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Mathematical Model for Prevention and Control of Cholera Disease in Nigeria

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Abstract

In this research work, we modified an existing mathematical model that can accommodate the gaps we discovered from the existing model. The modification centered on addition of a compartment called Isolation compartment into the existing model. The isolation is added as part of the control measures. This is one of the factors that make eradication of cholera impossible. We checked for the existence and uniqueness of the modified model and observed that the modified equations are unique and they exist. Maple 2023 and R studio software were used in carrying out the analysis. The disease-free equilibrium (DFE) state of the model was determined and used to compute the basic reproduction number R_0, as a threshold for effective disease management. The results from stability analysis for the disease-free equilibrium (DFEs) shows that it is locally asymptotically stable whenever the basic reproduction number is less than unity ($R_0 < 1$). The result obtained from sensitivity index of R_0 shows that the control parameters (isolation) of susceptible individual is crucial parameter to cholera management. It is recommended that isolation and awareness should be given prompt response

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as strategies in eradicating cholera disease so as to avoid prolonged illness and death.

Keywords: Cholera, Basic Reproduction Number, Parameter, Isolation, Disease-Free Equilibrium

INTRODUCTION

Cholera is a severe diarrhea infection upon consumption of food or water that is contaminated (Tainted) with the bacterium called vibrio cholera (Elimian *et al.,* 2019). It is an extremely noxious disease that can cause severe acute watery diarrhea, which can be symptomatic or asymptomatic. If the contaminated individuals do not get treatment, the acidic level of their body becomes excessive which can multiply the probability of cholera related death within 24 hours (Monje *et al.,* 2020). The most fatal among all the pandemic is third that occurred between 1852 and 1859 and cuts across all continents of the world excluding the Antartical and claim about 23, 000 in Great Britain (Piret and Boivin, 2010). Cholera is an example of a bacterial disease whose primary mode of infection is indirect; which is cause when individuals ingest fecal-contaminated water containing the bacteria V. cholera (Ali et al., 2017).Transmission between humans and reservoirs of pathogens implies that disease transmission includes an indirect route other than human-to-human contact.

The last few years have witnessed many cholera outbreaks in developing countries, including India in 2011,Congo in 2012, Iraq in 2012, Zimbabwe between 2011-2012, Vietnam in 2014, Nigeria in 2015. and Haiti(2015). In the year of 2015 alone, it is estimated that cholera affects 3-5 million people and causes 100.000-130,000 deaths in the world annually (Barua, 2016).

In essence, Cholera is an infection of the small intestine caused by the gram-negative bacterium, Vibrio cholera. Untreated individuals suffer severely from diarrhea and vomiting. The disease can cause a rapid dehydration and electrolyte imbalance, and can lead to death. Meanwhile, different transmission pathways are possible. For example, a cholera outbreak in a Singapore psychiatric hospital indicated that the direct human-to-human transmission was a driving force (Brown, 2018).

The dynamics of cholera involve multiple interactions between the human host, the pathogen, and the environment, which contribute to both direct human-to-human and indirect environment-to-human transmission pathways.

Due to its huge impact on public health, and social and economic development, cholera has been the subject of extensive studies in clinical, experimental and theoretical fields. It remains an important global cause of morbidity and mortality, capable of causing periodic epidemic disease (Farooqui et al. 2016).

(Jing Wang, 2019) considered three types of controls: vaccination, therapeutic treatment (including hydration therapy, antibiotics, etc), and water sanitation but he did not incorporate the role of education control strategy in their mode, also they did not consider a logistic growth of vibrio cholera.

Cholera is still endemic to sub-Saharan Africa mostly among countries with poor infrastructure (Legros, 2018). In 2019 the world cholera case death and fatality rate were put at 3499, 477, 2990 and 0.65 respectively (WHO, 2019).Mathematical modeling has been and will always remain a vital tool in the fight against diseases, mathematical modeling analysis has provided information for various countries in making public health policies in the ongoing COVID-19 pandemic (Enserink and Kupferchidt, 2020). Over the years, rigorous analytical and numerical analysis of model has contributed to the fight against cholera.

