402147707	-0.551079284789429	Unstable
0.030	-153.8635556813403	-27.1159505968098	7.1799979842951	-0.5510483500691	Unstable
0.0375	-578.9367232325274	-22.8116228962738	7.2705089745925	-0.5516086485719	Unstable
0.0450	-1680.364280844664	-20.955689424133	7.337286181894	-0.552121208243	Unstable
0.0525	-4223.271160778493	-19.721078469626	7.379806616197	-0.552630083585	Unstable
0.060	-9590.259366973847	-18.785359328819	7.404475528078	-0.553073445315	Unstable
0.0675	-20153.50382187567	-18.04193055810	7.41658838946	-0.55329581072	Unstable
0.07125	-28523.37541459641	-17.71182692062	7.41923510726	-0.55353702236	Unstable
0.0735	-34896.45855069797	-17.53624561912	7.41990260902	-0.55349892068	Unstable
0.0825	-74762.01294088454	-16.88852503356	7.41729687167	-0.55381336388	Unstable
0.090	-134550.9262181156	-16.4259261863	7.4099976886	-0.5541029670	Unstable
0.0975	-233542.9296624187	-16.0209634156	7.3993965980	-0.5543457613	Unstable
0.105	-392881.0377219479	-15.6595619514	7.3862795538	-0.5546171875	Unstable
0.1125	-643102.2387031537	-15.3429756073	7.3716793771	-0.5546984094	Unstable
0.120	-1027592.758041501	-15.054745183	7.355684829	-0.554830182	Unstable
0.1275	-1607083.434771557	-14.790710709	7.338619109	-0.555003973	Unstable
0.135	-2465929.821303217	-14.549804605	7.320900144	-0.555152387	Unstable
0.1425	-3718034.128378208	-14.327417689	7.302627169	-0.555316507	Unstable
0.14625	-4538088.494748818	-14.222465972	7.29336797	-0.555402420	Unstable
0.1485	-5105291.435448762	-14.164305968	7.287981311	-0.555372186	Unstable

Table 7: Effect of contact between susceptible and infected persons on the dynamical system

β_2	λ_1	λ_2	λ_3	λ_4	TOS
0.000011	-279.9180826108713	-32.7046959188386	10.8053312218446	-0.2841587390234	Unstable
0.000022	-156.4572482671883	-27.4673811577599	9.1574477632315	-0.3337019730729	Unstable
0.000033	-104.57220078335395	-25.4336228543098	8.4447235686995	-0.3763937440429	Unstable
0.000044	-75.941480702552610	-24.645579250602612	8.059197715008937	-0.413200887920538	Unstable
0.000055	-57.359786113535542	-24.755609557963712	7.826607965349210	-0.445120650131634	Unstable
0.000066	-43.517016920323471	-25.998114822145990	7.676124148093995	-0.473151685242553	Unstable
0.000077	-30.193790730120305	-30.193790730120305	7.574706660603323	-0.497853989239400	Unstable
0.000088	-26.746292078205638	-26.746292078205638	7.503857182535888	-0.519787905813366	Unstable
0.000099	-24.073830501017767	-24.073830501017767	7.451977938562727	-0.539471509118388	Unstable
0.0001045	-22.942541473776398	-22.942541473776398	7.431358634429062	-0.548564146162581	Unstable
0.0001078	-22.313569469611540	-22.313569469611540	7.420839594284378	-0.553690917901242	Unstable
0.000121	-20.163273116596745	-20.163273116596745	7.384056538958928	-0.573173256132916	Unstable
0.000132	-18.701031746903503	-18.701031746903503	7.360383640682048	-0.587761920803750	Unstable
0.000143	-17.467408351561645	-17.467408351561645	7.340708064730648	-0.601109797949579	Unstable
0.000154	-16.413564350254426	-16.413564350254426	7.323711742241775	-0.613373071913307	Unstable
0.000165	-15.503493356122398	-15.503493356122398	7.308474253470843	-0.624682347831496	Unstable
0.000176	-14.710093239144708	-14.710093239144708	7.294347612642705	-0.635147789812080	Unstable
0.000187	-14.012591442106537	-14.012591442106537	7.280873943461584	-0.644863013632623	Unstable
0.000198	-13.394811322422317	-13.394811322422317	7.267729961416242	-0.653908103977543	Unstable
0.000209	-12.843976554422454	-12.843976554422454	7.254688742598846	-0.662351989202810	Unstable
0.0002145	-12.590397927028128	-12.590397927028128	7.248152339771663	-0.666368085965177	Unstable
0.0002178	-12.444596670422705	-12.444596670422705	7.244214630212560	-0.668716208672557	Unstable

CONCLUSION AND RECOMMENDATION

This work on uncertainty and sensitivity analyses, a mathematical model of infectious disease of cholera in aquatic environment uses ODE45 numerical scheme. The study further shows that long term precise predictions of the concentration of infected cells during cholera infection could be difficult until the key parameters are correctly determined. On the contribution of contact between susceptible and the infected persons on the dynamical system, and variation of the rate of human exposure to contaminated water, predict a predominantly unstable steady state solution on the dynamical system.