Edward and Nkuba (2015) show in their work that the use of multiple control measure is far more effective than the application of single control.

Chen *et al.* (2016) proposed and analyzed a partial differential equation model to ascertain the effect of human diffusion and bacteria convection in cholera transmission; they also investigated the various factors that determine the spatial spread of cholera. Sun *et al.* (2017) develop a mathematical model to characterize the transmission process of cholera in China, the result of the analysis shows that improved environmental sanitation and provision of clean water is better strategy than vaccination. Yang *et al.* (2017) proposed two set of models to ascertain the impact of awareness/unawareness, their result highlight the importance of model validation as a prerequisite for adoption as the two closely related models have different dynamical behaviors.

More recently, Ayoade *et al.* (2018), in their work, shows the possibility of human to human transmission of cholera, that vaccination and treatment with drug remains sufficient to

eliminate cholera. Lemos-Paiao *et al.* (2019) proposed and analyzed a mathematical model for cholera considering vaccination, their analysis and simulation suggest that vaccination has the ability to stem down cases if started in good time earlier. Mokati *et al.* (2019), in their work, proposed a model to control cholera via Quarantine. Chayu (2020), in his work introduced the multi-scale modelling where he considered between and within host characteristics. Yang and Wang (2019), in their model, they studied the effect of medical resources in cholera transmission and fitted their model to the Yengen cholera outbreak during 2017- 2018.

Hailemarian and Kahsay (2020) proposed a model for eradication of cholera and validated their assumption using numerical simulation.

Kolayse *et al.* (2020) proposed the control of cholera via sensitization and sanitation.

Bakare and hoskovamayerora (2021), in their paper developed an optimal control model for cholera, their analysis shows that the four-control measure considers have the capacity to control and eradicate cholera in asymptomatic population. Phan *et al.* (2021) develop a stochastic model of cholera incorporating environmental fluctuation in the transmission dynamics.

Hezam *et al.,* (2021) propose an optimal mathematical model that integrate COVID-19 and cholera, their model aimed at minimizing infected person and other cost associated with the two diseases

Sharma and Signh (2021), in their research, established the backward bifurcation of cholera model with some treatment function.

METHODS

Introduction

In this research work, we extended the work done by Okolo et al (2020), by including isolation as a measure of controlling Cholera disease. This yielded a modified model in which we obtained a method of the solution of the problem.

Model Assumption

Here we considered the following assumptions

(i) Cholera disease is an infection that can affect all ages

(ii) We assume that death can occur in any of the compartment

(iii) Cholera is contagious and so infected individuals should be isolated

(iv) People without awareness suffer cholera disease the most

(v) Infected individuals without symptoms spread the disease faster.

Model Formulation

The equation of the existing model

$$\frac{dS}{dt} = \rho - (\alpha - \gamma\alpha)\frac{B}{K+B}S - (\beta - \gamma\beta)SI - (\varphi + \mathrm{q})S \quad (1)$$

$$\frac{dI}{dt} = (\alpha - \gamma\alpha)\frac{B}{K+B}S + (\beta - \gamma\beta)SI - (\sigma + \delta + \psi + u)I \quad (2)$$

$$\frac{dB}{dt} = \varepsilon I - (\emptyset + z)B \quad (3)$$

$$\frac{dR}{dt} = (\sigma + u)I + qS - \varphi R \quad (4)$$

With the non-negative initial condition.

$$S(O) \geq 0, I(O) \geq 0, B(O) \geq 0, R(O) \geq 0 \quad (5)$$

Parameters of the existing model

Table 1: (showing variable and parameter with their meaning).

Parameter	Meaning	Values	Source
ρ	Recruitment rate	0.00913	Hartley et al(2006)
α	Rate of injecting V. Cholera from contaminated sources	0.214	Falaye et al (2018)
K	Concentration of Vibrio Cholera in food and water that yield 50% chance of	0.000007	Codeco(2001)

	catching cholera Disease.		
β	human -to- human transmission rate	0.02	Hartley et al(2006)
Ψ	Human death rate	0.025	Falaye et al (2006)
q	Vaccination rate	0.04	Falaye et al (2006)
σ	Recovery rate of infected human	0.2	Hartley et al(2006)
δ	Disease induced death rate	0.013	Wang et al(2011)
Γ	The rate at which isolated recovered	0.2	Hartley et al(2006)
μ	Treatment rate	0.2	Falaye et al (2006)
ε	The rate of which isolated goes back to susceptible individual	0.42	Wang et al (2011)
Φ	Natural death rate of V cholera	0.33	Misra et al (2011)
Z	Water sanitation rate	0.01	Falaye et al (2006)

The systematic diagram of the existing model

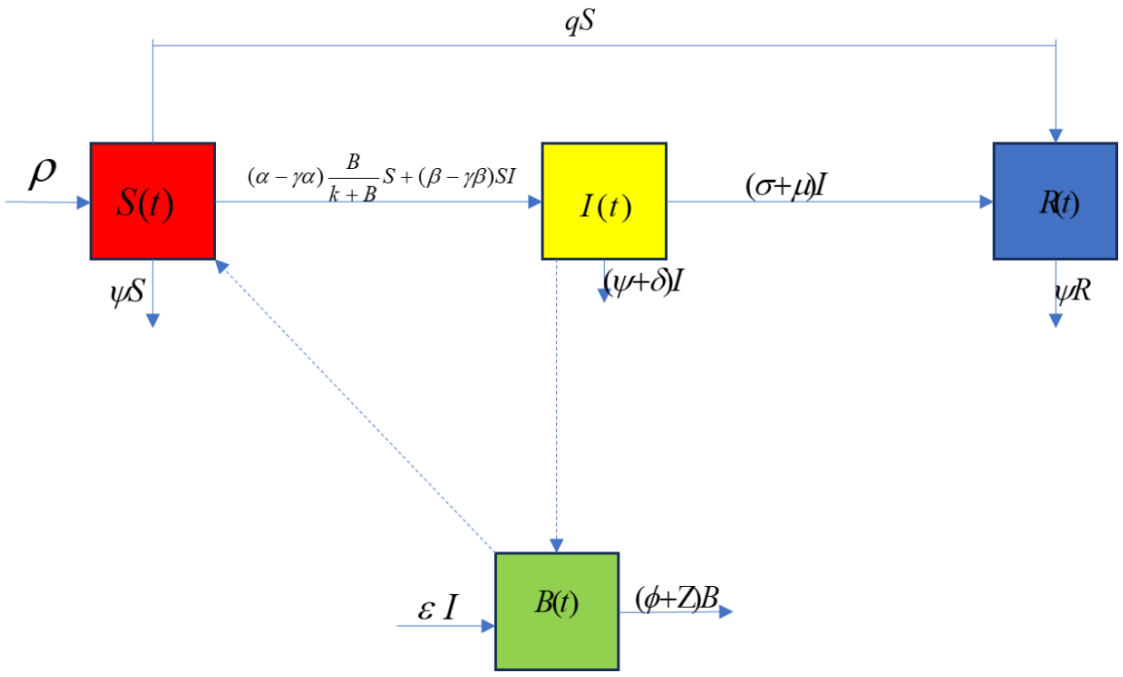


Figure 1: Schematic diagram of the existing mathematic model

Model Equation of the modified model

$$\frac{dS}{dt} = \rho - (\alpha - \gamma\alpha)\frac{B}{K+B}S - (\beta - \gamma\beta)SI - (\varphi + \mathrm{q})S + \lambda I_S - \eta_S \qquad (6)$$

$$\frac{dI}{dt} = (\alpha - \gamma\alpha)\frac{B}{K+B}S + (\beta - \gamma\beta)SI - (\sigma + \delta + \psi + u)I \quad (7)$$

$$\frac{dB}{dt} = \varepsilon I - (\emptyset + z)B \quad (8)$$

$$\frac{dR}{dt} = (\sigma + u)I + qS - \varphi R + \Gamma I_S \quad (9)$$

$$\frac{dI_S}{dt} = \eta_S - \lambda I_S - \Gamma I_S - \mu_1 \quad (10)$$

Variables and Parameters of the modified model

The following variable and parameter are use in the modified model

Table 2: (showing variable and parameter with their meaning).