REFERENCES

- Ecohard, R. (2010). Methodology of the sensitivity analysis used for modelling on infection disease. *Vaccine*, 28, 8132 –8140. doi:10.1016/j.vaccine.2010.09.099
- Edward, S., & Nyerere, N. (2015). A mathematical model for the dynamics of cholera with control measures. *Application of Computational Mathematics*, 4(2), 53 – 63.
- Fraser, C. (2012). Mathematical models on infectious disease transmission. *National Reservoir Micro Biology*, 6, 477 - 487.
- Gatelli, D. (2008). *Global sensitivity analysis*. John Wiley and Sons.
- Gomero, B. (2012). Latin hypercube sampling and partial rank correlation coefficient analysis applied to an optimal control problem. Master's Thesis, University of Tennessee. https://trace.tennessee.edu/utk_gradthes/1278
- Hornick, R. B. (1971). The broad street pump revisited: Response of volunteers to ingested cholera vibrios. *Bulletin of New York Academic Medicine*, 47(10), 1181 – 1190.
- Isere A. O., Osemwenkhae J. E. & Okuonghae D. (2014). Optimal control model for the outbreak of cholera in Nigeria. *African Journal of Mathematics, Computer Science Research*, 7(2), 24
- Kadeleka, S. (2011). Assessing the effects of nutrition and treatment in cholera dynamics: The case of Malawi. M.Sc. Dissertation, University of Deres Salaam.
- Keeling, M. (2007). *Modelling infectious disease in human and animal*. Princeton University Press.
- Mondal, P. K. & Kar, J. K. (2013). Global dynamics of waterborne disease model with multiple transmission pathways. *Applications and Applied Mathematics*, 8(1), 75 – 98.
- Morris, M. D. (1991). Factorial sampling plans for preliminary computational experiments. *Technometrics* 33, 161 – 174. doi.10.1080/00401706.1991.10484804.
- Mosler, J. & Kessely, H. (2015). Factors determining water treatment behaviour for the prevention of cholera treatment in Chad. *The American Journal of Tropical Medicine and Hygiene*, 93, 57 – 65.
- Numfor, E. S. (2010). Mathematical modeling, simulation, and time series analysis of seasonal epidemics. M.Sc. Thesis, East Tennessee State University.

- Nwagor, P. & Ekaka-a, E. N. (2017). Sensitivity of a mathematical model of HIV infection with a fractional order characterization. *International Journal of Pure and Applied Sciences*, 10(1), 86 – 92.
- Ochoche, J. M. (2013). A mathematical model for the transmission dynamics of cholera with control strategy. *International Journal of Scientific and Technology Research*, 2(11), 212 – 217.
- Panja, P. (2019). Optimal control analysis of a cholera epidemic model. *Biophysical Review and Letters*, 14, 27 – 48.
- Ray, C. J. (2008). A methodology for performing global uncertainty and sensitivity analysis in system biology. *Journal of Theoretical Biology*, 254, 178 – 196. doi:10.1016/j.jtbi.2008.04.011
- Rodrigues, H. S., Monteiro, M. T., & Torres, D. F. (2013). Sensitivity analysis in a dengue epidemiological model. <http://dx.doi.org/10.1155/2013/721406>
- Saltelli, A. (2007). An effective screening design for sensitivity analysis of large models. *Environment Modelling Software*, 22, 1509 – 1518. doi:10.1016/j.envsoft.2006.10.004
- Sobol, I. M. (1990). Sensitivity estimates for non-linear mathematical models. *Matematicheskoe modelirovanie*, 2, 112 – 118.
- Sobol, I. M. (2001). Global sensitivity indices for non-linear mathematical models and their Monte Carlo estimate. *Mathematical Computational Simulation*, 55, 271 – 280. doi:10.1016/S0378-4754/000027-6
- Stockholm, F. (2006). Methods for uncertainty and sensitivity analysis: Review and recommendations for implementation in ecology. *Eysicum*, 5, 23 – 29.
- Tarantola, S. (2008). *Global sensitivity analysis*. John Wiley and Sons.
- Umoh, E.S. (2022). Mathematical Modelling Approach for the Sensitivity and Stability Analyses of Cholera Diseases in Aquatic Environment. An M.Sc. Thesis in the Department of Mathematics and Statistics, Ignatius Ajuru University of Education, Port Harcourt, Rivers State.
- WHO (2019). Cholera – World Health Organization. <https://www.who.int/news-room/fact-sheets/detail/cholera>
- Wang, J. & Modnak, C. (2011). Modeling cholera dynamics with controls. *Canadian Applied Mathematics Quarterly*, 19(3), 255 – 273.
- Wang, X., & Wang, J. (2014). Analysis of cholera epidemics with bacteria growth and spatial movement. *Journal of Biological Dynamics*, 2, 23 – 31.