Variable	**Meaning**	**Values**	**Source**
S	Susceptible	3683	NCDC(2023)
I	Infected	2112	Assumed
B	Virus class	784	NCDC(2023)
R	Recover	567	Assumed
I_s	Isolation	220	WHO(2023)
Parameter	**Meaning**		
ρ	Recruitment rate	0.00913	Hartley et al(2006)
α	Rate of injecting V. Cholera from contaminated sources	0.214	Falaye et al (2018)
K	Concentration of Vibrio Cholera in food and water that yield 50% chance of catching cholera Disease.	0.000007	Codeco(2001)
β	human -to- human transmission rate	0.02	Hartley et al(2006)
Ψ	Human death rate	0.025	Falaye et al (2006)

q	Vaccination rate	0.04	Okolo et al (2020)
σ	Recovery rate of infected human	0.2	Hartley et al(2006)
δ	Disease induced death rate	0.013	Wang et al(2011)
λ	The rate at which susceptible are isolated	0.03	Assumed
Γ	The rate at which isolated recovered	0.2	Hartley et al(2006)
μ_1	Natural death from the Isolated	0.02	Assumed
μ	Treatment rate	0.2	Okolo et al (2020)
ε	The rate of which isolated goes back to susceptible individual	0.42	Wang et al (2011)
Φ	Natural death rate of V cholera	0.33	Misra et al (2011)
η	The rate at which isolated individuals recovered	0.05	Assumed
Z	Water sanitation rate	0.01	Okolo et al (2020)

The schematic diagram of the modified model.

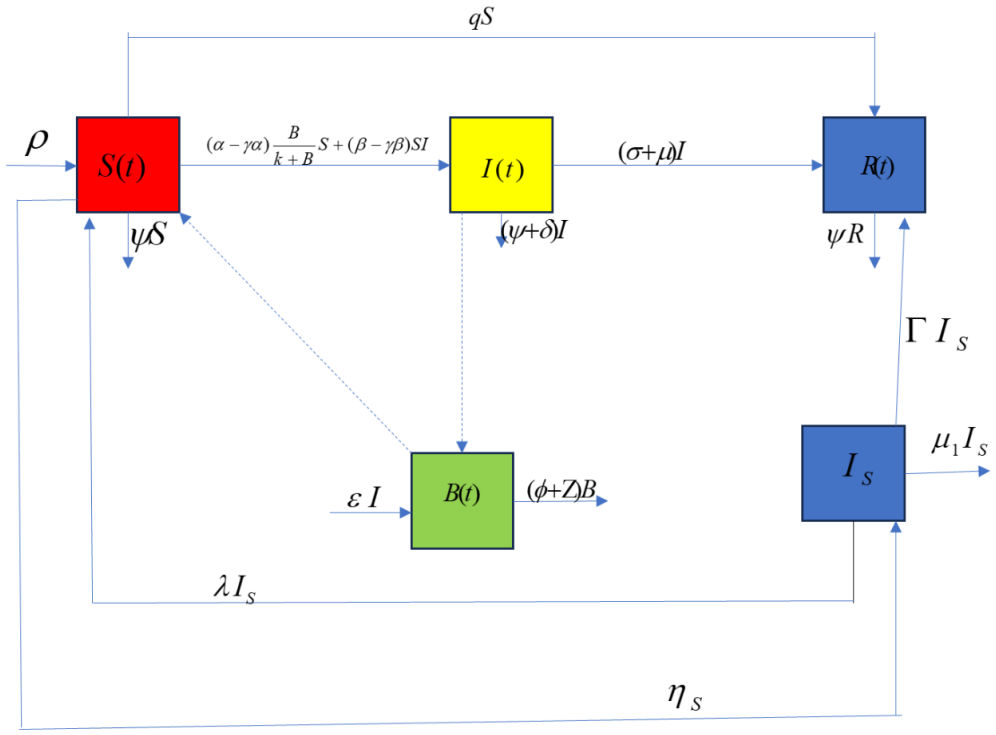


Figure 2: Schematic diagram of the modified mathematical model

Basic Properties of the model equation.

All model variable and parameter are assumed to be non-negatives for all t≤0 since the model monitor changes in the population

Existence of solution

Let X: $\mathbb{R}\rightarrow\mathbb{R}^5$

$t \rightarrow (S(t), I(t), B(t), R(t),$ I_s (t).

And

$\boldsymbol{F}: \mathbb{R}^{\mathbf{5}} \rightarrow \mathbb{R}^{\mathbf{5}}$

$$X(t) \rightarrow F(X(t)) = (\frac{dS(t)}{dt}, \frac{dI(t)}{dt}, \frac{dB(t)}{dt}, \frac{dR(t)}{dt}, \frac{dI_s(t)}{dt})$$

Then the system (6) – (10) becomes

$$X(t) = F(X(t)), X(0) = X_0$$

Disease – Free Equilibrium Point

In finding disease- free equilibrium (DFE), we consider

$\frac{dS}{dt} = \frac{dI}{dt} = \frac{dB}{dt} = \frac{dR}{dt} = \frac{dIs}{dt}$=0

{DFE} is obtained by making (S.I.R.B.I_S) each the subject.

$$\frac{dS}{dt} - \rho + (\alpha - \gamma\alpha)\frac{B}{K+B}S + (\beta - \gamma\beta)SI + (\varphi + \mathrm{q})S + \lambda I_S + \eta_S = 0$$

Making S the subject of the formula in the equation above gives,

Considering ϱ−(Ψ+q)s−ηs=0 it implies S=$\frac{\rho}{\Psi+q+\eta}$

Similarly in solving for I we have $-(\sigma + \delta + \psi + u)I$ =0 ==>,I =0

Similarly for B , let εI= 0 and $-(\emptyset + z)B$= 0 hence B = 0

Following the same vein for R. $-\varphi R$ = 0 hence R = 0.

Finally following the same path to solve I_s, where S = 0 and $-(\lambda + \Gamma + \mu)\mathrm{Is} = 0$ *hence* Is

Therefore $(S^*, I^*, R^*, B^*, I_S^*) = (\frac{\rho}{\Psi+q+\eta}, 0, 0, 0, 0)$

Therefore DFE = $[\frac{\rho}{\Psi+q+\eta}, 0, 0, 0, 0]$

Basic Reproduction Number

Basic Reproduction number is defined as the number of cases directly caused by an infected individual throughout his infected period. Basic reproduction number is used to determine the ability of a disease to spread with a given population. Usually, if $R_0 < 1$, the DFE is locally asymptomatically stable and the disease cannot invade the population, but if $R_0 > 1$, then the DFE is unstable and invasion is possible. if $R_0 < 1$, then on average, an infected individual produces less than one new infected individual over the cause of the infectious period, and once the infection cannot grow.

$$f = \begin{bmatrix} \frac{(\alpha - \gamma\alpha)BS}{K+B} \\ 0 \\ 0 \end{bmatrix}$$

$$F = \begin{bmatrix} 0 & \frac{(\alpha - \gamma\alpha)S}{K+B} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

$$v = \begin{bmatrix} (\sigma + \delta + \psi + \mu)I - (\beta - \gamma\beta)SI \\ (\phi + Z)B - \varepsilon I \\ (\lambda + \Gamma + \mu)I_S - \eta_S \end{bmatrix}$$

$$V = \begin{bmatrix} (\sigma + \delta + \psi + \mu) - (\beta - \beta\gamma)S & 0 & 0 \\ -\varepsilon & (\phi + Z) & 0 \\ 0 & 0 & (\lambda + \sigma + \mu) \end{bmatrix}$$

$$V^{-1} = \begin{bmatrix} \frac{\psi + q + \eta}{D1\eta + D1\psi + D1q - D2\rho} & 0 & 0 \\ \frac{\varepsilon(\psi + q + \eta)}{(D1\eta + D1\psi + D1q - D2\rho)D3} & \frac{1}{D3} & 0 \\ 0 & 0 & \frac{1}{D4} \end{bmatrix}$$

$$FV^{-1} = \begin{bmatrix} 0 \\ 0 \\ \frac{\alpha(1-\gamma)\rho\varepsilon}{(K+B)((D1\eta + D1\psi + D1q - D2\rho)D3} \end{bmatrix}$$

This shows that $\lambda 1 = 0,\ \lambda 2 = 0, \lambda 3 = \frac{\alpha(1-\gamma)\rho\varepsilon}{(K+B)((D1\eta + D1\psi + D1q - D2\rho)D3}$

Therefore $R_0 = \lambda 3$

$$R_0 = \frac{\alpha(1-\lambda)\rho\varepsilon}{(K+B)(D1\eta + D1\psi + D1q - D2\rho)D3}$$

Note: At disease-free Equilibrium, $B = 0,\ R_0 = \dfrac{\alpha(1-\lambda)\rho\varepsilon}{K(D1\eta + D1\psi + D1q - D2\rho)D3}$

Local Stability of Diseases Free Equilibrium

We investigate the local stability of the disease-free equilibrium of the modified model, using the theorem below

Theorem 3: The disease-free equilibrium of the modified model is locally asymptotically stable if $R_0 < 1 \textit{ and unstable if } R_0 > 1$

Proof:

Using Routh-Hurwhz theorem which state that an equilibrium state will be asymptotically stable if and only if the sum of the trace of all the Eigen values is < 0 and the determinant is > 0

$$J = \begin{bmatrix} & S & I & B & R & I_S \\ F1 & -(\psi + q + \eta) & (\beta - \gamma\beta)S & -(\alpha - \gamma\alpha)\dfrac{1}{K}S & 0 & \lambda \\ F2 & 0 & -(\sigma + \delta + \psi + \mu) & (\alpha - \gamma\alpha)\dfrac{1}{K}S & 0 & 0 \\ F3 & 0 & \varepsilon & -(\phi + Z) & 0 & 0 \\ F4 & q & \sigma + \mu & 0 & -\psi & \Gamma \\ F5 & \eta & 0 & 0 & 0 & -(\lambda + \Gamma + \mu_1) \end{bmatrix}$$

From the Jacobian matrix above; the trace of the Jacobian is

$$Trace\ of\ J_{EO} = -\left[(\psi + q + \eta) + (\sigma + \delta + \psi + \mu) + (\phi + Z) + (\psi) + (\lambda + \Gamma + \mu_1)\right] < 0$$

Looking at the trace of the Jacobian matrix, it shows that the asymptotically stable

Considering the determinant of the matrix, we have;

This also shows that the disease-free equilibrium is locally asymptotically stable

RESULTS

In this research work, we present the results of the sensitivity analysis and the numerical simulation

Sensitivity Analysis:

Sensitivity analysis helps to build confidence in the model by studying the uncertainties that are often associated with parameter change. Sensitivity indices allows us to measure the relative change in a state of variable when a parameter changes sensitivity analysis is commonly used to determine the robustness of model prediction to parameter values (since there are usually errors in data collection and we presumed parameter values.

This is used to investigate the sensitivity of the threshold quantity, Basic Reproduction Number with respect to the parameters through investigation. From this analysis, we will know which parameter causes high reduction in the Basic Reproduction number and the parameters that have high impact on the basic Reproduction Number. The sensitivity analysis shows how important each of the parameters is to the transmission of cholera disease.

The normalized forward sensitivity index of the variable to a parameter is the ratio of the relative change in the parameter.

Maple 2023 programming language was uses for the sensitivity analysis

The sensitivity index of $\alpha \; with \; respect \; to \; R_0$ is given as;

$$X_{\alpha}^{R_0} = \frac{\partial R_0}{\partial \alpha} \times \frac{\alpha}{R_0} = 1$$

$$X_{\gamma}^{R_0} = \frac{\partial R_0}{\partial \gamma} \times \frac{\gamma}{R_0} = -0.025798114$$

$$X_{\beta}^{R_0} = \frac{\partial R_0}{\partial \beta} \times \frac{\beta}{R_0} = 0.005871075964$$

$$X_{q}^{R_0} = \frac{\partial R_0}{\partial q} \times \frac{q}{R_0} = -0.3498682004$$

$$X_{\eta}^{R_0} = \frac{\partial R_0}{\partial \eta} \times \frac{\eta}{R_0} = -0.4373352504$$

$$X_{\sigma}^{R_0} = \frac{\partial R_0}{\partial \sigma} \times \frac{\sigma}{R_0} = -0.4593018612$$

$$X_{\psi}^{R_0} = \frac{\partial R_0}{\partial \psi} \times \frac{\psi}{R_0} = -0.9903660725$$

$$X_{\delta}^{R_0} = \frac{\partial R_0}{\partial \delta} \times \frac{\delta}{R_0} = -0.02985462098$$

$$X_{\varepsilon}^{R_0} = \frac{\partial R_0}{\partial \varepsilon} \times \frac{\varepsilon}{R_0} = 1$$

$$X_{Z}^{R_0} = \frac{\partial R_0}{\partial Z} \times \frac{Z}{R_0} = 0.2857142857$$

$$X_{K}^{R_0} = \frac{\partial R_0}{\partial K} \times \frac{K}{R_0} = -1$$

Table3: Table of the Sensitivity indices

The results of the sensitivity analysis are presented in table 3 below;

S/N	Parameters	Sensitivity Index
1	α	1
2	γ	-0.025798114
3	β	0.005871075964
4	q	-0.3498682004
5	η	-0.373352504
6	σ	-0.4593018612
7	ψ	-0.9903660725
8	δ	-0.02985062098
9	ε	1
10	Z	-0.2857142857
11	K	-1

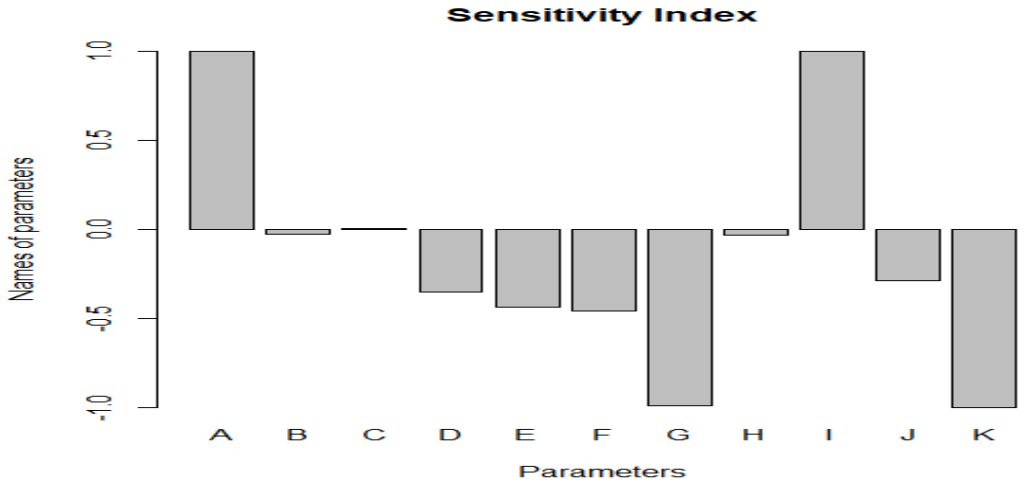


Figure 3: Graph of the Sensitivity indices

The letters in the chart represent the parameters that appeared in the sensitivity analysis.

$A=\alpha, B=\gamma, C=\beta, D=q, E=\eta, F=\sigma, G=\psi, H=\delta, I=\varepsilon, J=Z, K=K$

From the chart, we discovered that $\alpha, \varepsilon, \psi, K$ have high impact on the Basic reproduction Number.

CONCLUSION

This work formulated a deterministic Mathematical model for the study of cholera disease. The study focused on the control measure for the spread of cholera. The measures include the following; sanitation, isolation, vaccination, treatment and education. From the model, we found the existence and uniqueness of the model and discovered that the model exists and it is also unique. We obtained the Basic Reproduction number and the local stability of the model. We discovered that the model is asymptotically stable. We also performed the Sensitivity analysis on the Basic Reproduction Number, from which we have noted that the most sensitivity parameter include; $\alpha, \varepsilon, \psi, K$. This showed that control strategies need high attention in order to control cholera outbreak. From this study we conclude that for cholera to be eradicated from the community, control strategies should be highly implemented.

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